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Nutrición Hospitalaria

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Editorial

Trabajos Originales

Paciente crítico

Nutrición artificial

Pediatría

Obesidad y síndrome metabólico

Valoración nutricional

Epidemiología y dietética

Otros

Revisiones

Cartas al Director

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Sumario

Vol. 41 Julio-Agosto N.º 4

sumario

Nutrición Hospitalaria

Sumario

Vol. 41 Julio-Agosto N.º 4

sumario

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Vol. 41 Julio-Agosto N.º 4

sumario

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Summary

Vol. 41 July-August No. 4

summary

Nutrición Hospitalaria

Summary

Vol. 41 July-August No. 4

summary

Nutrición Hospitalaria

Summary

Vol. 41 July-August No. 4

summary

ISSN (electrónico): 1699-5198 - ISSN (papel): 0212-1611 - CODEN NUHOEQ S.V.R. 318

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Gestación tras cirugía bariátrica: una de cal y otra de arena

Pregnancy after bariatric surgery: blowing hot and cold

La obesidad materna es un factor de riesgo en la gestación, incrementando los resultados adversos materno-fetales. En los últimos años han aumentado los procedimientos de cirugía bariátrica (CB), la mitad en mujeres en edad fértil. Cada vez es más común atender a mujeres gestantes tras CB (MG-CB) y existen aspectos importantes a abordar en su manejo.

La valoración preconcepcional es imprescindible, advirtiendo a las mujeres que tras la CB aumenta la fertilidad y recomendándoles anticoncepción hasta poder planificar la gestación. Aunque el intervalo óptimo entre CB y gestación sigue siendo desconocido, suele plantearse una espera de 12-24 meses, debiendo valorarse individualmente el riesgo-beneficio de reducir o ampliar este intervalo (1,2).

Pese a una reducción del riesgo de diabetes *mellitus* gestacional (DMG) del 60-80 %, su prevalencia sigue siendo más elevada que en población general, posiblemente porque la mitad de MG-CB siguen siendo obesas periconcepcionalmente. Aunque no existen guías ni puntos de corte diagnósticos específicos, existe consenso en evitar las sobrecargas orales de glucosa como cribado y diagnóstico de DMG (al menos tras *bypass* gástrico), por su mala tolerancia y riesgo de hipoglucemia (3). De hecho, aunque los estudios son limitados, al menos la mitad de MG-CB presenta hipoglucemias durante el embarazo, independientemente de la técnica quirúrgica. Y lo que es más importante, se ha postulado una posible relación entre las hipoglucemias maternas y complicaciones fetales. La monitorización continua de glucosa es una ventana de oportunidad en MG-CB, permitiendo observar excursiones glucémicas, hipoglucemias, tiempo en rango y variabilidad, a fin de optimizar el manejo de hipoglucemias e individualizar mejor las necesidades y distribución de macronutrientes (4).

Las MG-CB presentan menor riesgo de estados hipertensivos del embarazo, corioamnionitis e infección de herida quirúrgica. Las tasas de cesárea parecen ser similares o ligeramente reducidas, si bien las MG-CB suelen tener edad más avanzada y mayor prevalencia de obesidad preconcepcional, existiendo una elevada variabilidad entre centros en la indicación de cesárea. No hay datos definitivos sobre reducción del riesgo de aborto (5).

En los aspectos fetales, se asume que la CB no tiene un impacto negativo importante en la morbimortalidad neonatal. Se ha observado reducción del riesgo de recién nacido grande para edad gestacional (del 30-80 %). Existen datos discrepantes sobre el aumento de riesgo de recién nacido pequeño para edad gestacional, aunque revisiones sistemáticas muestran un aumento de casi el doble respecto a mujeres no intervenidas. La CB no parece incrementar el riesgo de anomalías congénitas (5,6).

En alimentación no existe evidencia sólida en distribución o tipo de macronutrientes para MG-CB, asumiéndose las recomendaciones para población general obstétrica. Puede ser difícil alcanzar los requerimientos energéticos y proteicos por la restricción gástrica y la malabsorción, recomendándose consejo dietético individualizado y suplementos nutricionales si fuera necesario. El riesgo de deficiencia en vitaminas y minerales es muy elevado, por la CB y los requerimientos extra durante el embarazo. El manejo de estas deficiencias

editorial

requiere una evaluación y tratamiento protocolizados. Diferentes sociedades científicas recomiendan un suplemento polivitamínico específico para población post-CB, ya que los suplementos para población general obstétrica no cubren los requerimientos de muchos micronutrientes (7).

A pesar del aumento en el número de publicaciones en los últimos años sobre gestación y CB, la evidencia disponible sigue siendo limitada en todos los aspectos comentados. El tamaño muestral de estudios aislados es pequeño para poder extraer conclusiones rotundas, además de las consideraciones éticas de la investigación en gestantes y menores de edad. Ante la necesidad de investigación que analice los complejos aspectos materno-fetales que rodean a la gestación tras CB, Ángel Martínez y cols. publican en este número de la revista *Nutrición Hospitalaria* un estudio observacional retrospectivo de MG-CB frente a un grupo de mujeres gestantes no intervenidas con distintos grados de obesidad. Sus principales resultados son similares a los descritos en la literatura en los últimos años: un riesgo significativamente menor de DMG, en paralelo con un aumento del riesgo de crecimiento intrauterino retardado y menor peso del recién nacido, en las gestantes intervenidas (8). Además destaca como aspecto positivo en su cohorte de estudio la reducción en la tasa de cesáreas en el grupo intervenido; y como foco de atención para el manejo estrecho de estas pacientes, el riesgo de aborto espontáneo aumentado.

Como conclusión, la CB parece asociarse tanto a beneficios como a riesgos durante la gestación y el posparto. Sigue habiendo controversias en muchos puntos y quedan muchas incógnitas por aclarar en futuras líneas de investigación, como la ganancia ponderal adecuada, la dosis óptima de ácido fólico, la vía de parto más segura, el papel la homeostasis de la glucosa en los resultados materno-fetales y, sobre todo, la salud metabólica de recién nacido y madre a largo plazo. Por este motivo, las MG-CB requieren un seguimiento estrecho entre Endocrinología y Nutrición, Obstetricia, Cirugía, Anestesiología y Atención Primaria.

Conflicto de intereses: los autores declaran no tener conflicto de interés.

Inteligencia artificial: los autores declaran no haber usado inteligencia artificial (IA) ni ninguna herramienta que use IA para la redacción del artículo.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Paciente crítico

Validation of the nutritrauma concept for the detection of potential harmful effects of medical nutritional treatment in critically ill patients in real life

Validación del concepto de nutritrauma para la detección de posibles efectos adversos del tratamiento nutricional médico en pacientes críticos en la vida real

Jordi Parisi[1], Itzíar Martínez de Lagrán[1], Mateu Serra-Prat[2], María Roca[3], Raquel Merino[4], María del Carmen de la Torre[1], Lluis Campins[4], Juan Carlos Yébenes[1]

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Abstract

Introduction: medical nutritional treatment (MNT) can be complex and may be associated with potential metabolic complications, which has been recently described as nutritrauma.

Objective: the aim of our work is to describe whether the application of the nutritrauma concept in real life is feasible and useful to detect the metabolic complications associated with the prescription of MNT.

Material and methods: in this descriptive, prospective study at a single center we enrolled 30 consecutive critically ill patients in a 14-bed medical-surgical intensive care unit. The nutritrauma strategy implementation was based in four "M" steps: Metabolic screening, MNT prescription, biochemical Monitoring, and nutritional Management.

Results: we analyzed 28 patients (mean age, 69.7 ± 11.3 years; APACHE II, 18.1 ± 8.1; SOFA, 7.5 ± 3.7; Nutric Score, modified, 4.3 ± 2.01, and mean BMI, 27.2 ± 3.8). The main cause of admission was sepsis (46.4 %). Length of ICU stay was 20.6 ± 15.1 days; 39.3 % of subjects died during their ICU stay. Enteral nutrition (82.1 %) was more frequent than parenteral nutrition (17.9 %). During nutritional monitoring, 54 specific laboratory determinations were made. Hyperglycemia was the most frequent metabolic alteration (83.3 % of measurements). Electrolyte disturbances included hypocalcemia (50 %), hypophosphatemia (29.6 %) and hypokalemia (27.8 %). The most frequent lipid profile abnormalities were hypocholesterolemia (64.8 %) and hypertriglyceridemia (27.8 %). Furthermore, nutritional prescription was modified for 53.6 % of patients: increased protein dosage (25 %), increased calorie dosage (21.4 %) and change to organ-specific diet (17.8 %).

Conclusions: in conclusion, the application of the nutritrauma approach facilitates detection of metabolic complications and an evaluation of the appropriate prescription of MNT.

Keywords:

Metabolic complications. Critically ill. Nutritrauma. Medical nutrition therapy. Enteral nutrition. Parenteral nutrition.

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Artificial intelligence: the authors declare not to have used artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

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Resumen

Introducción: el tratamiento médico nutricional (TMN) puede ser complejo y asociarse a potenciales complicaciones metabólicas, lo que se ha descrito recientemente como "nutritrauma".

Objetivo: el objetivo de nuestro trabajo es describir si la aplicación del concepto de nutritrauma en la vida real es factible y útil para detectar las complicaciones metabólicas asociadas a la prescripción del TMN.

Materiales y métodos: en este estudio unicéntrico y prospectivo describimos el seguimiento de 30 pacientes críticos consecutivos en una unidad de cuidados intensivos médico-quirúrgica de 14 camas. La implementación de la estrategia nutritrauma se basó en cuatro pasos "M": valoración Metabólica, prescripción del TMN, Monitorización bioquímica y Manejo nutricional.

Resultados: se analizaron 28 pacientes (edad media: 69,7 ± 11,3 años; APACHE II: 18,1 ± 8,1; SOFA: 7,5 ± 3,7; Nutric Score modificada: 4,3 ± 2,01, e IMC medio: 27,2 ± 3,8). La principal causa de ingreso fue la sepsis (46,4 %). La duración de la estancia en UCI fue de 20,6 ± 15,1 días y el 39,3 % fallecieron durante la estancia en UCI. La nutrición enteral (82,1 %) fue más frecuente que la parenteral (17,9 %). Durante el seguimiento nutricional se realizaron 54 determinaciones analíticas específicas. La hiperglucemia fue la alteración metabólica más frecuente (83,3 % de las determinaciones). Las alteraciones electrolíticas fueron: hipocalcemia (50 %), hipofosfatemia (29,6 %) e hipopotasemia (27,8 %). Las alteraciones del perfil lipídico más frecuentes fueron la hipocolesterolemia (64,8 %) y la hipertrigliceridemia (27,8 %). Además, se modificó la prescripción nutricional en el 53,6 % de los pacientes: aumentar la dosis proteica (25 %), aumentar la dosis calórica (21,4 %) y cambiar a una dieta específica de órgano (17,8 %).

Conclusión: en conclusión, la aplicación de la estrategia nutritrauma facilitó la detección de complicaciones metabólicas y la evaluación de la adecuada prescripción del TMN.

Palabras clave:

Complicaciones metabólicas. Paciente crítico. Nutritrauma. Tratamiento médico nutricional. Nutrición enteral. Nutrición parenteral.

INTRODUCTION

Treatments for organ failure can present deleterious effects on critically ill patients, so adherence to institutional protocols is essential. However, despite the fact that having protocols is a basic step to improve healthcare practice, their existence does not guarantee their application (1), so in certain contexts some tools can be useful to facilitate the dissemination and implementation of protocols. Simplifying and grouping key elements of complex processes has been proven useful for implementing safety and/or quality strategies (2-4). Unequivocally, identifying the project facilitates the engagement, education, execution and evaluation of the protocol objectives. These 4 steps have been considered a useful methodology for the development of these strategies (5).

One of the resources to facilitate the implementation of protocols or strategies is to designate the process to be monitored unequivocally, if possible by associating it with a key concept through a specific name. To create a concept to group different events related with a cause or procedure can be useful to increase awareness and spread its existence. This is the case of barotrauma (6), to prevent injuries associated with mechanical ventilation, dialytrauma (7), to avoid injuries associated with renal replacement techniques in critically ill patients, or the bacteremia zero concept (8), to reduce catheter-related bacteremia.

Medical nutritional treatments (MNT) in critically ill patients can be complex, mainly during the first days of illness. The ideal prescription of calories, proteins, fiber or electrolytes is difficult because it can be affected by several factors such as basal patient conditions, impact of acute illness, endogenous production or route of administration, so a special monitoring is suggested (9,10). Over- and under-prescription of macronutrients is associated with worse prognosis. Moreover, critically ill patients can present comorbid conditions predisposing to refeeding syndrome (11,12).

Recently, with the idea to facilitate the monitoring of the metabolic effects of initial nutrition the concept nutritrauma was introduced to group together the potential metabolic complications associated with an inadequate medical nutritional treatment prescription (10). The idea was that by creating this concept, awareness about this kind of complications and their active detection, treatment and monitoring would be facilitated. However, while only conceptualization can be insufficient, it can facilitate the engagement and education of practitioners. Therefore, our idea was to implement a structured strategy based on engagement, education, execution and evaluation of the prevention of nutritrauma. The aim of this work was to describe the nutritrauma strategy implementation in real life, and analyze if it allows to detect metabolic complications and inappropriate prescription of MNT in critically ill patients.

MATERIALS AND METHODS

SUBJECTS AND STUDY DESIGN

A unicenter prospective study was developed in a medical-surgical intensive care unit with 14 beds at a university hospital. We included 30 consecutive critically ill patients that received MNT during the first trimester of 2020. Patients were monitored from admission to ICU discharge.

Inclusion criteria were patients admitted to intensive care unit, aged 18 or older, with at least 2 organ failures, who needed enteral or parenteral nutrition for at least 48 hours. Exclusion criteria were patients with a high subjective probability of receiving oral nutrition or dying during the first 72 h. The present study was approved by the Ethics Committee of the Consorci Sanitari del Maresme (Ref. 52/2019).

THE "NUTRITRAUMA STRATEGY" IMPLEMENTATION

The nutritrauma strategy was based on consecutive actions (Fig. 1) following the 4E strategy:

– *Engage and Educate:* A preliminary multidisciplinary formative session was conducted, in which the incidence of meta-

bolic complications and their incidence on the clinical evolution of critically ill patients was presented. We emphasized the concept that most of those complications can be easily detected and treated if a structured protocol is applied. A structured and validated protocol was redacted and diffused through the hospital's Nutritional Commission.

– *Execute:* Informative posters were designed (Fig. 2) and a specific biochemical profile was created in the biochemical laboratory petitionary. All patients with medical nutritional treatment should be evaluated periodically for the presence of nutritrauma. The strategy was structured in four M steps: Metabolic screening, MNT design, Monitoring, and Management (Fig. 3).
– *Evaluate:* Even though a daily analysis of nutritional requirements is mandatory, we proposed a weekly feedback clinical session, that was scheduled to discuss nutritional strategies and favor learning and engagement.

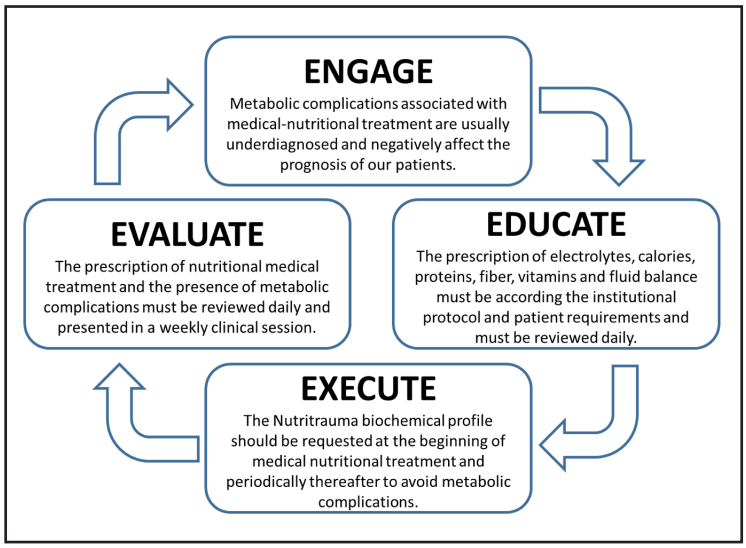

Figure 1.

The application of the 4E strategy (5) to translate knowledge to clinical practice.

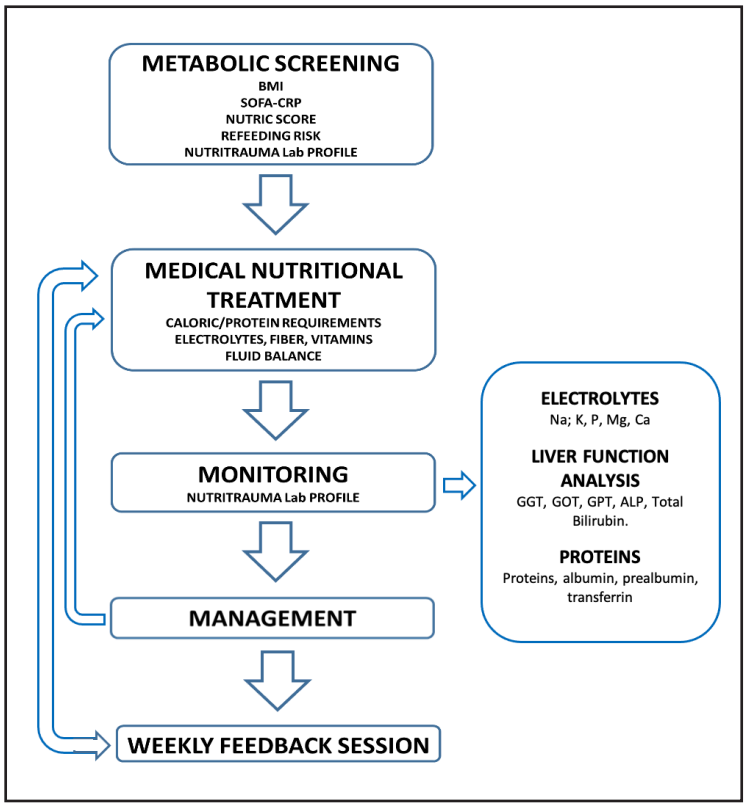

Figure 2.

Informative poster (Na: sodium; K: potassium; P: phosphorus; Mg: magnesium, Ca: calcium; GGT: gamma-glutamyl transferase; GOT: glutamic oxaloacetic transaminase; GPT: glutamic pyruvic transaminase; ALP: alkaline phosphatase; CRP: C-reactive protein).

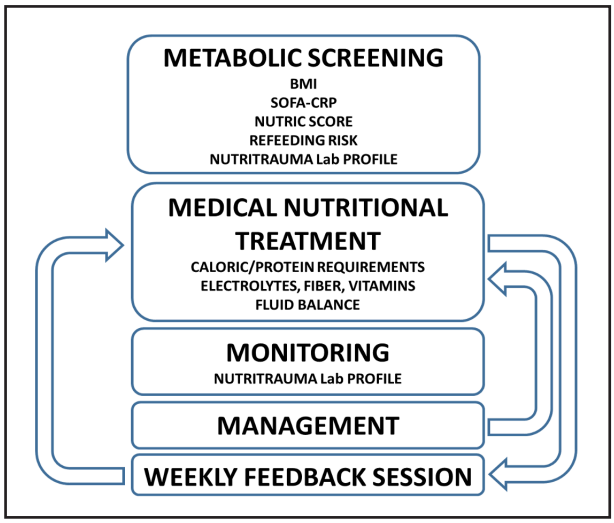

Figure 3.

Schema for "Execute" the nutritrauma strategy into clinical practice (BMI: body mass index; SOFA: Sequential Organ Failure Assesment; CRP: C-reactive protein; Lab: Laboratory).

THE EXECUTION OF THE NUTRITRAUMA STRATEGY

Metabolic screening

During the first 24 hours of admission, the severity of illness [Sequential Organ Failure Assessment (SOFA) (13), Acute Physiology and Chronic Health Evaluation II (APACHE II) (14)], nutritional risk evaluation (modified Nutric Score) (15), and risk of refeeding syndrome assessment (16) were performed.

Medical nutritional treatment prescription

Initial nutrition prescription was defined according to the institutional protocol. Caloric and protein requirements were estimated separately, using weight-based formulas (using adjusted weight if BMI was > 30). The initial calorie prescription was 10-15 kcal/kg/day if there was refeeding syndrome risk, and 20 kcal/kg/day if there was no risk. Calorie prescription was increased progressively according to clinical status. The enteral and/or parenteral route was used to achieve caloric objectives. Protein prescription was adjusted to clinical status (from 1.2 to 2 g/kg/day or 2 g/kg ideal weight/day if BMI was between 30 and 40) (17).

Biochemical monitoring

A specific blood profile was created (named Nutritrauma) that included:

- *Electrolytes:* sodium (Na); potassium (K), phosphorus (P), magnesium (Mg), calcium (Ca).
- *Liver function analysis:* gamma-glutamyl transferase (GGT), glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), total bilirubin (and indirect and direct bilirubin if it was abnormal).
- *Proteins:* total proteins, albumin, prealbumin, transferrin.
- *Lipids:* total cholesterol, triglycerides.
- *Inflammation:* C-reactive protein (CRP), lymphocytes.

Nutritional management

Physicians must design their patients' treatments according to institutional protocols, based on SEMICyUC Guidelines (17). The Nutritrauma blood analysis was performed at nutrition initiation (day 0), at clinical criteria in the presence of abnormal values or nutritional risk, on days 2 and 5, and weekly. Every Wednesday a one-hour multidisciplinary clinical session was performed, attended by the medical ICU staff, a nutritionist, a pharmacist, a rehabilitation physician, and a physiotherapist.

DATA COLLECTION

The study data included age, sex, weight, height, body mass index (BMI), APACHE-II, and SOFA. Blood levels of total proteins, albumin, prealbumin, transferrin, triglycerides, total cholesterol, CRP, liver function (GGT, GOT, GPT, ALP), and electrolytes (Na, K, Ca, Mg, P] were recorded for each study participant.

During the Wednesday multidisciplinary clinical session, nutritional treatment changes were collected, such as increase of protein and/or caloric dosage, change to an "organ-specific diet" (L-arginine-enriched diets, specific diabetic diets, and diet for enteral nutrition-associated diarrhea) or change to a fiber-enriched diet.

STATISTICAL ANALYSIS

Data were collected in Excel® through individual questionnaires, which were anonymized and exported for analysis to the SPSS version 26.0 statistical package (IBM SPSS, Armonk, NY, USA) to perform a descriptive analysis of means or medians based on normality for quantitative variables, and of proportions for descriptive variables. Normality was analyzed using the Shapiro-Wilk test. No comparative statistical analyses were performed, according to the descriptive nature of the study.

RESULTS

PATIENTS CHARACTERISTICS

From January to March of 2020, 30 consecutives patients were included. Two of them died before initiation of MNT. Mean age was 69.7 ± 11.3 years, 50 % were female with an admission APACHE II

of 18.1 ± 8.1, admission SOFA of 7.5 ± 3.7, and modified Nutric Score of 4.3 ± 2.01. Four patients (14.4 %) had risk of refeeding syndrome. The most frequent disease on admission was sepsis (46.4 %), followed by cardiovascular disease (21.4 %) and respiratory failure (17.8 %). The main MNT route of administration was enteral nutrition (82.1 %). The adequacy of starting time of the nutritional treatment was 92.8 % [understood as early initiation (24-48 hours) of MNT after hemodynamic stabilization]. The patients stayed 20.6 ± 15.1 days in the ICU and 39.3 % died during their ICU stay. The main characteristics of the 28 patients are described in table I.

Table I. Main patient´s characteristics

Main patient's characteristics	*n* = 28
Age (years); mean (± SD)	69.7 ± 11.3
Male / Female	14 (50 %) / 14 (50 %)
Weigh (Kg); mean (± SD)	77.4 (± 12.9)
BMI; mean (± SD)	27.2 (± 3.8)
APACHE II; mean (± SD)	18.1 (± 8.1)
SOFA Score; mean (± SD)	7.5 (± 3.7)
Nutric Score; mean (± SD)	4.5 (± 1.9)
Risk of refeeding syndrome; *n* (%)	4 (14.4 %)
Disease on admission; n (%)	
Sepsis	13 (46.4 %)
Cardiovascular	6 (21.4 %)
Respiratory	5 (17.8 %)
Miscellanea	4 (14.4 %)
Enteral / Parenteral nutrition	23 (82.1 %) / 5 (17.9 %)
Adequacy of starting time; *n* (%)	26 (92.8 %)
Hiperglycaemia; *n* (%)	23 (83.3 %)
Fluid overload; *n* (%)	28 (100 %)
Length of ICU stay (days); mean (± SD)	20.6 (± 15.1)
Mortality; *n* (%)	11 (39.3 %)

Kg: kilograms; BMI: body mass index; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; ICU: intensive care unit.

DETECTION OF METABOLIC COMPLICATIONS

During follow-up, 54 lab determinations were made (Table II). Hyperglycemia was the most frequent metabolic alteration during evolution (83.3 % of patients). Electrolyte disturbances were also frequent: hypocalcemia, adjusted for albumin (50 %), hypophosphatemia (29.6 %) and hypokalemia (27.8 %). After identifying ion deficit, supplementation was started in 100 % of the cases. Regarding liver function, 31.5 % of the patients had bilirubin elevated > 2 times above its baseline value, this not being associated with MNT. Similarly, 85.2 % of the patients presented cholestasis, none of them being treated with parenteral nutrition. Analyzing the lipid profile, hypocholesterolemia (64.8 %) was the most frequent laboratory abnormality followed by hypertriglyceridemia (27.8 %), and during serial tests both cholesterol and triglyceride levels normalized without specific treatment. All protein-related biochemical parameters were low during practically the entire follow-up: hypoproteinemia (90.7 %), hypoalbuminemia (88.8 %), low transferrin (87 %) and low prealbumin (72.2 %). Finally, 100 % of the patients presented anasarca in their evolution.

MEDICAL NUTRITIONAL TREATMENT MODIFICATIONS DURING MULTIDISCIPLINARY SESSIONS

During the multidisciplinary sessions inappropriate prescription was detected in 53.6 % of patients. All of them suffered at least one MNT modification, 3.6 % of the patients suffered two modifications, and another 3.6 % suffered three modifications during their evolution in the ICU. The most frequent modification made was increasing protein dosage (25 %), followed by increasing calorie dosage (21.4 %), and change to an organ-specific diet (17.8 %). A change to a fiber-enriched diet was made in 10.7 % of the patients (Table III).

Table II. Detected metabolic complications

Laboratory determinations		*n* = 54
Inflammation		
Lymphopenia; (*n* %)		31 (57.4 %)
C-reactive protein; mean (± SD)		16.5 ± 15.3
Glycaemia		
Hyperglycaemia; (*n* %)		48 (88.8 %)
Electrolytes		
Phosphorus	Hypophosphatemia	16 (29.6 %)
	Hyperphosphatemia	5 (9.2 %)
	Normal phosphorus	33 (61.1 %)

(Continues on next page)

Table II (cont.). Detected metabolic complications

Laboratory determinations		*n* = 54
Electrolytes		
Magnesium	Hypomagnesaemia	4 (7.4 %)
	Hypermagnesaemia	7 (12.9 %)
	Normal magnesium	28 (51.8 %)
Calcium	Hypocalcemia	27 (50 %)
	Hypercalcemia	3 (5.5 %)
	Normal calcium	24 (44.4 %)
Potassium	Hypokalaemia	15 (27.8 %)
	Hyperkalaemia	3 (5.5 %)
	Normal potassium	35 (64.8 %)
Lipids		
Cholesterol	Hypercholesterolaemia	3 (5.5 %)
	Hypocholesterolaemia	35 (64.8 %)
	Normal cholesterol	16 (35.2 %)
Triglycerides	Hypertriglyceridemia	15 (27.8 %)
	Low triglycerides	0 (0 %)
	Normal triglycerides	39 (72.2 %)
Liver function analysis		
Alteration of GGT and ALP		46 (85.2 %)
Alteration of bilirubin		17 (31.5 %)
Proteins		
Total proteins	Hypoproteinemia	49 (90.7 %)
	Normal proteins	5 (9.2 %)
Albumin	Hypoalbuminemia	48 (88.8 %)
	Normal albumin	6 (11.1 %)
Prealbumin	Low prealbumin	39 (72.2 %)
	High prealbumin	1 (1.8 %)
	Normal prealbumin	14 (25.9 %)
Transferrin	Low transferrin	47 (87 %)
	Normal transferrin	7 (12.9 %)

% expressed the number of described alterations with respect to lab determinations. GGT: gamma-glutamyl transferase; ALP: alkaline phosphatase.

Table III. Treatment modifications

Variable		*n* = 28
Patients with treatment modifications; n (%)		15 (53.6 %)
Number of modifications	1	15 (53.6 %)
	2	1 (3.6 %)
	3	1 (3.6 %)
Type of modification	Increase protein dosage	7 (25 %)
	Increase calorie dosage	6 (21.4 %)
	Change to organ-specific diet	5 (17.8 %)
	Diabetic diet	4 (14.2 %)
	L-arginine-enriched diet	1 (3.6 %)
	Change to fiber-enriched diet	3 (10.7 %)

DISCUSSION

Our work is the first clinical report of the application of the nutritrauma concept. In our experience, the grouping of the different complications associated with MNT under the nutritrauma concept facilitated the spread of the notion that inappropriate nutritional prescription can be associated with deleterious metabolic effects. The strategy allowed the detection that nearly 30 % of patients presented hypophosphatemia, 50 % hypoalbuminemia, and 83 % hyperglycemia. Moreover, the combination of the lab screening with periodical clinical multidisciplinary sessions facilitated the systematic reevaluation of MNT, modifying MNT in 53 % of patients.

Our strategy was based on two actions: first, an individual approach (the 4 Ms) to the characteristics and metabolic requirements of patients, and second, a collective approach (a 1-hour weekly session) with different healthcare profiles, including all intensive care physicians, with presence of nurses, pharmacists, physiotherapists, and nutritionists. The individual approach was facilitated by the dissemination of the institutional protocol and the creation of a laboratory profile that includes all the analytical variables to assess nutritional risk and monitor electrolyte and metabolic complications. This laboratory profile was called "Nutritrauma".

Optimal prescription of MNT requires taking into account different aspects that may not be obvious. Scores, such as Nutric Score (15), which has been validated for critically ill patients, can facilitate the evaluation of different conditions that can modify the initial prescription, which is why we consider it essential prior to the administration of MNT. Age, acute disease severity, multiple organ failure, presence of comorbidities, and level of inflammation are factors that define a clinical scenario of nutritional risk and allow the identification of patients who must be specially treated and monitored. However, not only is nutritional risk detected but the approach also allows identification of patients with a higher general risk, thus indicating that these patients will need a greater nursing workload and a physiotherapist, will spend more days in the ICU, and have a greater probability of dying (18-20). So, in our opinion, the Nutric Score should be calculated at the beginning of MNT and can be also useful in general for the critically ill patient.

Glucose blood level alteration is quite common in critically ill patients. Its prevalence is difficult to know as it depends on the cut-off point we consider for hyperglycemia. In our sample, 83.3 % of patients presented glucose levels above 150 mg/dL, data that is consistent with what the actual literature describes. Hyperglycemia may be related to overfeeding, insulin resistance in the acute phase of metabolic response, or even insufficient insulin treatment (21). It is described that hyperglycemia is associated with poor clinical outcomes, increased morbidity and mortality (22), altered immune response causing increased risk of infection, reductions of vascular reactivity and nitric oxide, therefore compromising blood flow and increasing proteolysis, and, being associated with a greater risk of cardiac and renal complications (23). Although treatment of hyperglycemia is associated with better results, strict control is not recommended due to its association with higher mortality. Hence most scientific societies recommend glucose levels between 140 and 180 mg/dL (24). Avoiding hyperglycemia is not enough, it is increasingly important to control glycemic variability, which is also associated with mortality (23,24).

Electrolyte disorders, such as hypocalcemia (50 %) and hypophosphatemia (29.6 %) were very frequent. Calcium is the most plentiful mineral in the body. It has skeletal functions, such as bone tissue building, and non-skeletal ones. The latter are divided into structural, like organelle or cell membrane formation, and regulatory, such as enzymatic reactions to modify cell functions (25). Hypocalcemia may have severe consequences, such as seizures, laryngospasm, prolonged QT or cardiac dysfunction (26). In critically ill patients, abnormal calcium values can be a marker of severity, and is often corrected spontaneously when the primary disease is solved. There is not enough evidence on the management of hypocalcemia, although generalized administration is discouraged to normalize its values, and it is concluded that treatment should be guided by basic decision-making principles (27).

Phosphate has several functions in the body (28) including an energy function (it is part of adenosine triphosphate, ATP), structural function (it is a component of phospholipids in cell membranes and nucleic acids), activation of proteins through phosphorylation, intracellular buffering effect, and mineralization of the bone matrix. Hypophosphatemia produces a wide spectrum of symptoms when there is a depletion of intracellular phosphate. Its deficit produces an increase in the affinity of hemoglobin for oxygen, reducing its delivery at the tissues, and ATP deficit produces alterations in the cellular functions affecting neurological, cardiopulmonary, muscular and hematological systems. In critically ill patients, hypophosphatemia, in addition to the above-described symptoms, is a risk marker for refeeding syndrome, a syndrome associated with high morbidity and mortality (16). As reflected in the latest ASPEN consensus recommendations on refeeding syndrome (29), the identification of hypophosphatemia can help identify patients at risk of presenting with refeeding syndrome.

During the nutritrauma strategy MNT prescription was optimized in 53.6 % of patients. In our experience, one of the most frequent difficulties of MNT for nonexpert physicians, is to adapt its prescription to the metabolic situation (30) and syndromic characteristics (31-33). Many studies show that the number of calories and proteins that critically ill patients receive is lower than the calculated requirements (34,35). This is associated with worse evolution (36). However, an evaluation of daily nutritional requirements may minimize this concern. Despite the fact that our patients were in a non-blinded observational study, underfeeding remained the most frequent complication related to doses. Consequently, increases in protein (25 %) and calorie dosages (20 %) were the most frequently made modifications.

The qualitative characteristics of diets can also affect a patient's evolution. We introduced changes in the prescription of organ-specific diets in 17.8 % of patients (31). The SEMICYUC

recommendations for specialized nutritional-metabolic management of the critical patient includes soluble and insoluble fiber diets to prevent complications such as diarrhea, constipation, and tolerance to enteral nutrition (37). We detected a significant percentage of patients that were not receiving a fiber-enriched diet, so the prescription of a fiber-enriched diet was very common (10.7 %).

The weekly feedback session was an essential tool in the strategy. Despite the fact that general recommendations for the prescription of MNT and the management of gastrointestinal complications are included in the institutional protocol, some doubts or errors regarding MNT may be detected (34). The weekly feedback sessions were a very useful learning tool for training non-expert clinicians in MNT. In addition, the presence of a pharmacist, nutritionist and physiotherapist makes it possible to incorporate different points of view and facilitate the transition from parenteral to enteral and from enteral to oral nutrition, as well as the continuity of nutritional management outside the ICU, in the wards. Frailty after ICU discharge is common, therefore MNT in critically ill patients should not end with ICU discharge. A transfer from the ICU to a ward may be associated with changes in the healthcare personnel involved in the patient's recovery (doctors, nurses, nutritionists, physiotherapists...). Therefore, there is a risk that the transfer of a critically ill patient to a ward may cause changes in or the partial withdrawal of the nutritional and physiotherapy treatments. In our experience, the weekly feedback session facilitated the presence of the nutritionist and physiotherapist who will treat patients after discharge from the ICU. However, the positive effects of multidisciplinary meetings are difficult to measure. In our experience, sharing weekly doubts and interpretations of nutritional practice with experts not only allowed the identification of wrong dosages and metabolic disorders, but also led to an increase in MNT knowledge.

Our work has some limitations. This is a non-blinded observational study designed to evaluate the applicability of the nutritrauma strategy. In our opinion, the main limitation is that it was developed in a single center with a low number of patients. Moreover, we cannot evaluate whether MNT modifications impact positively patient prognosis, which is the final objective of any clinical intervention. However, it is clear that, by facilitating metabolic monitoring, we increase the detection of metabolic alterations correlated with complications and worse prognosis, and allow therapeutic modifications. Despite these limitations, this is the first clinical application reported of the nutritrauma concept, and the benefits observed encouraged us to present our protocol and results.

CONCLUSIONS

The nutritrauma concept has been useful to spread the notion that MNT must be carefully designed and monitored to avoid harmful effects. The application of the nutritrauma strategy facilitates the detection of metabolic complications and the evaluation of the appropriate prescription of MNT. A weekly multidisciplinary session represents a powerful clinical and educational strategy.

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Nutrición Hospitalaria

Trabajo Original

Nutrición artificial

Tendencias en las características de los pacientes tratados con suplementos nutricionales en el Área Norte de Gran Canaria en el periodo 2016-2021

Trends in the characteristics of patients treated with nutritional supplements in the Northern Area of Gran Canaria in the period 2016-2021

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Resumen

Objetivo: valorar la prescripción de suplementos nutricionales orales (SNO) en el Área Norte de Gran Canaria en el periodo 2016-2021.

Material y métodos: basándonos en datos de receta electrónica, se analizó la primera prescripción de SNO durante 2016-2021 considerando edad, género, requerimientos nutricionales (RN), índice de masa corporal (IMC), porcentaje de pérdida de peso (PPP), albúmina y número de SNO prescritos.

Resultados: se identificaron 10.595 prescripciones correspondientes a 6661 pacientes con las siguientes características: 46,3 % varones, edad media 72,84 ± 15,93 años, IMC 20,60 ± 3,98 kg/m^2, PPP del 11,89 ± 8,32 %; albúmina 3,08 ± 0,63 g/dl. Las etiologías más frecuentes de la DRE fueron: neoplasias, 42,6 %; procesos degenerativos del SNC, 28,9 %; ictus, 3,9 %; intestino corto, 6,9 % y enfermedad inflamatoria intestinal (EII), 5,5 %. Los porcentajes de RN cubiertos por los SNO prescritos fueron del 100 % en el 8,9 % de los casos, del 50 % en un 36,9 % y del 25 % en el 54,2 %. Un 40,4 % de los pacientes recibió 1 SNO diario, un 36,3 % tomaron 2 SNO y un 23 % recibieron > 3 SNO diarios. Los mayores RN se asociaron con un mayor número de SNO ($p < 0,001$), pero el 40,8 % de los pacientes que precisaban cubrir > 50 % de RN recibían solo un SNO.

Conclusión: un porcentaje importante de pacientes con ~~DRE~~ no recibe SNO de acuerdo a sus RN.

Palabras clave:

Desnutrición relacionada con la enfermedad. Suplementos nutricionales orales. Necesidades nutricionales.

Abstract

Aim: ~~assess~~ the prescription of oral nutritional supplements (ONS) in the Northern Area of Gran Canaria in the period 2016-2021.

Materials and methods: based on electronic prescription data, the first ONS prescription during 2016-2021 was analyzed considering age, gender, nutritional requirements (NR), body mass index (BMI), percentage of weight loss (%WL), albumin and number of prescribed ONS per patient.

Results: 10,595 prescriptions were identified corresponding to 6661 patients with the following characteristics: 46.3 % men, mean age 72.84 ± 15.93 years, BMI 20.60 ± 3.98 kg/m^2, %WL 11.89 ± 8.32 %; albumin 3.08 ± 0.63 g/dl. The most frequent etiologies of DRE were: neoplasms 42.6 %; degenerative processes of the CNS 28.9 %; stroke 3.9 %; short ~~intestine~~ 6.9 %, and inflammatory bowel disease (IBD) 5.5 %. The percentages of NR covered by the prescribed ONS were: 100 % in 8.9 % of cases, 50 % in 36.9 %, and 25 % in 54.2 %; 40.4 % of patients received 1 unit of ONS daily, 36.3 % took 2 units of ONS, and 23 % received > 3 units of ONS per day. Greater NR were associated with a greater number of ONS ($p < 0.001$), but 40.8 % of patients who needed to cover > 50 % of NR received only one unit of ONS.

Conclusion: a significant percentage of patients with ~~DRM~~ do not receive a number of ONS according to their NR.

Keywords:

Disease-related malnutrition. Oral nutritional supplements. Nutritional requirements.

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INTRODUCCIÓN

La desnutrición relacionada con la enfermedad (DRE) se asocia con un aumento de la morbimortalidad en múltiples patologías y genera un mayor gasto sanitario (1,2).

Un manejo adecuado que incluya un diagnóstico precoz y un tratamiento adecuado de los pacientes desnutridos es fundamental para mejorar el pronóstico y evitar las complicaciones de diversas situaciones clínicas, incluyendo una reducción de la estancia hospitalaria y la mortalidad (3,4). En nuestro sistema de salud, esta responsabilidad es compartida entre los especialistas de atención primaria y de las diferentes especialidades de atención hospitalaria. El uso de suplementación nutricional oral (SNO) se ha mostrado útil en los pacientes afectos de DRE asociada al cáncer (5), en los pacientes que van a ser sometidos a cirugía gastrointestinal (6) y en los ancianos frágiles con sarcopenia en régimen ambulatorio (7).

La farmacoepidemiología es un método moderno y válido para evaluar el cumplimiento de las guías de práctica clínica en diferentes contextos sanitarios (8,9) y también puede aplicarse en la desnutrición.

En nuestro ámbito sanitario, la prescripción se realiza a través de la receta electrónica y debe ir asociada a un formulario en el que se recogen las características clínicas de los pacientes. La primera prescripción puede realizarla cualquier médico del sistema sanitario público, mientras que la continuidad debe contar con la autorización de los especialistas en Endocrinología y Nutrición y de la Inspección Médica.

No hemos encontrado ningún estudio en nuestro país en el que se hayan analizado estos parámetros y su evolución a lo largo del tiempo; tampoco en la comunidad autónoma de Canarias. Un estudio basado en la implantación de un sistema de cribado en un centro hospitalario demostró que los pacientes que recibieron intervención nutricional presentaron una menor estancia hospitalaria, menor tasa de mortalidad y menor probabilidad de ingresar en cuidados intensivos (10).

El objetivo primario de este trabajo es valorar las características de los pacientes tratados con suplementos nutricionales orales (SNO) en el Área Norte de Gran Canaria en el periodo 2016-2021.

MATERIAL Y MÉTODOS

Se trata de un estudio observacional retrospectivo en el que se recogen anualmente todas las solicitudes para la prescripción de SNO en el Área Norte de Gran Canaria en el periodo comprendido entre 2016 y 2021.

La población del estudio fueron los pacientes con diagnóstico de desnutrición a los que su médico prescribió SNO a través del formulario digital de la receta electrónica. En este estudio mostramos los resultados de la primera prescripción, que puede ser realizada por cualquier médico del Servicio Canario de Salud.

Los datos se obtuvieron de la base de datos anonimizada proporcionada por la Dirección del Área de Salud de Gran Canaria dependiente del Servicio Canario de Salud.

Las variables extraídas del formulario fueron: edad, género, desnutrición relacionada con la enfermedad (DRE), requerimientos nutricionales (RN), índice de masa corporal (IMC), porcentaje de la pérdida de peso (PPP) en 3 meses, albúmina y número de SNO prescritos.

El proyecto de investigación tiene la aprobación del Comité de Bioética de la Universidad de Las Palmas de Gran Canaria y cumple con La Ley Orgánica de Protección de Datos y garantía de los derechos digitales

ESTADÍSTICA

El análisis estadístico fue realizado con el programa SPSS 25.0 (IBM). En las variables cuantitativas se analizó si seguían una distribución normal a través de la prueba de Kolmogórov-Smirnov y se expresaron como media y desviación estándar (±). La comparación entre variables cuantitativas se realizó con la prueba de la t de Student. Se realizó un ANOVA de doble vía para el análisis factorial de la varianza. La prueba de igualdad de varianzas de Levene se utilizó para valorar la homocedasticidad.

Las variables cualitativas se expresan como frecuencias absolutas y porcentajes. La comparación entre variables se realizó con la prueba del chi-cuadrado. Se consideró significativo todo valor de p inferior a 0,05.

RESULTADOS

Se identificaron 10.595 prescripciones correspondientes a 6661 pacientes (46,3 % eran varones (3085) y 53,7 % eran mujeres (3576)). Esto representa un 3,09 % de la población de referencia del área de salud del Hospital Universitario de Gran Canaria Doctor Negrín (HUGCDrN), que abarca unas 342.566 personas según datos de 2019 (11).

Las características basales de la población estudiada fueron: edad media, 72,84 ± 15,93 años; el 44,5 % de los pacientes fueron mujeres; IMC, 20,60 ± 3,98 kg/m^2; PPP, 11,89 ± 8,32 %; tiempo medio de pérdida de peso, 5,15 ± 3,57 meses; albúmina, 3,08 ± 0,63 g/dl. El 18,3 %, 18,9 %, 24,1 %, 25,5 % y 13,2 % de las prescripciones correspondieron a pacientes en los rangos etarios de < 59 años, 60-69 años, 70-79 años, 80-89 años y > 90 años, respectivamente.

ETIOLOGÍA DE LA DESNUTRICIÓN (DRE)

Los síndromes más frecuentes asociados a DRE fueron: patología oncológica, 42,6 %; enfermedades neurológicas con disfagia, 28,9 %; ictus, 3,9 %; intestino corto, 6,9 %; enfermedad inflamatoria intestinal, 5,5 %. El 12,2 % de las prescripciones se excluyeron de este análisis por diagnósticos incongruentes y/o no documentados en la historia clínica. La distribución de las patologías por año se muestra en la figura 1. La distribución de las variables cuantitativas se muestra en la tabla I.

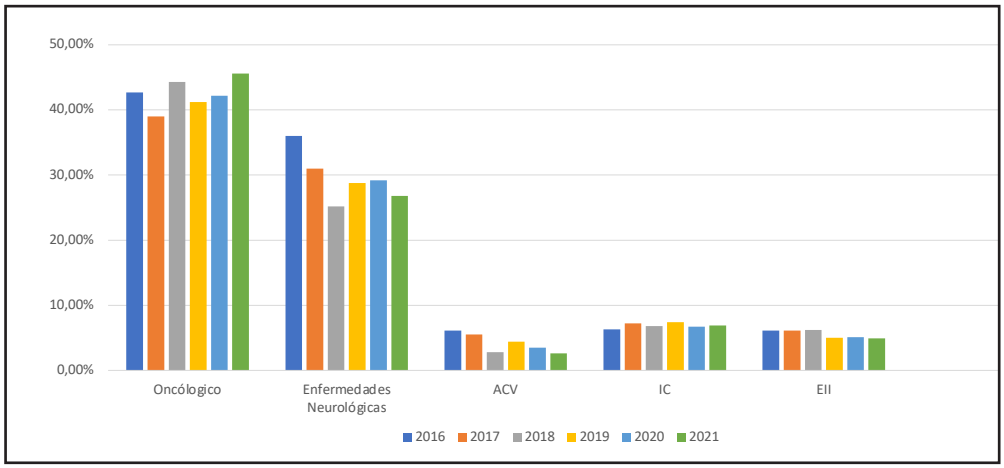

Figura 1.

Etiología de la DRE por años de observación. Porcentajes anuales (enfermedades neurológicas: enfermedades del SNC excluyendo el ACV; ACV: accidente vasculocerebral; IC: intestino corto; EII: enfermedad inflamatoria intestinal).

Tabla I. Características de la población en los años de seguimiento

	2016	2017	2018	2019	2020	2021	Total
n	653	1049	1208	1265	1203	1282	6660
Edad (años)	75,33 ± 15,55	74,88 ± 16,08	73,04 ± 15,80	72,39 ± 16,15	72,34 ± 15,05	70,60 ± 15,93	
n	603	982	1154	1205	1167	1241	6352
IMC (kg/m^2)	20,84 ± 4,03	20,90 ± 4,13	20,63 ± 3,96	20,54 ± 4,00	20,31 ± 3,76	20,50 ± 4,01	
n	575	897	1084	1153	1082	1153	5944
PPP (%)	12,62 ± 8,67	12,06 ± 7,91	12,29 ± 9,14	12,11 ± 7,91	11,59 ± 8,34	11,08 ± 7,89	
n	559	847	941	1049	988	1038	5422
MPP (meses)	5,46 ± 3,75	4,97 ± 3,17	5,02 ± 3,47	5,17 ± 3,75	5,09 ± 3,55	5,30 ± 3,67	
n	547	928	1118	1114	1154	1221	6082
Alb (g/dl)	3,12 ± 0,60	3,06 ± 0,60	3,07 ± 0,65	3,04 ± 0,66	3,06 ± 0,63	3,13 ± 0,65	

Alb: albúmina; IMC: índice de masa corporal; MPP: meses de pérdida de peso; PPP: % de pérdida de peso.

La edad media de la población que recibió el SNO disminuyó durante el periodo de observación. En el inicio del seguimiento, la edad media fue de 75,33 ± 15,56 años, en el 2017 fue de 74,88 ± 16,09 años, en el 2018 fue de 73,04 ± 15,80 años, en el 2019 fue de 72,39 ± 16,16 años, en el 2020 fue de 72,34 ± 15,50 años y en el 2021 fue de 70,60 ± 15,94 años. Se observó una disminución estadísticamente significativa de la edad de los pacientes tratados en 2016 frente a 2019, 2020 y 2021; entre los pacientes tratados en 2017 frente a 2019, 2020 y 2021, $p < 0,001$; y entre los pacientes tratados en 2018 con respecto a 2021 y entre pacientes tratados en 2019 con respecto a 2021 ($p < 0,001$). Existieron diferencias estadísticamente significativas en la edad media de inicio del SNO por sexos (mujeres, 74,73 ± 16,68 años frente a varones, 71,2 ± 15,08 años, $p < 0,001$).

Hubo tendencia a iniciar el tratamiento con IMC más bajos ($p = 0,021$) (Fig. 2) y pérdidas de peso menores ($p = 0,025$) (Fig. 3). Existieron diferencias estadísticamente significativas en el IMC por sexo (mujeres, 20,26 ± 4,11 kg/m^2 frente a varones,

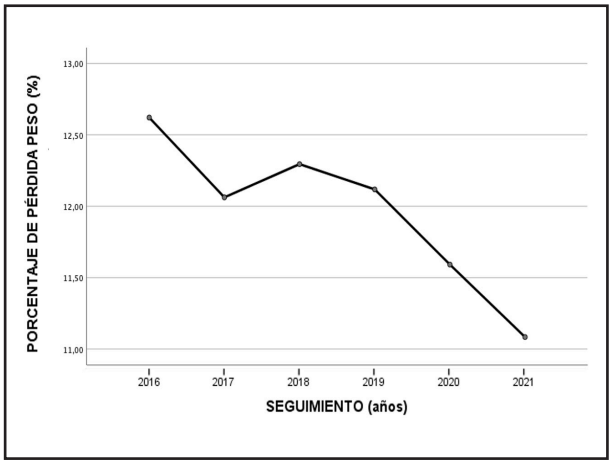

Figura 2.

Evolución del porcentaje de pérdida de peso de los pacientes en el momento de la prescripción a lo largo del seguimiento.

20,89 ± 3,84 kg/m^2, $p < 0,001$). Sin embargo, no se observó ninguna tendencia atendiendo a las cifras de albuminemia (Fig. 4), aunque sí que existieron diferencias estadísticamente significativas por sexos (mujeres, 3,06 ± 0,63 g/dl frente a varones, 3,10 ± 0,65 g/dl, $p = 0,018$).

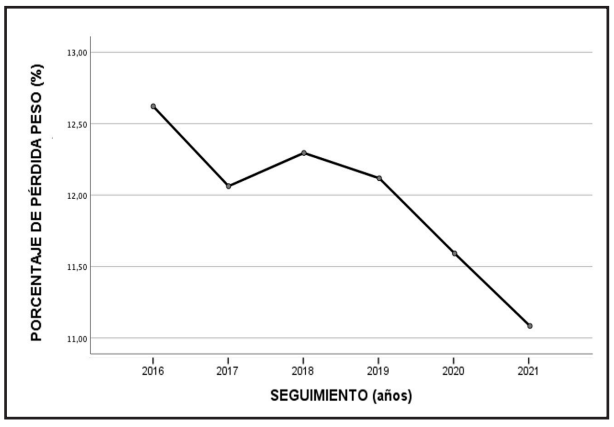

Figura 3.

Evolución del porcentaje de pérdida de peso de los pacientes en el momento de la prescripción a lo largo del seguimiento.

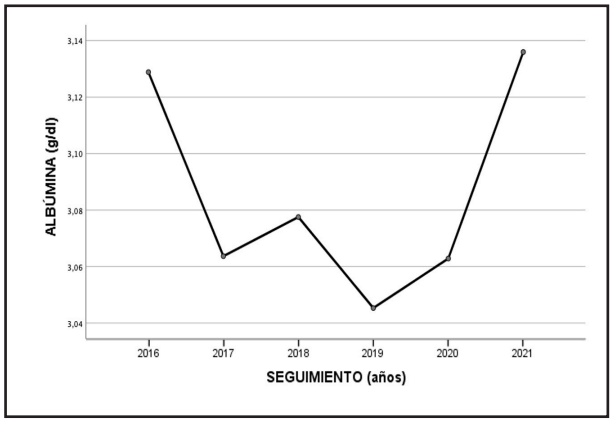

Figura 4.

Evolución de la albuminemia de los pacientes a lo largo del seguimiento.

Con respecto a la prevalencia de la desnutrición según los criterios GLIM, el 63,74 % de los sujetos ≥ 70 años presentaron un IMC < 22 kg/m^2; el 47,66 % de los < 70 años presentaron un IMC < 20 kg/m^2.

El 8,9 %, el 36,9 % y el 54,2 % de los pacientes precisaban cubrir los RN en un 100 %, un 50 % y un 25 %, respectivamente, según los datos del formulario (Fig. 5). Existieron diferencias estadísticamente significativas por sexos en los pacientes en que se cubría el 100 % de los RN (mujeres, 9,6 % frente a varones, 8,0 %, $p = 0,017$) y el 50 % de los RN (mujeres, 19,0 % frente a varones, 17,9 %, $p = 0,006$), pero no en el 25 %.

En relación con el número de SNO prescritos, el 40,4 %, el 36,6 % y el 23,0 % de los pacientes recibieron uno, dos o tres o más SNO. De los pacientes que tenían requerimientos nutricionales superiores al 50 %, el 40,8 % y el 41,6 % recibían solo 1 o 2 SNO, respectivamente. No existieron diferencias entre número de suplementos prescritos en el tiempo de observación (Fig. 5), ni por sexos.

En relación con la vía de administración, el 93,0 %, el 5,1 %, el 0,8 % y el 0,1 % recibían los SNO por vía oral, gastrostomía, sonda nasogástrica y yeyunostomía, respectivamente. No existieron diferencias según el sexo.

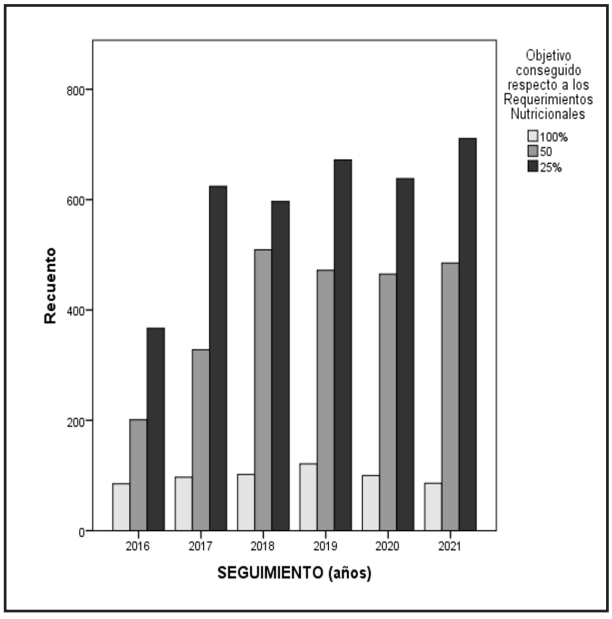

Figura 5.

Evolución del cumplimento de los requerimientos nutricionales con la pauta de suplementación nutricional a lo largo del seguimiento.

DISCUSIÓN

Este es el primer estudio poblacional que analiza el patrón de prescripción de suplementos nutricionales en nuestro país durante un periodo tan prolongado, incluyendo los años de pandemia de COVID, la cual condicionó forzosamente un cambio en la asistencia sanitaria.

Durante el periodo de observación no hubo cambios significativos en la etiología de la DRE, donde predominaban los pacientes oncológicos, lo que sugiere que la asistencia sanitaria de estos pacientes durante la pandemia de COVID fue lo más similar posible a los periodos convencionales. En estudios nacionales de la vida real, el soporte nutricional con SNO ha demostrado beneficio tanto en los parámetros nutricionales como en la calidad de vida de los pacientes oncológicos (12) y de los pacientes con enfermedad gastrointestinal y malabsorción (13).

La edad media del paciente que recibe suplemento nutricional es superior a los 70 años y en los primeros años de observación

fue superior a la reportada en otros estudios de base poblacional en Europa (14,15). Este hecho puede estar en relación con las mayores expectativas de vida que hay en nuestro país (16). No encontramos una explicación al descenso de 5 años en la edad media de los pacientes que reciben SNO. Una posibilidad es el aumento de la mortalidad superior a la esperada en la población anciana en los años de pandemia de COVID.

La gran mayoría de los pacientes cumplía el criterio de bajo peso según las guías GLIM (17) y hubo tendencia a iniciar el tratamiento con IMC más bajos, pero la diferencia numérica es tan pequeña que no la consideramos epidemiológicamente relevante.

A pesar de que hubo una tendencia a iniciar el tratamiento con pérdidas de peso menores, en este punto hay un amplio margen de mejora. Es importante recordar que dentro de los criterios GLIM se establece como punto de corte la pérdida del 5 % del peso a los 6 meses. La implantación de un cribado nutricional entre los pacientes en riesgo de desnutrición puede facilitar una identificación y tratamiento más precoz.

No se observó ninguna tendencia de prescripción de SNO según los niveles de albúmina plasmática (Fig. 5). Además, un porcentaje significativo de los formularios no tenían información sobre este parámetro. Esto posiblemente sea reflejo de la creciente importancia que tienen los criterios fenotípicos frente a los datos analíticos para el diagnóstico de la desnutrición. De hecho, éstos ni siquiera se mencionan dentro de los criterios GLIM. Por otra parte, la albuminemia puede verse afectada por otras comorbilidades o tratamientos, como la patología hepática y renal y la quimioterapia, si bien la albúmina puede ser un marcador indirecto de inflamación y pronóstico clínico (18).

Uno de los aspectos más destacables de nuestro estudio es la disociación entre las necesidades calóricas de los pacientes desnutridos y el número de suplementos nutricionales prescritos. Más del 80 % de los pacientes con prescripciones con intención de cubrir unos RN superiores al 50 % recibían únicamente 1 o 2 SNO, lo que no garantiza cubrir las necesidades calóricas ni proteicas, máxime teniendo en cuenta que las necesidades proteicas en enfermedades agudas o con alto nivel de inflamación pueden ser de hasta 1,5-2 g/kg/día. Este dato pone de manifiesto que casi la mitad de los pacientes podría considerarse infratratados.

Este punto resalta la importancia de adecuar la prescripción de soporte nutricional artificial a las necesidades reales de los pacientes. Si consideramos que, de promedio, un envase de SNO estándar aporta unas 300-400 kcal y 15-18 g de proteínas, difícilmente el objetivo se puede alcanzar en un paciente malnutrido si se emplea una única dosis diaria. Además, hay que individualizar la prescripción teniendo en cuenta la importancia de la adherencia a la pauta, ya que muchas veces el cumplimiento terapéutico implica las preferencias del paciente en cuanto a sabor y palatabilidad de la fórmula de SNO (19).

La asistencia a los pacientes con riesgo de desnutrición requiere conocer los criterios de desnutrición, calcular el déficit calórico que se produce entre la ingesta del paciente y el gasto energético total y prescribir los suplementos nutricionales adecuados a esta situación, además de comprender la fisiopatología de las enfermedades asociadas con desnutrición y su manejo óptimo con soporte nutricional. Esto implica una formación que solo está incluida en los programas de formación de los residentes de Endocrinología y Nutrición, aunque otros especialistas a través de la formación continuada pueden adquirir esos conocimientos.

Este estudio tiene algunas debilidades que debemos señalar: se trata de un estudio retrospectivo en la vida real, con lo que la exactitud de todos los datos antropométricos y bioquímicos no se puede garantizar.

Como fortalezas queremos destacar que el estudio abarc*ó* la casi totalidad de la población atendida por el sistema público por DRE en nuestra área de salud a la que se solicita un SNO, que además comprende un largo periodo de observación y que la albúmina se ha analizado durante todo el periodo de observación en un mismo laboratorio; todo ello nos garantiza que los principales hallazgos y conclusiones del estudio son sólidos.

Este estudio abre otras líneas de investigación, como valorar la adherencia a los SN o calcular el impacto que tiene la prescripción de SNO específicos sobre determinadas patologías en grupos específicos de pacientes ambulatorios. Es bien conocido el impacto positivo del tratamiento de la desnutrición en población hospitalaria (20), pero menos conocido es el impacto en población ambulatoria (21-27). Otra línea de trabajo podría ser analizar, en los pacientes que recibieron soporte nutricional durante más de 3 meses, la concordancia con el informe del especialista en Endocrinología y Nutrición.

CONCLUSIONES

En este estudio de base poblacional que analiza el patrón de prescripción de suplementos nutricionales durante 6 años no hay cambios significativos en las causas de desnutrición. Aunque hay una tendencia a una detección más precoz de la DRE, existe un margen importante de mejora: la instauración de programas de cribado en pacientes de riesgo puede ser útil en este sentido. Es fundamental que el médico que asista a estos pacientes tenga la formación suficiente para tratar adecuadamente a estos pacientes con el objetivo de evitar el infratratamiento.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Nutrición artificial

Mejorando la atención nutricional del paciente oncológico: validación de un protocolo multidisciplinar en el entorno clínico español

Improving the nutritional care of oncology patients — Validation of a multidisciplinary protocol in the Spanish clinical setting

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Resumen

Introducción: la desnutrición es un problema muy frecuente en el paciente oncológico y puede tener graves repercusiones. Un manejo nutricional adecuado es coste-efectivo en términos de salud y supervivencia en esta población, pero requiere de coordinación multidisciplinar, formación específica y seguimiento continuo.

Objetivo: validar la aplicabilidad y eficacia de un protocolo multidisciplinar de soporte nutricional en pacientes oncológicos.

Métodos: se desarrolló un protocolo nutricional multidisciplinar para pacientes oncológicos, con pautas para el cribado y valoración de la desnutrición, el tratamiento, la reevaluación y la gestión de los efectos secundarios, además de orientaciones sobre suplementación y patrones de alimentación. Se implementaría el protocolo en diversos centros clínicos, recogiendo datos a través de un cuestionario estructurado, registrando variables antes y después de la implementación.

Resultados: se implementó y se valoraron el protocolo y su impacto en 39 centros. Se observó una mejoría en la atención nutricional, evidenciada por un inicio más precoz de la valoración nutricional y un aumento en el número de pacientes que recibían atención adecuada tras la implementación del protocolo. Se identificaron problemas relacionados con una inadecuada codificación de la desnutrición en los centros, recursos limitados y la necesidad de mayor colaboración interdepartamental.

Conclusiones: la realización de este estudio ofrece información de cómo la implementación de un protocolo multidisciplinar de soporte nutricional puede contribuir a mejorar la atención nutricional que reciben los pacientes e informa de cuáles son los principales obstáculos para una implementación adecuada.

Palabras clave:

Atención nutricional. Paciente oncológico. Protocolo multidisciplinar. Desnutrición en cáncer. Implementación clínica. Validación de protocolo.

Abstract

Introduction: malnutrition is a very frequent problem in oncology patients and ~~can~~ have serious repercussions. Adequate nutritional management is cost-effective in terms of health and survival in this population, but it requires multidisciplinary coordination, specific training, and continuous follow-up.

Objective: to validate the applicability and efficacy of a multidisciplinary nutritional support protocol in oncology patients.

Methods: a multidisciplinary nutritional protocol was developed for oncology patients, with guidelines for screening and assessment of malnutrition, treatment, re-evaluation, and management of side effects, as well as guidance on supplementation and eating patterns. The protocol would be implemented in various clinical centers, collecting data through a structured questionnaire, registering variables before and after implementation.

Results: the protocol and its impact were implemented and evaluated in 39 centers. An improvement in nutritional care was observed, evidenced by an earlier initiation of nutritional assessment and an increase in the number of patients receiving adequate care following the protocol implementation. Problems related to inadequate malnutrition coding in the centers, limited resources, and the need for greater interdepartmental collaboration were identified.

Conclusions: the conduct of this study provides insights into how the implementation of a multidisciplinary nutritional support protocol can improve the nutritional care received by patients and informs about the main obstacles to adequate implementation.

Keywords:

Nutritional care. Oncology patient. Multidisciplinary protocol. Malnutrition in cancer. Clinical implementation. Protocol validation.

INTRODUCCIÓN

El cáncer es una de las causas más habituales de desnutrición relacionada con la enfermedad (DRE) (1). La desnutrición es un problema muy frecuente en los pacientes oncológicos, afectando al 19-73 % de estos, y se asocia con diferentes factores, incluyendo el tipo de tumor, el estadio de la enfermedad, la salud basal del individuo y el tratamiento oncológico utilizado (1). A nivel nacional, el estudio NUPAC muestra que la desnutrición (moderada-severa) está presente en el 52,2 % de los individuos con cáncer avanzado (2).

La desnutrición puede tener graves repercusiones en estos pacientes, como un aumento de las complicaciones posquirúrgicas (3), una menor tolerancia al tratamiento antitumoral (4,5), una menor eficacia del tratamiento (3), un peor pronóstico (6), una peor calidad de vida (7) y un aumento de los costes (8). Ante la importancia del estado nutricional en el paciente oncológico, las guías de la Sociedad Europea de Nutrición Clínica y Metabolismo (ESPEN) recomiendan la evaluación nutricional de todos los pacientes con cáncer en el momento del diagnóstico y el establecimiento de las maniobras de intervención específicas para cada paciente (1).

Un adecuado tratamiento médico nutricional es coste-efectivo en términos de salud y supervivencia en estos pacientes (9,10). El manejo de la nutrición a través de procesos asistenciales permite una respuesta integral al paciente oncológico, facilita la continuidad de la atención, hace un uso eficiente de los recursos y permite una evaluación adecuada de los resultados. Los recursos recomendados para este enfoque incluyen estructuras clínicas, personal médico especializado y material documental.

A fin de facilitar la organización de dichos elementos y estructuras de manera efectiva, se elaboró en 2022 un protocolo multidisciplinar de soporte nutricional en pacientes oncológicos que describía pautas para el cribado y valoración de la desnutrición, el tratamiento nutricional, la reevaluación periódica y la gestión de los efectos secundarios del tratamiento, además de proporcionar orientaciones sobre suplementación nutricional y patrones de alimentación específicos en esta población de pacientes (11).

El presente estudio tiene como finalidad validar la practicidad y eficacia de dicho protocolo en las diferentes realidades del entorno clínico español a través de una evaluación sistemática. Adicionalmente, buscamos analizar el posible impacto que puede generar la implementación de un protocolo de este tipo en la atención nutricional de los pacientes oncológicos con desnutrición.

MATERIAL Y MÉTODOS

El protocolo fue elaborado conjuntamente por un grupo multidisciplinar de autores (dos especialistas en Endocrinología y Nutrición, una especialista en Oncología Médica, una enfermera especializada en Oncología Radioterápica y Radiofísica y una nutricionista). La tabla I muestra el índice de contenidos del documento.

Tabla I. Tabla de contenidos del protocolo multidisciplinar de soporte nutricional en pacientes oncológicos (1.ª edición, que se distribuyó entre los participantes)

Introducción
1. Desnutrición en el paciente oncológico
1.1 ¿Es habitual la desnutrición en el paciente oncológico?
1.2 ¿Cuáles son las repercusiones derivadas de la desnutrición en el paciente con cáncer?
1.3 Importancia del abordaje de la desnutrición en Oncología
1.4 Procesos asistenciales en el abordaje nutricional del paciente oncológico
2. Cribado y valoración de la desnutrición
2.1 ¿Cómo evaluar el estado nutricional en el paciente oncológico?
2.2 Parámetros clásicos en Nutrición Clínica
2.3 Parámetros avanzados en Nutrición Clínica
2.4 Algoritmo diagnóstico de valoración nutricional en el servicio de Oncología
2.5 Codificación de la desnutrición
2.6 Algoritmos de valoración nutricional y flujo de pacientes
3. Tratamiento nutricional
3.1 Algoritmo terapéutico de cálculo requerimientos
3.2 Terapia nutricional según severidad del cuadro
3.3 Terapia nutricional según la ingesta
3.4 Algoritmo terapéutico en situaciones especiales
3.5 Algoritmo de selección de fórmula nutricional
4. Algoritmos de seguimiento y revisión
4.1 ¿Cómo y cuándo reevaluar la situación nutricional?
4.2 Importancia del trabajo multidisciplinar
4.3 Algoritmo y recomendaciones de actuación ante efectos secundarios del tratamiento
4.4 Preguntas frecuentes en relación con la suplementación nutricional
ANEXO I: Patrones de alimentación
5.1 ¿Cómo podemos enriquecer la dieta?
5. Abreviaturas utilizadas
6. Bibliografía

En junio de 2022, el protocolo (11) fue distribuido entre profesionales sanitarios con interés en la nutrición clínica del paciente oncológico, quienes fueron invitados a implementarlo en sus respectivos centros. Aunque trabajos anteriores han documentado cómo la implementación de un protocolo de nutrición enteral está asociada con mejoras significativas en indicadores como el momento de inicio de la nutrición enteral, la cantidad total de nutrición entregada o la satisfacción general de las necesidades calóricas de los pacientes y recomiendan que los protocolos de nutrición enteral sean parte del *standard of care* (12), se ha documentado también la existencia de una brecha entre actitudes y prácticas actuales en nutrición enteral que puede generar barreras en la implementación (13), por lo que se suele recomendar explorar las actitudes y experiencias de los profesionales sanitarios conjuntamente con la implementación de estos protocolos.

Así, además de la propia implementación, consideramos que era esencial recoger datos que nos permitieran entender cómo y por qué se usaban las diferentes herramientas incluidas en el protocolo y qué obstáculos aparecían en el proceso, por lo que se invitó a los participantes a completar un cuestionario en varias fases.

La validación del protocolo tuvo lugar a través de un cuestionario desarrollado por los autores del protocolo, siguiendo las recomendaciones para la elaboración de preguntas para encuestas de investigación y ensayos clínicos de la ICH (14) y de Edwards y cols. (15).

El cuestionario incluía 43 preguntas, tanto cerradas (de multielección y tipo Likert de 5 opciones) como abiertas (numéricas y de texto), organizadas en cuatro bloques:

- El bloque 1 contenía preguntas sobre la manera en que los centros solían abordar la desnutrición en pacientes oncológicos antes de valorar e implementar el protocolo.
- El bloque 2 se centraba en la valoración del protocolo, enfatizando en su utilidad clínica, facilidad y grado de implementación, y rango de acciones donde el protocolo fue valorado e implementado.
- El bloque 3 valoraba la implementación del protocolo y replicaba algunas de las variables principales del bloque 1 (relativas al centro), pero después de la implementación del protocolo para cuantificar su efecto.
- Finalmente, el bloque 4 se centraba en la valoración de las actitudes hacia el manejo nutricional.

Los profesionales sanitarios completaron el cuestionario durante el periodo de julio a diciembre de 2022 mediante una aplicación web creada específicamente a tal efecto.

Se aplicaron técnicas estadísticas descriptivas para el análisis de los resultados y las respuestas a preguntas abiertas se categorizaron para su evaluación.

Se midió el impacto del protocolo a través de la valoración subjetiva del impacto clínico por parte de los participantes (bloques 2 y 4) así como la comparación de resultados emparejados entre los bloques 1 (previo a la implementación) y 3 (posterior a la implementación). La tabla II proporciona un listado detallado de las variables recogidas.

Tabla II. Variables recogidas en el estudio

Bloque	Variable	Tipo de pregunta
Bloque 1. Variables del centro	1. Edad del participante	Campo numérico abierto
	2. Sexo del participante	Elección múltiple
	3. Tamaño del centro	Elección múltiple
	4. Profesión del participante	Elección múltiple
	5. Ubicación habitual de los pacientes	Elección múltiple
	6. Número de pacientes oncológicos atendidos en un mes	Campo numérico abierto
	7. Decisión de la actuación nutricional del paciente	Elección múltiple con opción de texto abierto
	8. Tipos de cáncer con riesgo nutricional/desnutrición atendidos	Elección múltiple con opción de texto abierto
	9. Número de pacientes con riesgo nutricional/desnutrición en un mes	Campo numérico abierto
	10. Estimación del porcentaje de pacientes oncológicos que deberían recibir atención nutricional en el centro	Campo numérico abierto
	11. Estimación del porcentaje real de pacientes oncológicos que reciben atención nutricional (previo al protocolo) en el centro	Campo numérico abierto
	12. Momento de inicio del abordaje nutricional en los pacientes	Elección múltiple
	13. Profesionales involucrados en el abordaje nutricional	Elección múltiple con opción de texto abierto
	14. Etapa evolutiva del cáncer en la que se valora el estado nutricional con mayor frecuencia	Campo abierto con porcentajes
	15. Tipos de tratamiento en los que se valora el estado nutricional	Campo abierto con porcentajes
	16. Existencia de materiales de entrega al paciente con recomendaciones nutricionales en el centro	Elección múltiple con opción de texto abierto
	17. Utilización de un sistema de codificación para la clasificación de la desnutrición en el centro	Elección múltiple
	18. Existencia previa de un protocolo similar en el centro	Elección múltiple
Bloque 2. Valoración del protocolo	19. Estimación de rango de actuaciones para valorar la implementación del protocolo	Elección múltiple
	20. Opinión sobre la adecuación/utilidad del protocolo	Escala de Likert de 1 a 5
	21. Opinión sobre la fiabilidad científica del protocolo	Escala de Likert de 1 a 5
	22. Lo más útil del protocolo	Campo de texto abierto
	23. Lo menos útil del protocolo	Campo de texto abierto
	24. Utilidad clínica de las herramientas del protocolo	Escala de Likert de 1 a 5
Bloque 3. Valoración del protocolo	25. Rango de implementación del protocolo	Elección múltiple
	26. Grado de implementación de las herramientas del protocolo	Campo de texto abierto con porcentajes
	27. Obstáculos en la implementación del protocolo	Campo de texto abierto
	28. Cambios positivos en el abordaje nutricional	Escala de Likert de 1 a 5
	29. Mejora en la atención nutricional	Escala de Likert de 1 a 5
	30. Estimación del porcentaje actual de pacientes que reciben atención nutricional	Campo de texto abierto
	31. Momento de inicio del abordaje nutricional	Campo de texto abierto con porcentajes
	32. Herramientas del protocolo que han aportado mayor cambio	Elección múltiple (seleccione tres)
Bloque 4. Actitudes/ opiniones respecto al abordaje nutricional en Oncología	33. Opinión sobre la valoración nutricional en el paciente oncológico	Escala de Likert de 1 a 5
	34. Opinión sobre la coordinación del abordaje nutricional	Escala de Likert de 1 a 5
	35. Mediciones/evaluaciones mínimas en el cribado/valoración nutricional	Elección múltiple
	36. Recursos materiales mínimos en el cribado/valoración nutricional	Elección múltiple
	37. Personal/equipo mínimo en el cribado/valoración nutricional	Elección múltiple
	38. Opinión sobre la ingesta de proteínas en pacientes oncológicos	Escala de Likert de 1 a 5
	39. Opinión sobre la importancia de los aminoácidos esenciales	Escala de Likert de 1 a 5
	40. Opinión sobre la selección de proteínas con diferentes perfiles de digestión	Escala de Likert de 1 a 5
	41. Opinión sobre la alta densidad calórica en los suplementos nutricionales	Escala de Likert de 1 a 5
	42. Opinión sobre las características clave de un suplemento nutricional	Escala de Likert de 1 a 5
	43. Opinión sobre el uso de fórmulas con inmunonutrientes en pacientes quirúrgicos	Escala de Likert de 1 a 5

RESULTADOS

NÚMERO DE PARTICIPANTES Y CARACTERÍSTICAS DE LOS CENTROS

El protocolo fue revisado y validado por 39 médicos (80 % especialistas en Endocrinología-Nutrición y 15 % médicos especialistas en Oncología Radioterápica y 5 % otros. El 53 % de los participantes trabajaba en centros con más de 500 camas y el 47 % en centros con entre 50 y 500 camas. Los participantes estimaron que veían un promedio de 77 pacientes oncológicos al mes.

INTERVENCIÓN NUTRICIONAL

En cuanto a la toma de decisiones en relación con la intervención nutricional, se registró que el 43 % de las decisiones se toman en unidades de nutrición. El 92 % de los participantes expresó que consideraban que, al menos, el 80 % de sus pacientes necesitaba atención nutricional. Sin embargo, se identificó una brecha en la atención nutricional que recibían los pacientes, con un 23 % de pacientes que no estaban recibiendo el tratamiento considerado necesario por el participante.

Respecto a la codificación de la desnutrición en los centros, la gran mayoría de centros (63 %) no utilizaba una codificación para la clasificación de la desnutrición (Fig. 1). Un 6 % utiliza sistemas de clasificación, pero no son codificados.

IMPLEMENTACIÓN DEL PROTOCOLO

Un 90 % de los participantes pudo implementar exitosamente el protocolo en su centro, y el 91 % afirmó que la implementación produjo cambios positivos en el abordaje nutricional del paciente oncológico. Los principales obstáculos para la implementación fueron la falta de recursos (85 %), la necesidad de colaboración interdepartamental (38 %) y un alto volumen de pacientes (24 %).

VALORACIÓN DEL PROTOCOLO

El protocolo fue valorado muy positivamente por los participantes: el 95 % estuvo de acuerdo o muy de acuerdo con considerarlo adecuado y útil y un 98 % lo consideró una propuesta científica fiable. Las aportaciones mejor valoradas del protocolo fueron la valoración nutricional completa, los algoritmos y flujos de pacientes, y el hecho de que fuese específico para Oncología. Al preguntar por las secciones menos útiles o innecesarias, un 36 % de los participantes respondió que ninguna parte les parecía poco útil.

IMPACTO EN LA ATENCIÓN NUTRICIONAL DEL PACIENTE ONCOLÓGICO DESNUTRIDO O EN RIESGO

Un 91 % de los participantes consideró que la implementación del protocolo había producido cambios positivos en el abordaje nutricional del paciente oncológico en su consulta o unidad. Las herramientas responsables de esa mejora fueron el cribado y valoración de la desnutrición, los algoritmos y recomendaciones de actuación ante efectos secundarios del tratamiento, los parámetros avanzados en nutrición clínica y la codificación de la desnutrición (Fig. 2).

Se observó una mejoría en el número de pacientes que recibían atención nutricional en un 82 % de los casos tras implementar el protocolo (Fig. 3). También se observó una mejoría en el momento de inicio de la valoración nutricional de los pacientes: antes de la implementación del protocolo, la mayoría de los centros iniciaba el abordaje nutricional en el momento del tratamiento o la aparición de efectos secundarios. Tras la implementación del protocolo, sin embargo, hubo una tendencia a iniciar el abordaje nutricional más temprano después de implementar el protocolo, principalmente en el momento del diagnóstico y en la primera visita (este desplazamiento hacia un abordaje más precoz se puede apreciar en la figura 4).

ACTITUDES RESPECTO AL TRATAMIENTO MÉDICO NUTRICIONAL

Por último, en relación con las actitudes y opiniones sobre el tratamiento médico nutricional, los participantes consideraron que la intervención nutricional es coste-efectiva y que el tratamiento médico nutricional debe cubrir los requerimientos proteicos y calóricos del paciente oncológico, teniendo como características principales para cubrir necesidades y favorecer la adherencia las siguientes: hiperproteico, aporte aminoácidos ramificados (en particular leucina), una mezcla de proteínas óptima (50 % caseína sérica y 50 % lactoproteína sérica) , alta densidad calórica ≥ 2 kcal/ml, bajo volumen y variedad de sabores.

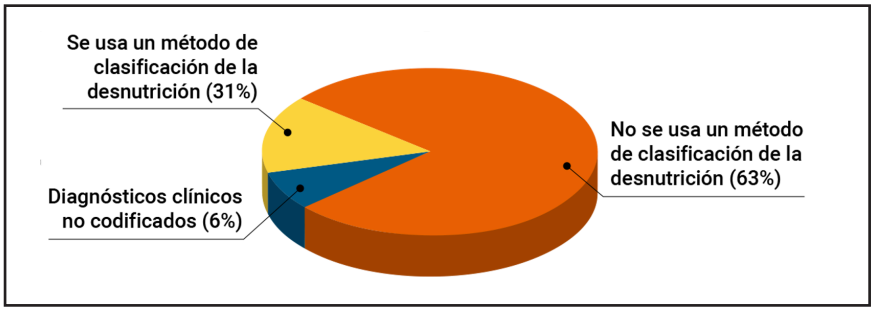

Figura 1.
Uso de codificación para la clasificación de la desnutrición previamente a la implementación del protocolo ($n = 39$).

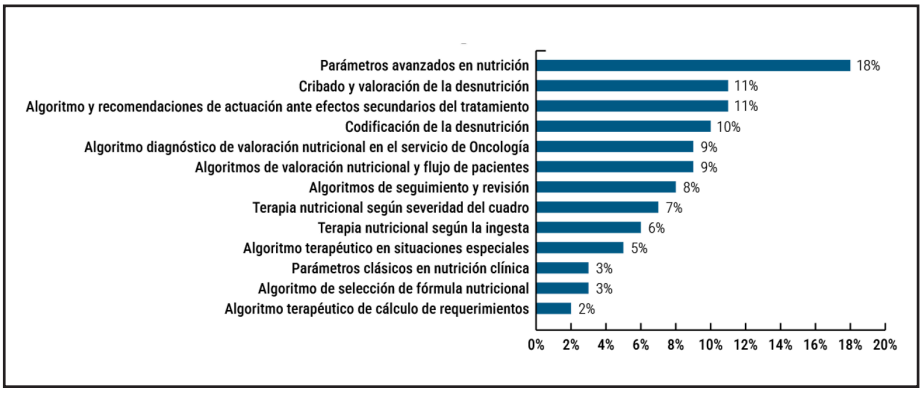

Figura 2.

Impacto estimado de cada herramienta en la mejor*ía* de la atención nutricional al paciente oncológico tras la implementación del protocolo ($n = 39$).

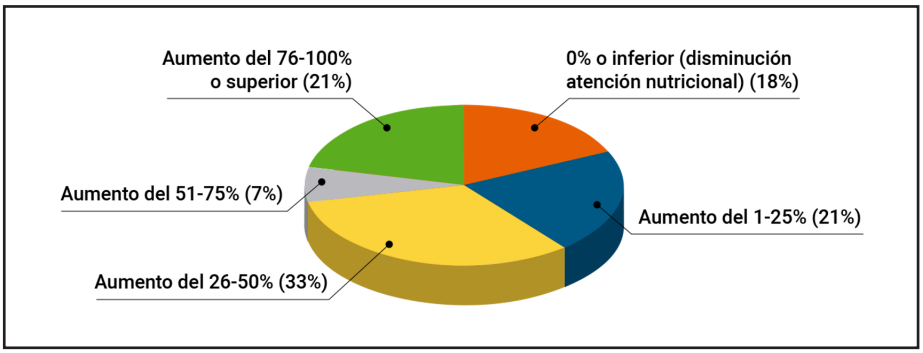

Figura 3.

Variación en el número de pacientes que recibía una atención nutricional adecuada tras la valoración e implementación del protocolo.

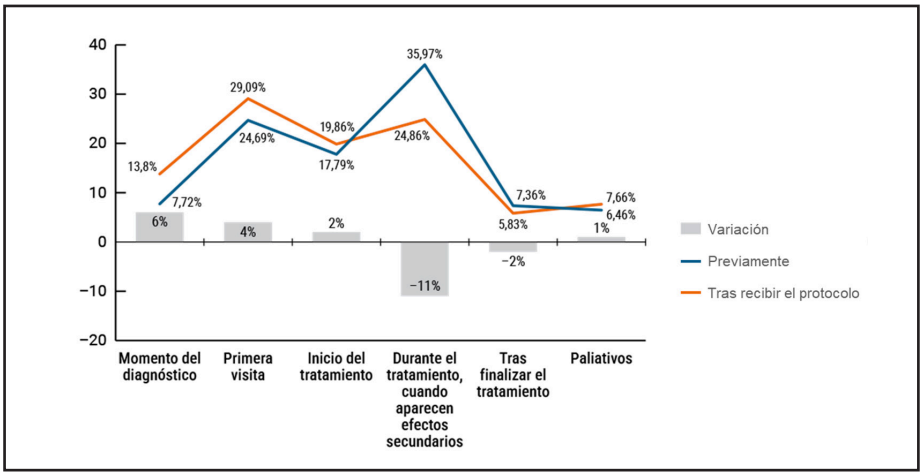

Figura 4.

Momento de inicio del abordaje nutricional previa o posteriormente al protocolo. En las barras, variación pospreimplentación. Como se ve, tras recibir e implementar el protocolo, hubo una tendencia a que la valoración nutricional se produjera en un momento más cercano al diagnóstico.

DISCUSIÓN

El resultado principal de este estudio es que nos ofrece varias medidas de cómo la implementación de un protocolo multidisciplinar de soporte nutricional contribuye a mejorar la atención nutricional que reciben los pacientes (en este caso, oncológicos).

La mejoría observada respecto al momento de inicio de la valoración y abordaje nutricional es de gran importancia, ya que la detección precoz de los pacientes desnutridos o en riesgo nutricional permite actuar cuando su estado nutricional no está demasiado deteriorado, haciendo así que el tratamiento nutricional sea menos intensivo, involucrando principalmente modificaciones dietéticas y suplementos. De este modo, esta detección temprana permite una reversión más rápida de la desnutrición, evitando así una hospitalización prolongada y previniendo incurrir en mayores costes de hospitalización y tratamiento (16). Pese a todo, un 39 % de los participantes consideró que en su centro existían pacientes que recibían menos atención nutricional de la que deberían, lo que estaría alineado con resultados procedentes de otros estudios en nuestro medio, que evidencian que el manejo nutricional del paciente con cáncer en la práctica clínica actual en España es subóptimo (17,18), que aproximadamente la

mitad de los pacientes no recibe ningún tipo de asesoramiento nutricional (17) y que se deben tomar medidas para fomentar la adopción de las recomendaciones nutricional en la práctica clínica y promover la educación nutricional de los profesionales de la salud (18).

Por otra parte, los resultados obtenidos nos ofrecen una aproximación de cómo se lleva a cabo actualmente el abordaje nutricional en los diferentes centros españoles.

Los datos en relación con la codificación de la desnutrición indican que, en una mayoría de los casos (63 %), no se codificaba la desnutrición o se codificaba inadecuadamente (6 %). Estos datos son relevantes porque, como sabemos, las repercusiones de la desnutrición en el entorno hospitalario aún no están bien cuantificadas (16), y la codificación es a menudo el primer paso necesario para poder garantizar que un paciente desnutrido reciba la atención nutricional adecuada y oportuna. Existen estudios en nuestro entorno donde se han evidenciado mejoras clínicas como un incremento en el peso medio de los pacientes desnutridos tras la implementación de mejoras en la codificación de la desnutrición (16). Esta necesidad de una codificación adecuada se vuelve aún más urgente a medida que la digitalización de los hospitales y procesos sanitarios avanza (19).

Los resultados contribuyen a poner de manifiesto la presencia de obstáculos significativos para una adecuada atención nutricional, entre los cuales destacan una falta generalizada de recursos y de tiempo, así como la necesidad de una mayor colaboración entre diferentes disciplinas en los centros de salud. Estos resultados están alineados con los resultados de estudios internacionales de nutrición enteral en el paciente oncológico, en el que las principales barreras al implementar estrategias de nutrición médica, son las objeciones de los colegas o problemas relacionados con los recursos (20). Si bien son carencias que muchos profesionales de la salud constatamos a diario, es importante que queden documentadas en una publicación como esta, a fin de poder contribuir a activar medidas que mejoren la calidad y eficiencia de la atención sanitaria que prestamos. Es fundamental implementar estrategias que permitan superar estas barreras, como la asignación adecuada de recursos y la promoción de una mayor interdisciplinariedad en los equipos de atención. Al hacerlo, se fortalecerá la capacidad de los centros para proporcionar una atención nutricional integral y efectiva a los pacientes en el momento adecuado.

Si bien el protocolo propuesto ofrecía referencias y recomendaciones para una adecuada atención nutricional, sigue siendo necesario adaptar las medidas y procesos a la realidad de cada centro (recursos, equipo, pacientes, etc.). En este sentido, muchos participantes valoraron positivamente que en un documento de este tipo se haga una distinción entre aquellas intervenciones que son mínimas imprescindibles y aquellas que son deseables (p. ej., parámetros avanzados en nutrición clínica). La estandarización, en cualquier caso, mediante un protocolo de estas características, ayuda a que los resultados obtenidos puedan compararse con estándares de referencia que ayuden a establecer el límite más allá del cual los niveles de cumplimiento pueden considerarse adecuados (21).

Una de las fortalezas de este estudio es que ha permitido contrastar la validez de unas recomendaciones y orientaciones en un entorno sanitario real. Normalmente, lo habitual es que se emitan documentos de recomendaciones basados en la evidencia, pero sin recibir una retroalimentación o corrección proveniente de la práctica clínica real que permita validar si esas recomendaciones están siendo comunicadas de una manera útil y eficaz. El presente estudio pretende contribuir a llenar ese vacío al evaluar las recomendaciones en un contexto práctico, lo que ha brindado una oportunidad única para verificar su relevancia y aplicabilidad en el campo de la atención nutricional. Este enfoque contribuye a fortalecer la base de conocimientos y mejorar la eficacia con la que se presenta. Así, por ejemplo, ese circuito de retroalimentación ha permitido aportaciones muy valiosas por parte de los participantes. Se destaca, por ejemplo, cómo en respuesta al *feedback* obtenido durante las sesiones de validación con todos los participantes, se incorporó un capítulo adicional sobre ejercicio al protocolo.

La principal limitación de este estudio es que las valoraciones del impacto clínico se han producido siempre de manera estimada y a partir de la consideración de los participantes, y por tanto están sujetas a la subjetividad y sesgos de los mismos. Sin embargo, creemos que la publicación de un estudio de validación de este tipo puede contribuir a fomentar la publicación de otros estudios de diseño y objetivos parecidos, pero que encuentren maneras de objetivar los resultados clínicos, ofreciendo resultados aún más sólidos en la validación y que redunden en un beneficio directo para los pacientes y la atención sanitaria en general.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Nutrición artificial

Comparison of two isocaloric parenteral nutrition regimens with different protein content — A propensity-score matched comparative study

Comparación de dos regímenes isocalóricos de nutrición parenteral con diferente contenido de proteínas: un estudio comparativo emparejado por puntuación de propensión

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Abstract

Objective: this study aimed to assess the effects of two isocaloric parenteral nutrition (PN) regimens with different protein content and non-protein calorie to nitrogen ratio (NPCNR) on the evolution of nutritional parameters and outcomes in adult inpatients.

Methods: this was a retrospective quasi-experimental study performed in a 400-bed tertiary hospital. Adult inpatients were initially eligible if they had received ≥ 4 days of PN with NPCNR ≥ 100 or ≤ 90 in a period of three years. Patients were propensity-score matched to adjust for differences, resulting in two final cohorts: Cohort "Medium-P" included patients receiving PN with NCPCNR ≥ 100 and cohort "High-P", receiving PN with NCPCNR ≤ 90. The main variables were differences in plasma albumin, prealbumin, cholesterol, and lymphocyte count, days requiring PN, length of stay, and mortality at 90 days.

Results: 202 patients were finally recruited and divided into the two equal cohorts. Patients were mainly male (122; 60.4 %), surgical (149; 73.8 %), critically ill (100; 49.5 %), with high nutritional risk (141; 69.8 %) and with a neoplasm (145; 71.8 %). PN provided 25 kcal/kg/day, but protein intake was 0.25 g/kg/day higher in the "High-P" cohort. Baseline characteristics and biochemistry were not different between the two cohorts. The "High-P" cohort presented a smaller difference at the end of PN for lymphocytes, more days with hyperglycaemia, and more days requiring PN. The rest of variables did not differ.

Conclusions: high doses of protein (lower NPCNR) did not present advantages compared to medium doses of protein (higher NPCNR) when providing isocaloric PN in adult inpatients.

Keywords:

Parenteral nutrition. Energy intake. Dietary proteins. Critical illness. Propensity score. Mortality.

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Resumen

Objetivo: este estudio tuvo como objetivo evaluar los efectos de dos regímenes de nutrición parenteral (NP) isocalórica con diferente contenido de proteínas y relación calorías no proteicas-nitrógeno (NPCNR) sobre la evolución de los parámetros nutricionales y los resultados en pacientes adultos hospitalizados.

Métodos: se trata de un estudio cuasiexperimental retrospectivo realizado en un hospital terciario de 400 camas. Los pacientes adultos hospitalizados eran inicialmente elegibles si habían recibido ≥ 4 días de NP con NPCNR ≥ 100 o ≤ 90 en un período de 3 años. Los pacientes fueron emparejados por puntuación de propensión para ajustar las diferencias, lo que resultó en dos cohortes finales: la cohorte "P media" incluyó pacientes que recibieron NP con NCPCNR ≥ 100 y la cohorte "P alta", que recibió NP con NCPCNR ≤ 90. Las principales variables fueron las diferencias en la albúmina plasmática, la prealbúmina, el colesterol y el recuento de linfocitos, los días que requirieron NP, la duración de la estancia hospitalaria y la mortalidad a los 90 días.

Resultados: finalmente se reclutaron 202 pacientes y se dividieron en dos cohortes iguales. Los pacientes fueron principalmente varones (122; 60,4 %), quirúrgicos (149; 73,8 %), críticos (100; 49,5 %), con alto riesgo nutricional (141; 69,8 %) y con neoplasia (145; 71,8 %). La NP proporcionó 25 kcal/kg/día, pero la ingesta de proteínas fue 0,25 g/kg/día mayor en la cohorte "P alta". Las características iniciales y la bioquímica no fueron diferentes entre las dos cohortes. La cohorte "P alta" presentó una diferencia menor al final de la NP para linfocitos, más días con hiperglucemia y más días que requirieron NP. El resto de variables no difirieron.

Conclusiones: las dosis altas de proteína (menor NPCNR) no presentaron ventajas en comparación con las dosis medias de proteína (mayor NPCNR) al proporcionar NP isocalórica en pacientes adultos

Palabras clave:

Nutrición parenteral.
Ingesta energética.
Proteínas dietéticas.
Enfermedad crítica.
Puntuación de propensión.
Mortalidad.

BACKGROUND

In the last years, the provision of clinical nutrition has focused on higher protein intake rather than higher energy intake, especially in severely ill (1) and surgical patients (2), but there is much controversy regarding protein and caloric needs. Current ESPEN guidelines for critically-ill patients recommend 1.3 g protein/kg/day and 20-25 kcal/kg/day (3). For surgical patients, there are currently no specific intake recommendations (4), but in the previous 2017 guidelines, requirements were estimated at 1.5 g protein/kg/day and 25-30 kcal/kg/day (5). ASPEN guidelines differ from these European guidelines, being 1.2-2 g protein/kg/day and 12-25 kcal/kg/day for critically ill patients (6) and without recent guidelines for surgical patients. In other recommendations, a moderately hypocaloric nutrition, 20 kcal/kg/day, along with a high protein content of 2 g/kg/day, was also proposed for hospitalized patients (7). However, high protein doses and hypocaloric nutrition have not been demonstrated to improve outcomes in critically ill patients (8,9). Most nutritional studies did not examine the relationship between energy and protein intakes (10). An additional variable combining both values could be a logical approach to assess it. This is the classic non-protein calorie to nitrogen ratio (NPCNR) (11), which was early proposed to maximise protein synthesis during clinical nutrition (11). It is worth noting that this is a counterintuitive parameter, the higher the values, the less protein is contained in the diet.

When NPCNR was calculated, the values ranged from 71 to 100 non-protein kcal/g nitrogen for the ESPEN guidelines, from 37.5 to 105 non-protein kcal/g nitrogen for ASPEN guidelines, and about 37.5 non-protein kcal/g nitrogen for hospitalized patients. As can be seen, the proposed nutritional intakes cover a wide range of values. The higher values double and even triple the lower ones. However, to the best of our knowledge, there are no recent studies assessing the influence of NPCNR on nutritional parameters and outcomes in patients receiving parenteral nutrition (PN).

This study aimed to assess the effects of two regimens of isocaloric PN with different NPCNR on the evolution of nutritional parameters and outcomes in adult inpatients requiring this nutritional therapy and receiving intakes close to those recommended.

MATERIALS AND METHODS

STUDY DESIGN

This was a retrospective quasi-experimental study based on prospectively collected data performed in a 400-bed university tertiary hospital in an urban area. All adult (≥ 18 years old) patients were initially eligible if they had received ≥ 4 days of PN, as initial exclusive nutritional therapy, with NPCN ≥ 100 or ≤ 90 between January 2015 and December 2017 during their hospital admission. Patients were excluded if they received long-term (> 90 days) or home PN or lacked recorded data.

Patients were then divided into two initial cohorts depending on their NPCNR: one that included patients who had received PN with an NPCNR ≥ 100 non-protein kilocalories/g of nitrogen and another that included patients who had received PN with an NPCNR ≤ 90 non-protein kilocalories/g of nitrogen. Subsequently, both initial cohorts were propensity-score matched to adjust for differences, resulting in two final cohorts: Cohort "Medium-P" included patients on PN with an NPCNR ≥ 100 who received less protein, and cohort "High-P", patients on PN with an NCPCNR ≤ 90 who received more protein.

ETHICAL APPROVAL

Ethics approval was obtained from the Comitè Etic d'Investigació, CEIC-Parc de Salut Mar (approval number 2021-9677).

PARENTERAL NUTRITION THERAPY

Overall, PN was designed to provide about 25 kcal/kg ideal body weight (IBW)/day and about 1.2-1.5 g protein/kg IBW/day. The composition of each PN was individually modified when necessary according to clinical conditions, evolution, and laboratory parameters.

PN was prepared following usual hospital practices as an "all-in-one" admixture and was administered in a 24-h perfusion. All patients received the same products used to prepare PN: glucose solutions, standard amino acid solution (Aminoplasmal L, B. Braun, Rubí, Spain), intravenous lipid emulsions (IVLE) (SMOFLipid 20 %, Fresenius Kabi, Barcelona, Spain or Clinoleic 20 %; Baxter; Ribarroja del Túria, Spain), vitamins (Cernevit, Baxter, Ribarroja del Túria, Spain), trace-element solution (Addamel, Fresenius Kabi, Barcelona, Spain or Supliven, Fresenius Kabi, Barcelona, Spain), and electrolytes.

The intravenous lipid emulsions (IVLE) containing fish oil (SMOFLipid 20 %) was used mainly in severely-ill patients or with moderate hypertriglyceridemia (triglyceridemia > 250-400 mg/dL). IVLE based on an olive oil emulsion (Clinoleic 20 %) was used in the remaining patients.

Additional energy sources such as propofol and glucose infusions were also considered.

DATA COLLECTION

Data collected at PN initiation were patient demographics, main diagnosis, anthropometric data (weight, height, body mass index (BMI), IBW (12), type of admission (emergent or elective), type of patient (medical or surgical), critically ill condition, the severity of illness at the beginning of PN, comorbidity, and nutritional risk. The severity was classified as minor (predicted mortality < 10 %), moderate (predicted mortality from 10 % to < 25 %), and major (predicted mortality ≥ 25 %) according to Mortality Probability Model-III (13) at PN initiation. Comorbidity was classified as mild (predicted mortality < 10 %), moderate (predicted mortality from 10 % to < 25 %), and severe (predicted mortality ≥ 25 %) according to the Elixhauser score (14). The nutritional risk was classified as low (score ≤ 1), moderate (score = 2), and high (score ≥ 3) according to the Nutritional Risk Score (NRS) 2002 (15).

Serum levels of biochemical parameters at the beginning and end of PN were also recorded: creatinine and estimated glomerular filtration rate (eGFR) by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (16), albumin, prealbumin, lymphocyte count, C-reactive protein (CRP), triglycerides, bilirubin, and alkaline phosphatase (ALP). Other parameters recorded were the number of days with hyperglycaemia (days with at least one glycemia > 180 mg/dL).

Nutritional data recorded were the mean amount of protein, glucose, IVLE, and energy administered per kg of IBW during PN, mean NPCNR, use of IVLE with fish oil, indication for PN, length of PN, and days between admission and PN initiation.

VARIABLES

Nutritional parameters considered were plasma albumin, prealbumin, cholesterol, and lymphocyte count. The number of patients who improved in at least three of these parameters at the end of the PN was also considered.

Outcomes considered were days requiring PN, admission in intensive care unit (ICU) or post-anaesthesia care unit (PACU) for ≥ 3 days during PN, length of stay (LOS), and mortality 90 days after the end of PN.

All patients were followed for at least 90 days after the end of PN or until death if it occurred before 90 days. Mortality was extracted from hospital records, primary-care records and a central register of the autonomous health authority.

STATISTICAL ANALYSIS

Propensity-score matching was performed to reduce biases in patient selection from the initial cohorts. Propensity scores were obtained by logistic regression and using one-to-one nearest neighbour matching without replacement with assignation to a Medium-P or High-P as a dichotomous dependent variable and sex, age, severity, comorbidity, BMI, plasma albumin, ICU admission, need for renal replacement therapy, all at PN initiation, as independent variables. The caliper was set to a width of twice the standard deviation of the propensity score logit value (17).

Categorical variables were presented as percentages, and continuous variables as mean and 95 % confidence intervals (95 %CI). Analyses were conducted using a chi-squared or Fisher's exact test for categorical variables and the Student's t-test for continuous variables. Survival was estimated with the Kaplan-Meier method, and the survival rate was compared using the Breslow test.

In all analyses, p-values were two-tailed and $p < 0.05$ was considered statistically significant.

Statistical analyses were performed using IBM SPSS Statistics 25.0 (IBM Co., Armonk, NY, U.S.A.).

OTHER OUTCOMES INVESTIGATED IN SUB-STUDIES AND IN SUBGROUPS

Based on the primary results, two sub-studies have been carried out in order to analyze the impact of critical illness and the use of fish oil in the IVLE administered, respectively.

RESULTS

All adult patients receiving PN during the study period were initially screened (Fig. 1). A total of 202 patients were finally recruited and divided into two equal cohorts of 101 patients each. Generally, patients were mainly male (122, 60.4 %), surgical (149; 73.8 %), about half of them critically ill at the beginning of PN (100; 49.5 %), with high nutritional risk (141, 69.8 %) and with neoplasm as the main diagnosis (145; 71.8 %). Detailed baseline characteristics of the two cohorts were presented in table I. The only difference between the two cohorts was the prevalence of diabetes *mellitus*, being about 15 % higher in the Medium-P cohort.

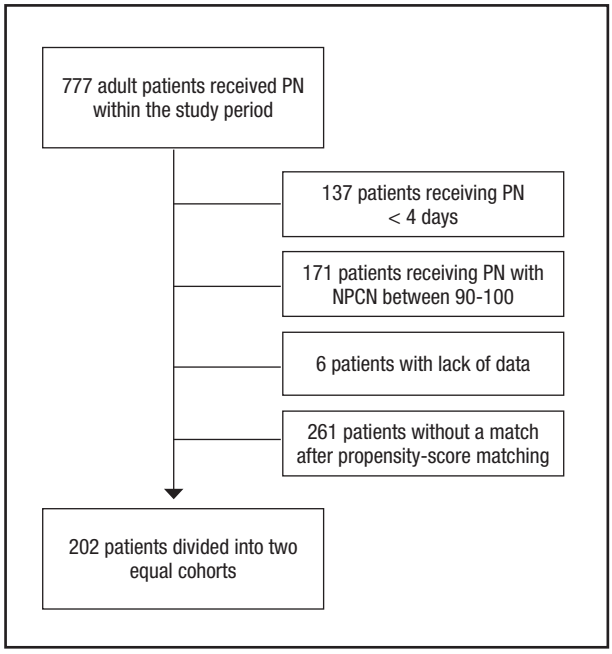

Figure 1.
Patient recruitment procedure for the study.

Baseline biochemistry at the start of PN was presented in table II. The parameters studied did not differ between the two cohorts. PN provided about 25 kcal/kg IBW/day in all patients, but there were differences in protein intake, being about 0.25 g/kg IBW/day higher in the High-P cohort. The dose of lipid emulsion provided was lower in the High-P cohort and NPCNR was lower in the High-P cohort. More patients received IVLE-containing fish oil in the High-P cohort.

Few differences were detected in the evolution of biochemical and nutritional parameters to the end of PN. Data were shown in table III. The difference in triglycerides and lymphocytes was lower in the High-P cohort. This cohort also presented more days with hyperglycaemia during PN.

Outcomes were not statistically different between the two cohorts, except for PN duration, which was longer in the High-P cohort (Table IV). Mortality reached a *p* value close to significance when analysed by a Kaplan-Meyer plot, as shown in figure 2.

The sub-study in critically ill patients included a total of 100 patients distributed as shown in table I. Baseline characteristics of both subgroups were similar without statistical differences except for the protein intake, sub-cohort Medium-P received 1.19 (1.13-1.25) vs. 1.45 (1.40-1.51) g/kg IBW/day received by sub-cohort High-P, $p < 0.001$, and, evidently, for NPCNR 108.5 (104.2-112.9) vs. 84.8 (83.2-86.5), respectively, $p < 0.001$.

Table I. Baseline characteristics

	Cohort Medium-P (*n* = 101)	Cohort High-P (*n* = 101)	*p*
Gender, male, *n* (%)	61 (60.4 %)	61 (60.4 %)	1.000
Age, years	71.2 (68.3-74.1)	71.1 (68.5-73.7)	0.969
Ideal body weight, kg	59.1 (58.1-60.0)	58.6 (57.7-59.5)	0.486
Body mass index, kg/m^2	25.8 (25.1-26.5)	26.1 (25.2-27.1)	0.562
Surgical patient, *n* (%)	77 (76.2 %)	72 (71.3 %)	0.523
Critically ill at the beginning of PN, *n* (%)	48 (47.5 %)	52 (51.5 %)	0.673
Renal replacement therapy during PN, *n* (%)	11 (10.9 %)	12 (11.9 %)	1.000
Emergent admission, *n* (%)	71 (70.3 %)	59 (58.4 %)	0.106
Surgical procedure 7 days prior to PN, *n* (%)	57 (56.4 %)	56 (55.4 %)	1.000
Days between admission and PN start	8.7 (6.3-11.1)	8.4 (6.6-10.2)	0.853
Diabetes *mellitus*, *n* (%)	45 (44.6 %)	30 (29.7 %)	0.041
Comorbidity			
Mild, *n* (%)	74 (73.3 %)	78 (77.2 %)	0.625
Moderate, *n* (%)	24 (23.8 %)	20 (19.8 %)	0.609
Severe, *n* (%)	3 (3.0 %)	3 (3.0 %)	1.000
Severity			
Minor, *n* (%)	46 (45.5 %)	53 (52.5 %)	0.398
Moderate, *n* (%)	34 (33.7 %)	29 (28.7 %)	0.544
Major, *n* (%)	21 (20.8 %)	19 (18.8 %)	0.865
Nutritional risk			
Low, *n* (%)	7 (6.9 %)	9 (8.9 %)	0.795
Moderate, *n* (%)	27 (26.7 %)	18 (17.8 %)	0.176
High *n* (%)	67 (66.3 %)	74 (73.3 %)	0.358

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Table I (cont.). Baseline characteristics

	Cohort Medium-P (*n* = 101)	Cohort High-P (*n* = 101)	*p*
Main diagnostics			
Lower digestive tract neoplasms, *n* (%)	26 (25.7 %)	25 (24.8 %)	1.000
Acute non-neoplastic lower gastrointestinal diseases, *n* (%)	18 (17.8 %)	21 (20.8 %)	0.722
Other neoplasms including haematological, *n* (%)	18 (17.8 %)	22 (21.8 %)	0.597
Upper digestive tract neoplasms, *n* (%)	6 (5.9 %)	9 (8.9 %)	0.593
Acute non-neoplastic upper gastrointestinal diseases, *n* (%)	6 (5.9 %)	5 (5.0 %)	1.000
Acute pancreatitis, *n* (%)	5 (5.0 %)	2 (2.0 %)	0.445
Other diseases, *n* (%)	28 (27.7 %)	23 (22.8 %)	0.517

Table II. Baseline biochemistry and nutrition related parameters

	Cohort Medium-P (*n* = 101)	Cohort High-P (*n* = 101)	*p*
Baseline biochemistry			
eGFR, mL/min/1.73 m^2	68.3 (61.4-75.1)	72.5 (66.5-78.5)	0.354
Creatinine, mg/dL	1.37 (1.13-1.61)	1.22 (1.00-1.45)	0.368
Bilirubin, mg/dL	0.70 (0.46-0.94)	1.26 (0.57-1.96)	0.131
ALP, U/L	93 (78-108)	118 (96-141)	0.071
Triglycerides, mg/dL	118.7 (103.9-133.6)	131.8 (106.2-157.4)	0.387
CRP, mg/dL	15.02 (12.61-17.43)	16.21 (13.58-18.83)	0.509
Albumin, g/dL	2.5 (2.4-2.7)	2.6 (2.5-2.7)	0.694
Prealbumin, mg/dL	10.2 (8.8-11.7)	10.9 (9.6-12.1)	0.489
Total cholesterol, mg/dL	94 (86-102)	98 (88-108)	0.476
Lymphocytes, x10^3 cell/mL	1.12 (1.00-1.25)	1.23 (0.94-1.51)	0.519
Parenteral nutrition			
kcal/kg IBW/day	25.0 (24.3-25.7)	24.8 (24.1-25.6)	0.754
Non-protein kcal/g N	108.6 (105.4-111.7)	84.3 (83.0-85.5)	< 0.001
Protein, g/kg IBW/day	1.19 (1.14-1.23)	1.43 (1.38-1.47)	< 0.001
Glucose, g/kg IBW/day	2.93 (2.85-3.01)	2.85 (2.75-2.95)	0.244
Lipids, g/kg IBW/day	0.85 (0.82-0.88)	0.77 (0.73-0.81)	0.001
Patient receiving IVLE containing fish oil	73 (72.3 %)	90 (89.1 %)	0.004
Fish oil received, g/kg IBW/day	0.07 (0.05-0.08)	0.08 (0.07-0.09)	0.065

ALP: alkaline phosphatase; eGFR: estimated glomerular filtration rate; CRP: C-reactive protein; IBW: ideal body weight.

Table III. Evolution of biochemical and nutritional parameters at the end of PN

	Cohort Medium-P (*n* = 101)	Cohort High-P (*n* = 101)	*p*
Biochemistry			
Difference in eGFR, mL/min/1.73 m^2	12.5 (7.9-17.0)	12.5 (7.1-17.9)	0.989
Difference in creatinine, mg/dL	-0.36 (-0.54-0.19)	-0.29 (-0.48-0.11)	0.591
Difference in bilirubin, mg/dL	0.04 (-0.12-0.21)	0.31 (-0.19-0.80)	0.318

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Table III (cont.). Evolution of biochemical and nutritional parameters at the end of PN

	Cohort Medium-P (*n* = 101)	Cohort High-P (*n* = 101)	*p*
Biochemistry			
Difference in ALP, U/L	73 (43-103)	122 (64-181)	0.143
Difference in triglycerides, mg/dL	63.2 (39.5-86.9)	24.1 (-2.5-50.8)	0.031
Difference in CRP, mg/dL	-8.55 (-11,01--6,10)	-7.26 (-10.50-4.01)	0.526
Difference in albumin, g/dL	0.4 (0.2-0.5)	0.2 (0.1-0.4)	0.145
Difference in prealbumin, mg/dL	7.1 (5.0-9.2)	5.7 (4.1-7.3)	0.273
Difference in total cholesterol, mg/dL	26 (18-34)	21 (8-35)	0.546
Difference in lymphocytes, x10^3 cell/mL	0.32 (0.17-0.47)	0.03 (-0.21-0.27)	0.047
Patients who improved in at least 3 nutritional parameters by the end of PN, *n* (%)	44 (43.6 %)	44 (43.6 %)	1.000
Days with hyperglycaemia during PN	4.0 (3.0-5.0)	6.3 (4.8-7.9)	0.011

Evolution, difference between values at the end of PN in relation the baseline values at PN initiation. ALP: alkaline phosphatase; eGFR: estimated glomerular filtration rate; CRP: C-reactive protein.

Table IV. Outcomes

	Cohort Medium-P (*n* = 101)	Cohort High-P (*n* = 101)	*p*
PN duration, days	11.0 (9.3-12.7)	15.7 (13.5-17.9)	0.001
Need for ICU or PACU admission, *n* (%)	3 (3.0 %)	8 (7.9 %)	0.214
Length of stay entire cohort, days	33.7 (28.2-39.2)	38.3 (33.3-43.3)	0.221
Length of stay, survivors, days	32.3 (26.6-38.1)	39.1 (32.4-45.8)	0.129
Mortality at 90 days after end of PN, *n* (%)	22 (21.8 %)	33 (32.7 %)	0.114

ICU: intensive care unit; PACU: post-anaesthesia care unit.

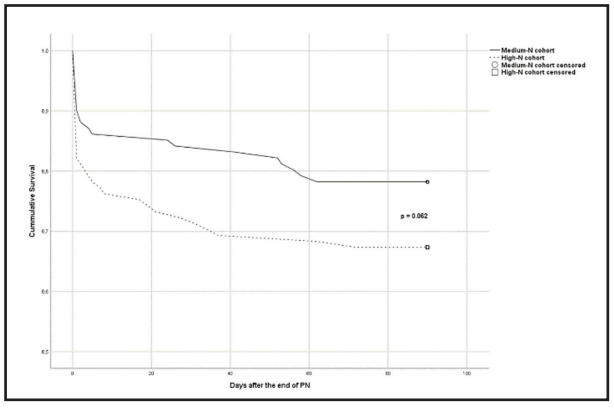

Figure 2.
Kaplan-Meyer plot for mortality of the two cohorts.

The results only differed in days requiring NPT, sub-cohort Medium-P 10.2 (8.4-12.0) vs. 16.9 (13.2-20.6) days in sub-cohort High-P, $p = 0.002$. Mortality rate was not different.

The sub-study in patients receiving fish oil in the IVLE included 163 patients distributed as shown in table II. Baseline characteristics of both subgroups were similar without statistical differences except for the protein intake 1.21 (1.17-1.25) vs. 1.42 (1.38-1.47) g/kg IBW/day, $p > 0.001$; non-protein kcal/g N 20.1 (19.5-20.7) vs. 19.1 (18.5-19.7) NP kcal/kg IBW/day, $p = 0.031$; and NPCNR 103.9 (102.2-105.7) vs. 84.4 (83.1-85.8), $p < 0.001$. Both sub-cohorts received the same fish oil intake, about 0.09 (0.08-0.10) g/kg IBW/day. Results differed only in difference in prealbumin 9.0 (6.1-12.0) vs. 6.0 (4.4-7.5) mg/dL, $p = 0.044$; and in days requiring NPT, 10,8 (8.1-13.6) vs. 18.0 (14.3-21.8), $p = 0.008$. In all cases, being the first values for the sub-cohort Medium-P and the second values for the sub-cohort High-P.

The results in these sub-studies are in consonance with the results obtained in the general study.

DISCUSSION

This study found no advantages in providing moderately high protein doses with lower NPCNR in adult patients receiving an isocaloric PN regimen versus medium protein doses with

higher NPCNR, even with several parameters worsening, e.g., days requiring PN, lymphocyte count evolution, or days with hyperglycaemic episodes. Mortality differences approached significance, being higher in the cohort receiving moderately high protein doses. The results of sub-analysis in critically-ill patients or in patients receiving fish oil in the IVLE did not differed significantly from the entire cohort. This study had several differences compared with most studies consulted. It included mixed patients, critically and non-critically ill, studied an isocaloric diet and the relationship between calories and protein delivered, provided protein doses close to those recommended, and it was performed with PN as the exclusive nutritional therapy. All these points, to our knowledge, have not been previously explored.

STUDIES FOCUSED ON PROTEIN PROVISION

Much controversy has been generated on protein provision in clinical nutrition (18) and most analyses have focused only on protein and critically ill patients. Three recent meta-analyses reviewed this topic. That of Fetterplace et al. included six trials with 511 critically ill patients receiving exclusively enteral nutrition (EN) (19). They found no differences in functional outcomes, mortality, and LOS between a high protein group (1.3 g protein/kg/day) and a low protein group (0.75 g/kg/day). The two groups also received different energy provisions (21 kcal/kg/day vs. 17 kcal/kg/day). NPCNR values were around 76 in the high and 116 in the low protein group. Lee et al. (20) included 19 randomized controlled trials (RCT) with a total of 1731 patients, only three of which were exclusively PN. They concluded that 0.48 g/kg/day higher protein delivery (1.31 ± 0.48 vs. 0.90 ± 0.30 g/kg/day) with similar energy provided (around 20 kcal/kg/d) had no significant effect on overall mortality, infectious complications, mechanical ventilation (MV) duration, and length of ICU and LOS. The only difference was muscle loss attenuated in the higher protein group. This difference was mostly attributed to enteral nutrition (EN) studies. When calculated, the NPCNR for the higher protein cohort was about 70, and about 114 for the lower protein cohort. A prior meta-analysis (21) also found no effects on mortality from different protein doses delivered (0.67 vs 1.02 g/kg/day).

In PN, protein doses were compared in the RCT of Ferri et al. (22) who found that providing 1.2 g of protein/kg/day vs 0.8 g/kg/day in a non-isocaloric regimen in critically ill patients improved handgrip strength, fatigue score, and muscle thickness, but with no differences in LOS, ventilator days, and mortality. The NPCNR in this study could be calculated as 98 for the high protein cohort and 148 for the low protein cohort. Additionally, a recent international study including data from 16,489 critically ill patients (23) found that an enteral or parenteral intake of 0.8-1.2 g protein/kg/day during the late acute phase was associated with lower hospital mortality versus a higher protein intake (> 1.2 g/kg day).

STUDIES FOCUSED ON THE PROVISION OF PROTEIN AND ENERGY SEPARATELY

Few additional studies have analysed both energy and protein delivered in clinical nutrition. These variables are usually studied separately. A metanalysis for protein delivered (24) included 14 RCTs with a total of 1690 patients. The protein doses compared were 1-2 g/kg/d vs. 0.5-0.9 g/kg/day. No changes were detected in daily living activities after discharge, handgrip strength, quality-of-life score, mortality, and LOS. A significant increase in muscle mass was noted with high protein delivery. Regarding energy, the same study meta-analysed 15 RCTs including 3892 critically ill patients. No outcome differences were detected between high (≥ 20 kcal/kg/day) versus low (< 20 kcal/kg/day) energy delivered. NPCNR could not be calculated from the data provided.

The prospective observational multinational EuroPN study (25) assessed nutritional practices in European ICUs, recruiting a total of 1172 critically ill patients. Protein and energy intakes were analysed separately, finding that 10-20 kcal/kg/day was associated with longer survival times and shorter invasive MV times and 0.8-1.2 g protein/kg/day was associated with earlier weaning from MV, but not survival.

STUDIES FOCUSED ON ENERGY PROVISION

Energy delivered and its effects were analysed in a recent review (26), where only six RCTs including 1143 critically ill patients addressing this question were found. It concluded that achieving energy balance with clinical nutrition may improve outcomes, but too many uncertainties remain to make this a strong statement.

STUDIES FOCUSED ON THE RELATIONSHIP BETWEEN PROTEIN AND ENERGY

This relationship has been much less explored. From early studies, a NPCNR of 100-150 was proposed to permit anabolism during the anabolic phases of convalescence (11). In a much more recent review, Kreymann et al. (10) found a non-linear relationship between total protein loss and the energy/nitrogen ratio provided. The study included 91 cohorts of patients and healthy subjects. They inferred a single equation for all cohorts. Hospitalized patients had a lower energy/nitrogen ratio than healthy subjects. Moderately ill patients had a mean calculated NPCNR of 166 and severely ill patients, 96. However, the variable energy/nitrogen ratio did not provide additional information to NPCNR as nitrogen is in the numerator, as calories provided by proteins, and also in the denominator as nitrogen itself. This ratio can be easily converted to NPCNR by just subtracting 25.

STUDIES FOCUSED ON VARIABLES AFFECTING MORTALITY

In two different studies, the effects of nutrition therapy on mortality, amongst other variables, were evaluated. In critically ill patients requiring artificial nutrition (PN, EN, or mixed), Servia et al. (27) analyzed 639 patients finding that providing more protein and fewer calories was protective for 28-day mortality. However, they provided only a mean of 16 kcal/kg/day and 0.8 g of protein/kg/day. In a similar study, Mateu and Retamero (28) analyzed 634 mixed patients exclusively receiving PN, finding that the provision of more energy was protective for 90-day mortality. In this study, patients received a mean of 25 kcal/kg IBW/day. Protein delivery did not affect mortality.

Taken together, our results seemed to agree with the conclusions from all these studies. The provision of higher protein doses has no notable advantages compared to most "conventional" doses.

This study had several limitations. First, its retrospective nature, although a propensity-score matching was performed to reduce biases. This is a single-center study. The results could not be extrapolated to special populations such as patients with obesity or low BMI, with high risk of refeeding syndrome, burns, under extracorporeal membrane oxygenation, or severe polytrauma. The extrapolation to EN could also be difficult since PN could negatively modify gut hormones, bile acids (29), microbiota (30), and metabolism (31). Variation parameters for muscle mass or performance were not been included in the study as they are not routine practices in clinical settings. Time of PN initiation (early versus late) was also not studied, although days from admission to PN initiation were similar between cohorts. Neither were the different energy and protein doses in the early phase of PN studied. This study had a quasi-experimental design and a further RCT would confirm the results.

In conclusion, in adult patients requiring PN, the provision of energy close to that recommended with moderately high protein doses and lower NPCNR did not present any advantages and even worsened some secondary parameters compared to providing the same energy with medium doses of protein with higher NPCNR. Differences in mortality approached significance, being higher in the cohort receiving moderately high doses of protein.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Pediatría

Sobrepeso y obesidad en niños de 5 a 11 años en México en el periodo 1999-2021: ¿por qué es necesario un abordaje interdisciplinario?

Overweight and obesity in children aged 5-11 years in Mexico — Why is necessary an interdisciplinary approach?

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Resumen

Introducción: el sobrepeso y la obesidad en niños son serios problemas de salud pública en México.

Objetivo: analizar el comportamiento de la prevalencia de sobrepeso y obesidad en niños de 5 a 11 años y presentar proyecciones sobre su prevalencia para el periodo 2022-2026.

Metodología: estudio ecológico y retrospectivo cuyas unidades de análisis fueron grupos de niños con sobrepeso y obesidad en el periodo 1999-2021, de acuerdo con información recabada en seis Encuestas Nacionales de Salud y Nutrición en México. Para las proyecciones se utilizó el método clásico de mínimos cuadrados, con el que se realizó un análisis de tendencia de ambas condiciones para el periodo 2022-2026.

Resultados: el sobrepeso en niñas y la obesidad en niños muestra una elevada prevalencia en el periodo 1999-2021, aun cuando el análisis de tendencia para el periodo 2022-2026 muestra un ligero decremento en el sobrepeso para el grupo de niños y un ligero incremento en el sobrepeso para las niñas, así como en la obesidad para ambos grupos.

Conclusión: Debido a la elevada prevalencia de sobrepeso y obesidad en niños de 5 a 11 años en México, se precisa de su abordaje interdisciplinario para identificar qué dimensiones (bioquímica, psicológica, interpersonal y social) participan en el problema, considerando tres ambientes que contribuyen al desarrollo psicológico y social de los niños, el ecológico-social, el familiar y el escolar.

Palabras clave:

Sobrepeso. Obesidad. Prevalencia. Interdisciplina. Ambientes.

Abstract

Introduction: overweight and obesity in children are serious public health problems in Mexico.

Objective: to analyze the behavior of the prevalence of overweight and obesity in children from 5 to 11 years of age and to present projections on the prevalence for the period 2022-2026.

Methodology: ecological and retrospective study whose units of analysis were groups of children of Mexico with overweight and obesity in the period 1999-2021, according to information collected from six National Health and Nutrition Surveys. For the projections the classical method of least squares was used, for a trend analysis of both conditions for the period 2022-2026.

Results: overweight in girls and obesity in boys shows a high prevalence in the period 1999-2021, even though the trend analysis for the period 2022-2026 shows a slight decrease in overweight for the group of boys and a slight increase in overweight for girls, as well in obesity for both groups.

Conclusions: due to the high prevalence of overweight and obesity in children from 5 to 11 years of age in Mexico, an interdisciplinary approach is required to identify which dimensions (biochemical, psychological, interpersonal and social) participate in the problem, considering three environments contributing for psychological and social development of children, the ecological-social, the family and the school.

Keywords:

Overweight. Obesity. Prevalence. Interdisciplinary. Environments.

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INTRODUCCIÓN

La primera Encuesta Nacional de Nutrición (ENN 1988) se condujo en México con los auspicios de la Secretaría de Salud en el gobierno federal (1), en tanto que la segunda se administró una década después (ENN 1999), con los auspicios del Instituto Nacional de Salud Pública — INSP (2). Investigadores de esta institución han asumido desde entonces la responsabilidad de diseñar y administrar las subsecuentes encuestas, destacando por su importancia las Encuestas Nacionales de Salud y Nutrición (ENSANUT) 2000 (3), 2006 (4), 2012 (5) y 2018-2019 (6), renombradas recientemente como Encuestas Nacionales de Salud Nutrición COVID-19 (ENSANUT COVID-19) de 2020 (7) y 2021 (8).

Si bien las ENN de 1988 y 1999 se centraron, entre otras cosas, en la cuantificación del estado nutricional y las prácticas alimentarias en niños, adolescentes y adultos de ambos sexos, a partir de la ENSANUT 2000 se adicionó información sobre: a) la utilización de los servicios de salud, atención ambulatoria y hospitalaria; b) la prevalencia de enfermedades crónicas como la hipertensión, la diabetes y distintos tumores malignos; y c) la prevalencia de condiciones como el sobrepeso y la obesidad. La importancia de estas últimas reside en que su justa prevalencia en los diferentes grupos etarios se ha venido incrementando de manera preocupante a partir de 1999, aunado al hecho de que se ha demostrado que ambas constituyen factores de riesgo que potencian diferentes enfermedades crónicas, como es el caso de los accidentes cerebrovasculares y los cardiovasculares (9-12).

Lo antes dicho es preocupante porque, si bien es cierto que la tasa de mortalidad infantil (en menores de 15 años, por cada 100 mil habitantes) en México muestra una clara tendencia a la baja desde la década de los cincuenta del pasado siglo y hasta el año 2020, merced a que se han logrado controlar y/o abatir enfermedades infecto-contagiosas y problemas relacionados con el nacimiento y el puerperio (13,14), también lo es que en los grupos etarios de los 5 a los 9 y de los 10 a los 14 años, los tumores malignos y las enfermedades del corazón han figurado dentro de los 10 primeros lugares como causa de mortalidad en los cinco años recientes; son, asimismo, enfermedades a las que posteriormente se suman la diabetes *mellitus* y las cerebrovasculares, por mencionar a dos de las más importantes (15-17).

Entender el rol clave que desempeñan el sobrepeso y la obesidad en niños de los 5 a los 11 años es necesario, sobre todo si se trata de impulsar estrategias y programas de acción tendientes a su prevención y control, cuyo objetivo es el de contribuir en el mediano y largo plazo a la reducción tanto de su prevalencia como de su impacto sobre el desarrollo de múltiples enfermedades crónicas no transmisibles. No podemos omitir el hecho, como inclusive lo reconoció recientemente el Fondo de las Naciones Unidas para la Infancia (UNICEF), que México ocupa uno de los primeros lugares en obesidad infantil y en adultos (18), por lo que una tarea urgente que se propuso en la agenda 2019-2024 fue la de consolidar un Sistema Nacional de Protección de los Niños y Adolescentes, dentro del cual la promoción de su desarrollo integral y la erradicación de la desnutrición son dos de sus principales campos de actuación.

Con base en estas consideraciones se planteó el presente trabajo, con el objetivo de analizar el comportamiento de la prevalencia del sobrepeso y la obesidad en niños de entre 5 y 14 años en México en el periodo 1999-2021, así como presentar proyecciones de ambos problemas de salud pública para el periodo 2022-2026.

MATERIALES Y MÉTODO

El presente estudio es de tipo ecológico y retrospectivo, cuyas unidades de análisis fueron grupos de niños de México con sobrepeso y obesidad, de acuerdo con datos recabados en 6 Encuestas Nacionales de Nutrición (ENN) y de Salud y Nutrición (ENSANUT) en el periodo 1999-2021. Las encuestas se basaron en un diseño probabilístico, estratificado y por conglomerados, con representación en áreas urbanas y rurales de todo el país (19). Los datos sobre la prevalencia del sobrepeso y obesidad se obtuvieron a partir de la revisión exhaustiva de la ENN 1999, de las ENSANUT 2006, 2012 y 2018-2019, así como de las ENSANUT COVID-19 de 2020 y 2021.

Para los fines del presente trabajo, se procedió a revisar de cada encuesta el apartado correspondiente a los capítulos intitulados "Nutrición", información que aparece desagregada por grupos etarios, de los cuales se seleccionó el de los niños de los 5 a los 11 años. Para cada grupo se consideraron datos de la muestra (N), el número en miles (que corresponde al factor de expansión) y el porcentaje de quienes fueron evaluados según los estándares internacionales de medición del índice de masa corporal (IMC). Como se observa en la tabla I, las muestras (N) variaron de manera importante entre encuestas para cada grupo por condición (sobrepeso y obesidad) y por sexo (hombres y mujeres), con una reducción considerable en su valor en los años 2020 y 2021, quizá atribuible a la irrupción de la COVID-19 y a las medidas de confinamiento instrumentadas para su control en nuestro país.

Para el tratamiento e interpretación de los datos se compararon los porcentajes entre niños y niñas, especificando el incremento o decremento en la prevalencia de sobrepeso y obesidad en el periodo de estudio. Por otro lado, para efectuar un análisis de proyección del comportamiento de ambas condiciones en el periodo 2022-2026 se utilizó el método clásico de mínimos cuadrados, haciendo la aclaración que en cada caso "x" representa el año; por ejemplo, el porcentaje del sobrepeso en niños para el año 2022, estimado según el modelo de ajuste lineal, es $S_H(2022) = -0{,}0383(2022) + 94{,}773 = 17{,}33$.

- Sobrepeso en niños: $S_H(x) = -0{,}0383x + 94{,}773$
- Sobrepeso en niñas: $S_M(x) = 0{,}167x - 316{,}58$
- Obesidad en niños: $O_H(x) = 0{,}6723x - 1336{,}2$
- Obesidad en niñas: $O_M(x) = 0{,}3242x - 640{,}37$

Tabla I. Porcentajes de sobrepeso y obesidad en niños, por sexo, en el periodo 1999-2021 en México

Encuesta y año	Sobrepeso hombres	Sobrepeso mujeres	Obesidad hombres	Obesidad mujeres
ENN 1999	N = 5 530	N = 5 679	N = 5 530	N = 5 679
	NM = 7 542,2	NM = 7 847,7	NM = 7 542,2	NM = 7 847,7
	18,6 %	*17,2 %*	*9,6 %*	*8,3 %*
ENSANUT 2006	N = 1 279	N = 1 392	N = 774	N = 684
	NM = 1 297,7	NM = 1 432,4	NM = 739,0	NM = 689,0
	16,5 %	*18,1 %*	*9,4 %*	*8,7 %*
ENSANUT 2012	N = 8 195	N = 8 156	N = 8 195	N = 8 156
	NM = 8 327,4	NM = 8 116,7	NM = 8 327,4	NM = 8 116,7
	19,5 %	*20,2 %*	*17,4 %*	*11,8 %*
ENSANUT 2018-2019	N = 3 093	N = 3 173	N = 3 093	N = 3 173
	NM = 5 479,1	NM = 5 512,5	NM = 5 479,1	NM = 5 512,5
	17,7 %	*18,4 %*	*20,1 %*	*15,0 %*
ENSANUT 2020	N = 1 003	N = 941	N = 1 003	N = 941
	NM = 7 567,2	NM = 7 506,2	NM = 7 567,2	NM = 7 506,2
	17,7 %	*21,6 %*	*21,5 %*	*15,6 %*
ENSANUT 2021	N = 1 286	N = 1 283	N = 1 286	N = 1 283
	NM = 8 124,4	NM = 7 547,9	NM = 8 124,4	NM = 7 547,9
	16,6 %	*21,2 %*	*23,8 %*	*13,1 %*

N corresponde a la muestra en número de participantes. NM corresponde al número en miles por el factor de expansión.

RESULTADOS

Tal y como se observan los datos sobre los porcentajes de la prevalencia de sobrepeso y obesidad (Tabla I) en el periodo 1999-2021, sobresalen los siguientes: primero, una reducción de dos puntos porcentuales en la prevalencia del sobrepeso en niños, así como un incremento sostenido, equivalente a 3,1 puntos porcentuales, en la prevalencia en niñas. Segundo, en sentido opuesto se observa un fuerte incremento de 14,2 puntos porcentuales en la prevalencia de obesidad en niños, así como un incremento moderado, de 4,8 puntos porcentuales, en el grupo de niñas. Llama la atención, sin embargo, que en los casos del sobrepeso para ambos grupos los porcentajes más altos se registraron en la ENSANUT 2012, para luego mostrar una reducción sostenida en el caso de los niños y un incremento más claro a partir del año 2000. Contrasta el comportamiento del sobrepeso con la obesidad, pues en ambos grupos los incrementos más importantes se empezaron a registrar con la ENSANUT 2018-2019, siendo sostenidos en el caso de los niños, con incrementos y decrementos fluctuantes en el caso de las niñas (Fig. 1).

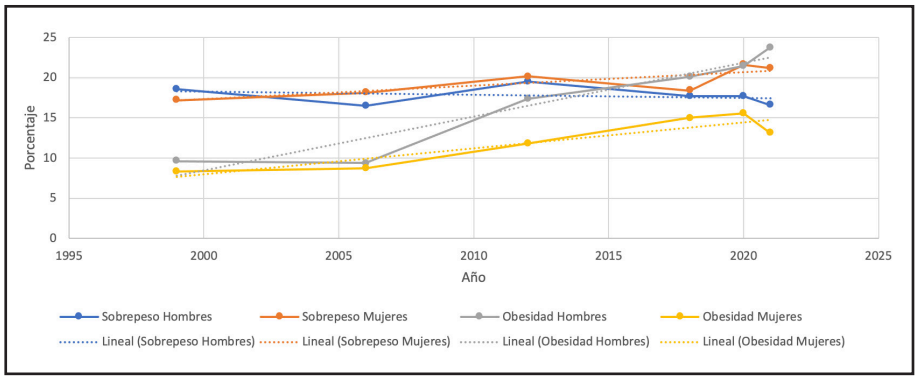

Figura 1.
Representación gráfica de la prevalencia de sobrepeso y obesidad en niños, por sexo, en el periodo 1999-2021 en México.

Tabla II. Proyecciones basadas en los ajustes lineales para el comportamiento de la prevalencia de sobrepeso y obesidad en niños, por sexo, en el periodo 2022-2026

Año	Sobrepeso hombres	Sobrepeso mujeres	Obesidad hombres	Obesidad mujeres
2022	*17,33*	*21,09*	*23,19*	*21,09*
2023	17,29	21,26	23,86	21,26
2024	17,25	21,42	24,53	21,42
2025	17,21	21,59	25,20	21,59
2026	*17,17*	*21,76*	*25,87*	*21,76*

Con relación a las proyecciones en el comportamiento de la prevalencia de sobrepeso y obesidad para el periodo 2022-2026, los datos se muestran en la tabla 2. Con excepción del sobrepeso en niños, donde se observa una ligera tendencia a la baja, el sobrepeso en niñas y la obesidad para ambos grupos muestra una ligera tendencia al alza, un poco más acentuada en los niños, lo que confirmaría el comportamiento del indicador observado desde la ENN 1999 y hasta la ENSANUT COVID-19 de 2021, de acuerdo con los datos que se presentaron en la tabla I.

DISCUSIÓN

La elevada prevalencia de sobrepeso y obesidad en niños de 5 a 11 años en México constituye un serio problema de salud pública que precisa de estrategias y programas de acción que contribuyan a su prevención y eventual control. Con todo y que en México se han venido impulsando diferentes propuestas para cumplir con ambos cometidos (20,21), el hecho inequívoco, a juzgar por los datos y las proyecciones antes presentados, es que los resultados obtenidos al día de hoy en las estrategias y programas específicos de acción han sido magros. En efecto, basta con tener presente que lo que los autores dieron en llamar una "actualización" de la ENSANUT de Medio Camino de 2016 (22), en un análisis del riesgo o del sobrepeso y de la obesidad como tal en tres grupos etarios (menores de 5 años, de los 5 a los 11 y de los 12 a los 19 años) estudiados entre 2012 y 2016, se encontró que la prevalencia de ambas condiciones en niños y adolescentes era todavía alta, afectando en casi un tercio (33 %) de los niños mayores de 5 años. Son datos que coinciden con sendos estudios de corte transversal conducidos en distintas entidades del país.

Por ejemplo, en uno que se condujo entre 2017 y 2018, el cual incluyó a una amplia muestra de 24.600 niños de 6 a 11 años del estado de Morelos (en la región centro), se reportó que en general el sobrepeso ascendió a 19,7 % y la obesidad a 16,0 %, si bien la prevalencia de ambas condiciones en niños de 6 años fue de 25,4 %, lo mismo que aumentó de manera considerable a 41,1 % en el grupo de niños de 11 años (23). Una situación similar se reportó en un análisis realizado en el estado de Jalisco (región pacífico sur) en niños de los 5 a los 11 años y de los 12 a los 19 años; en el caso de los primeros, el sobrepeso en hombres pasó en del 16,5 % en 2006 a 22,1 % en 2012, mientras que en las mujeres bajó del 29,3 % en 2006 a 25,6 % en 2012, aun cuando para este subgrupo con edades entre los 12 a los 19 años se observó un incremento porcentual del 22,5 % al 27,0 %, entre 2012 y 2018. El problema, con relación a la obesidad, es que ésta pasó del 11,4 % en 2006 al 15,1 % en 2018 para los hombres, y del 14,6 % al 14,1 %, en el mismo periodo, para el subgrupo de mujeres (24).

Cuando líneas atrás mencionamos que los resultados arrojados tanto por las estrategias generales como en los programas de acción específicos eran magros, por supuesto que lo hicimos en el pleno convencimiento de que una elevada prevalencia de sobrepeso y obesidad en niños y adolescentes precisa de propuestas innovadoras y con sentido multidisciplinario para su abordaje; nos referimos a una diversidad de acciones que van desde la prevención, hasta su manejo y su control efectivo en distintos ambientes, de acuerdo con lo que se propone en la figura 2.

Como se muestra en la figura 2, se parte del reconocimiento de las dimensiones implicadas en el problema del sobrepeso y la obesidad. Dichas dimensiones, que consideran niveles de complejidad creciente (lo que se representa gráficamente por el tamaño de los rectángulos), debieran intersectarse de cara a proponer líneas de investigación que permitan dilucidar cómo opera cada dimensión y cómo es potencialmente afectada, directa y/o indirectamente, por otras, de manera tal que los resultados aporten elementos para el diseño de las políticas públicas y los programas de acción-intervención particulares. Abordar un problema complejo como el del sobrepeso y la obesidad requiere de una propuesta como la que aquí se presenta, considerando cuatro ambientes (ecológico-social, familiar, escolar e institucional) y cuatro dimensiones (bioquímica, psicológica, interpersonal y social) para su estudio sistemático y para los fines de entender mejor cómo es que estas dimensiones interactúan.

Se plantea, por tanto, la propuesta en esos términos, partiendo del entendido de que dadas ciertas condiciones bioquímicas, los procesos de aprendizaje durante el desarrollo psicológico adquieren particular relevancia en los entornos ecológico-social (cómo se establecen las relaciones entre personas, en la forma de costumbres), familiar y escolar (ambos basados en sistemas

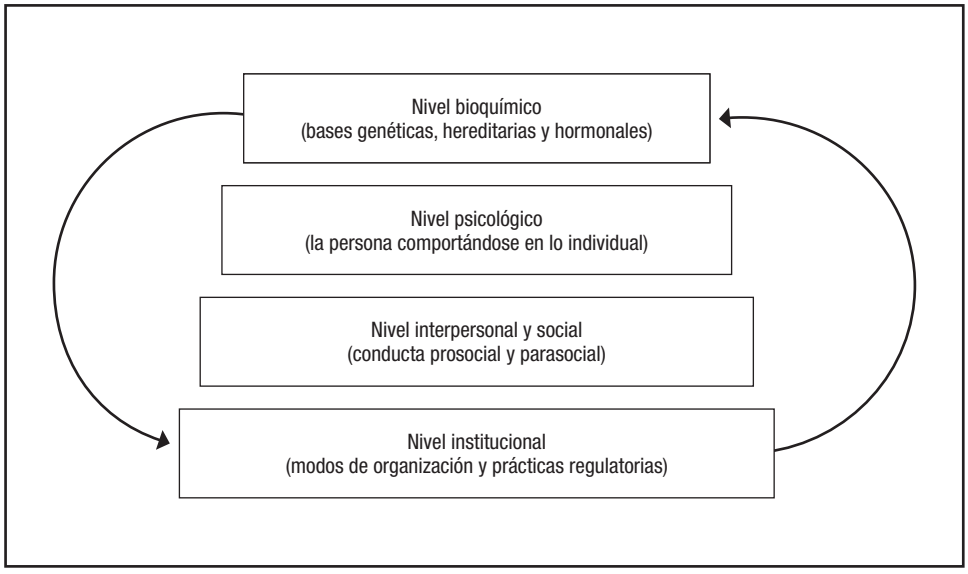

Figura 2.
Niveles de análisis de los factores participantes en el problema del sobrepeso y la obesidad.

de relaciones específicas a las que se requieren ajustar los niños y niñas según sean las demandas propias de cada entorno), en los que se esperaría se adquieran las que se dan en llamar competencias de vida, que consisten en conocimientos, habilidades y destrezas que les permitan responder de manera eficiente a los requerimientos que imponen las circunstancias que se enfrentan día a día en las esferas de la salud, la nutrición, la recreación y el tiempo y el ocio, entre otras (25,26).

Buscar colindancias entre las disciplinas implicadas en el ámbito de la salud debería ser una preocupación constante, si de lo que se trata es de procurar estudios de corte interdisciplinario que aporten información sustantiva sobre cómo, cada dimensión participante, interactúa con las demás y, como consecuencia, qué tipos de programas y estrategias se tienen que diseñar, instrumentar y evaluar para los fines de incidir positivamente sobre la conducta de los niños, de sus pares en el entorno ecológico-social, de sus padres y hermanos en el entorno familiar, y de los maestros y pares en el entorno escolar. Modificar la conducta de unos u otros no es tarea fácil; precisa la colaboración interdisciplinaria y la necesidad de entender que la conducta humana (psicológica, interpersonal y social) no ocurre en el vacío. Entrenar en competencias de y para la vida requiere de profesionales de la conducta y de la comunicación que hayan sido formados y entrenados en programas competenciales; hay que saber qué información se transmitirá y cómo; hay, también, que saber qué tipos de competencias hay que entrenar en los distintos entornos, según sean los requerimientos o demandas particulares (27-29). Algunos ejemplos que apuntan al reconocimiento de esta manera de abordar el problema del sobrepeso y la obesidad (y su relación con la diabetes) se han venido realizando en nuestro país, desde una perspectiva eminentemente conductual o de corte cognoscitivo-conductual (30-32), de las cuales en el ámbito de la salud pública se puede aprender mucho; de ello no tenemos la menor duda.

CONCLUSIÓN

Considerando que el sobrepeso y la obesidad en niños mexicanos constituye un serio problema de salud pública, para su manejo óptimo y su eventual control se precisa de un abordaje interdisciplinario del problema, del cual aquí se presenta una propuesta inicial que se está desarrollando con mayor amplitud en sendos trabajos relacionados con la diabetes y el conjunto de enfermedades crónicas no transmisibles. Es una propuesta que apunta a dar cumplimiento a la necesidad urgente de que ese abordaje interdisciplinario se lleve a cabo cabalmente, como recientemente lo plantearon profesionales de la salud desde diferentes campos de actuación (33), con 10 recomendaciones, 2 de las cuales incluyeron el entender que la obesidad debe considerarse como una enfermedad crónica, compleja y multifactorial, así como el que para su abordaje se requiere de un enfoque centrado en la persona.

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Trabajo Original

Pediatría

Effects of COVID-19 lockdown on children´s sleep quality, physical activity, screen time, and diet

Efectos del confinamiento por COVID-19 en la calidad del sueño, la actividad física, el tiempo de pantallas y la alimentación en los niños

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Abstract

Background: this study aimed to assess how the COVID-19 lockdown (March to June 2020) affected children's sleep quality, physical activity, screen time, and nutrition.

Material and methods: the survey consisted of 479 children from the SENDO project, a pediatric cohort in Spain, aged 4-5 years. The BEAR questionnaire was used to evaluate sleep quality. Hierarchical models with two-level clustering were used to account for intra-cluster correlation between siblings, and the difference regression method was used to study the association between changes in screen consumption and physical activity and changes in sleep quality.

Results: the results showed an increase in the consumption of homemade pastries and snacks. Sleep quality worsened significantly during confinement, with a mean score on the BEAR scale of 0.52 before, 1.43 during, and 1.07 after confinement. Although sleep quality improved significantly after the end of confinement, it remained worse than before. The average daily screen time increased from 1.13 hours before confinement to 2.65 hours during confinement. Physical activity decreased during confinement, with the mean number of hours per day decreasing from 1.27 to 0.79. Children who spent more time on screens during confinement had worse sleep quality, as indicated by their higher scores on the BEAR scale. We used the difference regression method to identify a statistically significant association between the increased screen time for leisure hours and the worsening of children's sleep quality during confinement.

Conclusion: we observed a significant relationship between confinement and reduced sleep quality. Although the end of the lockdown led to a slight improvement, the average BEAR scale score remained higher post-confinement, suggesting that the consequences of the lockdown may persist over time.

Keywords:

Sleep quality. Screen time. Physical activity. Food. Confinement. SENDO project.

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Resumen

Introducción: el objetivo del estudio es evaluar el impacto del confinamiento por COVID-19 (marzo-junio 2020) en la calidad de sueño, actividad física, tiempo de pantallas y alimentación de los niños.

Material y métodos: los participantes son 479 niños del proyecto SENDO. Los criterios de inclusión en el Proyecto fueron niños de 4-5 años, residentes en España, con un seguimiento periódico por medio de cuestionarios. Se utilizó el cuestionario BEAR para valorar la calidad del sueño. Se utilizaron modelos jerárquicos teniendo en cuenta la correlación entre hermanos, método de regresión de diferencias y la regresión lineal múltiple.

Resultados: se objetiva un aumento de consumo de bollería casera y *snacks*. La puntuación media de la escala BEAR fue de 0,52; 1,43; y 1,07 antes, durante y después del confinamiento, respectivamente, por lo que la calidad de sueño empeoró significativamente durante el confinamiento y mejoró tras el fin, pero persistiendo peor que previo al mismo. El tiempo medio de pantallas por ocio al día es de 1,13 horas previo al confinamiento, con aumento significativo durante el mismo a 2,65. La media de horas al día de actividad física previo al confinamiento es de 1,27 descendiendo a 0,79 durante el mismo. Los niños que se encuentran en el tercil superior de consumo de pantallas tienen significativamente ($p < 0,05$) mayor puntuación en la escala BEAR (peor calidad de sueño). Observamos una asociación estadísticamente significativa entre el aumento de exposición a pantallas y el empeoramiento de la calidad de sueño.

Conclusiones: el periodo de confinamiento se asoció a una disminución de la actividad física, un mayor tiempo de consumo con pantallas y una peor calidad del sueño. La peor calidad del sueño persistió al acabar ese periodo, confirmando las tendencias previas a la pandemia.

Palabras clave:

Calidad de sueño. Pantallas. Actividad física. Alimentación. Confinamiento. Proyecto SENDO.

INTRODUCTION

The COVID-19 pandemic profoundly altered people's lives worldwide, producing long-term consequences for public health, the economy, and social interactions (1).

The lockdown measures implemented due to COVID-19 significantly changed children's routines. They experienced changes in nutrition, physical activity, television/screen use, social activity, schoolwork schedules, and attendance (2). Moreover, several studies have associated the COVID-19 lockdown with higher levels of anxiety and depression in children (3).

The confinement condition can lead to forced inactivity and increased sedentary behavior, which are known to increase the risk for psycho-physical adverse conditions such as obesity, muscle atrophy, and cardiovascular vulnerability (4), as well as symptoms of anxiety and depression (5).

Another critical aspect of children's lifestyles that has changed during the COVID-19 pandemic is nutrition. Feeding patterns have also changed during the pandemic, especially during the lockdown (6,7). Social distancing measures may have contributed to worsening food patterns, such as increased consumption of unhealthy snacks and sugar-containing foods (8).

This confinement could have adverse effects on children's physical and mental health as they did not get to play with their friends, participate in sports groups, or have regular exercise in school physical education classes (9). This is especially concerning as previous studies have shown that most children and adolescents did not reach the recommended 60 minutes of moderate to vigorous physical activity per day set by the World Heart Association and the World Health Organization even before the pandemic (10). A further reduction of physical activity during the pandemic could have harmful effects as physical activity during youth is an essential determinant for future physical activity (11), is an antecedent for mental health (12), and helps prevent future health challenges such as obesity and cardiovascular diseases (13).

The social isolation caused by the COVID-19 pandemic greatly reduced physical activity levels in both male and female students (14,15). Physical activity is crucial in promoting positive mood (16), maintaining a healthy weight, and fostering self-esteem in children and adolescents (17). Vigorous physical activity has been shown to substantially reduce adolescents' stress, anxiety, and depression (18), providing protection against metabolic syndrome (19).

In addition to food and physical exercise, screen usage changed drastically due to the COVID-19 lockdown (20). Studies suggest a widespread, immediate, and potentially adverse impact on children's screen time due to the COVID-19 lockdown (21-23). The two crucial negative impacts of screen time on the physical health of children and adolescents are sleep problems (24,25) and an increased risk of myopia (26). Excessive screen exposure has been linked to physical health symptoms like eye strain, sleep disturbances, carpal tunnel syndrome, and neck pain. Psychologically, excess screen time is linked to impaired concentration, obsession, and even diagnosable mental illnesses such as anxiety, depression, and attention-deficit hyperactivity disorder (27-31).

Furthermore, the dramatic lifestyle changes and stressors associated with this pandemic pose a threat to mental health and have the potential to exacerbate risk factors for suicide (32).

A previous report focused on assessing the changes in sleep quality in Spanish children during the lockdown (33). This study aimed to determine changes in nutrition patterns, physical activity, screen time, and sleep quality in Spanish children during the lockdown between March and June 2020.

MATERIALS AND METHODS

STUDY AIM, DESIGN, AND SETTING

The SENDO project (*S*eguimiento de *E*scolares *N*avarros para un *D*esarrollo *Ó*ptimo) evaluates the impact of diet and lifestyle on the health of children and adolescents. It is a prospective, dynamic, multipurpose pediatric cohort that started in 2015. The study collects self-reported data through online questionnaires completed by parents and children. The inclusion criteria for the SENDO project were children aged 4-5 years living in Spain. The participants were aged 4-11 years at the time of questionnaire

completion in May 2021, depending on when they joined the study. More details on this cohort study design have been published elsewhere (34).

PARTICIPANTS

Until September 2020, 832 participants were recruited. Of these, 485 completed an additional questionnaire to report various lifestyle changes during the lockdown period. However, 14 participants with incomplete information —meaning they needed more information on four or more questions regarding sleeping quality, physical activity, or screen time— were excluded from the analysis. The remaining participants who had missed only a few items were contacted to complete the information. After excluding the ineligible participants, the final sample comprised 471 participants.

VARIABLES

The SENDO project collects data on various sociodemographic, lifestyle, and diet-related factors through baseline and annual questionnaires (Q0, Q1, Q2, etc.). In May 2021, a new questionnaire focused on emotional, nutritional, physical activity, screen time, sleeping habits, and other lifestyle factors was introduced.

To assess sleeping habits in children, we used the BEAR questionnaire, a widely used screening tool to identify sleep problems. The BEAR questionnaire has already been validated in Spain and includes questions related to bedtime reluctance, difficulty falling asleep, awakening during the night, and regularity and duration of sleep (35,36). Points were assigned to each answer based on their frequency of occurrence. A score was calculated for each participant by adding the points for the four questions.

Each participant completed the BEAR questionnaire before the lockdown (using the last annual questionnaire they finished) and twice in May 2021 (covering periods during and after the lockdown). We calculated the total score for each participant before, during, and after the lockdown. The final scores ranged from 0 to 12, with higher scores indicating more sleeping problems.

Dietary information was collected through a previously validated semi-quantitative FFQ, which included 149 food items (37). For each food item, a portion size was specified. Parents reported how often their child consumed each food item over the previous year by choosing one of nine consumption frequencies ranging from "never or rarely" to "6 or more times/d". For dietary changes during lockdown, we present a descriptive analysis of the consumption of food groups.

Diet quality was assessed with the KIDMED index, an *a priori*-defined dietary index to evaluate adherence to the MedDiet pattern in children and adolescents (38). The KIDMED index consists of 16 items: 12 scored 0 or 1; 4 scored −1 or 0. Thus, the score in the KIDMED index ranges from −4 to 12 points. Participants' adherence to the MedDiet was classified as poor (≤ 3 points), medium (4-7 points), or high (≥ 8 points) according to their score.

The study gathered data about physical activity through a questionnaire that included 17 different types of activities and 10 response options, ranging from never to over 10 hours per week. The Spanish version of the questionnaire was validated in the "Seguimiento Universidad de Navarra" study (39). The variable was defined as moderate or intense activity, measured hours per day. Physical activities can be classified according to their intensity. Moderate-intensity activities require 3 to 6 METs, whereas vigorous-intensity activities require more than 6 METs. The target heart rate for moderate exercise intensity is 50 %-70 % of your maximum heart rate, while for vigorous exercise intensity, it is 70 %-85 % (40). The guidelines defined moderate activity as brisk walking and other moderate-intensity activities, such as dancing. In contrast, vigorous intensity was defined as activities that require high-intensity exercise, such as jogging, running, fast cycling, fast swimming, and team sports (41).

In addition, screen time was assessed by averaging the daily hours spent watching TV, using a computer, playing video games, or similar.

STATISTICAL ANALYSIS

Participant characteristics were analyzed by sex. Mean values and standard deviations (SD) were used for quantitative variables, while percentages were used for categorical ones. The Student t-test was applied for quantitative variables and χ^2 tests for qualitative ones to compare between-group differences.

BEAR questionnaire scores were compared across the three periods (before, during, and after lockdown) using repeated measures for each participant. Similarly, physical activity and screen time were also compared, but only with two periods (before and during lockdown) due to the lack of information after lockdown.

Hierarchical models with two levels of clustering were used to account for the intra-cluster correlation between siblings. The interaction between time and *a priori* selected variables, such as sex, number of siblings, number of cohabitants, parental education, having a pet, having a mobile phone, physical activity (METS), BMI (kg/m^2), moderate or intense activity (hours/week), and adherence to the Mediterranean diet, was assessed by introducing the interaction term into the model and calculating a likelihood ratio test.

The regression of differences method was employed to study the association between changes in screen consumption and sleep quality and between changes in physical activity and sleep quality. Participants were divided into tertiles, and multiple linear regression was used to study the relationship between tertiles of screen consumption, physical activity, and sleep quality.

The analysis was conducted using the software STATA 15.0 (Stata Corporation, College Station, TX, USA). All *p*-values were two-tailed, and statistical significance was determined at the conventional cut-off point of $p < 0.05$.

ETHICAL CONSIDERATIONS

The SENDO project adheres to the ethical principles for medical research in human beings, as stated in the Declaration of Helsinki. This study has been approved by the Ethics Committee for Clinical Research of Navarra (Pyto 2016/122). Informed consent was obtained from the parents of all participants during recruitment.

RESULTS

This study involved 471 participants, 223 females and 248 males, with an average age of 7.5 years (SD: 1.8). Table I provides relevant information regarding the participants' baseline characteristics. There were no significant differences between the groups regarding the sociodemographic and lifestyle characteristics of the children or the family characteristics.

During the lockdown, the consumption of most food groups remained relatively unchanged, except for snacks and homemade bakery items. 32 % of participants reported consuming more or much more snacks and 62 % of them reported consuming more or much more homemade baked goods during lockdown (Table II).

Children spent an average of 1.27 hours (SD 0.99) on moderate to vigorous physical activity daily before lockdown. However, this value decreased significantly during confinement to 0.79 (SD 0.96) ($p < 0.001$).

Before lockdown, the average daily screen time spent on leisure activities was 1.13 hours (SD: 0.81). During confinement, it increased significantly to 2.65 hours (SD: 1.69) ($p < 0.001$).

The BEAR scale was used to examine children's sleep quality before, during, and after confinement. The results showed that the mean score of the BEAR scale was 0.52 (SD 1.25), 1.43 (SD 1.99), and 1.07 (SD: 1.55) for before, during, and after confinement, respectively. All comparisons indicated a statistically significant worsening of sleep quality during confinement with little recovery afterward.

The study also investigated the relationship between sleep quality during confinement, measured by the BEAR score, and physical activity levels in tertiles. However, no statistically significant differences were found (Table III).

Regarding screen time, children who spent the most leisure time on screens during confinement (upper tertile) had significantly higher BEAR scale scores (indicating worse sleep quality) compared to children who spent less time on screens (lower tertile) ($p = 0.005$), as shown in table III.

Also, a significant association was found between increased screen time for leisure and worsened sleep quality in confined children ($p = 0.04$).

Table I. SENDO project participants' baseline characteristics. Numbers are expressed as % or mean (± SD)

	Boys	Girls	*p* value
n	**248**	**223**	
Age (years)	7.45 ± 1.73	7.49 ± 1.95	0.832
Number of siblings	1.27 ± 1.23	1.40 ± 0.95	0.191
Numbers of cohabitants	3.48 ± 1.35	3.79 ± 3.00	0.137
BMI (kg/m^2)	16.08 ± 1.78	16.18 ± 2.06	0.544
z-BMI	-0.03 ± 0.92	0.02 ± 1.07	0.545
Physical activity (METS-hours/week)	48.90 ± 33.90	41.13 ± 28.11	0.007
Moderate or intense activity (hours/week)	9.64 ± 7.99	8.10 ± 5.45	0.016
Screen time (hours/day)	1.14 ± 0.80	1.12 ± 0.82	0.835
Punctuation KIDMED[1]	5.85 ± 1.94	6.10 ± 1.82	0.154
BEAR score[2]	0.52 ± 1.26	0,52 ± 1.19	0.997
Maternal age (years)	42.43 ± 4.06	42.19 ± 4.37	0.436
Paternal age (years)	43.42 ± 5.37	43.26 ± 5.31	0.958
Smoking (% exposed to secondhand smoke)	5.62	8.00	0.544
Pet ownership (% of children with pets)	23.39	26.46	0.441
Mobile phone (% of children with a mobile phone)	0.4	1.79	0.142
Parents´ education (% of children with mother or father with at least a college education)[3]	87.50	85.20	0.467

[1]Adherence to the Mediterranean diet. [2]Sleep quality. [3]University alone or university plus master or doctorate.

Table II. Changes in food consumption frequency before and during lockdown (% of participants)

	Much more	More	Similar	Fewer	Much fewer
Fruits	4 %	17 %	67 %	10 %	2 %
Vegetables	3 %	16 %	72 %	8 %	1 %
Fast food	1 %	11 %	58 %	21 %	10 %
Homemade baked goods	5 %	57 %	31 %	4 %	3 %
Industrial bakery	1 %	7 %	53 %	24 %	15 %
Sugary drinks	1 %	6 %	67 %	11 %	15 %
Snacks	3 %	29 %	52 %	9 %	7 %

Table III. Mean (SD) BEAR questionnaire scores during lockdown by terciles of physical activity and screen time

Physical activity	Low (1st tertile)	Medium (2nd tertile)	High (3rd tertile)
BEAR questionnaire score (mean)	1.48 (2.07)	1.48 (2.01)[a]	1.26 (1.81)[b]
Screen time	**Low (1st tertile)**	**Medium (2nd tertile)**	**High (3rd tertile)**
BEAR questionnaire score (mean)	1.35 (1.87)	1.39 (1.83)[c]	2.02 (2.37)[d]

[a]Medium vs. low: p = *0.971; [b]High vs. low:* p = *0.433; [c]Medium vs. low:* p = *0.785; [d]High vs. low:* p = *0.005.*

DISCUSSION

In this study of 471 children from the SENDO project, we discovered that the lockdown enforced in Spain between March and June 2020 due to the COVID-19 pandemic resulted in a significant increase in screen time and a marked decrease in moderate and vigorous physical activity. Additionally, we observed a considerable decline in sleep quality that persisted after the end of the lockdown. Our analysis revealed that the greater the increase in screen time, the more pronounced the worsening of sleep quality, highlighting a potential link between screen time and poor sleep quality. However, we did not find any significant association between the decrease in physical activity and the deterioration of sleep quality. This may be because the quality of physical exercise could have been better, as outdoor activities were restricted during the lockdown.

Our findings underscore the importance of evaluating sleep quality in children and implementing preventive measures anticipating potential future lockdowns. It also highlights the risks of increased screen time and decreased physical activity. However, we do not have to wait for another lockdown to consider this issue. Rapid technological advancements have increased screen time in recent years, resulting in sedentary lifestyles and greater inactivity in children (42,43). The lockdown has only exacerbated this growing trend, making it necessary to establish public health policies to combat this critical issue, particularly during the childhood obesity pandemic.

Prior studies also reported measurable reductions in physical activity among children and adolescents during the COVID-19 lockdown (16,17), which may have contributed to poor sleep quality. Therefore, it is essential to enhance access to resources that promote physical activity to ensure good health and social functioning among children and adolescents during pandemic recovery efforts (44). The use of electronic devices has increased during the lockdown (24,45), and its excessive use has been linked to poor sleep quality (22,23). Hence, targeted health promotion interventions are required to encourage the judicious use of screens for education and entertainment and emphasize the adverse health effects of excess screen time.

Most food groups remained the same regarding dietary habits, except for increased beverages and homemade bakery consumption. Some studies have also reported higher caloric intake during confinement, increased alcohol consumption, and a generally unhealthier diet with more snacking (46,47). This data highlights the need for dietary guidelines to prevent or mitigate potential weight gain during the period of self-isolation, especially for individuals with overweight and obesity.

Our results should be considered alongside specific study limitations. First, the cross-sectional design precludes the determination of causality. The use of self-reported information is susceptible to misclassification bias. However, since the SENDO project information is updated annually through online questionnaires, families are used to this data collection method, which may reduce the risk of systematic error in the reported data.

Another limitation is the demographic composition of SENDO. SENDO project participants are mostly white children from families with higher educational attainment. While this may limit the generalizability of our results, it increases the validity of the responses and reduces potential confounding by socioeconomic status. Due to the observational design, we cannot rule out the possibility of residual confounding by uncontrolled variables. When interpreting the results or generalizing findings to broader populations, these limitations should be considered.

In conclusion, many studies have associated the COVID-19 pandemic and ensuing lockdown with psychological and lifestyle changes. Our study contributes to this body of knowledge by revealing reduced physical activity and worsened sleep quality associated with increased screen time. Helping children to maintain healthy habits despite challenging circumstances and providing early psychological support is important for preventing negative (and potentially persistent) psycho-physical symptoms resulting from lockdown.

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Trabajo Original

Pediatría

Determination of inflammation by TNF-alpha and IL-10 levels in obese children and adolescents

Determinación de la inflamación mediante los niveles de TNF-alfa e IL-10 en niños y adolescentes con obesidad

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Abstract

Background: childhood obesity is one of the major health problem worldwide. Obesity is associated with low-level chronic inflammation resulting from inflammatory cytokine release in white adipose tissue. We aim to specify inflammatory markers tumor necrosis factor-alpha (TNF-alpha) and interleukin-10 (IL-10) in children and adolescents to determine their relationship with obesity.

Materials and methods: forty obese patients and 46 controls were included in the study from the pediatric clinic. Blood samples from the study group were centrifuged, and the sera were stored at -80 °C after separation. Serum levels of TNF-alpha and IL-10 were determined using Human ELISA kits for TNF-alpha and IL-10.

Results: serum samples from 86 children, including 45 girls (52.3 %) in the study group, were analyzed for TNF-alpha and IL-10 levels. TNF-alpha levels in the obese and control groups were 1.04 ± 0.79 and 0.60 ± 0.72 pg/ml, respectively ($p = 0.010$). Also, IL-10 levels in the obese and control groups were 0.76 ± 0.62 and 1.54 ± 0.71 pg/ml, respectively ($p < 0.001$). Gender was not identified as a factor for serum TNF-alpha and IL-10 levels ($p = 0.281$ and $p = 0.477$, respectively). Moreover, white blood cell (WBC) and serum C-reactive protein (CRP) levels were higher in the obese patient group than in the control group ($p = 0.002$ and $p = 0.010$, respectively).

Conclusion: TNF-alpha levels were higher than control in obese patients and it was important in terms of showing that obesity triggers inflammation in the body. IL-10 levels, which inhibit inflammation, were lower in obese patients than controls.

Keywords:

Obesity. Child. TNF-alpha. Interleukin-10. Inflammation. Cytokine.

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Resumen

Antecedentes: la obesidad infantil es uno de los principales problemas de salud a nivel mundial. La obesidad está asociada con una inflamación crónica de bajo nivel, resultado de la liberación de citocinas inflamatorias en el tejido adiposo blanco. Nuestro objetivo es especificar los marcadores inflamatorios factor de necrosis tumoral-alfa (TNF-alfa) e interleucina-10 (IL-10) en niños y adolescentes para determinar su relación con la obesidad.

Materiales y métodos: cuarenta pacientes obesos y 46 controles fueron incluidos en el estudio desde la clínica pediátrica. Las muestras de sangre del grupo de estudio se centrifugaron, y los sueros se almacenaron a -80 °C después de la separación. Los niveles séricos de TNF-alfa e IL-10 se determinaron utilizando *kits* ELISA humanos para TNF-alfa e IL-10.

Resultados: se analizaron muestras de suero de 86 niños, incluidas 45 niñas (52,3 %) en el grupo de estudio, para los niveles de TNF-alfa e IL-10. Los niveles de TNF-alfa en los grupos de obesos y control fueron de 1,04 ± 0,79 y 0,60 ± 0,72 pg/ml, respectivamente ($p = 0,010$). Además, los niveles de IL-10 en los grupos de obesos y control fueron de 0,76 ± 0,62 y 1,54 ± 0,71 pg/ml, respectivamente ($p < 0,001$). El género no se identificó como un factor para los niveles séricos de TNF-alfa e IL-10 ($p = 0,281$ y $p = 0,477$, respectivamente). Además, los niveles de glóbulos blancos (WBC) y proteína C-reactiva (PCR) en suero fueron más altos en el grupo de pacientes obesos que en el grupo de control ($p = 0,002$ y $p = 0,010$, respectivamente).

Conclusión: los niveles de TNF-alfa fueron más altos ~~que en el grupo de control en pacientes obesos~~, lo que es importante para mostrar que la obesidad desencadena ~~la~~ inflamación en el ~~cuerpo.~~ Los niveles de IL-10, que inhiben la inflamación, fueron más bajos en pacientes obesos que en controles.

Palabras clave:

Obesidad. Niño. TNF-alfa. Interleucina-10. Inflamación. Citocina.

INTRODUCTION

Obesity has become a significant global health problem due to its strong association with diseases such as insulin resistance, type 2 diabetes, atherosclerosis, and ischemic heart disease, which reduce life expectancy and have significant economic and societal impacts. Obesity is associated with inflammatory cytokine (IC) release in white adipose tissue (AT), triggering local inflammation, as well as with low-grade chronic inflammation in adipocytes (1,2). Furthermore, the pathogenesis of obesity-related metabolic disorders is known to play a crucial role in chronic inflammation. Low-grade inflammation has been clearly linked to metabolic disorders such as type 2 diabetes *mellitus* (DM). Increased AT mass leads to elevated pro-inflammatory markers such as C-reactive protein (CRP) and its inducer, interleukin (IL)-6. Interestingly, elevations in CRP and IL-6 were found to predict the development of type 2 DM (3,4). AT also causes the production of inflammatory mediators known as adipokines; when released into the circulation, these transport the local inflammation caused by obesity to other parts of the body, including cardiovascular tissues (5).

In obesity and diabetes, tumor necrosis factor-alpha (TNF-α) has been identified as a pro-inflammatory product of AT which links obesity and inflammation (6). A previous study revealed that mice with inactivated insulin receptors are protected from obesity-related insulin resistance and inflammation (1). This shows that in obesity, the insulin receptor plays a key role in macrophage activation and inflammation (2). Accordingly, obese children also had increased circulating levels of pro-inflammatory cytokines (e.g., leptin, TNF-α, IL-6, and CRP) compared to normal-weight children and adolescents aged 2-18 years (3). Specifically, TNF-α activates macrophages in host defense mechanisms, inducing the production of pro-inflammatory nitric oxide and reactive oxygen species (7).

IL-10 has been recognized as an anti-inflammatory and immunosuppressive factor. As an anti-IC, IL-10 suppresses the ability of human monocytes and macrophages to produce pro-ICs, including IL-6 (8). IL-10 is produced by activated immune cells (T and B lymphocytes, mast cells, granulocytes, macrophages) which acts as a potent negative feedback regulator and controls inflammation (7). Within lean AT, anti-ICs secreted by resident AT macrophages (ATMs) help maintain insulin sensitivity by counteracting inflammatory responses. Indeed, treatment of adipocytes with IL-10 alleviated the insulin resistance (IR) induced by TNF-α (9).

To the best of our knowledge, no study has evaluated the role of IL-10 in childhood obesity. This study aimed to identify pro-inflammatory and anti-inflammatory markers present in children and adolescents to determine their relationship with obesity.

MATERIALS AND METHODS

Children and adolescents (40 obese, 46 controls) were recruited from the pediatric outpatient department of the hospital of Tokat Gaziosmanpasa University School of Medicine, Tokat, Turkey. The study was conducted in accordance with the Helsinki Declaration of the World Medical Association and local ethical standards; this was approved by the Ethics Committee of Gaziosmanpasa University School of Medicine (approval no. 17-KAEK-014). Since can cause inflammation, subjects with symptoms or signs of infection, fever, or/and endocrinologic disorders such as thyroiditis or rheumatologic diseases such as arthritis or rash were excluded. The study group was classified according to the age and sex-adjusted body mass index (BMI) reference curve for Turkish children. Participants with BMI above the 95th percentile were classified as obese, while those between the 5th and 84th percentiles as normal (10) (Table I).

Serum samples were obtained from fasting blood samples and stored at -80 °C. TNF-α and IL-10 were measured using an ELISA kit (Elabscience Biotechnology Co., Wuhan, China). Laboratory tests, including complete blood count, glucose, blood urea nitrogen, serum creatinine (sCre), CRP, aspartate transaminase (AST), and alanine transaminase (ALT), were obtained from fasting blood samples of all participants. Insulin levels and thyroid function tests were measured in obese participants only. Serum fasting glucose, insulin, AST, ALT, and sCre were measured using reagent kits from Roche Diagnostics adapted to the COBAS

Table I. Distribution of the study group and inflammatory markers according to gender

		Group		*p*	Inflammatory marker		*p*
		Obese *n* (%)	Control *n* (%)		TNF-α (pg/mL)	IL-10 (pg/mL)	
Sex	Female	24 (60.0)	21 (45.7)	0.184	0.89 ± 0.84	1.12 ± 0.83	0.281
	Male	16 (40.0)	25 (54.3)		0.71 ± 0.72	1.24 ± 0.70	0.477
Total		40 (100)	46 (100)		0.81 ± 0.78	1.17 ± 0.77	

E601 system (Roche Diagnostics, Mannheim, Germany). Statistical analysis of the data was performed using SPSS 19 (IBM SPSS Statistics 19, SPSS Inc., Somers, NY, USA), and $p < 0.05$ was considered significant.

RESULTS

Serum TNF-α and IL-10 levels were measured in 40 obese children and 46 controls, who had mean ages of 12.7 ± 3.2 and 13.1 ± 2.3 years, respectively ($p = 0.698$). Among the participants, 53.5 % were female. When grouped according to sex, there were no significant differences in TNF-α and IL-10 levels. TNF-α levels were 0.892 ± 0.835 and 0.708 ± 0.716 pg/mL in females and males, respectively ($p = 0.281$). IL-10 levels were 1.117 ± 0.832 and 1.238 ± 0.705 pg/mL in females and males, respectively ($p = 0.477$) (Table II).

Serum TNF-α levels were significantly higher in obese individuals versus controls (1.04 ± 0.79 vs. 0.60 ± 0.72 pg/mL, $p = 0.010$) IL-10, known for its anti-inflammatory properties, was lower in obese individuals versus controls (0.76 ± 0.62 vs. 1.54 ± 0.71 pg/mL, $p < 0.001$).

Table II. Distribution of TNF-α and IL-10 serum levels and laboratory parameters by groups

Variables	Group			*p*
	Total (*n* = 86)	Control (*n* = 46)	Obese (*n* = 40)	
	Mean ± SD	Mean ± SD	Mean ± SD	
IL-10 (pg/ml)	1.174 ± 0.773	1.545 ± 0.709	0.756 ± 0.618	*< 0.001*
TNF-α (pg/ml)	0.806 ± 0.782	0.602 ± 0.722	1.035 ± 0.792	*0.010*
Age (year)	12.8 ± 3.0	12.7 ± 3.2	13.1 ± 2.3	0.698
Height (cm)	152.86 ± 14.05	151.41 ± 17.24	154.52 ± 9.04	0,672*
Body weight (kg)	54.25 ± 18.24	47.36 ± 15.28	62.18 ± 18.32	0,138*
BMI (kg/m^2)	22.77 ± 5.95	20.33 ± 5.72	25.58 ± 4.92	0,342*
TSH	2.437 ± 1.299	2.311 ± 1.18	2.711 ± 1.53	0.298
fT4	1.206 ± 0.583	1.126 ± 0.486	1.408 ± 0.756	0.092
Glucose	90.49 ± 9.82	91.69 ± 10.87	87.72 ± 6.27	0.166
Insulin	24 ± 18.01	20.29 ± 15.83	24.87 ± 18.82	0.659
Hemoglobin	12.99 ± 1.34	12.99 ± 1.42	12.98 ± 1.12	0.973
White blood cells	7.25 ± 2.1	6.79 ± 1.82	8.6 ± 2.35	0.002
Platelets	298.87 ± 66.33	284.93 ± 58.66	341.6 ± 72.13	0.003
CRP	6.69 ± 24.52	2.69 ± 5.04	30.01 ± 62.24	0.010
AST	21.55 ± 6.39	21.43 ± 6.58	21.88 ± 6.01	0.809
ALT	16.79 ± 10.48	15.48 ± 7.51	20.32 ± 15.77	0.104

*TNF-α: tumor necrosis factor-alpha; IL-10: interleukin-10; BMI: body mass index; TSH: thyroid stimulating hormone; fT4: serum free thyroxin; CRP: C-reactive protein; AST: aspartate transaminase; ALT: alanine transaminase. The values presented are means ± standard deviation (SD). The p-values represent the statistical significance for the comparison between the control and obese groups. *Correction for age and gender was performed by covariance analysis.*

DISCUSSION

Chronic inflammation, as seen in obesity, can occur due to excess production of inflammatory mediators when clearance mechanisms are insufficient or even under normal physiological changes. Circulating inflammatory mediators and activated monocytes have been associated with metabolic and cardiovascular complications in obesity (5). In this study, we aimed to assess inflammation by determining the levels of inflammatory markers TNF-α and IL-10. Notably, TNF-α, which triggers inflammation by promoting macrophage activation and oxygen radical production (8), was higher in obese children and adolescents. IL-10, which has anti-IC actions and suppresses monocyte/macrophage stimulation and cytokine production, especially IL-6 (7), was lower in obese children and adolescents.

Previous studies have associated subclinical chronic inflammation with obesity (11). AT acts not only as a fat depot but also as an active endocrine organ which releases numerous peptides and cytokines into the circulation (12). In obesity, there is a shift in the balance among these molecules; enlarged adipocytes produce more pro-ICs (e.g., TNF-α and IL-6) and fewer anti-inflammatory peptides (e.g., adiponectin) (13). The infiltration of macrophages into AT was also found to increase with the severity of obesity, which is associated with decreased insulin sensitivity (14). The dysregulation of these adipokines reportedly plays a significant role in obesity-related metabolic and cardiovascular disorders (15). Severely obese adolescents with increased BMI and CRP have an increased risk of impaired fasting glucose and hypertension (16). Similarly, regardless of the association with metabolic complications, we also found elevated TNF-α levels in obese children and adolescents. Kopp et al. reported that TNF-α levels decreased alongside weight loss in obese patients with metabolic syndrome (17). Thus, weight loss can possibly achieve inflammation control in obesity-related metabolic disorders.

Protective factors, such as adiponectin, reportedly decrease in cases of increased BMI and elevated CRP (18). IL-10 is considered a good and protective cytokine in human metabolism (19). In atherosclerosis, IL-10 is speculated to be produced in the atherosclerotic plaques by stimulated monocytes/macrophages and lymphocytes, and it may provide more protection from excessive pro-inflammatory responses (20). Jung et al. showed that an increase in IL-10 was dependent on the degree of weight loss and improvement in metabolic disorders (21). In our study, IL-10 levels were low in obese adolescents and children. Since we did not observe the effects of weight loss, we cannot make interpretations about the changes in this cytokine. In contrast, it has been suggested that IL-10 release is related to TNF-α and could help limit the pro-inflammatory effect of TNF-α (21).

These studies have shown that low-grade systemic inflammation is present in childhood obesity. Consequently, it has been proposed that metabolic dysfunction associated with excessive AT mass could result from an imbalance in the expression of pro- and anti-inflammatory adipokines, thereby contributing to the development of obesity-related complications (5,22).

A limitation of this study is the lack of investigation into the relationship between metabolic disorders and inflammatory markers. Nevertheless, as a case-control study, the clear differences in these markers highlight the importance of our findings.

In conclusion, this study examined two inflammatory markers in childhood obesity, TNF-α and IL-10. Inflammatory mediators differed between obese and lean control groups. These ICs may be part of the inflammatory connection between obesity and its metabolic and cardiovascular complications. Thus, these can be potential targets for the early detection and prevention of these complications.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

A randomized double-blind controlled clinical trial demonstrating efficacy of different probiotic strains on serum lipids and glycemic biomarker

Un ensayo clínico controlado aleatorizado, doble ciego, que demuestra la eficacia de diferentes cepas de probióticos en los lípidos séricos y el biomarcador glucémico

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Abstract

Background: the aim of this randomized placebo-controlled study was to investigate the effect of probiotics mainly on plasma lipids, homocysteine levels, glycemic biomarkers and inflammatory marker in people with hyperlipidemia, compared to a placebo.

Methods: a randomized, double-blind placebo-controlled study was completed with a total of 51 men and women who have diagnosed with hyperlipidemia. The three study interventions were: 1) probiotic group I asked to take once a day 1 x 10^6 colony forming unit (CFU) *Lactobacillus rhamnosus GG* microorganism ($n = 18$) capsule; 2) probiotic group II asked to take once a day of a combined *Lactobacillus acidophilus* 1 x 10^9 CFU and *Bifidobacterium animalis* subsp.*lactis* 1 x 10^9 CFU probiotic capsule ($n = 17$); and 3) placebo group: emptied capsule ($n = 16$), plasma lipids, homocysteine, and glycemic biomarkers were were performed at baseline and week 8. Also, hs-CRP levels was assessed as inflammatory parameter.

Results: compared to baseline there was a significant decrease in triglyceride and total cholesterol levels of the both intervention groups compared to the placebo group. Regarding the glycemic biomarkers. both intervention groups significantly alter the HOMA-IR values compared to the placebo group ($p < 0.05$). When homocysteine values were evaluated. a statistically significant decrease was observed only in the group using the combined strain ($p < 0.05$). Results demonstrated that regular and strain-specific use of probiotics have effective and favorable consequences on plasma lipids and glycemic biomarkers.

Conclusion: probiotics containing *Lactobacillus* or *Bifidobacterium* could be effective in hypercholesterolemic patients, reducing serum lipids as well as homocysteine and glycaemia.

Keywords:

Serum lipids.
Cardiovascular disease.
Cholesterol. Hyperlipidemia.
Probiotic.

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Ethical approval and consent to participate: before participating in the study, all participants were asked to sign a written consent form declaring that they wanted to voluntarily participate in the study, after being informed about the study.

Authors' contributions: Okburan G, Bas M and Ogmen S equally contributed to the conception and design of the research; Okburan G contributed to the design of the research; Okburan G contributed to the acquisition and analysis of the data; Okburan G and Ogmen S contributed to the interpretation of the data; Okburan G drafted the manuscript. Okburan G wrote the article with the supervision of Bas M. All authors critically revised the the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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Resumen

Objetivo: el objetivo de este estudio aleatorizado controlado con placebo fue investigar el efecto de los probióticos principalmente en los lípidos plasmáticos, los niveles de homocisteína, los biomarcadores glucémicos y el marcador inflamatorio en personas con hiperlipidemia, en comparación con un placebo.

Métodos: se realizó un estudio doble ciego aleatoria controlado con placebo con un total de 51 hombres y mujeres a quienes se les había diagnosticado hiperlipidemia. Las tres intervenciones del estudio fueron: 1) un grupo probiótico que tomaban una vez al día 1 x 10^6 cápsulas de unidades formadoras de colonias (UFC) del microorganismo *Lactobacillus rhamnosus GG* ($n = 18$); 2) un grupo probiótico II que tomaba una vez al día una cápsula probiótica combinada de *Lactobacillus acidophilus* 1 x 10^9 CFU y *Bifidobacterium animalis* subsp.*lactis* 1 x 10^9 CFU ($n = 17$); y 3) un grupo placebo: cápsula vacía ($n = 16$), lípidos plasmáticos. Se realizaron biomarcadores de homocisteína y glucémico al inicio y también en la semana 8. Los niveles de hs-CRP se evaluaron como parámetro inflamatorio.

Resultados: en comparación con el valor inicial, hubo una disminución significativa en los niveles de triglicéridos y colesterol total de ambos grupos de intervención en comparación con los del grupo de placebo. En cuanto a los biomarcadores glucémicos, ambos grupos de intervención alteran significativamente los valores de HOMA-IR en comparación con el grupo placebo ($p < 0,05$). Cuando se evaluaron los valores de homocisteína, se observó una disminución estadísticamente significativa solo en el grupo que utilizó la cepa combinada ($p < 0,05$). Los resultados demostraron que el uso regular y específico de cepas de probióticos tiene consecuencias favorables sobre los lípidos plasmáticos y los biomarcadores glucémicos.

Conclusión: los probióticos que contienen *Lactobacillus* o *Bifidobacterium* podrían ser eficaces en pacientes hipercolesterolémicos, reduciendo los lípidos séricos, así como la homocisteína y la glucemia.

Palabras clave:

Lípidos en sangre.
Enfermedad cardiovascular.
Colesterol. Hiperlipidemia.
Probiótico.

INTRODUCTION

Hypercholesterolemia is a major risk factor for coronary artery disease and myocardial infarction (1,2). Regarding the lifestyle intervetion, dietary management, behavioural modifications and exercise are advised in order to lower the plasma cholesterol level (3,4). However, in some cases, these precautions may not be efficient and sufficient to manage the plasma lipids. Despite changes in lifestyle, in individuals with resistant high serum lipids they may require additional pharmacological treatment yet those treatment may associated with some adverse effects (5). In this context, for the treatment of high cholesterol level, alternative therapies or options are being investigated. One of the non-pharmacological approach for improving plasma lipids is the use of safe and strain-specific probiotics (6). Probiotics are defined as "live microorganisms which when administered in adequate amount confer health benefits to the host" (FAO/WHO, 2002) (7). Since the scientific evidence which is pointing the beneficial effects of probiotic on human health is becoming increasingly popular, there is an intense focus on probiotic bacteria and their health benefits (8). Some of the *in vitro* and animal studies indicated that strain-specific probiotics have cholesterol lowering effect via different mechanisms. Possible mechanisms than can be attributed to the hypocholesterolemic effect of probiotics include; deconjugation of bile acids by bile salt hydrolase (9), production of short chainf fatty acids (SCFAs) (10), and assimilation of cholesterol and fatty acids into the cell surface of the organism which makes cholesterol less available for absorption into the circulation (11). Regarding the hypocholesterolemic effect of probiotics, in contrast to *in vitro* and animal studies (12,13), human studies are not as consistent as *in vitro* studies (14-16). The reason for inconsistent results may attributed to the different type of strains that have been used, doses of probiotics, delivery matrix, study duration, and study population. The present study is one of the scarce studies that evaluated the effects of different probiotic strains on serum lipids, glycemic parameters, CRP and homocysteine. This double blind, placebo controlled study was conducted to demonstrate the efficacy of different probiotic strain use on serum lipids and glycemic biomarkers in healthy adults with hypercholesterolemia. In addition, it was evaluated whether different strains of probiotics differed on serum lipids and which could cause a more effective reduction.

EXPERIMENTAL METHODS

STUDY POPULATION AND DESIGN

A double-blind, placebo-controlled, parallel design randomised clinical trial was conducted in the Internal Medicine Department of Famagusta State Hospital to determine the effects of different probiotics on hyperlipidemia for 8 weeks. Patients diagnosed with hypercholesterolemia (defined as a total cholesterol ≥ 200 mg/dL) during a routine check-up in the Internal Medicine Department of Famagusta State Hospital, were eligible to participate in the study. Participants age ranges were between 30-64 (18 males, 33 females). Participants who met the the inclusion criteria were randomly assigned to either *Lactobacillus* group or *Lactobacillus* plus *Bifidobacterium* group or placebo group. Five visits were conducted; one prior to the study to screen and collect baseline data and to record food consumption and physical activity, anthropometry, and body composition measurements; the remaining interviews were every 15 days during the study period. Nutrient composition was determined with BEBIS Nutrition Data Base Software, physical activity was assessed on the same day with dietary records by average daily physical activity and expressed as physical activity level (PAL). Blood samples of the participants were collected twice: at the begining and at the end of the study. Participants in all groups were instructed to maintain their normal daily activity and nutritional habits during the study period. In order to remind the participants about the study capsules, daily messages was sent via Whatsapp. Prior to the contribution, each volunteer provided written informed consent.

ELIGIBILITY CRITERIA

All individuals who met the inclusion and exclusion criteria were invited to participate in the study. The inclusion criteria were: had a repeated total cholesterol level ≥ 200 mg/dL prior to allocate to the study group and to declined conventional lipid lowering medical treatment. Those with any chronic conditions other than hypercholesterolaemia, inherited lipid metabolic disorders, chronic gastrointestinal disease, immunodeficiency, malignancy, mental disabilities. patients currently using any lipid lowering drugs, or an alternative treatment to lower plasma cholesterol (such as probiotics) and individuals who have used antibitoics in the previous three months prior to study and pregnant or lactating women were excluded from the study. Participants were informed that they could withdraw the study at any time.

ETHICAL CONSIDERATIONS

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the ethics committee (with a document number; 2018/60-26). Written informed consent were voluntarily obtained from all participants and the study was registered on public clinical trials registry of U.S. National Library of Medicine Clinical Trial and had a registration ID number as NCT04701775.

INTERVENTION

Participants were randomly divided into three groups. Randomisation was carried out by utilising a random number table; for this, an independent coordinator, not otherwise involved in the study, created the allocation sequence assigning participants as following simple randomization procedures (computerized random numbers): 1) probiotic group who take once a day 1 x 10^6 colony forming unit (CFU) *Lactobacillus rhamnosus GG* microorganism (n = 18) capsule; 2) probiotic group II who take once a day a combination of *Lactobacillus acidophilus* 1 x 10^9 CFU and *Bifidobacterium animalis* subsp.*lactis* 1 x 10^9 CFU probiotic capsule (n = 17); and 3) placebo group: emptied capsule (n = 16) (Fig. 1). A total of 63 patients diagnosed with hypercholesterolemia, 51 were recruited into the study. The investigator and patients were blinded to the intervention. The code to the randomization sequence was only revealed to the main investigator after the final data analysis. An identification number

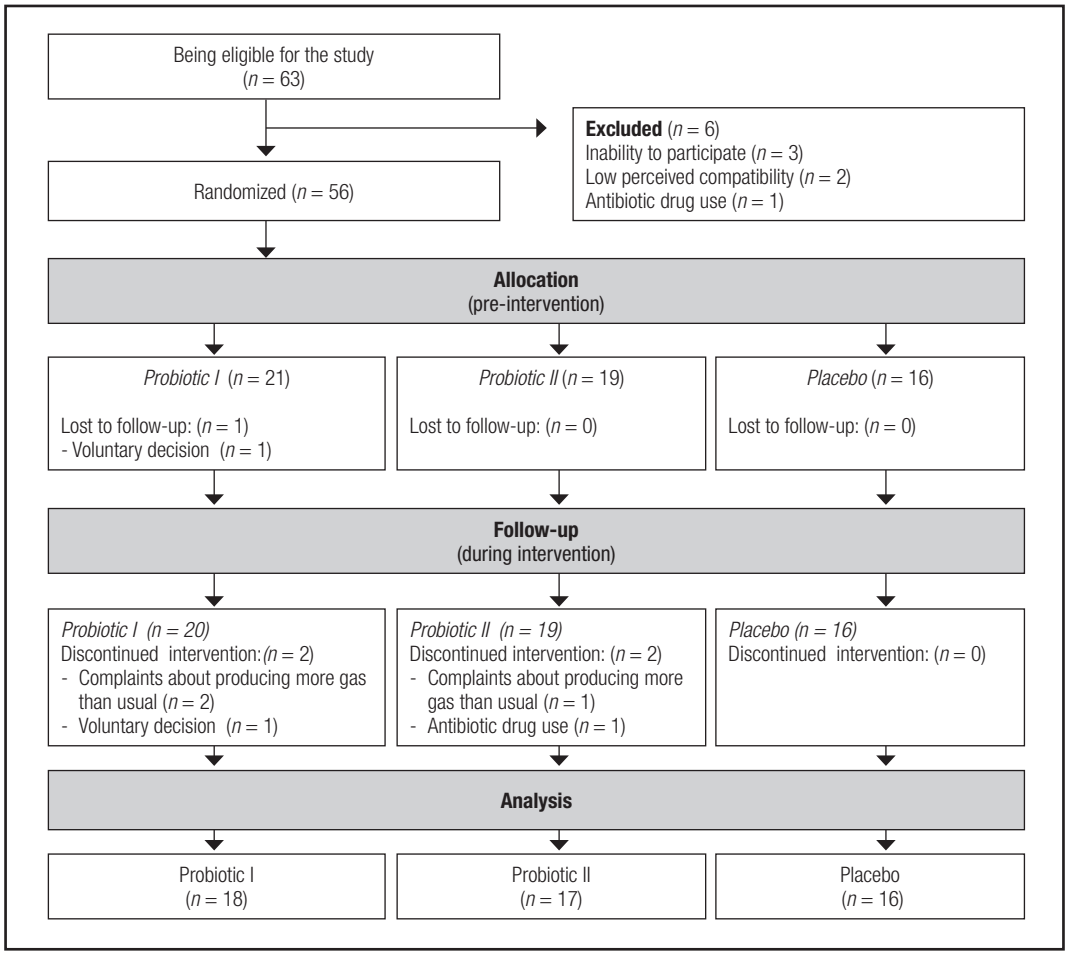

Figure 1.
Study flow chart and enrolment.

was generated for each participant and it was recorded by the pharmacist in three capsules of the product to which the person was allocated.

Pharmacist assigned participants to their group (the order of assignment was hidden by the independent coordinator until the moment of assignment), oral and written dietary instruction about their regimen was informed by independent coordinator. However, the pharmacist did not participate in data collection and/or analysis. Both participants and other research team members (with the exception of the mentioned pharmacist) were blinded to treatment allocation until the database was unlocked and data analysis was complete. Except for the interventionist (pharmacist), investigators and staff were kept blind to supplementation assignment of the participants. All investigators and participants were kept masked to outcome measurements and trial results. Study products was packed in duly labeled package and also in order to preserve the study blinding, identical placebo capsules were used to matched for size, shape, colour, texture and packaging which and consecutively numbered for each participants according to the randomisation schedule. One capsule a day were asked to be consumed by the recruited participants for the study duration and in order to ensure that all participants consume the product under the same conditions, it is requested to be consumed immediately after breakfast. Each participant was assigned an order number and received the capsules in the corresponding prepacked packages. All participants were informed of the risks and benefits of the study and were aware that they could leave the study at any time and for any reason.

ANTHROPOMETRY AND BODY COMPOSITION

All anthropometric measurements were reported by a dietitian according to the method described by Lohman et al. (17). Body weight and percentage of body fat were measured using a body composition analyser (Bioimpedance analyzer; Tanita-BC 420 s). Participants' body composition was measured while they were wearing light clothing and were barefoot with bare hands, with a precision of 0.5 kg. Height was measured using a stadiometre with 0.5 cm precision in a normal standing position without shoes. BMI was calculated as BW/height (m^2) and waist circumference (WC) were measured at the midpoint between the iliac crest and the lower rib while standing. All participants were instructed to fast for 12 h (an overnight fast). the participants were also instructed to avoid exercising, consuming alcohol for 48 h before the test. Moreover, 30 min before, the test participants were asked to fully urinate and not to consume water. A senior investigator performed these measurements before and after the intervention.

PLASMA MEASUREMENTS

At the beginning and end of the study, blood samples were drawn into vacutainer tubes containing Na2EDTA (1 g/L final concentration) from the antecubital vein after an overnight fast. The tubes were then immediately stored into ice water. Within 2 h, plasma was seperated by centrifugation at 2500 g for 20 min at 4 °C**.** All the measurments were made immediately after the plasma collection. Glucose concentrations were measured by glucose oxidase and peroxidase reactions. Total cholesterol was measured by cholesterol esterase, cholesterol oxidase and peroxidase reactions. Total TAG was measured by glycerol-phosphate-oxidase and peroxidase reactions. The method for direct determination of HDL-cholesterol uses polyethylene glycol (PEG) based system in which sulfated α-cyclodextrin, dextran sulfate, and $MgCl^2$ form water soluble complexes with the non-HDL lipoproteins present in a sample, after which pegylated cholesterol esterase and cholesterol oxidase are introduced. LDL cholesterol concentration were calculated using the Friedewald formula: (total cholesterol) - (HDL cholesterol) - (VLDL cholesterol) = LDL cholesterol. VLDL cholesterol concentrations were estimated as TAG divided by 5 when concentrations are expressed in mg/dL (18).

STATISTICAL ANALYSIS

Estimation of an appropriate sample size was conducted using the G*Power analysis method. The power value of the study was calculated as 96 % with an effect size of 0.5. Rationale for sample size was based on a previous study evaluating different probiotic capsules in hyperlipidemic patients. This study revealed an effect size for blood cholesterol of 0.5 after the probiotic capsule ingestion. A sample size of fifteen per group was determined with an effect size of 0.5, and 80 % power at the predetermined level of $\alpha = 0.05$. To account for potential subject attrition, it was planned to recruit an extra five participants per group, which increased the final sample size to twenty participants per group. Main statistical analysis were analyzed by statistical analytical systems software (package 20.0). The normality of data was confirmed using One-Sample Kolmogrow-Smirnov test. The mean ± SD were determined, and the differences among baseline, control diet, and probiotic groups were compared by analysis of paired sample t-test. Pearson correlation test was used because of the normal distribution of the data set from the relationships between the biomarkers. Nutrient intake (total fat, saturated fatty acid (SFA), mono-unsaturated fatty acid (MUFA), and polyunsaturated fatty acid (PUFA) were also compared with the changes of plasma lipid concentrations. Also, chi square was used in order to make an assumption and compare the two qualitative (categorical) variables. The level of significance was considered $p < 0.05$.

RESULTS

As shown in figure 1, in total 51 hypercholesterolemic subjects completed the trial as detailed in the study protocol. A total 51 patients were allocated into three groups: 18 participants allocated in the probiotic group I (only *Lactobacillus*), 17 participants

allocated in the probiotic group II (combined *Lactobacillus* and *Bifidobacterium*), and 16 participants were allocated in the the placebo group. Before the randomisation, 6 subject declined to participate in the study becuase of the inability to participate, low perceived compatibility and antibiotic drug use. A total of 56 patients were allocated into 3 study groups, 56 of the 51 patients completed the assigned protocol. Table I shows the demographic characteristics of the participants in all 3 groups who provided outcome measures. Mean age was 46 years (SD = 8) for the only *Lactobacillus* group, 44 years (SD = 9) for combination of *Lactobacillus* and *Bifidobacterium* group, and 45 years (SD = 8) for the placebo group. Most participants in all three groups were female and it has also been shown that the ratio of men to women in the 3 study groups was similar. As seen in table I, all groups were matched according to their age and sex.

Body composition measurements for pre-interveniton and post-intervemtion are shown in table II. During the study period, no statistically significant difference was found between the body composition measurements of the participants in all groups ($p < 0.05$). Participants' body composition was closely monitored throughout the study, as body weight is an important factor that may influence the outcome of the study and biochemical biomarkers. Body composition measurements, especially body weight, BMI, and body fat may affect serum plasma lipids and other biochemical biomarkers. As seen in table II, there was no statistically significant difference between body composition measurements taken at the beginning and at the end of the study in all groups ($p < 0.05$).

Participants´ nutrient intake during the study is shown in table III. As shown in table III, the energy intake of the participants in the probiotic group II is statistically higher than the other 2 study groups ($p = 0.03$). Consequently, as expected, the high energy intake has led to a parallel increase in macronutrient intake. Thus, the nutrient intake of participants in this group was found to be significantly higher than the other two groups.

Mean baseline, final and change in serum lipids levels in study groups are seen in table IV. Also, figure 2 shows the change in serum lipids of participants with probiotic intervention. Baseline evaluation (pre-intervention) revealed no differences among study groups except triglyceride levels. Among the groups, the initial triglyceride levels were compared and it was determined that the mean triglyceride levels in group I was significantly higher than the other groups. There was a statistically significant difference especially between the I group and the placebo group ($p = 0.02$). As seen in table IV, after the intervention period, participants of both group who used the probiotic capsules showed a statictically signifcant reduction in total cholestrol and triglyceride ($p < 0.05$) than the group that received a placebo.

Mean baseline, final and change in fasting blood glucose values are shown in table V. There was a statistically significant decrease in fasting blood glucose level ($p = 0.000$) of both probiotic groups. Regarding the mean baseline and final changes in hs-CRP and homocysteine levels, there was a statistically significant mean difference in the probiotic group using the combined capsule, as seen in table V. However, there were no significant changes in the *Lactobacillus* or placebo group.

Table I. Demographic characteristics of the participants

Measures	Probiotic I (*n* = 18)		Probiotic II (*n* = 17)		Placebo (*n* = 16)		Total (*n* = 51)	
	n	%	n	%	n	%	n	%
Gender n (%)								
Female	11	61.1	11	64.71	11	68.75	33	64.71
Male	7	38.89	6	35.29	5	31.25	18	35.29
Age, yr	46.78 ± 8.42		44.12 ± 9.07		45.62 ± 6.84		45.53 ± 8.11	

Table II. Initial and final body composition measurements of participants

Measures	Group	Pre-intervention			Post-intervention			
		$\bar{\chi} \pm s$	p_1	Difference	$\bar{\chi} \pm s$	p_2	Difference	p_3
Body weight (kg)	Probiotic I	69.62 ± 11.74	0.153		69.93 ± 11.89	0.128		0.103
	Probiotic II	77.84 ± 12.83			78.02 ± 12.68			0.492
	Placebo	71.38 ± 6.86			71.64 ± 6.72			0.338
Height (cm)	Probiotic I	166.44 ± 9.18	0.074		166.44 ± 9.18	0.074		1.000
	Probiotic II	173 ± 9.12			173 ± 9.12			1.000
	Placebo	167.06 ± 9.42			167.06 ± 9.42			1.000

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Table II (cont.). Initial and final body composition measurements of participants

Measures	Group	Pre-intervention			Post-intervention			
		$\bar{\chi} \pm s$	p_1	Difference	$\bar{\chi} \pm s$	p_2	Difference	p_3
BMI (kg/m^2)	Probiotic I	27.51 ± 6.93	0.848		27.87 ± 6.66	0.721		0.080
	Probiotic II	26.23 ± 7.67			26.42 ± 7.28			0.297
	Placebo	27.54 ± 8.16			27.83 ± 7.99			0.178
Waist circumference (cm)	Probiotic I	82.33 ± 14.06	0.606		82.44 ± 14.03	0.638		0.157
	Probiotic II	85.29 ± 9.12			85.44 ± 9.21			0.317
	Placebo	83.06 ± 7.38			83.13 ± 7.65			0.563
Hip circumference (cm)	Probiotic I	100.17 ± 10.36	0.430		100.17 ± 10.36	0.430		1.000
	Probiotic II	101 ± 6.41			101 ± 6.41			1.000
	Placebo	101.69 ± 6.53			101.69 ± 6.53			1.000
Waist/hip ratio	Probiotic I	0.82 ± 0.07	0.731		0.82 ± 0.07	0.731		1.000
	Probiotic II	0.83 ± 0.07			0.83 ± 0.07			1.000
	Placebo	0.81 ± 0.06			0.81 ± 0.06			1.000
Body fat (kg)	Probiotic I	19.09 ± 5.22	0.691		19.26 ± 5.16	0.793		0.250
	Probiotic II	20.35 ± 6.69			20.73 ± 6.82			0.080
	Placebo	21.06 ± 5.07			21.62 ± 5.18			0.010*
FFM (fat free mass)	Probiotic I	50.57 ± 10.58	0.042*	1-2[a]	50.19 ± 10.4	0.059		0.039*
	Probiotic II	57.56 ± 10.7		2-3[c]	57.23 ± 10.7			0.256
	Placebo	49.59 ± 7.53			49.38 ± 7.6			0.364
TBW %	Probiotic I	50.4 ± 4.88	0.370		49.91 ± 4.61	0.391		0.017*
	Probiotic II	51.26 ± 4.94			50.95 ± 5.2			0.087
	Placebo	48.75 ± 4.48			48.34 ± 4.62			0.011*

BMI: body mass index; TBW: total body water. Values are means ± s.d., $n = 51$. p_1*: differences among study groups in pre-intervention period;* p_2*: differences among study groups in post intervention period;* p_3*: differences among pre and post study .* [a]*Statistical difference between group 1-2.* [b]*Statistical difference between groups 1-3.* [c]*Statistical difference between groups 2-3. For* p_1 *and* p_2*: independent t-test, and for* p_3*: paired sample t-test was used. The level of significance was* $p < 0.05$.

Table III. Nutrient composition of the study groups during the study period

Measures	Group	Pre-intervention $\bar{\chi} \pm s$	p_1		Post-intervention $\bar{\chi} \pm s$	p_2		p_3
Energy (kcal)	Probiotic I	1474.66 ± 279.87	0.003*	1-2[a]	1487.46 ± 272.37	0.007*	1-2[a]	0.500
	Probiotic II	2137.47 ± 1203.33		2-3[c]	2138.7 ± 1197.44		2-3[c]	0.619
	Placebo	1456.13 ± 289.8			1527.64 ± 281.71			0.039*
Protein (g)	Probiotic I	76.55 ± 16.25	0.801		75.41 ± 19.31	0.054		0.446
	Probiotic II	94.55 ± 55.32			105.46 ± 56.54			0.005*
	Placebo	77.17 ± 16.45			76.76 ± 17.67			0.796
Fat (g)	Probiotic I	52.52 ± 9.66	0.009*	1-2[a]	53.52 ± 10.66	0.042*	1-2[a]	0.360
	Probiotic II	75.13 ± 40.95		2-3[c]	73.41 ± 40.09		2-3[c]	0.287
	Placebo	51.84 ± 9.9			55.22 ± 10.46			0.179
Carbohydrate (g)	Probiotic I	164.94 ± 39.27	0.001*	1-2[a]	167.8 ± 35.12	0.011*	1-2[a]	0.616
	Probiotic II	254.68 ± 143.93		2-3[c]	251.31 ± 144.87		2-3[c]	0.287
	Placebo	161.2 ± 39.78			172.06 ± 39.86			0.179

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Table III (cont.). Nutrient composition of the study groups during the study period

Measures	Group	Pre-intervention $\bar{\chi} \pm s$	p_1		Post-intervention $\bar{\chi} \pm s$	p_2		p_3
Fiber (g)	Probiotic I	30.33 ± 12.97	0.158		26.07 ± 10.23	0.001*	1-2[a]	0.557
	Probiotic II	41.96 ± 31.01			37.79 ± 17.44		2-3[c]	0.723
	Placebo	29.1 ± 11.6			28.37 ± 10.56			0.756
Saturated fat (g)	Probiotic I	12.92 ± 2.93	0.378		14.40 ± 2.93	0.226		0.094
	Probiotic II	17.55 ± 9.09			20.66 ± 14.36			0.136
	Placebo	13.05 ± 2.95			14.98 ± 2.87			0.020*
Mono-unsaturated fat (g)	Probiotic I	13.36 ± 2.83	0.073		12.82 ± 3.58	0.036*	1-2[a]	0.528
	Probiotic II	18.94 ± 10.2			19.08 ± 10.9		2-3[c]	0.906
	Placebo	13.55 ± 2.92			13.66 ± 3.3			0.836
Polyunsaturated fat (g)	Probiotic I	16.03 ± 7.65	0.022*	1-2[a]	15.09 ± 8.23	0.235		0.102
	Probiotic II	24.63 ± 13.26		2-3[c]	21.46 ± 14.43			0.124
	Placebo	16.11 ± 7.67			16.28 ± 8.62			0.352
Dietary cholesterol (mg)	Probiotic I	213.82 ± 99.89	0.952		198 ± 83.42	0.586		0.446
	Probiotic II	213.59 ± 115.35			281.55 ± 222.41			0.039*
	Placebo	214.92 ± 82.42			196.65 ± 69.32			0.438
Omega 3 (g)	Probiotic I	2.35 ± 1.58	0.331		2.42 ± 1.72	0.516		0.794
	Probiotic II	3.04 ± 1.48			2.83 ± 1.34			0.962
	Placebo	2.39 ± 1.53			2.52 ± 1.71			0.856
Omega 6 (g)	Probiotic I	13.44 ± 6.36	0.019*	1-2[a]	12.53 ± 6.87	0.244		0.133
	Probiotic II	19.47 ± 6.28		2-3[c]	16.42 ± 7.17			0.068
	Placebo	13.71 ± 6.24			13.6 ± 7.32			0.255

p_1: *differences among study groups in pre-intervention period;* p_2: *differences among study groups in post intervention period;* p_3: *differences among pre and post study.* [a]*Statistical difference between group 1-2.* [b]*Statistical difference between groups 1-3;* [c]*Statistical difference between groups 2-3. For* p_1 *and* p_2*: independent t-test, and for* p_3*: paired sample t-test was used. The level of significance was* $p < 0.05$.

Table IV. Mean baseline and final change in serum lipids levels in study groups

	Group	Pre-intervention		Post-intervention		p_3	Diff.	95 % CI	
		$\bar{\chi} \pm s$	p_1	$\bar{\chi} \pm s$	p_2			Low	Up
Cholesterol	Probiotic I	241 ± 37.22		215.39 ± 42.86		0.001*	-25.61	-40.22	-11.00
	Probiotic II	226 ± 30.74	0.232	201.47 ± 31.18	0.455	0.002*	-24.53	-35.83	-13.23
	Placebo	221.63 ± 34.81		215.31 ± 33.63		0.088	-6.31	-13.07	0.45
LDL-cholesterol	Probiotic I	156.5 ± 36.08		156 ± 40.51		0.862	-0.50	-10.97	9.97
	Probiotic II	143.35 ± 29.03	0.168	137.82 ± 30.4	0.23	0.142	-5.53	-14.51	3.45
	Placebo	136.19 ± 37.1		134.75 ± 33.78		0.451	-1.44	-7.04	4.16
HDL-cholesterol	Probiotic I	57.67 ± 13.61		56.22 ± 13.33		0.2	-1.44	-4.04	1.15
	Probiotic II	63.41 ± 9.64	0.287	59 ± 10.95	0.819	0.09	-4.41	-7.29	-1.54
	Placebo	59.81 ± 12.5		59.19 ± 11.43		0.815	-0.63	-4.07	2.82

(Continues on next page)

Table IV (cont.). Mean baseline and final change in serum lipids levels in study groups

	Group	Pre-intervention		Post-intervention		p_3	Diff.	95 % CI	
		$\bar{\chi} \pm s$	p_1	$\bar{\chi} \pm s$	p_2			Low	Up
Triglyceride	Probiotic I	151 ± 72.1	0.002*	123.89 ± 69.78	0.451	0.004*	-27.11	-44.11	-10.12
	Probiotic II	121.71 ± 37.61		96.82 ± 29.9		0.006*	-24.88	-39.84	-9.92
	Placebo	83.81 ± 21.03		88.81 ± 26.84		0.776	5.00	-5.61	15.61
HDL:LDL	Probiotic I	2.9 ± 1.08	0.189	2.98 ± 1.19	0.125	0.661	0.08	-0.13	0.28
	Probiotic II	2.29 ± 0.49		2.38 ± 0.56		0.174	0.09	-0.05	0.23
	Placebo	2.36 ± 0.67		2.33 ± 0.61		0.949	-0.03	-0.22	0.16
Total:HDL	Probiotic I	4.43 ± 1.39	0.204	4.06 ± 1.39	0.456	0.014*	-0.37	-0.71	-0.03
	Probiotic II	3.61 ± 0.55		3.48 ± 0.58		0.171	-0.13	-0.30	0.04
	Placebo	3.82 ± 0.76		3.74 ± 0.69		0.801	-0.08	-0.37	0.20

LDL: low-density lipoprotein; HDL: high density lipoprotein. p_1*: differences among study groups in pre-intervention period;* p_2*: differences among study groups in post intervention period;* p_3*: differences among pre and post study. For* p_1 *and* p_2*: independent t-test, and for* p_3*: pairedsample t-test was used. The level of significance was* $p < 0.05$.

Table V. Mean baseline and final change in gylycemic and other biomarkers in study groups

	Group	Pre-intervention		Post-intervention		p_3	Diff.	%95 CI	
		$\bar{\chi} \pm s$	p_1	$\bar{\chi} \pm s$	p_2			Low	Up
FBG	Probiotic I	97.89 ± 7.42	0.956	87.61 ± 6.39	0.188	0.000*	-10.28	-13.78	-6.77
	Probiotic II	100.76 ± 18.55		90.59 ± 11.81		0.000*	-10.18	-16.23	-4.12
	Placebo	97.06 ± 8.24		92.06 ± 6.77		0.003*	-5.00	-9.09	-0.91
CRP	Probiotic I	0.24 ± 0.22	0.519	0.23 ± 0.17	0.014*	0.777	-0.01	-0.12	0.11
	Probiotic II	0.25 ± 0.22		0.28 ± 0.26		0.410	0.02	-0.03	0.07
	Placebo	0.19 ± 0.16		0.18 ± 0.13		0.280	-0.04	-0.08	0.00
Homosis-tein	Probiotic I	13.76 ± 8.6	0.089	11.77 ± 6.37	0.235	0.085	-1.98	-3.69	-0.28
	Probiotic II	9.68 ± 3.03		8.78 ± 2.78		0.044*	-0.89	-1.61	-0.18
	Placebo	8.83 ± 2.11		9.64 ± 2.13		0.006*	0.81	0.30	1.32
Insulin	Probiotic I	10.24 ± 6.05	0.583	9.52 ± 3.86	0.402	0.372	-0.72	-4.45	-1.57
	Probiotic II	9.56 ± 5.4		8.47 ± 3.54		0.277	-1.09	-3.83	-2.24
	Placebo	8.01 ± 4.64		7.91 ± 3.97		0.877	-0.1	-3.91	-3.72
HOMA-IR	Probiotic I	2.48 ± 0.55	0.756	2.05 ± 0.59	0.384	0.004*	-0.43	-0.34	-0.27
	Probiotic II	2.37 ± 0.48		1.89 ± 0.28		0.002*	-0.48	-0.26	-0.17
	Placebo	1.91 ± 0.32		1.80 ± 0.27		0.089	-0.11	-0.44	-0.15

fbg: fasting blood glucose. p_1*: differences amon gstudy groups in pre-intervention period;* p_2*: differences among study groups in post intervention period;* p_3*: differences among pre and post study. For* p_1 *and p2: independent t-test, and for* p_3*: paired sample t-test was used. The level of significance was* $p < 0.05$.

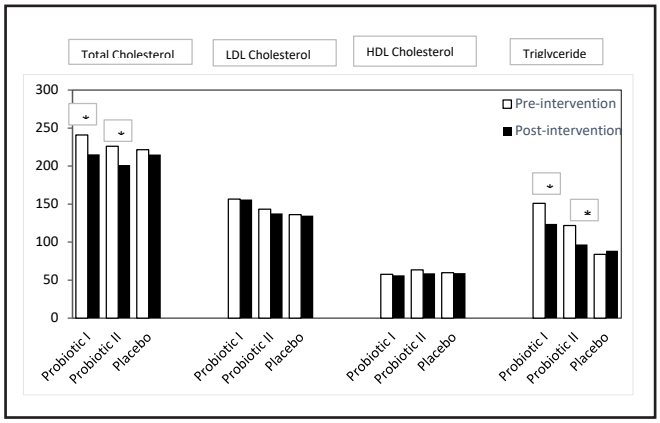

Figure 2. Effects of 8 weeks of different probiotic consumption on serum lipids compared with placebo (*$p < 0.05$ statistically significant difference).

DISCUSSION

Current double blind randomized controlled study demonstrated that 1 x 10^6 colony forming unit (CFU) *Lactobacillus rhamnosus GG* microorganism and combination of 1 x 10^9 CFU *Lactobacillus acidophilus* and 1 x 10^9 CFU *Bifidobacterium animalis* subsp. *lactis* both probiotic capsules over eight weeks had efficient role in lowering serum total cholesterol and triglyceride levels as well as showing an efficient reduction on fasting plasma glucose level, insulin and HOMA-IR levels in patients with hypercholesterolemia. Contrary to this finding, in the plasebo group there was no significant decrease was observed in plasma lipids and plasma glucose levels. Current study findings mostly indicated parallel results with the majority of previous studies evaluating the cholesterol lowering effects of probiotics (19-21). Most of the previous studies have shown that probiotic capsules have a lowering effect especially on total cholesterol and LDL cholesterol, but many of the same studies have demonstrated that probiotic use does not affect triglyceride levels (19-23). Unlike other studies, the two different types of probiotics used in the current study significantly reduced total cholesterol and especially triglyceride levels, while not having any effect on LDL cholesterol. A current new research revealed the similar findings and strenghten the current study results (24). Jaff et al. compared body composition, serum lipid and serum glucose levels between groups receiving probiotics and those not receiving probiotics. According to the Jaff et al. study results, although there was a decreasing trend in all serum lipids, no statistically significant decrease was shown, including LDL cholesterol levels. However, although a decrease in LDL cholesterol was not found to be statistically significant in this study, statistically significant decreases were detected in the average total cholesterol and triglyceride levels of participants using probiotics (probiotic I and probiotic groups II), respectively 26 mg/dL (10.7 %) and 25 mg/dL (11.1 %). While the triglyceride levels of the participants in the probiotic group I decreased by an average of 18.5 % compared to the pre-intervention, this rate was found to be 20.6 % in the probiotic group II. In the placebo group, no significant decreases in total cholesterol and triglyceride levels were observed during the study. The study of Ahn et al. (25), which supports the findings of the present study, provides parallel results; reported a decrease in triglyceride levels of 18.3 % in patients with hypertriglyceridemia who took probiotics as a combination of *Lactobacillus plantarum* and *Lactobacillus curvatus* for 12 weeks. Contrary to some previous clinical studies (19-23), an expected decrease in LDL cholesterol (LDL-C) was not detected in the current study. Although there was a tendency for a decrease in LDL-C levels of the participants using combination of *Lactobacillus acidophilus* and *Bifidobacterium animalis* subsp. *lactis* (probiotic group II), no significant decrease was determined in all 3 study groups ($p > 0.05$). As mentioned in some previous studies (26,27), it has been stated that for the therapeutic effect of probiotics, the intervention should be longer than 6 weeks if possible, and thus a stronger lowering effect on LDL-C can be observed with longer interventions. As Jiang et al. (26) showed in their meta-analysis, the duration of probiotic supplementation was positively associated with the LDL-C lowering effects of probiotics. This is consistent with the results of a recent review (27), which indicated that trials lasting longer than 8 weeks had more significant lowering effects on LDL-C than those shorter than 8 weeks (27).

In addition to this, it is thought that another reason why the decrease in LDL cholesterol is not significant may be related to the probiotic dose used. In previous studies, participants taking higher doses of probiotics showed greater effectiveness on LDL-C. As Jiang et al. (2020) indicated in their metaanalyses (26), high-dose probiotics more effectively reduced LDL-C levels than low-dose probiotics. Additionally, another study by Zhang et al. (28) found that the survival of probiotic strains through the gastrointestinal passage is a key requirement for the efficacy of probiotics. Since some probiotic strains may have a low survival rate, the administration of high-dose probiotics can maximize the likelihood of gut colonization (28). Jiang et al. underlined that subgroup analyses made according to probiotic dosage showed that probiotic supplementation was only effective in reducing LDL-C levels when the dosage exceeded 10^9 CFU/day. In contrast, no changes in LDL-C levels were observed in patients given dosages below 10^9 CFU/day (26). In this study, while no decrease was observed in LDL-C levels in probiotic group I, a decrease was detected in probiotic group II, probably because the dosage used by participants was 10^9 CFU/day. However, it is thought that the reason why the decrease is not statiscally significant is likely related to the study duration.

Based on *in vitro* studies, the effect of probiotics in lowering plasma cholesterol is associated with different mechanisms; such as assimilation of cholesterol during growth by *L. Acidophilus,* binding of cholesterol to the cellular surface (29,30,) disruption of cholesterol micelles (29), and deconjugation of bile salt and bile salt hydrolase activity (30,31). A recent study has found that *L. acidophilus* reduces cholesterol absorption through the down-regulation of Niemann-Pick C1-like 1 in Caco-2 cells (32). While decreases in blood lipids were expected in people using probiotics through all the mentioned mechanisms, more significant decreases were expected especially in individuals in group II using combined strains. Since, studies indicated that combined strains are more effective in lowering plasma lipids than using a single strain (33,34).

Once the effect of probiotic intervention on glycemic biomarkers was evaluated, this study showed that the fasting insulin levels of group II participants who took capsules containing *Lactobacillus acidophilus* and *Bifidobacterium animalis* subsp.*lactis* decreased by 11.4 %, insulin levels of participants who took capsules containing only *Lactobacillus rhamnosus GG* (group I) decreased by 7.3 %, while this decrease was only 1.1 % in the placebo group. Similar results were observed in fasting serum glucose levels; after the intervention, there was a 12.5 % reduction in fasting serum glucose levels in probiotic group I, while a 9.5 % decrease was observed in probiotic group II. A decrease was also found in the placebo group (5.2 %), but not as significant as in probiotic intervention groups (Table IV). The present study, which has parallel findings with the meta-analysis previously compiled by

Ruan et al. (35) showed significant decreases in HOMA-IR values of probiotic supplemented participants. HOMA-IR value, which is an indicator of insulin resistance, decreased by 0.43 in probiotic group I, while a decrease of 0.48 was found in probiotic group II ($p < 0.05$) (Table IV). In this regard, the results of the present study show that both single and combined strains of probiotics, which are used regularly for 8 weeks, positively affect fasting blood glucose, fasting insulin level and therefore HOMA-IR. Similar results were obtained in a recent clinical study conducted with probiotic supplementation, and a decrease in blood glucose, insulin and HOMA-IR levels was detected in the group using probiotics compared to the placebo group (24).

It is known that high serum homocysteine levels are an independent risk factor for coronary heart disease (36). However, it is not possible to reach a definitive conclusion due to the small number of clinical studies examining the effect of probiotics on cardiovascular diseases through the homocysteine mechanism. In the present study, the effect of probiotic use on homocysteine level was evaluated and a significant decrease was associated only in the probiotic group II who were receiving the combined strain (Table IV). Parallel to this study, Valentini et al. (37) carried out a study in order to determine the effect of probiotic use on oxidative stress and inflammation biomarkers. Valentini et al., allocated participants into two groups and one group had only dietary intervention and the other group had dietary intervention plus VSL #3 probiotic strains (*Lactobacillus acidophilus, delbrueckii* subsp. *Bulgaricus, casei, plantarum, Bifidobacteria breve, B. Longum, infantis, Streptococcus salivarius* subsp. *thermophilus*). According to the results of this study, dietary intervention alone reduced fasting total cholesterol and glucose levels, while diet intervention plus probiotic supplementation has been shown to statistically improve folate, vitamin B12 and homocysteine levels. Barreto et al. (38) conducted an intervention study to examine the effect of probiotic use on homocysteine levels. During the study, participants in the intervention group ($n = 12$) were given fermented milk (80 mL/day) containing *Lactobacillus plantarum* for 90 days, while participants in the control group ($n = 12$) were given unfermented milk (80 mL/day) for 90 days and evaluation has been made. The findings of the study are consistent with those of Valentini et al. (37) and showed parallel results to the findings of the current study, showing that participants who consumed fermented milk for 90 days had a decrease in glucose and homocysteine levels compared to the control group.

The role of inflammation in the propagation of atherosclerosis and susceptibility to cardiovascular (CV) events is well established. Of the wide array of inflammatory biomarkers that have been studied, high-sensitivity C-reactive protein (hsCRP) has received the most attention for its use for the prediction of cardiovascular disease (39). Although there are studies showing that the use of probiotics reduces hs-CRP levels, some studies show that probiotic use does not affect hs-CRP levels (40-42-40). Ryan et al. (40) showed in their study in 12 individuals with hyperlipidemia that the use of 5.6 x 10^{10} *S. boulardii* for 8 weeks did not reduce hsCRP levels. This finding is in line with studies showing that probiotics have no effect on hs-CRP levels (41,42). Similar to studies showing that probiotic use has no effect on hs-CRP, this study also showed that probiotic use did not make a significant difference on hs-CRP levels compared to the baseline ($p > 0.05$) (Table IV).

There are strengths and limitations of the current study. It was a double-blind randomized controlled study conducted with good compliance to daily probiotic consumption during the study period (8 weeks). It is one of the scarce studies in which combined strain and single strain are compared at the same time. However, current study intervetion period was based on recommendations of similar studies that have been carried out in this area yet it would be significant for further studies to extend the duration of the intervention for a better understanding of the probiotic effect over time. The probiotic dose used in the current study was similar to others studies (30-34) but for therapeutic effect it would be better to use higher doses. Based on current study, it would be better for further studies to conduct the studies with a longer follow-up periods and different daily doses of probiotics.

CONCLUSION

As a conclusion, the results of this study showed that strains containing *Lactobacillus or Bifidobacterium* could be effective in hypercholesterolemic patients not treated with conventional lipid-lowering drugs and could reduce serum lipids as well as homocysteine and glycemic biomarkers. In order to determine the effectiveness of probiotics on cardiovascular disease, further studies are needed using different bacterial strains and different dosages to determine the potential role for probiotic bacteria in the management of hyperlipidaemia.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Obesidad y síndrome metabólico

Impacto de la cirugía bariátrica en los resultados materno-fetales de la gestación en comparación con mujeres con obesidad no operadas

Impact of bariatric surgery on maternal-fetal outcomes during pregnancy compared to non-operated obese women

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Resumen

Objetivo: el objetivo de nuestro estudio es evaluar el efecto de la cirugía bariátrica en los resultados obstétricos.

Material y métodos: se realizó un estudio de cohortes retrospectivo que incluyó 47 gestaciones postcirugía bariátrica y 219 gestaciones en mujeres con obesidad no operadas, reclutadas en el Hospital Álvaro Cunqueiro de Vigo (Galicia, noroeste de España), en el periodo comprendido entre diciembre de 2018 y enero de 2023. Se evaluaron diversas características, tanto maternas como obstétricas, abarcando desde datos basales hasta los resultados anteparto, intraparto, posparto y neonatales.

Resultados: la cirugía bariátrica mostró una significativa reducción del riesgo de diabetes gestacional (DMG) en un 69 % ($p = 0,045$) y del riesgo de cesáreas en un 63,1 % ($p = 0,014$), pero también un aumento notable del riesgo de aborto (3,5 veces más, $p = 0,046$) y del retraso del crecimiento intrauterino (35 veces más, $p = 0,009$). La cirugía bariátrica se asoció a una prolongación significativa de la estancia hospitalaria posparto (7,5 veces más, $p = 0,001$) y a una disminución del peso promedio del recién nacido (213,71 g, $p = 0,006$).

Conclusión: la gestación postcirugía bariátrica presenta beneficios, como una reducción del riesgo de diabetes gestacional (DMG) y de cesárea, pero presenta desafíos, como un mayor riesgo de aborto y un retraso del crecimiento intrauterino (CIR). Estos resultados resaltan la importancia de una atención obstétrica especializada para optimizar los resultados materno-fetales en las gestantes con antecedentes de cirugía bariátrica.

Palabras clave:

Cirugía bariátrica. Obesidad. Embarazo. Resultados obstétricos. Diabetes gestacional.

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Abstract

Objective: the aim of our study was to assess the effect of bariatric surgery on obstetric outcomes.

Material and methods: a retrospective cohort study was conducted, including 54 pregnancies post-bariatric surgery and 219 pregnancies in non-operated obese women, from December 2018 to January 2023. Various maternal and obstetric characteristics were evaluated, ranging from baseline data to antepartum, intrapartum, postpartum, and neonatal outcomes.

Results: bariatric surgery showed a significant 69 % reduction in the risk of gestational diabetes (GDM) ($p = 0.045$) and a 63.1 % reduction in cesarean sections ($p = 0.014$), but also a notable increase in the risk of miscarriage (3.5 times more, $p = 0.046$) and intrauterine growth restriction (35 times more, $p = 0.009$). Bariatric surgery was associated with a significant prolongation of postpartum hospital stay (7.5 times more, $p = 0.001$) and a decrease in the average weight of the newborn (213.71 g, $p = 0.006$).

Conclusion: pregnancy after bariatric surgery presents benefits, such as a reduced risk of gestational diabetes (GDM) and cesarean section, but also presents challenges, such as an increased risk of miscarriage and intrauterine growth restriction (IUGR). These results highlight the importance of specialized obstetric care to optimize maternal-fetal outcomes in pregnant women with a history of bariatric surgery.

Keywords:

Bariatric surgery. Obesity. Pregnancy. Obstetric outcomes. Gestational diabetes.

INTRODUCCIÓN

La obesidad ha alcanzado proporciones epidémicas a nivel mundial, convirtiéndose en un desafío crítico para la salud maternofetal. La obesidad materna ha surgido como un factor de riesgo gestacional predominante, evidenciando su impacto significativo en las últimas décadas (1). Este fenómeno no solo se vincula con complicaciones obstétricas tales como la diabetes gestacional y la HTA gestacional (2); también conlleva riesgos a largo plazo para la salud fetal, incluyendo el desarrollo de malformaciones congénitas y trastornos metabólicos a largo plazo (2,3).

En la actualidad, la cirugía bariátrica destaca como el abordaje más efectivo para tratar la obesidad severa, exhibiendo resultados notables en la pérdida de peso y mejorías en las condiciones de salud asociadas. Un fenómeno notable en los últimos años es el aumento de las intervenciones quirúrgicas en las mujeres en edad fértil (4).

La cirugía bariátrica podría ser beneficiosa para las mujeres que buscan concebir, al mejorar la fertilidad y reducir las complicaciones gestacionales asociadas con la obesidad. Sin embargo, también presenta potenciales riesgos, como deficiencias nutricionales debido a la reducción de la absorción de nutrientes, lo que podría afectar el desarrollo fetal (5) Es crucial, por tanto, un manejo integral y una monitorización continua durante el embarazo de estas gestantes para garantizar la salud óptima tanto de la madre como del feto (6).

MATERIAL Y MÉTODOS

Se trata de un estudio retrospectivo observacional de cohortes. El objetivo de nuestro estudio es evaluar el efecto de la cirugía bariátrica en los resultados obstétricos.

Se incluyeron 47 gestaciones postcirugía bariátrica y 219 gestaciones de mujeres con obesidad no operadas, 119 con obesidad de grado 1 (IMC: 30-34,9 kg/m^2) y 100 con obesidad de grado 2 y 3 (IMC > 35 kg/m^2), que fueron reclutadas durante su seguimiento en las consultas del Servicio de Endocrinología y Nutrición del Hospital Álvaro Cunqueiro de Vigo en el periodo comprendido entre diciembre de 2018 y enero de 2023.

Se evaluaron como características basales al inicio de la gestación: la edad materna, las características antropométricas maternas al inicio de la gestación, la ganancia ponderal gestacional, el número de embarazos, el número de partos, la diabetes *mellitus*, la hipertensión arterial, el tipo de cirugía bariátrica, los meses transcurridos entre la intervención de cirugía bariátrica y la gestación, la depresión, el hipotiroidismo gestacional, el tabaquismo, la anemia materna (definida como una hemoglobina materna < 11 g/dL) y la terapia de fertilidad.

Los resultados maternofetales examinados incluyeron las complicaciones anteparto (diabetes gestacional, hipertensión gestacional, ruptura prematura de membranas, placenta previa, desprendimiento prematuro de placenta, corioamnionitis, aborto espontáneo), las complicaciones intraparto (parto inducido, parto vaginal asistido, necesidad de cesárea, distocia de hombros), las complicaciones posparto (hemorragia posparto, anemia a los 6 días posparto (hemoglobina < 10 mg/dL), desgarro posparto, tromboembolismos venosos, larga estancia hospitalaria (> 6 días de ingreso hospitalario), asistencia a Urgencias durante el primer mes de posparto) y las neonatales (sexo del recién nacido, retraso de crecimiento intrauterino (CIR), pequeño y grande para edad gestacional según las tablas de población española, malformaciones congénitas, necesidad de UCI neonatal).

La variable "edad de las gestantes" se recoge como variable cuantitativa y categórica en tres segmentos (< 25 años, 25-34 años, > 34 años). A pesar de que la edad media de las gestantes españolas actualmente es de 32,5 años, se eligieron estos tramos de edad dado que existen diferencias en los riesgos y complicaciones obstétricas asociados con la edad materna. Por ejemplo, las mujeres menores de 25 años pueden tener un mayor riesgo de parto prematuro mientras que las mujeres mayores de 34 años pueden enfrentarse a un aumento de las complicaciones relacionadas con la edad, como la preeclampsia. Establecer estos tramos puede permitir investigar y comprender mejor las tasas de concepción y los desafíos asociados a los diferentes grupos de edad.

ANÁLISIS ESTADÍSTICO

Análisis univariante

Las variables cuantitativas se presentan con la media y la desviación típica y se analizan, después de comprobar que cumplen los criterios de normalidad, con la prueba de la t. Las variables

categóricas se presentan con recuento y porcentaje y se analizan con el test del chi^2 o el test exacto de Fisher si la frecuencia esperada en una celda es menor de 5.

Análisis multivariante

Para obtener los riesgos relativos (RR) y las diferencias de medias (DM), ajustados por las variables de confusión, se utilizan modelos de regresión que dependen del tipo de variable dependiente: regresión logística en el caso de las variables categóricas binarias; regresión logística multinomial en el caso de las variables categóricas con más de dos categorías; regresión lineal múltiple en el caso de la variable cuantitativa continua.

Las variables de confusión que se han tenido en cuenta en estos modelos de regresión han sido: edad materna, número de embarazos, diabetes *mellitus*, hipotiroidismo, depresión, tabaco, alcoholismo, tratamiento de fertilidad y anemia. En alguna variable dependiente se han introducido algunas variables más de confusión, detalladas en la tabla resumen.

Para seleccionar las variables de confusión introducidas en cada análisis multivariante de cada variable dependiente se han seguido los tres criterios habituales.

Se considera estadísticamente significativo un valor bilateral de $p < 0,05$. Los análisis estadísticos se han realizado con el programa Stata 16.1.

ASPECTOS ÉTICOS Y LEGALES

El estudio fue aprobado por el Comité de Ética e Investigación de Galicia, con Código de Registro 2016/534, en la fecha 17/01/17. Los investigadores han seguido las normas éticas y legales aplicables. Se obtuvo el consentimiento informado por escrito para participar de todos los participantes individuales incluidos en el estudio. El estudio aseguró el cumplimiento de la legislación española de protección de datos, especialmente conforme a la Ley Orgánica 3/2018, de 5 de diciembre.

El estudio ha sido desarrollado de acuerdo con las recomendaciones de la guía STROBE para estudios observacionales.

RESULTADOS

En la tabla I comparamos las características basales al inicio de la gestación de ambos grupos (mujeres sometidas a cirugía bariátrica y mujeres con obesidad no operadas).

En cuanto a los datos antropométricos, al inicio de la gestación, la media del peso gestacional y el IMC fueron inferiores en el grupo de cirugía bariátrica, ambas variables con significación estadística. Cabe destacar que, a pesar de lo dicho anteriormente, en el grupo de cirugía bariátrica la mayoría de las pacientes permanecen con obesidad tras la cirugía: $n = 27$ (58,32 %).

Si clasificamos las pacientes operadas de cirugía bariátrica según el IMC al inicio de la gestación, se obtienen los siguientes segmentos: normopeso, $n = 3$ (6,38 %); sobrepeso, $n = 17$ (35,4 %); obesidad de grado 1, $n = 14$ (29,16 %); obesidad de grado 2, $n = 10$ (21,27 %) y obesidad de grado 3, $n = 3$ (6,38 %).

En el grupo de mujeres con obesidad no operadas, $n = 219$, observamos la siguiente clasificación según el IMC al inicio de la gestación: obesidad de grado 1, $n = 119$ (54,33 %); obesidad de grado 2, $n = 60$ (27,39 %); obesidad de grado 3, $n = 40$ (18,26 %).

No se apreciaron diferencias en la ganancia ponderal gestacional, ni en el número de partos o gestaciones. En el grupo bariátrico hay un mayor número absoluto de gestaciones (47) que de partos (44) debido a que se produjeron 3 abortos espontáneos.

Según el tipo de cirugía bariátrica, la mayoría fueron sometidas a bypass gástrico en Y de Roux (79,63 %). Las restantes, un 18,52 %, fueron sometidas a derivación biliopancreática con cruce duodenal y un 1,85 % a gastrectomía vertical. Con respecto a los meses transcurridos entre la cirugía bariátrica y la gestación, de media se obtuvieron 60,77 meses (es decir, la mayoría cumplieron el periodo de espera de 12 meses para quedarse embarazadas tras la cirugía bariátrica).

En cuanto a las comorbilidades médicas previas analizadas, las pacientes de ambos grupos obtuvieron resultados similares en la mayoría de las variables (hipertensión arterial, tabaquismo y terapia de fertilidad) exceptuando la diabetes *mellitus* pregestacional, que fue más frecuente en el grupo bariátrico (el doble) pero sin significación estadística. Sin embargo, en el grupo de cirugía bariátrica fue estadísticamente significativa la mayor frecuencia de hipotiroidismo gestacional, trastornos depresivos y anemia materna definida como hemoglobina materna < 11 g/dL, esta última comorbilidad posiblemente por causas de malabsorción de hierro y vitamina B_{12}.

Ajustando las variables de edad materna, número de embarazos, diabetes *mellitus*, hipotiroidismo, depresión, tabaco, tratamiento de fertilidad y anemia materna, los resultados de nuestro estudio revelan un impacto significativo de la cirugía bariátrica en la gestación, abordando diversos aspectos cruciales (Tabla II).

En primer lugar, en las complicaciones anteparto se observó una disminución sustancial del riesgo de diabetes gestacional con una reducción estadísticamente significativa de un 69 % (factor de 0,310). Este hallazgo sugiere que la cirugía bariátrica emerge como un factor protector en la aparición de la diabetes gestacional. También disminuye el riesgo de hipertensión gestacional, de ruptura prematura de membranas y de placenta previa, pero estas diferencias no fueron significativas.

En contraste, se evidenció un aumento significativo del riesgo de aborto postcirugía bariátrica, con un incremento de 3,5 veces (factor de 3,533). Este aumento sustancial destaca la necesidad de una atención prenatal especializada y una evaluación individualizada para gestionar este riesgo potencialmente elevado. También se observó un aumento del riesgo de preeclampsia y corioamnionitis, pero no fue significativo.

En las complicaciones intraparto, la cirugía bariátrica demostró una reducción sustancial del riesgo de cesárea, con un factor de 0,369 que indica una disminución del 63,1 %. Este resultado

sugiere que la cirugía bariátrica podría contribuir positivamente a la reducción de las tasas de cesárea en las mujeres gestantes. La cirugía bariátrica, también, disminuye el riesgo de parto vaginal asistido, parto inducido y distocia de hombros, pero no se obtuvo la significación estadística.

En las complicaciones posparto, la cirugía bariátrica aumenta de forma significativa el riesgo de experimentar una estancia hospitalaria prolongada, definida como más de 6 días (hay un riesgo 7,5 veces mayor). También se asoció con un mayor riesgo de hemorragia posparto, anemia posparto y tromboembolismo venoso, pero no fue significativo. En contraste, la cirugía bariátrica disminuye el riesgo de infección periparto, desgarros postparto y necesidad de asistencia a Urgencias en el primer mes posparto, pero tampoco se alcanzó la significación.

En cuanto a las complicaciones neonatales, la cirugía bariátrica se asoció significativamente con un incremento llamativo del riesgo de retraso del crecimiento intrauterino (CIR) con un factor de 35,047. También se asoció con una disminución media significativa de 213,71 gramos en el peso del recién nacido.

La cirugía bariátrica disminuye el riesgo de macrosomía fetal, pero de manera no significativa. Por otro lado, se asoció a un aumento del riesgo de tener un feto pequeño para la edad gestacional, malformaciones congénitas y necesidad de una UCI neonatal, aunque los resultados tampoco fueron significativos.

Tabla I. Características basales de ambos grupos de estudio antes del inicio de la gestación

Características generales	Cirugía bariátrica (*n* = 47)	Obesidad (*n* = 219)	Valor *p*
Edad materna, años (media ± DT)	34,61 ± 4,87	32,27 ± 5,42	0,004*
< 25 (*n*, %)	2; 3,70 %	19; 8,68 %	0,483
25-34 (*n*, %)	27; 50,00 %	122; 55,71 %	0,298
> 34 (*n*, %)	25; 46,30 %	78; 35,62 %	0,262
Peso pregestacional, kg (media ± DT)	85,19 ± 13,77	94,97 ± 15,52	0,001*
Talla pregestacional, cm (media ± DT)	162,29 ± 5,56	162,92 ± 6,24	0,503
IMC pregestacional, kg/m^2 (media ± DT)	32,40 ± 5,26	35,73 ± 5,21	0,001*
Ganancia ponderal gestacional, kg (media ± DT)	7,28 ± 5,30	7,28 ± 5,73	0,99
Número de gestaciones (n, %)			
1	17; 36,17 %	82; 37,44 %	0,078
2-3	29; 61,70 %	111; 50,68 %	0,098
> 3	1; 2,13 %	26; 11,87 %	0,091
Número partos (n, %)			
1	25; 56,82 %	100; 46,08 %	0,146
2-3	19; 43,18 %	106; 48,85 %	0,323
> 3	0; 0,00 %	11; 5,07 %	0,243
Tipo de cirugía bariátrica (n, %)			
Gastrectomía vertical	1; 1,85 %		
Bypass gástrico en Y de Roux	43; 79,63 %		
Derivación biliopancreática con cruce duodenal	10; 18,52 %		
Meses transcurridos entre cirugía bariátrica y gestación, meses (media ± DT)	60,77 ± 42,34		
HTA pregestacional, w(*n*, %)	2; 3,70 %	16; 2,74 %	0,659
Diabetes pregestacional, (*n*, %)	3; 5,56 %	6; 2,74 %	0,387
Hipotiroidismo, (*n*, %)	10; 18,52 %	14; 6,39 %	0,012*
Depresión, (*n*, %)	7; 14,89 %	1; 0,46 %	0,001*
Tabaquismo, (*n*, %)	12; 22,22 %	32; 18,7 %	0,173
Anemia materna pregestacional, (*n*, %)	10; 18,87 %	2; 0,91 %	0,001*
Terapia de fertilidad, (*n*, %)	1; 2,13 %	5; 2,28 %	1,000

DT: desviación típica.

Tabla II. Análisis comparativo entre ambos grupos de los resultados materno-fetales al inicio de la gestación

Resultados	Método	RR	IC 95 %	Valor *p*	%RR
Complicaciones anteparto					
Hipertensión gestacional	RLo	0,195	0,026-1,451	0,114	
Diabetes gestacional	RLo	0,310	0,099-0,974	0,045	
Ruptura prematura de membranas	RLo	0,748	0,272-2,060	0,575	
Placenta previa	RLo	0,012	0,000-9999	1	-69 %
Desprendimiento prematuro de placenta	RLo	220	0,001-6766	1	
Corioamnionitis	RLo	2,656	0,240-29,346	0,426	
Aborto espontáneo	Rlo	3,533	1,022-12,219	0,046	253,3 %
Complicaciones intraparto					
Necesidad de cesárea	RLo	0,369	0,168-0,814	0,014	-63,1 %
Inducción del parto	RLo	0,584	0,284-1,199	0,143	
Parto vaginal asistido	RLo	0,662	0,329-1,332	0,248	
Distocia de hombros	Rlo	0,004	0,000-999,9	0,595	
Complicaciones posparto					
Hemorragia posparto	RLo	1,011	0,120-8,502	0,992	
Anemia posparto (hemoglobina < 10 mg/dL)	RLo	1,211	0,553-2,654	0,631	
Tromboembolismo venoso	RLo	214	0,000-9999	0,168	
Infección periparto	RLo	0,354	0,048-2,620	0,309	
Desgarros posparto	RLo	0,936	0,546-1,607	0,812	
Larga estancia hospitalaria (> 6 días)	RLo	7,459	3,000-18,548	0,001*	
Asistencia a Urgencias	Rlo	0,003	0,000-9999	0,604	645,9 %
Resultados neonatales					
Sexo (*n*, varón)	RLo	0,701-	0,475-1,035	0,074	
Peso recién nacido, g	RLm	213,71	-366,82-60,603	0,006	
Retraso del crecimiento intrauterino	RLo	35,047	4,327-283,878	0,009	
Pequeño para la edad gestacional (percentil de peso < 10)	RLo	2,381	0,805-7,049	0,117	3404,7 %
Grande para la edad gestacional (percentil de peso > 90)	RLo	0,357	0,088-1,451	0,150	
Malformaciones congénitas	RLo	1,665	0,166-16,711	0,665	
UCI neonatal	Rlo	5,300	0,338-83,000	0,235	

RR: riesgo relativo; RRR: reducción relativa del riesgo; RLo: regresión logística binomial; RLm: regresión lineal múltiple.

DISCUSIÓN

La cirugía bariátrica se ha consolidado como una herramienta eficaz en el manejo de la obesidad, generando notables impactos en la pérdida de peso y en la mejoría de las complicaciones metabólicas (7).

Con un número creciente de mujeres que buscan la maternidad después de estos procedimientos, es crucial explorar en detalle los efectos de la gestación postcirugía bariátrica. Aunque se han registrado beneficios significativos, como la reducción de la diabetes gestacional y mejoras en la salud materna, es esencial abordar también los posibles riesgos asociados, como las deficiencias nutricionales y desafíos metabólicos que podrían incidir en la gestación (6).

En este estudio, al igual que en otras investigaciones previas, se destaca una disminución sustancial del riesgo de diabetes gestacional en las pacientes que habían sido sometidas a un procedimiento bariátrico (6,8,9). Este beneficio se atribuye a múltiples mecanismos, como la pérdida de peso y la redistribución de la grasa corporal (en particular, la reducción de la grasa visceral), que han demostrado que contribuyen a normalizar la función metabólica, reduciendo la resistencia a la insulina. Además, la cirugía bariátrica impacta en las hormonas relacionadas con el apetito y el metabolismo, favoreciendo la homeostasis glucémica. Estos hallazgos respaldan la conclusión de que la cirugía bariátrica puede ser un factor protector contra la diabetes gestacional (10).

Tras la investigación se ha evidenciado un aumento del riesgo de aborto en las mujeres gestantes sometidas a cirugía bariátrica, tendencia previamente identificada en otros estudios que puede atribuirse a deficiencias nutricionales, especialmente en las técnicas como el bypass gástrico y las técnicas malabsortivas, que podrían afectar a la absorción de nutrientes esenciales para el desarrollo fetal.

Factores como la pérdida rápida de peso, los cambios en la anatomía del tracto digestivo y las dificultades para satisfacer las necesidades nutricionales durante el embarazo contribuyen también al riesgo de aborto. Es esencial brindar un cuidado prenatal especializado para asegurar un embarazo más saludable (11,12).

Desde el punto de vista obstétrico se observó que haber sido sometida a cirugía bariátrica disminuye el riesgo de cesáreas en

las gestantes, posiblemente debido a mejoras en la salud materna y a la reducción de las complicaciones asociadas con la obesidad, como la diabetes gestacional y la hipertensión (13,14).

Sin embargo, se identificó un mayor riesgo de estancia prolongada en la hospitalización posparto de las pacientes que han sido intervenidas con fines bariátricos. Los cambios anatómicos y metabólicos postcirugía pueden influir en la velocidad de recuperación posparto y las posibles complicaciones, como deficiencias nutricionales o desequilibrios electrolíticos, que pueden llegar a requerir una monitorización más intensiva (15,16).

En relación con los resultados neonatales se ha observado un aumento del riesgo de retraso del crecimiento intrauterino (17) y un menor peso de los recién nacidos de gestantes anteriormente sometidas a cirugía bariátrica (16,18). Esto se atribuye a la limitación en la absorción de nutrientes esenciales durante el embarazo, consecuencia de la cirugía bariátrica, y resalta la importancia de una vigilancia obstétrica más estrecha (19,20).

En cuanto a las limitaciones del estudio, hay que destacar que se trata de un estudio de cohortes retrospectivas, y este diseño presenta limitaciones inherentes que es necesario considerar. La naturaleza retrospectiva podría introducir sesgos de selección y memoria, mientras que la heterogeneidad en el grupo de la obesidad no operada y la falta de aleatorización pueden afectar a la comparabilidad. Las diferencias en la atención prenatal y el tamaño muestral limitado también deben ser tenidas en cuenta a la hora de interpretar los resultados. A pesar de estas limitaciones, consideramos que este estudio proporciona información valiosa sobre los resultados obstétricos postcirugía bariátrica, instando a futuras investigaciones prospectivas para confirmar y ampliar estos hallazgos.

CONCLUSIÓN

La gestación postcirugía bariátrica presenta beneficios, como la reducción del riesgo de diabetes gestacional y cesáreas, pero también desafíos, como un mayor riesgo de retraso del crecimiento intrauterino y de aborto. Es necesaria una atención obstétrica especializada y una evaluación cuidadosa de las mujeres con historial de cirugía bariátrica, para optimizar sus resultados maternofetales.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Validity of bioelectric impedance analysis for body composition assessment in interstitial lung disease patients

Validación del análisis de bioimpedancia eléctrica para la evaluación de la composición corporal en pacientes con enfermedad pulmonar intersticial

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Abstract

Background: changes in body composition (BC) are common in interstitial lung disease, which leads to an increased risk of complications and infections, and are associated with poor quality of life and worse outcomes. BC assessment is important to identify malnutrition and sarcopenia. However, gold-standard techniques are not available in all clinical settings.

Aims: this study aimed to evaluate the agreement and reliability of body composition estimated by bioelectric impedance analysis (BIA) and measured using dual-energy X-ray absorptiometry (DEXA) in women with interstitial lung disease.

Methods: this is a cross-sectional study. BC (fat mass and appendicular skeletal muscle mass) were assessed using BIA multifrequency and DEXA in standardized conditions. Agreement and reliability between techniques were evaluated using Bland-Altman plots and the intraclass correlation coefficient (ICC).

Results: a total of 50 women were evaluated. No differences were observed for FM (BIA, 25.8 ± 10.2 kg and DEXA, 26.3 ± 10.0 kg, $p = 0.77$) and ASMM (BIA, 14.1 ± 2.7 kg and DEXA, 13.9 ± 2.3 kg, $p = 0.83$). Based on ICC, good reliability was observed for FM (ICC, 0.98) and ASMM (ICC, 0.93).

Conclusion: BC estimated by BIA showed good agreement and reliability with DEXA measurements. In the absence of this method, BIA can replace the DEXA technique for body composition assessment.

Keywords:

Interstitial lung disease. Appendicular skeletal muscle mass. Body composition. Fat mass.

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Artificial intelligence: the authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

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Resumen

Introducción: los cambios en la composición corporal son comunes en la enfermedad pulmonar intersticial, lo cual incrementa el riesgo de complicaciones e infecciones, además de asociarse a peor calidad de vida y peores desenlaces clínicos. La evaluación de la composición corporal es importante para identificar la desnutrición y la sarcopenia, sin embargo, las técnicas consideradas "estándar de oro" no se encuentran disponibles en todos los entornos clínicos.

Objetivo: este estudio tiene por objetivo evaluar la validez y concordancia de los parámetros de composición corporal obtenidos por análisis de bioimpedancia eléctrica (BIA) en comparación con la técnica de absorciometría de rayos X de doble energía (DEXA) en mujeres con enfermedad pulmonar intersticial.

Métodos: estudio transversal donde se midió la composición corporal (masa grasa y masa muscular apendicular esquelética) utilizando un equipo de bioimpedancia eléctrica multifrecuencia y DEXA en condiciones estandarizadas. Se evaluó la concordancia y validez entre las técnicas utilizando gráficos Bland-Altman y el coeficiente de correlación intraclase (CCI).

Resultados: se evaluaron un total de 50 mujeres. No se observaron diferencias en los valores de masa grasa (BIA: 25,8 ± 10,2 kg y DEXA: 26,3 ± 10,0 kg, $p = 0,77$), ni en los de masa muscular apendicular esquelética (BIA: 14,1 ± 2,7 kg y DEXA: 13,9 ± 2,3 kg, $p = 0,83$). Acorde a los valores del CCI, se observa una validez buena para los valores de masa grasa (CCI: 0,98) y de masa muscular apendicular esquelética (CCI: 0,93).

Conclusión: la composición corporal estimada por BIA muestra una buena concordancia y validez con el resultado obtenido por DEXA en mujeres con enfermedad pulmonar intersticial. En ausencia de este método, la BIA puede utilizarse para la valoración de la composición corporal en este grupo de pacientes.

Palabras clave:

Enfermedad pulmonar intersticial. Masa muscular apendicular esquelética. Composición corporal. Masa grasa.

INTRODUCTION

Interstitial lung diseases (ILD) are a heterogeneous group of pulmonary disorders characterized by various degrees of inflammation and/or fibrosis that are characterized by dyspnea, increased metabolic requirements, depression, and anxiety (1,2). These symptoms, in addition to the use of certain drugs such as corticosteroids and immunosuppressives agents, are associated with vomiting, diarrhea, nausea, anorexia, and dysgeusia (3). Due to these complications, changes in body composition (BC) are common in this population (4), which leads to an increased risk of complications and infections, and are associated with poor quality of life (5) and predicts hospitalization (6). Additionally, fat mass (FM), fat-free mass (FFM, includes lean soft tissue and bone mineral density), and appendicular skeletal muscle mass (ASMM, includes lean soft tissue in legs and arms) were associated with diverse outcomes such as exercise capacity, disease severity (7,8), and increased mortality (9-11). In chronic obstructive pulmonary disease (COPD) patients, low muscle mass and sarcopenia is associated with reduced FEV_1 (12).

Dual-energy X-ray absorptiometry (DEXA) is considered a gold standard for BC assessment, but this method is expensive and not available in all clinical settings (13). Bioelectric impedance analysis (BIA) estimates the FM and FFM through the resistance and reactance measurement (14) and has been proposed as a safe and low-cost alternative (13). Accuracy between both methods was studied in cystic fibrosis, breast cancer, heart failure, and liver disease (15-19) populations and reports high variability between techniques using mono-frequency or multi-frequency BIA devices. There is a lack of evidence about BC assessment using BIA multifrequency and their agreement with DEXA in the ILD population.

This study aimed to evaluate the agreement and reliability of body composition estimated by BIA and DEXA in women with ILD.

METHODS

STUDY POPULATION

This is a cross-sectional analysis from an institutional cohort of women patients with ILD in the Institute of Respiratory Diseases (INER) diagnosed according to the American Thoracic Society/European Respiratory Society (ATS/ERS) 2013 guidelines (1). This study protocol was reviewed and approved by the Institutional Review Board of the National Institute of Respiratory Diseases.

DATA COLLECTION

Demographic and clinical information, including age and drug prescription, were collected from patient records.

BODY COMPOSITION ASSESSMENT

Patients were instructed to wear lightweight clothing and to avoid food intake 8 h previous to DEXA and BIA scans. Previous procedures, participants removed all metal jewelry from the body. Once removed, body weight and height were measured (SECA 769, Germany). Body mass index (BMI) was calculated and classified using World Health Organization criteria (14). Height and weight measurements were inputted into the BIA and DEXA devices.

DEXA measurements were made using a total-body scanner (Lunar Prodigy Advance, GE Healthcare, UK) with the participant in the supine position according to manufacturer recommendations. System quality assurance protocols were performed daily by the manufacturer's instructions. Regional lean mass, total- FM in kilograms, and percentage were calculated using enCORE 2010 software using scan modes

(thick, standard, or thin) suggested by the software. At the end of the scan, all BC analyses were thoroughly checked for random measurement errors (i.e., regions of interest errors or metal artifacts) and were manually adjusted for the region of interest for regional BC estimations (arms, legs, and trunk). All scans were performed by a single certified technician to decrease the potential introduction of interoperator differences. ASMM was calculated as the sum of the lean mass in the legs and arms.

BIA was performed with the patient in a supine position after the DEXA scan using a multi-frequency device (InBody S10®, InBody Co., Ltd., Seoul, Korea) according to the manufacturer's guidelines. This instrument uses eight tactile electrodes, with four in contact with the palm and thumb of both hands and the other four in contact with the anterior and posterior aspects of the sole of both feet. A total of 30 impedance measurements are obtained using 6 different frequencies (1 kHz, 5 kHz, 50 kHz, 250 kHz, 500 kHz, 1000 kHz) at the 5 following segments of the body: right and left arms, trunk, right and left legs. Data output (phase angle-PhA-, ASMM, and FM), as calculated by using the manufacturer's algorithm, were recorded from the machine output.

STATISTICAL ANALYSIS

Data analysis was performed using the Stata V14 software package. Normality was evaluated with the Shapiro-Wilk test. Data are expressed as means and standard deviations (SD) or median and interquartile range (IQR). A Bland Altman analysis was performed to evaluate the agreement of both methods (DEXA and BIA), including an analysis with the Student's *t*-test for the means to assess the differences in the real and estimated measurements compared with zero. Intraclass correlation coefficient (ICC) was evaluated, which calculates reliability between the body composition estimated by BIA and the measured by DEXA. Reliability was defined as good (> 0.75), moderate (0.5 to 0.75), and poor (< 0.5). A posteriori power analysis for the sample was performed and showed that the analyzed sample size is sufficient to detect a correlation > 0.90 between methods with a power of 80 %. A significance level of $p < 0.05$ was set.

RESULTS

Fifty women with ILD diagnosis were included, 58 % of cases were secondary to autoimmune disease; all patients were receiving immunosuppressant treatment (mycophenolate mofetil or azathioprine), some with steroids or nintedanib. The mean age was 60.8 ± 11 years (minimum 27, maximum 83 years).

The phase angle for the total sample was 5.2 ± 0.9°. Demographic characteristics are summarized in table I.

According to the BMI, 30 % of the sample had overweight and 32 % obesity. No statistical differences were observed for BC results between both techniques. BIA underestimates FM (25.8 ± 10.2 kg) in comparison to DEXA (26.3 ± 10.0 kg) without statistical significance ($p = 0.77$) (Table II). Oppositely, ASMM was overestimated (14.1 ± 2.7 kg) by BIA vs DEXA (13.9 ± 2.3) ($p = 0.83$). Based on ICC, good reliability was observed for FM (ICC, 0.98) and ASMM (ICC, 0.93) (Fig. 1).

Table I. Demographic, nutritional and pulmonary functional characteristics

	***n* = 50**
Age, years	61 ± 11
Diagnosis, n (%)	
Hypersensitivity pneumonitis	21 (42)
Interstitial lung disease secondary to autoimmune disease	29 (58)
Treatment, n (%)	
AZA	2 (4)
MMF	13 (26)
MMF + prednisone	25 (50)
MMF + nintedanib	3 (6)
MMF + nintedanib + prednisone	4 (8)
MMF + MTX + prednisone	1 (2)
MTX + AZA + prednisone	1 (2)
MTX + prednisone	1 (2)
Body composition	
Body mass index	
< 18.5 kg/m^2	3 (6 %)
18.5-24.9 kg/m^2	16 (32 %)
25-29.9 kg/m^2	15 (30 %)
> 30 kg/m^2	16 (32 %)
Weight (kg)	61.1 ± 14.1
Phase angle (°)	5.2 ± 0.9
Fat mass (kg)	
DEXA	26.3 ± 10.0
BIA	25.8 ± 10.2
Fat free mass (kg)	
BIA	35.2 ± 5.1
Appendicular skeletal muscle mass (kg)	
DEXA	13.9 ± 2.3
BIA	14.1 ± 2.7

AZA: azathioprine; MMF: mycophenolate mofetil; MTX: methotrexate. Mean ± standard deviation.

Table II. Agreement between the estimated and measured fat mass and appendicular skeletal muscle mass in patients with interstitial lung disease

	Bland-Altman*	95 % CI	t-test	ICC
ASMM kg	0.19	-1.59 to 1.89	0.77	0.93
FM kg	-0.41	-3.4 to 2.58	0.83	0.98

*CI: confidence interval; ICC: intraclass correlation coefficient; ASMM: appendicular skeletal muscle mass; FM: fat mass. *Analysis of differences (estimated body composition by BIA – body composition by DEXA).*

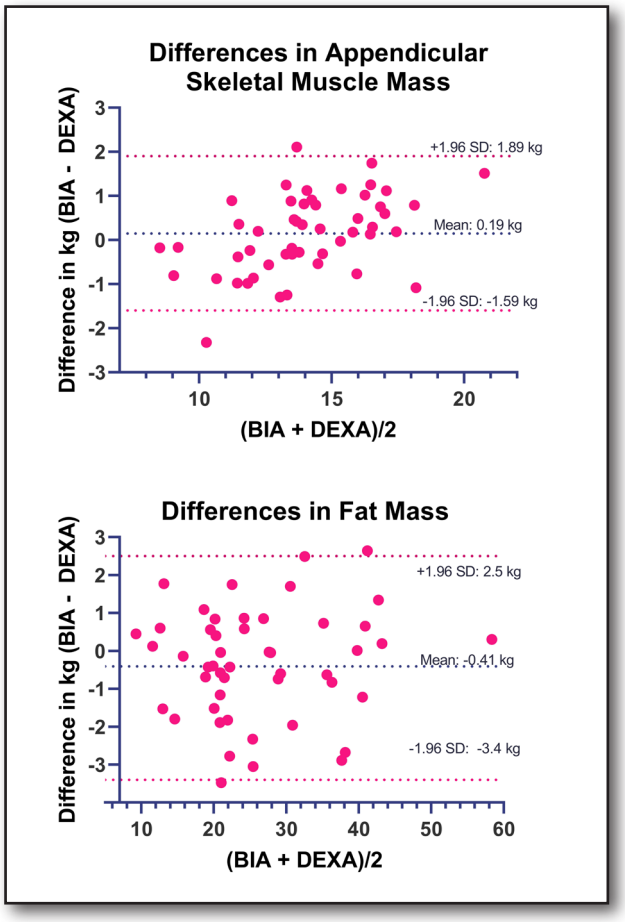

Figure 1.

Bland-Altman plots for differences in appendicular skeletal muscle mass and fat mass between BIA and DEXA.

DISCUSSION

In this sample of outpatient women with ILD, BC assessment using BIA shows good agreement and reliability for ASMM (mean difference of 0.19 kg and ICC = 0.93) and FM (mean difference of -0.41 kg and ICC = 0.98).

A study conducted by McLester in a healthy population found an underestimation of FM percentage and an overestimation of FFM using BIA in comparison to DEXA (20). Discrepancy data were reported in clinical populations; in cystic fibrosis patients, Ziai et al. found that BIA underestimated FM (-10.2 %) and overestimated FFM (8.04 %) (16). Grover et al report a good agreement between DEXA and BIA for FM (mean difference BIA-DEXA = 1.18, 95 % CI: 0.54 to 1.81 kg) and FFM (mean difference BIA-DEXA = -1.16, 95 % CI: -2.21 to -1.11 kg) assessment in patients with cirrhosis (15). Both suggested that BIA can be used for monitoring purposes but, for an accurate measurement of BC, DEXA is an irreplaceable tool. Shah et al. found differences in measurements between DEXA and BIA techniques in patients with heart disease, where BIA underestimates FM (mean difference BIA-DEXA = -5.1, 95 % CI: -11.7 to 1.5 kg) and overestimates lean mass (mean difference BIA-DEXA = 5.5, 95 % CI: -1.3 to 12.3 kg) (19). Saito et al. report a low agreement between BIA and DEXA for ASMM (mean difference = -1.19, 95 % CI: -1.47 to -0.91) in heart failure hospitalized patients, and poor agreement in diagnosing low ASMM (Cohen's kappa coefficient: 0.294, 95 % CI: 0.17 to 0.42) (17). In patients with breast cancer, Bell et al. found that BIA overestimated FFM (mean difference BIA-DEXA 4.1 ± 3.4 kg) using DEXA as the gold standard (18). The clinical characteristics of this study are different from those of ILD patients, which can explain the differences in agreement and reliability observed in our sample. Considering these results, an assessment of agreement and concordance of BIA with gold-standard methods is recommended before the incorporation of this technique into routine clinical care and nutritional monitoring.

Our study compared ASMM and FM measured by BIA and DEXA in patients with ILD. ASMM could be a better indicator than FFM when BIA is applied. In women with ILD, BIA can replace DEXA to estimate ASMM and FM to assess and monitor nutritional status and to identify patients who should benefit from a nutritional intervention. However, some factors can affect the accuracy of BC results such obesity, edema, pleural effusion, or chronic kidney disease (21).

PhA derived from BIA is another nutritional marker that is related to poor quality of body mass cells and cell membrane integrity (22). During a pro-inflammatory state, PhA responds over the lower capacitance of damaged cell membranes. This indicator was studied in other clinical conditions, such as cirrhosis (23), chronic kidney disease (24), or COPD (12). In the ILD context, it could be used as a biomarker of higher degrees of inflammation (22); however, more studies were needed to assess the validity and associations of PhA with other clinical outcomes in men and woman with ILD.

The limitations of this study consist of the number of participants, as they were only fifty women, so it makes it difficult to extrapolate our results to all women and the male population with ILD. Additionally, this study was conducted in a heterogenous sample, and inflammation status was not assessed; it may be an opportunity to consider future research on inflammation biomarkers to correlate with BC.

CONCLUSION

Body composition estimated by BIA showed good agreement and reliability with DEXA measurements. In the absence of this method, BIA can replace the DEXA technique for body composition assessment in women with interstitial lung disease.

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ARÁN

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Trabajo Original

Valoración nutricional

Symptom clusters and nutritional status in primary liver cancer patients receiving transcatheter arterial chemoembolization

Grupos de síntomas y estado nutricional en pacientes con cáncer hepático primario que reciben quimioembolización arterial transcatéter

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Abstract

Introduction: symptom clusters (SCs) are highly prevalent among patients diagnosed with primary liver cancer. Malnutrition poses a heightened risk for a more pronounced total symptom cluster score.

Objective: this study aimed to identify SCs and assess the nutritional status of patients undergoing transcatheter arterial chemoembolization (TACE). Furthermore, it aimed to investigate the association between nutritional status and symptom clusters.

Methods: primary liver cancer patients who were scheduled to receive TACE were recruited. Symptoms data were collected using the MD Anderson Symptom Inventory (MDASI-C) and the Symptom Module specific to Primary Cancer (TSM-PLC). Nutritional assessment relied on the Nutritional Risk Screening-2002 (NRS-2002) and blood biochemistry. The SCs were extracted using exploratory factor analysis, while the relationship between SCs and nutritional status was evaluated using Spearman correlation analysis.

Results: the study included 226 patients, four distinct symptom clusters emerged: emotional-psychological symptom cluster, upper gastrointestinal symptom cluster, post-embolization-related symptom cluster, and liver function impairment symptom cluster. 68.14 % of patients were found to be at high risk of malnutrition. Our study revealed significant differences in Scs scores between patients at risk of malnutrition and those without such risk ($p < 0.050$). Notably, we observed a positive correlation between NRS-2002 scores and the scores of all symptom clusters ($r = 0.205$ to 0.419, $p < 0.001$), while a negative correlation was observed between prealbumin levels and the scores of all symptom clusters ($r = -0.183$ to -0.454, $p < 0.001$).

Conclusion: the study highlights the high risk of malnutrition among liver cancer patients receiving TACE and the positive correlation between high malnutrition risk and Scs scores.

Keywords:

Primary liver cancer. Transcatheter arterial chemoembolization (TACE). Symptom cluster. Exploratory factor analysis. Malnutrition.

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Resumen

Introducción: los grupos de síntomas (SC, por sus siglas en inglés) son altamente prevalentes entre los pacientes diagnosticados de cáncer primario de hígado. La desnutrición aumenta el riesgo de que la puntuación total de los grupos de síntomas sea más pronunciada.

Objetivo: este estudio estaba dirigido a identificar los SC y a evaluar el estado nutricional de los pacientes sometidos a quimioembolización arterial transcatéter (TACE, por sus siglas en inglés). Adicionalmente, estaba dirigido a investigar la asociación entre el estado nutricional y los grupos de síntomas.

Métodos: se reclutaron pacientes con cáncer primario de hígado que tenían programado recibir TACE. Los datos de los síntomas se recolectaron mediante el Inventario de síntomas del MD Anderson (MDASI-C) y el Módulo de síntomas específicos del cáncer primario (TSM-PLC). La evaluación nutricional se basó en el cribado de riesgo nutricional 2002 (NRS-2002) y la bioquímica sanguínea. Los SC se extrajeron mediante un análisis factorial exploratorio, mientras que la relación entre los SC y el estado nutricional se evaluó mediante un análisis de correlación de Spearman.

Resultados: el estudio incluyó 226 pacientes, de los cuales surgieron cuatro grupos de síntomas distintos: grupo de síntomas emocionales-psicológicos, grupo de síntomas gastrointestinales superiores, grupo de síntomas relacionados con la postembolización y grupo de síntomas de deterioro de la función hepática. El 68,14 % de los pacientes presentaban un alto riesgo de desnutrición. Nuestro estudio reveló diferencias significativas en las puntuaciones de los SC entre los pacientes con riesgo de desnutrición y aquellos sin dicho riesgo ($p < 0,050$). En particular, observamos una correlación positiva entre las puntuaciones del NRS-2002 y las puntuaciones de todos los grupos de síntomas (r = 0,205 a 0,419, $p < 0,001$), mientras que se observó una correlación negativa entre los niveles de prealbúmina y las puntuaciones de todos los grupos de síntomas (r = -0,183 a -0,454, $p < 0,001$).

Conclusión: el estudio destaca el alto riesgo de desnutrición entre los pacientes con cáncer de hígado que reciben TACE y la correlación positiva entre el alto riesgo de desnutrición y las puntuaciones de los SC.

Palabras clave:

Cáncer primario de hígado. Quimioembolización arterial transcatéter (TACE). Grupo de síntomas. Análisis factorial exploratorio. Desnutrición.

INTRODUCTION

Liver cancer is currently the sixth most prevalent malignancy globally and ranks as the third leading cause of cancer-related mortality (1). Projections indicate that the number of new liver cancer cases and associated fatalities will surge by over 50 % in the next two decades (2). In China, liver cancer ranks as the 4th most common cancer type and the second leading cause of cancer-related deaths, posing a significant threat to public health and well-being (3).

The primary approach for treating early-stage primary liver cancer includes resection, transplantation, and local ablation; however, early detection is possible for only approximately 30 % of patients (4). TACE is the preferred treatment for unresectable patients with intermediate to advanced disease (5). Given the multivessel, multifocal, and highly recurrent nature of primary liver cancer, multiple TACE treatments are often required (6). Research indicates that patients undergoing TACE often experience a spectrum of symptoms attributable to both the primary disease and the treatments they receive (7,8).

Many patients concurrently suffer from a cluster of symptoms, termed a "symptom cluster" (SC). This term denotes the occurrence of two or more interrelated symptoms that manifest together and have synergistic effects on patients (9). Such clusters can have more adverse effects than individual symptoms, impacting patients' quality of life and overall survival. The study of symptom clusters is currently considered a promising area within the field of symptom research (10). Numerous studies have investigated symptom clusters in patients with various cancer types, such as lung cancer (11-13), breast cancer (14,15), and gastrointestinal cancer (16,17). Despite liver cancer's prevalence, there is a limited understanding of symptom clusters in patients undergoing TACE. A recent qualitative study by Liang Fu et al. on liver cancer patients revealed that diagnosis significantly impacts their daily life and health, highlighting three key themes.

Patients receiving TACE treatment for liver cancer often experience concurrent liver dysfunction and cirrhosis, leading to abnormal nutritional metabolism, inadequate nutrient intake, digestive and absorption disorders, and compromised protein synthesis. Therefore, varying degrees of malnutrition may occur (18). Numerous studies have reported that malnutrition can adversely affect cancer patients' quality of life and increase the incidence of complications. For instance, Sánchez et al.'s study indicated an association between malnutrition and the presentation of anxious and depressive symptoms in cancer patients (19). Guo et al. reported that malnutrition is common among gastric cancer patients and significantly impacts their quality of life (20). To our knowledge, few studies have investigated the correlation between nutritional status and symptom clusters experienced by primary liver cancer patients undergoing TACE treatment.

This study aimed to examine the frequency and severity of symptoms, as well as the nutritional status of liver cancer patients undergoing TACE. It also identified symptom clusters and explored their correlation with nutritional status.

METHODS

PATIENTS AND SETTINGS

The Ethics Committee of our university approved this study under the approval code No. JNU20221201IRB39. This analysis represents a cross-sectional observational study. For principal component analysis, approximately 10 patients were needed for each variable (21). Consequently, the desired sample size was 190 patients, as both the MDASI-C and TSM-PLC questionnaires consist of 19 symptoms. Between June 2022 and March 2023, we recruited 230 liver cancer patients who were undergoing TACE. Inclusion criteria were as follows: 1) Child-Pugh class was A or B; 2) ≥ 18 years; 3) clear consciousness, normal comprehension, and language expression function; and 4) provision of informed consent. Patients with severely impaired vital organ function or involvement in oth-

er clinical trials that could interfere with symptom assessment were excluded from this study. Three patients withdrew from the study due to exhaustion and difficulty understanding the questionnaires, while one died from upper gastrointestinal bleeding. Ultimately, 226 patients were enrolled in the study.

ASSESSMENT OF SYMPTOMS

MDASI-C

The MDASI is a self-assessment tool for cancer patients developed by the University of Texas Anderson Cancer Center (22) and translated into Chinese by Wang et al. in 2004 (23). This tool comprises two parts: the first part primarily assesses the severity of 13 common cancer-related symptoms, including pain, nausea, vomiting, and fatigue, while the second part assesses the impact of these symptoms on six aspects of daily life: activities, work, mood, walking, relationships with others, and life joy. The 19 items are rated on a numerical scale from "0" (no symptoms) to "10" (worst imaginable). For this study, we focused on the first section of the questionnaire.

TSM-PLC

The TSM-PLC is a symptom checklist specifically designed for primary liver cancer patients. This list includes six common symptoms experienced by liver cancer patients, such as abdominal distension, itching, and jaundice (24). The six items are rated using the same format as the first part of the MDASI, ranging from 0 to 10.

ASSESSMENT OF NUTRITIONAL STATUS

The Nutritional Risk Screening-2002 (NRS-2002) was utilized to assess nutritional risk (25). The NRS-2002 evaluates nutritional status in three sections: First, it considers unconscious weight loss and food intake; second, it assesses increases in daily calorie intake related to disease occurrence and treatment type; finally, it adds an age score. The total score ranges from 0 to 7, with a NRS2002 score of 3 or higher indicating a high nutritional risk (26).

Fasting blood samples for the assessment of albumin (ALB), prealbumin (pre-ALB), total protein (TP), hemoglobin, and lymphocyte (LYM) were collected within 24 hours of the patient's admission to the hospital. Laboratory data were measured using standard laboratory methods.

PROCEDURES

The NRS-2002, a validated nutrition assessment tool, was assessed by researchers within 24 hours of admission to the hospital. The MDASI-C and TSM-PLC questionnaires were completed by the patients 72 hours after TACE. For patients unable to write, an investigator read and marked their answers, which were subsequently reviewed by researchers to ensure accuracy.

Body weight and height were measured without shoes, and the body mass index (BMI) was calculated by dividing weight by the square of height.

Clinical information including age, sex, BMI, diagnosis duration, BCLC stage, and systemic comorbidities, was extracted from hospital records.

STATISTICAL ANALYSIS

Data were analyzed using SPSS statistical software. (IBM SPSS Statistics, Version 26.0). Descriptive statistics and frequency distributions were used to calculate demographic information, clinical data, symptom prevalence, nutritional status, and summary statistics.

Principal Component Analysis (PCA) with varimax rotation was employed to investigate the interrelationships among symptoms and identify symptom clusters. Following the approach of Kim et al. uncommon symptoms (prevalence < 20 %) were excluded from the analyses to ensure the accurate representation of key cluster symptoms (9). The selection of factors was based on specific criteria, including a factor eigenvalue > 1, symptom factor loadings > 0.5, and at least two items loading (21). The internal consistency and reliability of the derived clusters were assessed using Cronbach's alpha. Factors (symptom clusters) were named based on the predominant symptom in each cluster. Spearman's correlations were used to investigate the relationship between nutritional status and the scores of symptom clusters. The score for a symptom cluster was obtained by averaging the scores of all individual symptoms within that cluster. The T-test was used to compare the mean symptom cluster scores between patients with and without nutritional risk, while Wilcoxon rank-sum tests were used to analyze variables with skewed distributions. A significance threshold of $p < 0.05$ was set for all analyses.

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

A total of 226 primary liver cancer patients were enrolled in this study, with 191 males and 35 females, representing 95.46 % of married individuals. The average age of participants was 60.16 years (SD = 10.47; 34-87). Among them, 182 cases (80.53 %) had completed junior high school education or higher, 138 cases (61.06 %) were diagnosed within 12 months, and 68.14 % of patients were considered at risk of malnutrition. Table I presents a comprehensive summary of demographic and medical details.

SYMPTOM FREQUENCY AND SEVERITY SCORES

Symptom prevalence ranged from 3.98 % to 93.69 %. The five most common symptoms were fatigue in 211 patients (93.69 %), drowsiness in 197 (87.16 %), sleep disturbance in 195 (86.28 %),

distress in 191 (84.51 %), and sadness in 182 cases (80.53 %). The five symptoms with the highest severity scores were fatigue (5.07 ± 2.03), sleep disturbance (5.00 ± 2.65), pain (4.35 ± 3.52), fever (4.01 ± 3.85), and lack of appetite (3.86 ± 2.44) (Table II).

Table I. Sample demographic and clinical characteristics (n = 226)

Variable	*n*	%
Sex		
Male	191	84.51
Female	35	15.49
Age (years)		
< 65	126	55.75
≥ 65	100	44.25
Education level		
Primary school or below	44	19.47
Junior high	123	54.42
Senior high	48	21.24
University or above	11	4.87
Occupation status		
Unemployed or retired	203	89.82
Employed	23	10.18
Marital status		
Single	8	3.54
Married	218	96.46
Time since diagnosis		
≤ 12 m	138	61.06
> 12 m	88	38.94
Stage (BCLC)		
A	14	6.19
B	160	70.80
C	52	23.01
Child-Pugh class		
A	175	77.43
B	51	22.57
Nutritional risk		
No nutritional risk (< 3 points)	72	31.86
Nutritional risk (≥ 3 points)	154	68.14
Body mass index		
Low	27	11.95
Normal	160	70.80
High	39	17.26
Hypertension	82	36.28
Diabetes	48	21.24

Normal body mass index = 18.5-23.9.

Table II. Prevalence and severity of symptoms (n = 226)

Symptom	Prevalence *n* (%)	Rank order	Severity Mean (SD)	Rank order
Fatigue	211 (93.69)	1	5.07 (2.03)	1
Distress	191 (84.51)	4	3.78 (1.99)	6
Sadness	182 (80.53)	5	3.32 (1.98)	8
Sleep disturbance	195 (86.28)	3	5.00 (2.64)	2
Lack of appetite	178 (78.76)	6	3.86 (2.44)	5
Dry mouth	159 (70.35)	10	2.88 (2.06)	11
Pain	160 (70.80)	9	4.35 (3.51)	3
Nausea	133 (58.84)	11	3.31 (3.28)	9
Vomiting	126 (55.75)	13	2.83 (2.95)	12
Shortness of breath	35 (15.48)	16	0.62 (1.56)	16
Impaired memory	30 (13.27)	18	0.38 (1.07)	18
Drowsiness	197 (87.16)	2	3.49 (1.69)	7
Numbness	9 (3.98)	19	0.12 (0.60)	19
Abdominal distension	175 (77.43)	7	3.27 (2.11)	10
Diarrhea	34 (15.04)	17	0.59 (1.52)	17
Weight loss	163 (72.12)	8	2.48 (1.88)	13
Jaundice	72 (31.86)	15	1.25 (1.91)	15
Itch	74 (32.74)	14	1.31 (1.95)	14
Fever	133 (58.84)	11	4.01 (3.85)	4

SD: standard deviation.

SYMPTOM CLUSTERING BASED ON SYMPTOM OCCURRENCE

Principal component analysis with varimax rotation was utilized for an exploratory factor analysis. In this study, the KMO measure yielded a value of 0.808, and Bartlett's test of sphericity was < 0.001. After TACE, symptoms with a prevalence of < 20 %, including diarrhea, numbness, shortness of breath, and memory problems were excluded. The remaining 15 symptoms were subjected to principal component analysis, resulting in the identification of four clusters: the emotional-psychological symptom cluster (Cluster 1) included sadness, distress, drowsiness, sleep disturbance, and fatigue; the upper gastrointestinal symptom cluster (Cluster 2) included nausea, vomiting, lack of appetite, and weight loss; the post-embolization-related symptom cluster (Cluster 3) included pain, fever, dry mouth, and abdominal distension; the symptom cluster of liver function impairment (Cluster 4) included jaundice and itch. These four factors collectively explained 71.77 % of the overall variance. With internal consistency Cronbach's alpha coefficient was highest for Cluster 2 (0.884), followed by Cluster 4 (0.857), Cluster 1 (0.843) and cluster 3 (0.781) (Table III).

NUTRITIONAL STATUS IN PATIENTS

A total of 72 patients (31.86 %) had NRS-2002 scores < 3, while 154 (68.14 %) had scores ≥ 3. Significant differences were observed in hemoglobin, albumin, prealbumin, and lymphocyte values between both groups ($p < 0.050$, $p < 0.001$) (Table IV).

As shown in table V, the incidence rate of nutrition risk demonstrated statistically significant differences in Child-Pugh classification of liver function, BCLC stage, BMI, and elderly patients ($p < 0.001$). However, no significant differences were observed in terms of sex, hypertension, and diabetes ($p > 0.050$).

Table III. Factor loadings from the principal component analysis of symptoms (n = 226)

Symptoms	Cluster 1	Cluster 2	Cluster 3	Cluster 4	Final communality
Sadness	*0.817*	0.177	0.106	0.079	0.715
Distress	*0.793*	0.143	0.171	0.103	0.689
Drowsiness	*0.744*	0.142	0.142	-0.062	0.598
Sleep disturbance	*0.731*	0.144	0.204	-0.061	0.601
Fatigue	*0.617*	0.383	0.200	0.110	0.579
Nausea	0.117	*0.888*	0.253	-0.042	0.867
Vomiting	0.096	*0.876*	0.270	-0.069	0.855
Lack of appetite	0.442	*0.719*	0.179	0.020	0.745
Weight loss	0.399	*0.723*	0.092	0.070	0.696
Fever	0.075	0.162	*0.853*	0.063	0.763
Abdominal distension	0.302	0.171	*0.753*	0.083	0.694
Dry mouth	0.142	0.172	*0.791*	0.051	0.678
Pain	0.353	0.307	*0.571*	-0.049	0.547
Jaundice	0.060	-0.023	0.105	*0.922*	0.866
Itch	0.010	-0.003	0.017	*0.933*	0.871
% of variance	22.59	20.10	17.18	11.91	
Cronbach's alpha	0.843	0.884	0.781	0.857	

Bold-typeface values indicate the specific symptoms within each of the symptom clusters.
The four symptoms that did not meet our specific criterion for inclusion in the exploratory factor analyses were shortness of breath, impaired memory, numbness, and diarrhea.

Table IV. Comparison of blood biochemical indexes between the two groups

Variable	NRS-2002 score (1~2) *M (P25-P75)*	NRS-2002 score (≥ 3) *M (P25-P75)*	Wilcoxon signed-ranks test Z	*p*
Hemoglobin (g/L)	139.50 (124.25, 151.00)	117.00 (103.75, 132.00)	-6.472	0.000
Total protein (g/L)	68.50 (64.90, 71.53)	67.10 (63.08, 72.03)	-1.316	0.188
Serum albumin (g/L)	39.20 (36.90, 41.68)	34.15 (30.70, 37.30)	-7.778	0.000
Serum prealbumin (mg/L)	179.20 (155.50, 212.88)	115.60 (85.48, 166.13)	-6.905	0.000
Lymphocytes	1.20 (0.90, 1.60)	1.00 (0.70, 1.30)	-2.546	0.011
BMI (kg/m^2)	24.37 (22.50, 25.89)	20.61 (18.98, 22.72)	-8.054	0.000

BMI: body mass index.

Table V. Difference in clinical characteristics between the two groups

Variable	NRS-2002		χ^2/Z	*p*-value
	1-2 *n* = 72	≥ 3 *n* = 154		
Sex (%)				
Female	10 (28.57)	25 (71.42)	0.206	0.650
Male	62 (32.46)	129 (67.54)		
Age (years) (%)				
< 65	54 (42.86)	72 (57.14)	15.868	< 0.001
≥ 65	18 (18.00)	82 (82.00)		
Child-Pugh stage (%)				
A	67 (38.28)	108 (61.71)	14.757	< 0.001
B	5 (9.80)	46 (90.20)		
BCLC stage (%)				
A	7 (50.00)	7 (50.00)	16.319	< 0.001
B	60 (37.50)	100 (62.50)		
C	5 (9.62)	47 (90.38)		
Hypertension (yes, %)	31 (38.27)	51 (62.96)	2.096	0.148
Diabetes (yes, %)	17 (35.42)	31 (64.58)	0.355	0.551
BMI *M (P25-P75)*	24.37 (22.50, 25.89)	20.61 (18.98, 22.72)	-8.054	0.000

NRS-2002: Nutritional Risk Screening 2002.

CORRELATIONS BETWEEN SYMPTOM CLUSTERS AND NUTRITIONAL INDICATORS

The scores of symptom clusters exhibited significant variations by the NRS-2002 score ($p < 0.001$, $p < 0.05$) (Table VI).

As shown in table VII, symptom cluster scores displayed a significant positive correlation with NRS-2002 scores (r = -0.234 to -0.453, $p < 0.001$). Prealbumin was negatively correlated with all scores of symptom clusters (r = -0.183 to -0.454, $p < 0.001$), while hemoglobin and lymphocyte counts were negatively correlated with the emotional-psychological symptom cluster's score (r = -0.180 to -0.255, $p < 0.001$). BMI exhibited a negative correlation with both the emotional-psychological and upper gastrointestinal symptom cluster scores (r = -0.234 to -0.287, $p < 0.001$).

Table VI. Comparison of symptom cluster scores for two groups (*n* = 226)

SC	NRS-2002		Wilcoxon signed-ranks test Z
	1-2 *M (P25-P75)*	≥ 3 *M (P25-P75)*	
Emotional-psychological SC	15.50 (8.25, 19.75)	24.00 (20.00, 28.00)	-7.559†
Upper gastrointestinal SC	3.50 (0.00, 11.00)	15.00 (9.00, 22.00)	-7.101†
Post-embolization-related SC	6.00 (0.00, 15.50)	20.00 (11.75, 24.00)	-7.071†
Liver function impairment SC	0.00 (0.00, 2.00)	0.00 (0.00, 8.00)	-2.979*

*SC: symptom cluster; NRS-2002: Nutritional Risk Screening 2002. *p < 0.050; †p < 0.001.*

Table VII. Correlations between symptom clusters and each nutritional indicator (*n* = 226)

Symptom clusters	BMI	NRS-2002	Albumin	Prealbumin	Hemoglobin	Lymphocytes
Emotional-psychological SC	-0.234†	0.453†	-0.242†	-0.284†	-0.255†	-0.180†
Upper gastrointestinal SC	-0.287†	0.399†	-0.184†	-0.183†	-0.157*	-0.115
Post-embolization-related SC	-0.141*	0.438†	-0.241†	-0.277†	-0.153*	-0.082
Liver function impairment SC	-0.092	0.234†	-0.320†	-0.454†	-0.158*	-0.111

*SC: symptom cluster; NRS-2002: Nutritional Risk Screening 2002. *p < 0.050; †p < 0.001*

DISCUSSION

SYMPTOM BURDEN AND NUTRITIONAL STATUS

This study reveals that patients undergoing TACE simultaneously experience a range of symptoms, including clinical concerns such as pain and vomiting. Additionally, it sheds light on often-neglected symptoms like fatigue, drowsiness, sleep disturbance, distress, and sadness. Fatigue, in particular, emerged as the most prevalent and severe symptom, aligning with prior research findings (27,28). However, compared to Cao's study (27), our study observed a slightly lower incidence of nausea and vomiting, which could be attributed to the use of antiemetic drugs during TACE procedures.

Notably, prior studies have reported malnutrition rates of 34-45.3 % in patients with various cancers, such as lung, leukemia, and nasopharyngeal cancer (29,30). In our study, 68.14 % of primary liver cancer patients receiving TACE were identified as at high risk of malnutrition. Managing malnutrition in at-risk patients involves a comprehensive approach that includes nutritional status assessment, dietary counseling, oral nutritional supplements (ONS), enteral nutrition (EN), and parenteral nutrition (PN). The high prevalence of malnutrition may be linked to poor liver function or post-embolization syndrome (PES) or with advanced stage of liver cancer in our patient population (31). Previous studies have discussed the nutritional treatment of patients with malnutrition and the impact of malnutrition on mental state and quality of life of cancer patients (19,20,32). In contrast, this study focuses on the association between nutritional status and symptom clusters.

SYMPTOM CLUSTERS IN POST-TACE PATIENTS

Research on symptom clusters in patients undergoing TACE for liver cancer is relatively scarce. In contrast, emotional-psychological symptom clusters have been reported in previous studies involving patients with other types of cancer (16,33,34). The unique emphasis on TACE patients in our study reveals that they exhibit the largest explained variance in symptom clusters, a phenomenon unique to liver cancer patients. The absence of a standardized treatment duration for TACE requires frequent hospital visits for evaluations and treatment, which may contribute to this phenomenon. Additionally, the financial burden, physical discomfort, and fear of disease recurrence and death can induce hormonal changes and alter psychological states.

The presence of an upper gastrointestinal symptom cluster has been reported in several previous studies (35,36). While other studies focused on chemotherapy patients, our study was based on patients treated with TACE. The occurrence of post-TACE nausea and vomiting may be attributed to several factors. Firstly, operation trauma and aseptic inflammation during TACE can release various transmitters due to ischemia and hypoxia. Secondly, chemotherapeutic drugs administered during TACE, such as epirubicin and platinum, pose a moderate to high emetic risk. These drugs are injected through the branches of the celiac trunk or superior mesenteric artery, which directly supply the gastrointestinal tract (37).

The post-embolization-related symptom cluster is unique to TACE patients and likely arises from the embolization of tumor blood supply vessels. This leads to ischemia in the vessel's blood supply area, local tissue hypoxia, tumor necrosis, capsule swelling, ectopic embolization, or cytokine release and inflammatory responses (38).

The liver function impairment symptom cluster, including jaundice and pruritus, is a specific symptom cluster associated with liver cancer patients. This observation aligns with Cao's study (27), where these two symptoms were also grouped into a single symptom cluster. Liver dysfunction, caused by chemotherapy and embolization agents mainly staying in the tumor during TACE, can also affect normal liver tissue around the tumor, leading to elevated bilirubin and bile acid levels and resulting in this symptom cluster. Clinicians should prioritize liver function preservation, closely monitor jaundice development, and offer comprehensive skincare guidance.

EFFECTS OF NUTRITION STATUS ON SYMPTOM CLUSTERS

We assessed nutritional status using the NRS-2002 score and blood biochemistry. The results from both NRS-2002 and blood biochemistry were congruent. The NRS-2002 is a valuable tool for identifying early-stage nutritional risk in liver cancer patients with a high nutritional risk. Malnutrition is a prevalent issue among cancer patients. The central findings of this study are twofold: First, a significant difference in symptom cluster scores was observed between patients with normal nutrition and those at risk of malnutrition; second, nutritional status correlated with symptom cluster scores. These findings underscore the widespread malnutrition among liver cancer patients, necessitating follow-up nutrition interventions and support.

LIMITATIONS

The following limitations need to be considered. Firstly, potential bias may exist due to the exclusion of symptoms with low incidence (prevalence < 20 %) . Secondly, this cross-sectional study only suggests a correlation between symptom clusters and nutritional status, necessitating further longitudinal studies to confirm the causal relationship. Thirdly, this study included patients with various TACE regimens and stages, making it challenging to isolate potential confounding factors. This is a single-center with a small sample size, further multi-center and large sample studies are advocated to clarify this correlation.

CONCLUSION

This study highlights a significantly higher prevalence of malnutrition among liver cancer patients undergoing TACE. Additionally, it identifies four distinct symptom clusters and demonstrates the impact of nutritional status on these clusters. Therefore, healthcare providers should prioritize nutritional status assessments and consider early interventions to manage nutritional risk in liver cancer patients during TACE. Future research should explore the implementation of comprehensive in-hospital and home nutrition intervention programs. These programs would provide timely and evidence-based nutritional interventions to enhance patients' tolerance of antitumor therapy and evaluate their effectiveness in improving nutritional status, symptom clusters, and quality of life.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Agreements between the Global Leadership Initiative on Malnutrition using left calf circumference as criterion for reduced muscle mass and the Patient-Generated Subjective Global Assessment, and the Global Leadership Initiative on Malnutrition using the appendicular skeletal muscle index for the diagnosis of malnutrition in gastric cancer patients

Concordancias entre la Iniciativa Global de Liderazgo sobre la Desnutrición utilizando la circunferencia de la pantorrilla izquierda como criterio de masa muscular reducida y la Evaluación Global Subjetiva Generada por el Paciente, y la Iniciativa Global de Liderazgo sobre la Desnutrición utilizando el índice de músculo esquelético apendicular para el diagnóstico de desnutrición en pacientes con cáncer gástrico

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Abstract

Objective: this study aimed to explore the agreements between the Global Leadership Initiative on Malnutrition (GLIM) using left calf circumference (CC) as criterion for reduced muscle mass and the Patient-Generated Subjective Global Assessment (PG-SGA), or GLIM using appendicular skeletal muscle index (ASMI) for the diagnosis of malnutrition in gastric cancer patients.

Methods: the Nutritional Risk Screening 2002 (NRS 2002) was used as nutritional risk screening. PG-SGA and GLIM were applied for malnutrition diagnosis. Agreements were evaluated by Kappa, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and area under the curve (AUC).

Results: a total of 405 gastric cancer patients were included. The values of Kappa, sensitivity, specificity, PPV, NPV, accuracy and AUC were 0.463, 67.9 %, 87.3 %, 92.9 %, 52.8 %, 73.6 % and 0.776, and 0.496, 76.7 %, 78.0 %, 89.4 %, 57.9 %,77.0 % and 0.773, respectively, between GLIM using CC with or without NRS 2002 and PG-SGA. All values of agreement were higher than 0.800 or 80.0 % between GLIM using left CC and GLIM using ASMI.

Conclusion: the agreements were both acceptable between GLIM using left CC and PG-SGA, and GLIM using ASMI. Left calf circumference can be one of the credible references indicating a reduced muscle mass in patients with gastric cancer.

Keywords:

Agreement. GLIM. Calf circumference. PG-SGA. Malnutrition. Gastric cancer.

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Resumen

Objetivo: este estudio tenía como objetivo explorar los acuerdos entre la Iniciativa Global de Liderazgo sobre la Desnutrición (GLIM) utilizando la circunferencia de la pantorrilla izquierda (CC) como criterio de masa muscular reducida y la Evaluación Global Subjetiva Generada por el Paciente (PG-SGA), o la GLIM utilizando el índice de músculo esquelético apendicular (ASMI) para el diagnóstico de desnutrición en pacientes con cáncer gástrico.

Métodos: se utilizó el Cribado de Riesgo Nutricional 2002 (NRS 2002) como cribado de riesgo nutricional. PG-SGA y GLIM se utilizaron para el diagnóstico de desnutrición. Los acuerdos se evaluaron mediante Kappa, sensibilidad, especificidad, valor predictivo positivo (VPP), valor predictivo negativo (VPN), exactitud y área bajo la curva (AUC).

Resultados: se incluyó un total de 405 pacientes con cáncer gástrico. Los valores de Kappa, sensibilidad, especificidad, VPP, VPN, exactitud y AUC fueron de 0,463, 67,9 %, 87,3 %, 92,9 %, 52,8 %, 73,6 % y 0,776, y de 0,496, 76,7 %, 78,0 %, 89,4 %, 57,9 %, 77,0 % y 0,773, respectivamente, entre la GLIM utilizando CC con o sin NRS 2002 y PG-SGA. Todos los valores de concordancia fueron superiores a 0,800 u 80,0 % entre la GLIM utilizando la CC izquierda y la GLIM utilizando el ASMI.

Conclusión: los acuerdos fueron aceptables entre la GLIM utilizando la CC izquierda y la PG-SGA, y la GLIM utilizando el ASMI. La circunferencia de la pantorrilla izquierda puede ser una de las referencias creíbles que indiquen reducción de la masa muscular en los pacientes con cáncer gástrico.

Palabras clave:

Acuerdo. GLIM. Circunferencia de la pantorrilla. PG-SGA. Desnutrición. Cáncer gástrico.

INTRODUCTION

Malnutrition is one of the most common health problems that anyone can face. Cancer patients are one of the groups at highest risk for malnutrition, especially patients with gastric cancer (1,2). The prevalence of malnutrition in gastric cancer patients can be higher than 60 % (1). And the diagnosis of malnutrition in gastric cancer patients may have its own specificity. In addition, malnutrition is also negatively associated with adjuvant chemotherapy compliance, survival, mortality, length of stay, hospitalization costs, and postoperative complications in patients with gastric cancer (3-7). Although it is crucial to perform an accurate diagnosis of malnutrition in cancer patients, there is no gold standard for diagnosing malnutrition to date.

Numerous methods have been developed and applied to the diagnosis of malnutrition in clinical practice and scientific research, such as the Patient-Generated Subjective Global Assessment (PG-SGA), the Subjective Global Assessment (SGA), the European Society of Clinical Nutrition and Metabolism (ESPEN) Consensus Statement, and so on (8-10). However, there has long been no consensus on the diagnosis of malnutrition. In January 2016, the Global Leadership Initiative on Malnutrition (GLIM) was developed under the cooperation of several core global clinical nutrition societies, including ESPEN, the American Society of Parenteral and Enteral Nutrition (ASPEN), the Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismmo (FELANPE) and the Parenteral and Enteral Nutrition Society of Asia (PENSA) (11).

GLIM is a two-step approach. The first step is malnutrition risk screening to identify the "at risk" status by using any validated screening tool. The second step is the diagnosis and severity grading of malnutrition. The diagnosis of malnutrition requires at least one phenotypic criterion and one etiologic criterion. Phenotypic criteria involve weight loss, low body mass index, and reduced muscle mass. Etiologic criteria include reduced food intake or assimilation, and inflammation (11). Several studies have been performed to validate GLIM in practical applications, and its consistency with other diagnostic tools (12,13). However, the operational standards of this process have not yet been fully validated, especially in gastric cancer patients. Some criteria lack clearly defined cut-off values (14), such as the threshold value of calf circumference (CC). Considering the accessibility of assessment tools or equipment, CC is one of the simplest and most effective methods for reduced muscle mass, especially in low- and middle-income countries and in rural areas where the bioelectrical impedance analysis (BIA) or other assessing equipment may be unavailable. In addition, it is not clear how the use and non-use of the screening tool will affect the outcome of the GLIM process.

Considering that the consistency between GLIM and current clinical practice is still unclear in gastric cancer patients, it is crucial to explore the validation of GLIM using left calf circumference as the criterion for reduced muscle mass for malnutrition diagnosis, and the impact of screening tools on the diagnostic performance of GLIM. The PG-SGA was developed by Ottery, and is a nutritional status assessment method initially designed for cancer patients (10). The PG-SGA has been widely used in different patient populations and is known as the "semi-gold standard" for diagnosing malnutrition. As the reference values of appendicular skeletal muscle mass index (ASMI) were suggested in the GLIM consensus, GLIM using ASMI as the criterion for reduced muscle mass was also chosen as the complementary alternative "semi-gold standard" for assessing the validation of GLIM using left calf circumference as the criterion for reduced muscle mass (11). Therefore, the purpose of this study was to investigate agreements between GLIM using left CC as the criterion for reduced muscle mass and PG-SGA, and between GLIM using left CC and GLIM using ASMI for malnutrition diagnosis in patients with gastric cancer, and establish its validation.

MATERIAL AND METHODS

STUDY DESIGN AND PARTICIPANTS

This cross-sectional study was carried out at the Department of Gastrointestinal Surgery, Department of Hepatobiliary and Pancreatic Surgery, and Department of Medical Oncology, Affiliated Jinhua Hospital, Zhejiang University School of Medicine (Jinhua Municipal Central Hospital) from December 2020 to May 2022.

The inclusion criteria were as follows: a) aged 18 years or above; b) gastric cancer was confirmed by pathology; c) Eastern Cooperative Oncology Group Performance Status (ECOG-PS) lower than four; d) planned to undergo antitumor surgery or have already undergone antitumor surgery; and e) have not receive any treatment for gastric cancer at this admission; and 6) able to give informed consent. The exclusion criteria were: a) uncontrolled diabetes *mellitus*; b) receiving glucocorticoid therapy; c) liver and/or renal failure; and d) other conditions not suitable for inclusion in the study. We calculated the required sample size for our study using the 'kappaSize' package, which is freely available in the R version 4.2.1 software (15,16). The 'CIBinary' function in the kappaSize package uses a confidence interval perspective to estimate the sample size needed to test the value of Kappa. The preliminary studies indicated that the initial value of Kappa was 0.483 with a margin of 0.2 on each side (17,18), suggesting that the expected lower and upper confidence limits for Kappa were 0.283 and 0.683, respectively. We also assumed that the proportion of malnutrition was 0.742 based on the results of a previous study (17). Based on the information from these preliminary studies, the estimated sample size required is at least 129 cases at a 5 percent level of significance (i.e., alpha = 0.05). Therefore, with a 20 % dropout rate, the selected sample size ($n = 405$) is sufficient for the current study.

ETHICAL STATEMENT

This study was conducted in accordance to the Helsinki Declaration, and approved by the Medical Ethics Committee of Jinhua Municipal Central Hospital -(研)2022-伦理审查-210, (研)2021-伦理审查-142, (研)2020-伦理审查-240, (研)2020-伦理审查-298 and (研)2022-伦理审查-87). The informed consent was signed voluntarily by all patients.

GENERAL INFORMATION

Gender, age (years), tumor location, histopathological diagnosis, cancer stage, duration science diagnosis (days), cancer therapy phase were obtained through the electronic medical record system. Weight (kilogram [kg]), height (centimeter (cm)), educational level, occupation status, marital status, residence status and financial pressure were obtained by asking patients and caregivers. The financial pressure is a patient's self-evaluation of their own financial burden, which was self-reported via one item "Do you feel any financial pressure?" with four options "Not at all, A little bit, Somewhat, and Very much." Body mass index (BMI), and ECOG-PS score were measured and assessed by the research nurses.

NRS 2002

The Nutritional Risk Screening (NRS 2002) was applied as a screening tool (11). The NRS 2002 was developed by Kondrup et al., involving impaired nutritional status with 0 to 3 points, severity of disease with 0 to 3 points, and age with 0 to 1 point. The total score is 0 to 7 points. Malnutrition risk was defined as a score of 3 or above. This is step 0: Screening (19) (Fig. 1).

GLIM

Malnutrition was diagnosed using the Global Leadership Initiative on Malnutrition (GLIM) criteria that at least one phenotypic criterion and one etiologic criterion should be present (11). Three phenotypic criteria were: a) weight loss > 5 % within the past 6 months, or > 10 % beyond 6 months; b) body mass index (BMI) < 18.5 kg/m^2 if < 70 years, or < 20 kg/m^2 if ≥ 70 years (Asia); and c) reduced muscle mass. Two etiologic criteria were: a) reduced food intake or assimilation; and b) inflammation. A left calf circumference (CC) < 30 cm (male) or < 29.5 cm (female), or an appendicular skeletal muscle mass index (ASMI) < 7 kg/m^2 (male) or < 5.7 kg/m^2 (female) were considered as reduced muscle mass (11,20). The left CC were measured by research nurses using a flexible and non-elastic tape (20). ASMI were measured by technicians using body composition analyzer (InBody 720, Biospace, Korea) based on bioelectrical impedance analysis (BIA). Gastric cancer was identified as reduced food intake or assimilation. This is step 1: Diagnosis (Fig. 1).

Phenotypic metrics for grading severity as moderate (stage 1) malnutrition and severe (stage 2) malnutrition are proposed. Moderate malnutrition required one phenotypic criterion that meets this grade: a) weight loss 5-10 % within the past 6 months, or 10-20 % beyond 6 months; b) BMI < 18.5 kg/m^2 if < 70 years, or < 20 kg/m^2 if ≥ 70 years (Asia); 3) CC < 30 cm (male) or < 29.5 cm (female) (11,20). Severe malnutrition required one phenotypic criterion that meets this grade: 1) weight loss > 10 % within the past 6 months, or > 20 % beyond 6 months; 2) BMI < 17.0 kg/m^2 if < 70 years, or < 17.8 kg/m^2 if ≥ 70 years (Asia); and c) CC < 28 cm (male) or < 27.5 cm (female) (11,20). Regarding GLIM using ASMI, malnutrition severity was graded by weight loss and BMI due to there is no consensus on the grading reference values. This is step 2: Severity (Fig. 1).

PG-SGA

The Patient-Generated Subjective Global Assessment (PG-SGA) has a patient component and a professional component. The patient component includes weight, food intake, symptoms, and activities and function. The professional component involves scoring weight loss, disease and its relation to nutritional requirements, metabolic demand, physical exam, and global assessment categories (10). In this study, a score of four or above was identified as malnutrition (moderate malnutrition), and severe malnutrition was nine points or above.

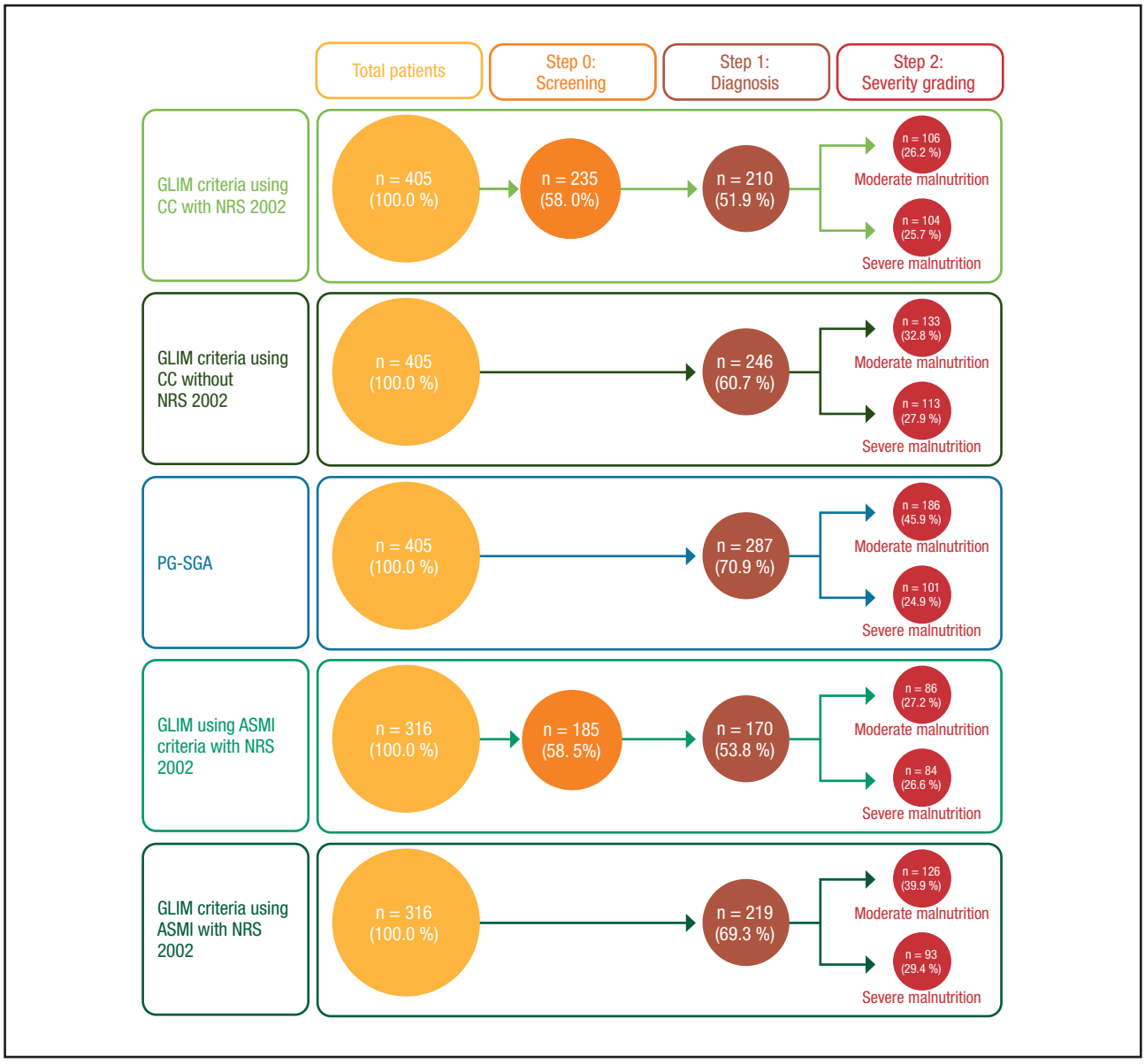

Figure 1.

Comparisons of diagnosis of malnutrition by the GLIM process with and without screening and by the PG-SGA method. The circles represent the number and prevalence of patients being identified at each of the steps. Nutritional risk was screened by NRS 2002 (orange circles): score ≥ 3. The diagnosis of malnutrition was based on GLIM criteria with NRS 2002, GLIM criteria without NRS 2002 and PG-SGA (brown circles). The severity of malnutrition was graded both according to GLIM and PG-SGA (red circles).

STATISTICAL ANALYSES

The Statistical Package for the Social Sciences (SPSS) version 26.0 was used for data analysis. Categorical variables were described as frequencies (percentages). The normality of continuous variables was tested using the Kolmogorov-Smirnov (K-S) test. Normally distributed data were described as mean (standard deviation [SD]), whereas non-normally distributed data were shown as median (25^{th}-75^{th} percentile). The agreements were assessed using Cohen's kappa (k) value (14). A k value of 0.41-0.60 is considered moderate agreement, and > 0.80 is recommended (14,21). Considering PG-SGA or GLIM using ASMI a gold standard, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and area under the curve (AUC) of GLIM using left CC and GLIM using ASMI were calculated using the methods described in a recent guidance (14). All p values were two-tailed with a statistical significance level of $p < 0.05$.

RESULTS

PATIENT CHARACTERISTICS

A total of 418 gastric patients were recruited, of which 13 were excluded due to missing PG-SGA data. Of the included 405 patients with gastric cancer, 291 (71.9 %) were men, the median age was 66.0 (57.0-72.0) years, the median weight was 55.0 (50.0-63.5) kg, 373 (92.1 %) were married, 377 (93.1 %) did not live alone, and the median duration since diagnosis was 41.5 (5.8-322.3) days. Only 19 (4.7 %) participants had university or above degrees, 28 (6.9 %) reported financial pressure very much, and 38 (9.4 %) were diagnosed with cancer stage IV (Table I).

Table I. Demographic and clinical characteristics of the participants

Characteristics	All participants (*n* = 405)
Gender, n (%)	
Male	291 (71.9)
Female	114 (28.1)
Age, year, n (%)	
< 70 years	246 (60.7)
≥ 70 years	159 (39.3)
Weight, kg, median (25^{th}-75^{th} percentile)	55.0 (50.0-63.5)
Height, cm, median (25^{th}-75^{th} percentile)	165.0 (158.0-170.0)
BMI, kg/m^2 (5^{th}, 15^{th} percentile)	
< 70 years	16.2, 17.8
≥ 70 years	16.4, 17.3
Left calf circumference, cm (5^{th}, 15^{th} percentile)	
Male	28.5, 29.9
Female	28.4, 29.5
ASMI, kg/m^2 (5^{th}, 15^{th} percentile)[a]	
Male	5.6, 6.2
Female	4.7, 5.0
Education level	
Primary school or below	236 (58.3)
High school	150 (37.0)
University or above	19 (4.7)
Occupation status	
Unemployed	269 (66.4)
Employed	136 (33.6)
Marital status	
Single	32 (7.9)
Married	373 (92.1)

(Continues on next column)

Table I (cont.). Demographic and clinical characteristics of the participants

Characteristics	All participants (*n* = 405)
Solitude	
No	377 (93.1)
Yes	28 (6.9)
Financial pressure	
Not at all	208 (51.4)
A little bit	123 (30.4)
Somewhat	46 (11.4)
Very much	28 (6.9)
ECOG-PS score	
0	144 (35.6)
1	187 (46.2)
2	48 (11.9)
3	26 (6.4)
Excessive alcohol consumption[b]	
No	234 (63.4)
Yes	135 (36.6)
Smoking status[b]	
No	284 (77.0)
Yes	85 (23.0)
Tumor location[c]	
Upper third	128 (32.3)
Middle third	97 (24.5)
Low third	161 (40.7)
Mixed tumor location	10 (2.5)
Histopathological diagnosis[d]	
Adenocarcinoma	314 (79.9)
Non-adenocarcinoma	58 (14.8)
Mixed histopathological diagnosis	21 (5.3)
Cancer stage[e]	
I	69 (17.5)
II	99 (25.1)
III	188 (47.7)
IV	38 (9.6)
Duration since diagnosis, day, median (25^{th}-75^{th} percentile)	41.5 (5.8-322.3)
Cancer therapy phase	
Before operation	118 (29.1)
After operation before chemotherapy	126 (31.1)
After operation undergoing chemotherapy	67 (16.5)
After operation after chemotherapy	94 (23.2)

n = 405. BMI: body mass index; ASMI: appendicular skeletal muscle mass index; ECOG-PS: Eastern Cooperative Oncology Group performance status. [a]n = 316, [b]n = 369, [c]n = 396, [d]n = 393, [e]n = 394.

THE RESULTS OF THE GLIM CRITERIA

The proportion of weight loss > 5 % within the past 6 months or > 10 % beyond 6 months in gastric cancer patients was 26.9 % (Table II). The percentage of BMI < 18.5 kg/m^2 if < 70 years or < 20 kg/m^2 if ≥ 70 years was 19.3 %; 50 (12.3 %) patients with gastric cancer were classified as left calf circumference < 30 cm (male) or < 29.5 cm (female). Of the 405 participants, 316 participants underwent a BIA with another 89 being excluded due to missing BIA data, and the number of subjects with ASMI < 7 kg/m^2 (male) or < 5.7 kg/m^2 (female) was 151 with a proportion of 47.8 %.

MALNUTRITION DIAGNOSED WITH GLIM AND NRS 2002

In the step 0 of screening, 235 (58.0 %) and 185 (58.5 %) gastric cancer patients were considered at risk for malnutrition, respectively (Fig. 1). In the step 1 of diagnosis, 210 (51.9 %) and 170 (53.8 %) participants were diagnosed with malnutrition by GLIM using left CC or ASMI with NRS2002, respectively. The final step 2 was severity grading, and the number of subjects with moderate malnutrition and severe malnutrition were 106 (26.2 %) and 104 (25.7 %) by GLIM using left CC, and 86 (27.2 %) and 84 (26.6 %) by GLIM using ASMI, respectively.

Table II. The results of the GLIM criteria

Criteria	*n*	%
Phenotypic criteria		
Weight loss > 5 % within past 6 months or > 10 % beyond 6 months	109	26.9
Weight loss > 10 % within the past 6 months or > 20 % beyond 6 months	74	18.3
BMI < 18.5 kg/m^2 if < 70 years or < 20 kg/m^2 if ≥ 70 years	78	19.3
BMI < 17.0 kg/m^2 if < 70 years or < 17.8 kg/m^2 if ≥ 70 years	50	12.3
Left calf circumference < 30 cm (male) or < 29.5 cm (female)	50	12.3
Left calf circumference < 28 cm (male) or < 27.5 cm (female)	12	3.0
ASMI < 7 kg/m^2 (male) or < 5.7 kg/m^2 (female)*	151	47.8
Etiologic criteria		
Reduced food intake or assimilation	405	100.0
Inflammation*	65	20.6

n = *405. BMI: body mass index; ASMI: appendicular skeletal muscle mass index.* *n = *316.*

Table III. Agreements between GLIM using left CC and PG-SGA

	Classification	GLIM using left CC	PG-SGA (≥ 4)	Kappa (95 % CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC (95 % CI)
GLIM using CC with NRS 2002	Malnutrition	210	287	0.463 (0.383-0.543)	67.9	87.3	92.9	52.8	73.6	0.776 (0.728-0.824)
	Moderate/Severe malnutrition	106/104	186/101	0.324 (0.255-0.393)	-	-	-	-	54.3	-
GLIM using CC without NRS 2002	Malnutrition	246	287	0.496 (0.410-0.582)	76.7	78.0	89.4	57.9	77.0	0.773 (0.721-0.825)
	Moderate/Severe malnutrition	133/113	186/101	0.339 (0.266-0.412)	-	-	-	-	56.0	-

n = 405. GLIM: Global Leadership Initiative on Malnutrition; CC: calf circumference; PG-SGA: Patient-Generated Subjective Global Assessment; NRS 2002: Nutritional Risk Screening 2002; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve.

MALNUTRITION DIAGNOSED WITH GLIM WITHOUT NRS 2002

For GLIM without NRS 2002, the step 0 screening was not included in the diagnosis process. In the step 1 of diagnosis, there were 246 (60.7 %) and 219 (69.3 %) patients with gastric cancer diagnosed with malnutrition by GLIM using left CC or GLIM using ASMI, respectively. Finally, 133 (32.8 %) and 126 (39.9 %) patients were classified as moderate malnutrition, and 113 (27.9 %) and 93 (29.4 %) were severe malnutrition in the step 2 severity grading (Fig. 1).

MALNUTRITION DIAGNOSED WITH PG-SGA

In the PG-SGA assessment, 287 (70.9 %) were diagnosed with malnutrition in the step 1 (Fig. 1). In the following step 2, 186 (45.9 %) and 101 (24.9 %) participants were graded as having moderate and severe malnutrition, respectively.

VALIDATION OF GLIM USING LEFT CC

The agreement between GLIM using left CC and PG-SGA is shown in table III. When comparing GLIM using left CC with NRS 2002 and PG-SGA, the Kappa coefficients were 0.463 (95 % CI: 0.383-0.543) in the distribution of malnutrition and non-malnutrition, and 0.324 (95 % CI: 0.255-0.393) in the categorization of severe malnutrition, moderate malnutrition and non-malnutrition. When PG-SGA was set as gold standard, the specificity, PPV, and AUC of GLIM using left CC with NRS 2002 were 87.3 %, 92.9 %, and 0.776 (95 % CI: 0.728-0.824) for malnutrition versus non-malnutrition. In the comparison between GLIM using left CC without NRS 2002 and PG-SGA, the Kappa coefficients were 0.496 (95 % CI: 0.410-0.582) and 0.339 (95 % CI: 0.266-0.412), respectively, in binary variables (malnutrition/non-malnutrition) and tripartite variables (severe malnutrition/moderate malnutrition/non-malnutrition). The specificity, PPV, and AUC of GLIM using left CC without NRS 2002 were 78.0 %, 89.4 %, and 0.773 (95 % CI: 0.721-0.825) in the categorization of malnutrition and non-malnutrition.

As presented in table IV, the Kappa coefficients for malnutrition versus non-malnutrition were 0.470 (95 % CI: 0.378-0.562) and 0.574 (95 % CI: 0.474-0.674) between GLIM using ASMI with or without NRS 2002 and PG-SGA. When PG-SGA was set as the gold standard in the categorization of malnutrition and non-malnutrition, the specificity, PPV, and AUC were 86.5 %, 92.9 %, and 0.781 (95 % CI: 0.726-0.836) for GLIM using ASMI with NRS 2002, as well as 73.0 %, 89.0 %, and 0.795 (95 % CI: 0.735-0.855) for GLIM using ASMI without NRS 2002. Table V indicates the agreement between GLIM using left CC and GLIM using ASMI. The Kappa coefficients were ranging from 0.840-0.975. The values of sensitivity, specificity, PPV, NPV, accuracy, and AUC were all higher than 80.0 % or 0.800.

Table IV. Agreements between GLIM using ASMI and PG-SGA

	Classification	GLIM using ASMI	PG-SGA (≥ 4)	Kappa (95 % CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC (95 % CI)
GLIM using ASMI with NRS 2002	Malnutrition	170	227	0.470 (0.378-0.562)	69.6	86.5	92.9	52.7	74.4	0.781 (0.726-0.836)
	Moderate/Severe malnutrition	111/104	186/101	0.354 (0.276-0.432)	-	-	-	-	55.6	-
GLIM using ASMI without NRS 2002	Malnutrition	219	227	0.574 (0.474-0.674)	85.9	73.0	89.0	67.0	82.3	0.795 (0.735-0.855)
	Moderate/Severe malnutrition	157/112	186/101	0.419 (0.337-0.501)	-	-	-	-	60.0	-

n = 316. *GLIM: Global Leadership Initiative on Malnutrition; ASMI: appendicular skeletal muscle mass index; PG-SGA: Patient-Generated Subjective Global Assessment; NRS 2002: Nutritional Risk Screening 2002; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve.*

Table V. Agreements between GLIM using left CC and GLIM using ASMI

	Classification	GLIM using left CC	GLIM using ASMI	Kappa (95 % CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC (95 % CI)
GLIM with NRS 2002	Malnutrition	165	170	0.968 (0.941-0.995)	97.1	100.0	100.0	96.7	98.4	0.985 (0.970-1.000)
	Moderate/Severe malnutrition	81/84	86/84	0.975 (0.953-0.997)	-	-	-	-	98.8	-
GLIM without NRS 2002	Malnutrition	196	219	0.840 (0.777-0.903)	89.5	100.0	100.0	80.8	92.7	0.947 (0.923-0.972)
	Moderate/Severe malnutrition	103/93	126/93	0.891 (0.848-0.934)	-	-	-	-	94.1	-

n = 316. GLIM: Global Leadership Initiative on Malnutrition; CC: calf circumference; ASMI: appendicular skeletal muscle mass index; NRS 2002: Nutritional Risk Screening 2002; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve.

DISCUSSION

The prevalence of patients with nutritional risk was 58.0 % in this study. Yang et al. study found 61.4 % of patients with gastric cancer were at nutritional risk by NRS 2002 (22). Mao et al. reported 53.8 % of gastric cancer patients were on malnutrition risk when screened with NRS 2002 (23). The results of this study were similar to those of previous studies on nutritional risk rates. According to GLIM using left CC with NRS 2002, the prevalence of malnutrition in this study was 51.9 % with 26.2 % moderate malnutrition and 25.7 % severe malnutrition. The findings in Li et al. study indicated the incidence of malnutrition was 53.0 %, of which 26.0 % and 27.0 % were identified as moderate and severe malnutrition (2). Matsui et al. reported 54.0 % of patients with advanced gastric cancer classified as malnutrition, and the prevalence of moderate malnutrition and severe malnutrition were 29.5 % and 24.5 %, respectively (24). Regarding GLIM using left CC without NRS 2002, 60.7 % (32.8 % moderate and 27.9 % severe) of gastric cancer patients were diagnosed as malnutrition. When screening tools were not used, the prevalence of malnutrition diagnosed by GLIM was higher than when screening tools were used. Similar results have been reported in the study of Rosnes et al. and Henriksen et al (12,25). In this study, the prevalence of malnutrition in patients with gastric cancer was as high as 70.9 % when malnutrition was assessed using PG-SGA. The malnutrition prevalence was 80.4 % and 71.6 % based on PG-SGA in similar studies (26,27). In fact, the prevalence of malnutrition may be overestimated when using PG-SGA for diagnosis (12). Moreover, the prevalence of malnutrition is often higher in patients with gastric cancer than in patients with other types of tumors (1,28).

In the phenotypic criteria, the positivity proportions of left calf circumference were much lower than the positivity proportions of weight loss, BMI, and ASMI. Most studies of GLIM in patients with gastric cancer have used skeletal muscle index as evidence of reduced muscle mass (4,29,30). There are fewer studies that use calf circumference as evidence of reduced muscle mass in gastric cancer patients. However, calf circumference assessment may be the best alternative when other assessment methods for reduced muscle mass are not available, especially in many low- and middle-income countries and rural areas. Li et al. applied calf circumference as the criterion for reduced muscle mass in GLIM diagnosis and used malnutrition to predict overall survival in gastric cancer patients (2). The fifth percentile (p5) and 15th percentile (p15) of the calf circumference were calculated as moderate malnutrition and severe malnutrition, but no specific thresholds were reported (2). In the mixed cancer patients, the cut-off values of calf circumference were reported, male 30 cm or female 29.5 cm for moderate malnutrition and male 28 cm or female 27.5 cm for severe malnutrition (20). Similar cut-off values of calf circumference were commonly applied in GLIM malnutrition diagnosis among patients with other types of tumors, distinguishing between patients' sexes or not (31-33). Our findings can

provide further good real-world value to this field with limited evidence, especially in Chinese patients with gastric cancer. In fact, measuring calf circumference is one of the most convenient and cost-effective ways to rate a patient's muscle mass.

Moderate concordances were found between GLIM using left CC and PG-SGA, as well as between GLIM using ASMI and PG-SGA. The moderate concordances were also reported between GLIM and PG-SGA for the diagnosis of malnutrition both in patients with gastric cancer and other cancer patients (4,17,18,34-36). With PG-SGA as the gold standard, the sensitivity, specificity, PPV, NPV, AUC and accuracy of GLIM using left CC and GLIM using ASMI were all acceptable. Most studies showed the values of sensitivity and specificity were 48 %-98 % between GLIM with or without NRS 2002 and PG-SGA (12,18,34-38). The PPV and NPV were 47 %-98 % (4,18,35,36). The results of AUC were also moderate and similar to previous studies, from 0.632 to 0.800 (18,34,35,37). The results of this study were similar to those of previous studies. Though few studies have reported accuracy between GLIM and PG-SGA in cancer patients, similar results were found in other populations between GLIM and Subjective Global Assessment (SGA) (39). However, several studies showed the values of Kappa coefficient, PPV and NPV were lower between GLIM with/without NRS 2002 and PG-SGA in cancer patients (12,37,38). In these studies, the assessment results of PG-SGA were divided into well-nourished (A), moderately malnourished or suspected malnourished (B) or severely malnourished (C), which were different from this study (12,37,38). In future similar studies, it is important to pay attention to the threshold of PG-SGA for diagnosing malnutrition, as this may lead to inconsistent findings. In the categorization of severe malnutrition, moderate malnutrition and non-malnutrition, the agreements were all lower than malnutrition versus non-malnutrition between GLIM and PG-SGA. With GLIM using ASMI as the gold standard, higher concordances were demonstrated between GLIM using left CC and GLIM using ASMI with or without NRS 2002, indicating that the two have consistent diagnostic efficacy for malnutrition. Few studies have used GLIM using ASMI as a gold standard to validate GLIM using left CC. Wang et al. evaluated the validity of GLIM using CC or GLIM using ASMI with the Malnutrition Universal Screening Tool (MUST) in diagnosing malnutrition/non-malnutrition compared with PG-SGA among ambulatory cancer patients (36). The values of Kappa coefficient, sensitivity, specificity, PPV and NPV were 0.565, 55.3 %, 97.9 %, 94.9 % and 75.3 % for GLIM using CC, and 0.586, 57.4 %, 97.9 %, 95.1 % and 76.2 % for GLIM using ASMI (36). The agreements were highly consistent between GLIM using CC and GLIM using ASMI when PG-SGA was used as the gold standard. Our findings in this study further confirmed the results in the above study. However, the positivity proportion of left CC was much lower than that of ASMI in this study, which may be related to the different calf circumference thresholds used. The muscle mass reduction (MMR) is defined as CC < 34 cm in men or CC < 33 cm for women in their study (36). It is recommended that future studies explore and analyze the diagnostic process between the two in more detail.

The strengths of this study are as follows: a) the GLIM using left CC was validated according to the recommendations of van der Schueren et al. (14); b) the study population was a single type of gastric cancer patient; c) the sample size was already large for gastric cancer patients. The possible limitations were: a) this is a single-center study, and the findings may not be generalized to all patients with gastric cancer; b) only patients with ECOG-PS scores less than 4 were included in the study, but patients with an ECOG-PS score of 4 may no longer be suitable for effective nutritional interventions or treatments due to their medical condition; and c) considering the differences in body composition across races, the results of this study may only be applicable to Chinese patients.

CONCLUSIONS

The prevalence of nutritional risk and malnutrition were higher in patients with gastric cancer. The prevalence of malnutrition diagnosed through PG-SGA was higher than with GLIM using left CC without NRS 2002, and the prevalence of malnutrition diagnosed by GLIM using left CC without NRS 2002 was higher than that of GLIM using left CC with NRS 2002. The agreements were acceptable both between GLIM using left CC and PG-SGA, and between GLIM using left CC and GLIM using ASMI. The left calf circumference can be one of the credible references that indicating the reduced muscle mass in patients with gastric cancer. The agreements regarding malnutrition versus non-malnutrition were better than those for tripartite variables (severe malnutrition/moderate malnutrition/non-malnutrition).

AUTHOR´S CONTRIBUTIONS

Liang Fu: conceptualization, formal analysis, funding acquisition, methodology, software, writing original draft. Xiaoqian Xu, Haixia Shi, Qiaohui Guan, Lijun Zhang and Yanting Hu: conceptualization, data curation, formal analysis, investigation. Yaoqi Zhang, Jianxiang Jin and Sha Zhu: conceptualization, data curation, methodology, project administration, resources. Bo Zhuang: conceptualization, resources. Lushan Zheng and Xianghong Ye: conceptualization, supervision, validation, visualization, writing original draft, writing review & editing. All authors contributed to and approved the final version of the manuscript.

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ARÁN

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Trabajo Original

Valoración nutricional

Comparison of the Global Leadership Initiative on Malnutrition and the Patient-Generated Subjective Global Assessment for diagnosing malnutrition in patients undergoing surgery for hepatobiliary and pancreatic malignancies

Comparación de la Iniciativa Global de Liderazgo sobre la Desnutrición y la Evaluación Global Subjetiva Generada por el Paciente para diagnosticar la desnutrición en pacientes operados de tumores malignos hepatobiliares y pancreáticos

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Abstract

Objective: to analyse the differences in malnutrition assessment between the Global Leadership Initiative on Malnutrition (GLIM) criteria and the Patient-Generated Subjective Global Assessment (PG-SGA) among patients with hepatobiliary and pancreatic malignancies.

Method: this study was a cross-sectional study and included 126 hospitalised patients who underwent surgery for hepatobiliary and pancreatic malignancies between November 1, 2019 and August 1, 2020. The patients' clinical data were collected, and malnutrition assessments were completed using the different nutritional assessment tools. The consistency of both tools was analysed using Cohen's kappa coefficient.

Results: the prevalence of malnutrition showed a difference in diagnosis results between the GLIM criteria (36.51 %) and the PG-SGA (55.56 %). The two methods had moderate consistency (kappa = 0.590, $p < 0.01$). The sensitivity of a malnutrition diagnosis using a combination of GLIM and PG-SGA was 65.7 % (53.3 % and 76.4 %, respectively), and specificity was 100 % (92 % and 100 %, respectively). When malnutrition was evaluated using only PG-SGA, sensitivity was 88.9 % (95 % confidence interval (CI) 63.9 % to 98.1 %), whereas when only the GLIM score was used for malnutrition evaluation, sensitivity was 98.2 % (95 % CI, 92.8 % to 99.7 %). In addition, the PG-SGA score and the GLIM score had significant correlations.

Conclusion: GLIM performed better than PG-SGA in the correlation analysis of nutritional indicators. GLIM is more suitable for patients with hepatobiliary and pancreatic malignancies than PG-SGA.

Keywords:

Nutritional assessment. Hepatobiliary and pancreatic malignant tumour. Global Leadership Initiative on Malnutrition. Subjective global assessment of patients.

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Ethics approval and consent to participate: this study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the First Hospital of Ningbo University (2020-R306). A written informed consent was obtained from all participants.

Availability of data and materials: all data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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Authors' contributions: Wang J conceived the study. Wang J, Xie HF, Xu QH, Yang L, Hu Y, Cai HN and Li HC were involved in the implementation of the programme and acquisition of data. Wang J and Hu Y performed the statistical analysis. Wang J and Xie HF wrote the paper. Wang J finalised the paper. All authors were involved in the interpretation of the data analysis, drafted or reviewed the paper, and approved this version for publication.

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Resumen

Objetivo: analizar las diferencias en la evaluación de la desnutrición en pacientes con tumores malignos hepatobiliares y pancreáticos entre los criterios de la Iniciativa Global de Liderazgo en Desnutrición (Global Leadership Initiative on Malnutrition, GLIM) y la Evaluación Global Subjetiva Generada por el Paciente (PG-SGA).

Métodos: el estudio fue un estudio transversal que incluyó a 126 pacientes hospitalizados que fueron operados de tumores malignos hepatobiliares y pancreáticos entre el 1 de noviembre de 2019 y el 1 de agosto de 2020. Recopilar datos clínicos de pacientes y completar la evaluación de la desnutrición con diferentes herramientas de evaluación nutricional. La consistencia de las dos herramientas se analizó utilizando el coeficiente Kappa de Cohen.

Resultados: los criterios GLIM (36,51 %) y PG-SGA (55,56 %) presentan diferencias en los resultados diagnósticos de desnutrición. Ambos métodos tienen una consistencia moderada (kappa = 0590, $p < 0,01$). La sensibilidad de GLIM y PG-SGA para el diagnóstico conjunto de desnutrición es del 65,7 % (53,3 % y 76,4 %, respectivamente). La especificidad fue del 100 % (92 % y 100 %, respectivamente). Cuando solo se utilizó la PG-SGA para evaluar la desnutrición, la sensibilidad fue del 88,9 % (intervalo de confianza del 95 % (IC) 63,9 % a 98,1 %), mientras que cuando solo se utilizó la GLIM para evaluar la desnutrición, la sensibilidad fue del 98,2 % (IC del 95 %: 92,8 % a 99,7 %. Además, la puntuación PG-SGA tuvo una correlación significativa con la puntuación GLIM.

Conclusión: en el análisis de correlación de los indicadores nutricionales, GLIM es mejor que PG-SGA. GLIM es más adecuado para pacientes con tumores malignos hepatobiliares y pancreáticos que PG-SGA.

Palabras clave:

Evaluación nutricional. Tumores malignos hepatobiliares y pancreáticos. Iniciativa Global de Liderazgo sobre la Desnutrición. Evaluación global subjetiva del paciente.

INTRODUCTION

Hepatobiliary and pancreatic malignancies include hepatocellular carcinoma and gallbladder, bile duct and pancreas cancers (1). The prevalence of malnutrition in patients with gastrointestinal malignancies ranges between 45 % and 80 %, and is higher than that of patients with other tumours (2,3). The incidence of malnutrition in hepatobiliary and pancreatic malignancies, which are included within the gastrointestinal malignancies, is between 2.7 % and 36.3 % (4). Patients with malignant tumours are prone to malnutrition due to the high metabolism caused by rapid cancer growth that constantly consumes nutrients from the body (5). The trauma caused by surgery aggravates the state of malnutrition, leading to a long postoperative recovery time and an increase in complications, seriously affecting survival time and quality of life (4).

Studies have shown that assessing patient nutritional status (protein energy malnutrition) with hepatobiliary and pancreatic malignancies is an important diagnostic and treatment tool for providing reasonable nutritional support (6). Although there is no gold standard for malnutrition assessment, many nutritional screening tools are commonly used in clinical practice (7). The Patient-Generated Subjective Global Assessment (PG-SGA) is a globally accepted tool for evaluating cancer patient nutritional status (8,9). Nevertheless, the PG-SGA is often deemed excessively time-consuming and challenging to comprehend for medical staff (10). Meanwhile, the Global Leadership Initiative on Malnutrition (GLIM) criteria, published in 2019, have been increasingly recognised for diagnosing malnutrition in clinical settings (11). Recent studies have demonstrated the applicability and reliability of the GLIM criteria in diagnosing malnutrition in various types of cancer, including lung and gastric cancer (12-14). Interestingly, the GLIM criteria define a lower prevalence of malnutrition in patients with hepatobiliary and pancreatic diseases compared with the PG-SGA (14). However, agreement between the GLIM criteria and PG-SGA in hospitalised patients undergoing hepatobiliary-pancreatic surgery remains unexplored.

In this study, the GLIM criteria and PG-SGA were chosen to assess the prevalence of malnutrition and the nutritional status of patients undergoing surgery for hepatobiliary and pancreatic malignancies, and a comprehensive comparison was carried out to select the most suitable nutritional assessment tool for clinical use.

MATERIALS AND METHODS

PARTICIPANTS

Patients attending a tertiary city hospital between November 1, 2019 and August 1, 2020 to undergo surgery for hepatobiliary and pancreatic malignancies were selected as the population for this study. The inclusion criteria were as follows: 1) patients with hepatobiliary and pancreatic malignancies diagnosed and pathologically confirmed; 2) patients aged over 18 years with indications for malignant tumours and opting to undergo hepatobiliary and pancreatic surgery for them; 3) patients who were conscious and had the ability to communicate clearly; and 4) patients who were willing to participate in this study and gave informed consent. The exclusion criteria were as follows: 1) patients with critical conditions that were difficult to assess; 2) patients with unknown diagnoses and advanced malignancy; 3) patients with malnutrition due to other reasons, such as cirrhosis or pancreatitis; and 4) patients receiving enteral nutritional support before surgery. This study was approved by the Ethics Committee of the First Affiliated Hospital of Ningbo University (ethical batch number: 2020R306), and all patients provided written informed consent before participating in the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Using the cross-sectional survey sample size estimation formula $N = Z^2 \times (1 - P) / (\varepsilon^2 \times P)$, where ε represents the desired accuracy as a percentage of the expected incidence rate, and P represents the expected incidence rate, the study's required sample size was determined. According to relevant literature, the nutritional incidence rate for gastrointestinal malignancies is approximately 70 %, with P equal to 70 %. With a confidence level of 90 %, Z is 1.64. Given that the true population rate is within 10 %, ε is set to 10 %. Therefore, $n = 1.642 \times (1 - 0.7) / (0.122 \times 0.7)$, indicating that a sample size of 115 participants is required for this research.

RESEARCH METHODOLOGY

General patient information was collected within 48 h of admission by reviewing the patients' medical records and having face-to-face meetings with them to obtain their medical histories. A qualified nutritionist assessed the patients 1 day before their scheduled surgeries, using the GLIM criteria and PG-SGA. The nutritional indicators used were body mass index (BMI), upper-arm circumference (AC) and triceps skinfold thickness (TSF). Laboratory tests were conducted for haemoglobin (Hb), serum albumin (ALB) and serum pre-albumin (PA).

Global Leadership Initiative on Malnutrition assessment

The GLIM assessment consists of two steps: malnutrition diagnosis and grading of the severity of the malnutrition (15). The diagnosis of malnutrition involves various criteria. Here, the manifestation criteria included: 1) weight loss > 5 % in the past 6 months or > 10 % over 6 months; 2) aged < 70 years with a BMI of < 18.5 kg/m^2 or aged > 70 years with a BMI of < 20 kg/m^2; 3) mild to moderate muscle loss (i.e. calf circumference ≤ 30 cm in men or ≤ 29 cm in women); and 4) severe muscle loss. If a patient had a positive score for 1 to 3 of the above indicators, they were given 1 point. The aetiological criteria included: 1) energy intake ≤ 50 % for > 1 week or reduced energy intake > 2 weeks; and 2) the presence of any chronic gastrointestinal disease (affecting the digestion and absorption of food) or acute illness/injury or inflammatory state associated with chronic disease. If one or two of the above indicators were positive, the patient was given 1 point. The manifestation criteria score plus the aetiological criteria score could result in a maximum score of 2. A score of 2 was assessed as malnutrition, while a score of 0 or 1 was considered absence of malnutrition.

Malnutrition severity was graded according to various performance indicators: 1) moderate malnutrition: weight loss of 5 %-10 % in the last 6 months or 10 %-20 % in more than 6 months, a BMI loss of < 20 kg/m^2 in patients aged < 70 years or < 22 kg/m^2 in patients aged > 70 years and a calf muscle circumference of < 30 cm in men and < 29 cm in women; and 2) severe malnutrition: weight loss > 10 % in the last 6 months or > 20 % in more than 6 months, a BMI loss of < 18.5 kg/m^2 in patients aged < 70 years or < 20 kg/m^2 in patients aged > 70 years and a calf muscle circumference of < 27 cm in men and < 26 cm in women.

Patient-Generated Subjective Global Assessment rating

The PG-SGA is designed for the nutritional assessment of oncology patients based on the subjective global assessment. The main evaluation of the PG-SGA consists of two parts, the patient's subjective assessment and the healthcare worker's assessment, which includes eight aspects: weight, eating status, symptoms, activity and physical fitness, weight loss, the relationship between disease and nutritional needs, metabolic stress status and physical examination (15).

The patient completed the first part of the PG-SGA, recording their weight, eating status, physical fitness and symptoms and activity. Points for weight and symptoms were cumulative, and points for eating status and activity and physical fitness were based on the highest score obtained from patient verification. The healthcare worker assessed the second part. 1) Weight loss was scored using January's weight data or, if those data were unavailable, the weight data from the last 6 months. An additional point was added if there had been some weight loss in the previous 2 weeks. 2) The relationship between disease and nutritional requirements was recorded if the patient had cancer, acquired immunodeficiency syndrome, pulmonary or cardiac cachexia, a decubitus ulcer, an open wound or fistula, trauma or was > 65 years, with 1 point for each condition. 3) Metabolic stress was assessed based on three factors: fever, duration of fever and glucocorticoid dosage. One point was given for mild stress, 2 for moderate stress and 3 for severe stress. 4) A physical examination assessed mainly fat, muscle and body fluids. Points were given depending on the degree of effort, with 0 points given for no exertion, 1 for mild exertion, 2 for moderate exertion and 3 for severe exertion. Finally, all the scores were added for a measurement evaluation, and a plan was developed based on the scores. A score of 0 or 1 on scale A indicated good nutrition, a score of 2-8 on scale B indicated uncertain or moderate malnutrition and a score of 9 or higher on scale C indicated severe malnutrition.

All diagnoses were made individually by two specialist dietitians, and where there was disagreement, the final diagnosis was discussed. Each patient was assessed for malnutrition using both methods.

STATISTICAL ANALYSIS

The statistical analysis was conducted using SPSS 19.0 software. The measurement data were expressed as mean and standard deviation, and the data were tested for normality using the Shapiro-Wilk test. Two independent sample t-tests were used to compare continuous variables with a normal distribution. The Mann-Whitney U-test was used for comparing continuous variables with a non-normal distribution, and count data were tested using the chi-square test. The correlation analysis was carried out using Spearman's rank correlation coefficient, and the consistency of different tools was analysed using Cohen's kappa coefficient. Statistically, $p < 0.05$ indicated a statistically significant difference, and $p < 0.01$ indicated a highly significant difference.

RESULTS

BASIC INFORMATION ON THE STUDY POPULATION

This study included 126 patients with perioperative hepatobiliary and pancreatic surgical malignancies. The patient's age was

≥ 65 years in 58 cases and < 65 years in 68 cases. Ninety-four patients were men, and 32 patients were women. The patients' BMI was < 18.5 kg/m^2 in 7 cases (5.6 %), 18.5-24 kg/m^2 in 69 cases (54.8 %) and > 24 kg/m^2 in 50 cases (39.7 %). There was one underlying disease present in 52 cases (41.3 %), two or more underlying diseases in 28 cases (22.2 %), and no underlying disease in 46 cases (36.5 %). As table I shows, there were malignant tumours in the biliary tract in 30 cases (23.8 %), malignant tumours in the pancreas in 29 cases (23.0 %) and malignant tumours in the liver in 67 cases (53.2 %).

ANALYSIS OF CONSISTENCY BETWEEN THE NUTRITIONAL RATINGS OF THE TWO TOOLS

The GLIM assessment showed that 80 patients were well-nourished (63.5 %), 36 patients were moderately malnourished (28.6 %) and 10 patients were severely malnourished (7.9 %) (Fig. 1). The PG-SGA assessment showed that 56 patients were well-nourished (44.4 %), 52 patients were moderately malnourished (41.3 %) and 18 patients were severely malnourished (14.3 %) (Table II). The chi-squared test showed a kappa value of 0.542 (95 % confidence interval (CI), 0.424-0.672, $p < 0.01$), indicating a difference between the tools' ratings.

Seventy percent of the patients diagnosed as well-nourished by the PG-SGA were found to be well-nourished on the GLIM scale. In addition, 77.8 % of the patients diagnosed as moderately malnourished by the PG-SGA were diagnosed as moderately malnourished according to the GLIM criteria, while 20 % were diagnosed as severely malnourished and 27.5 % were diagnosed as well-nourished. Furthermore, when the PG-SGA and the GLIM criteria were combined, severe malnutrition was diagnosed in 80 % of the participants, while the GLIM diagnosed good nutrition in 2.5 % and moderate nutrition in 22.2 %. This further suggests consistency in diagnosis between the PG-SGA and the GLIM criteria.

Table I. General information of patients

Item		Cases (n = 126)	Percentage
Age (years)	≥ 65	58	46.03 %
	< 65	68	53.97 %
Sex (cases)	Male	94	74.60 %
	Female	32	25.39 %
BMI (kg/m^2)	< 18.5	7	5.56 %
	18.5-24	69	54.76 %
	24	50	39.68 %
Underlying disease	1	52	41.27 %
	2 or more	28	22.22 %
	None	46	36.51 %
Diagnosis	Malignant neoplasm of biliary tract	30	23.81 %
	Malignant neoplasm of pancreas	29	23.02 %
	Malignant neoplasm of liver	67	53.17 %

Underlying disease: hypertension, diabetes mellitus, *coronary heart disease, chronic obstructive pulmonary disease, chronic kidney disease, etc. BMI: body mass index.*

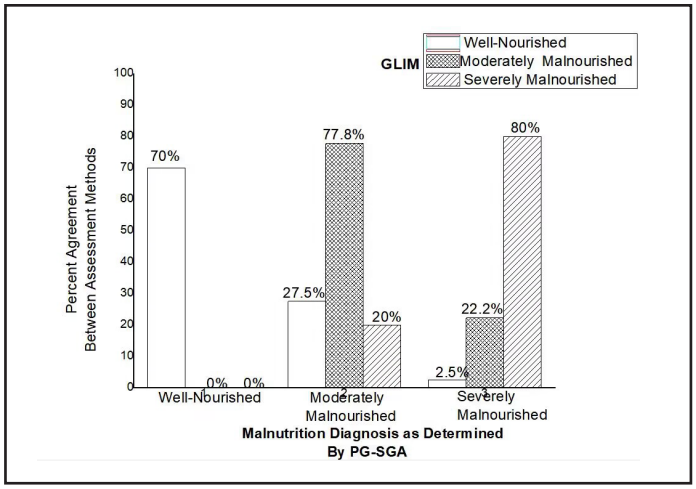

Figure 1.

Comparison of subjective patient assessment and global malnutrition assessment standards.

Table II. Analysis of GLIM and PG-SGA results

GLIM	PG-SGA			Total	Kappa	*p*
	Good nutrition	Moderate malnutrition	Severe malnutrition			
Good nutrition	56	22	2	80	0.542	< 0.01
Moderate malnutrition	0	28	8	36		
Severe malnutrition	0	2	8	10		
Total	56	52	18	126		

COMPARISON OF THE SENSITIVITY AND SPECIFICITY OF THE TWO ASSESSMENT TOOLS

The sensitivity and specificity of the GLIM criteria versus those of the PG-SGA were calculated. An analysis of the GLIM's and the PG-SGA's diagnoses of malnutrition showed that the sensitivity rate of 65.7 % (95 % CI: 53.3 %-76.4 %) was moderate, and the specificity rate of 100 % (95 % CI: 92 %-100 %) was good. For the diagnosis of malnutrition, the GLIM criteria, with a sensitivity distribution of 88.9 % (95 % CI: 63.9 %-98.1 %), showed good sensitivity compared with the PG-SGA grade C, which had moderate specificity at 72.2 % (95 % CI: 62.6 %-80.2 %). When the GLIM diagnosis of severe malnutrition was compared to the PG-SGA diagnosis of grade C malnutrition, the specificity was good at 98.2 % (95 % CI: 92.8 %-99.7 %), the sensitivity decreased to 44.4 % (95 % CI: 22.4 %-68.7 %) (Table III).

CORRELATION BETWEEN ASSESSMENT OF MALNUTRITION AND VARIOUS NUTRITIONAL INDICATORS BY THE TWO TOOLS

The GLIM criteria classified 80 participants as well-nourished and 46 participants as malnourished. When comparing the nutritional status groups based on GLIM, statistically significant differences in the nutritional indicators, including ALB, PA, calf circumference, AC, TSF and PG-SGA scores, were observed ($p < 0.05$), except for Hb (Table IV).

Conversely, the PG-SGA assessment categorised 56 participants as well-nourished and 70 as malnourished. The analysis revealed significant differences in all indicators across the nutritional status groups determined by PG-SGA, except for Hb, ALB, and TSF, where the differences were not statistically significant ($p < 0.01$) (Table IV).

Table III. Comparison of sensitivity and specificity between GLIM and PG-SGA

Parameters	GLIM Malnutrition vs PG-SGA B and C	GLIM Malnutrition vs PG-SGA Class C	GLIM Severe Malnutrition vs PG-SGA Class C
Sensitivity (%)	65.71 % (53.31 %, 76.38 %)	88.89 % (63.93 %, 98.05 %)	44.40 % (22.40 %, 68.65 %)
Specificity (%)	100 % (92 %, 100 %)	72.22 % (62.64 %, 80.20 %)	98.15 % (92.81 %, 99.68 %)

Table IV. Comparison of GLIM and PG-SGA assessment of malnutrition with various one-way indicators

Projects	Good nutrition	Malnutrition	t/z values	*p*-value
GLIM				
Number of people	80	46	-	-
HB (g/L)	127.30 ± 24.56	118.30 ± 24.84	-1.673	0.094
ALB (g/L)	38.40 ± 5.03	35.92 ± 5.81	-2.200	0.028
PA (mg/L)	19.68 ± 7.93	15.29 ± 7.08	3.111	0.002
Calf circumference (cm)	33.91 ± 3.98	31.67 ± 3.61	-3.043	0.002
AC (cm)	27.31 ± 2.81	24.67 ± 3.08	-4.498	0.000
TSF (mm)	9.62 ± 2.83	8.33 ± 3.43	-2.842	0.004
PG-SGA score	1.75 ± 2.18	6.13 ± 2.76	-9.836	0.000

(Continues on next page)

Table IV (cont.). Comparison of GLIM and PG-SGA assessment of malnutrition with various one-way indicators

Projects	Good nutrition	Malnutrition	t/z values	*p*-value
PG-SGA				
Number of people	56	70	-	-
HB (g/L)	124.00 ± 25.85	124.03 ± 24.39	-0.02	0.984
ALB (g/L)	38.15 ± 4.52	36.97 ± 6.06	1.120	0.228
PA (mg/L)	20.45 ± 8.22	16.18 ± 7.12	3.125	0.002
Calf circumference (cm)	34.20 ± 4.22	32.20 ± 3.57	-2.707	0.007
AC (cm)	27.50 ± 2.64	25.42 ± 3.27	-3.673	0.000
TSF (mm)	9.59 ± 2.898	8.79 ± 3.26	-1.863	0.062
GLIM score	0.21 ± 0.41	1.40 ± 0.87	-9.336	0.000

HB: haemoglobin; ALB: serum albumin; PA: serum pre-albumin; AC: upper-arm circumference; TSF: triceps skinfold thickness.

Table V. Correlation analysis of each nutritional indicator with GLIM and PG-SGA

	GLIM		PG-SGA	
	r	*p*	r	*p*
HB (g/L)	-1.150	0.094	-0.002	0.984
ALB (g/L)	-0.197	0.027	-0.075	0.403
PA (mg/L)	-0.245	0.006	-0.234	0.008
Calf circumference (cm)	-0.272	0.002	-0.242	0.006
AC (cm)	-0.402	0.000	-0.329	0.000
TSF (mm)	-0.254	0.004	-0.167	0.062
GLIM score	-	-	0.642	0.000

HB: haemoglobin; ALB: serum albumin; PA: serum pre-albumin; AC: upper-arm circumference; TSF: triceps skinfold thickness.

Table V provides insights into the correlation analysis between GLIM and PG-SGA assessments and individual nutritional indicators. The results indicated negative correlations between the GLIM criteria and indicators such as ALB, PA, calf circumference, AC and TSF, while no significant correlation was observed with Hb.

In contrast, the PG-SGA assessments exhibited negative correlations with all individual nutritional indicators, except for Hb, ALB and TSF. In addition, it is noteworthy that both PG-SGA and GLIM scores demonstrated significant correlations across all patients ($p < 0.001$) (Table V).

DISCUSSION

This study compared two nutritional assessment tools, the GLIM and the PG-SGA, within the context of patients undergoing surgery for hepatobiliary and pancreatic malignancies. These malignancies present a considerable risk of malnutrition, making accurate diagnoses crucial. The study's findings revealed several significant differences and insights into these two assessment tools.

Initially, the GLIM assessment criteria, which necessitate the presence of positive nutritional screening alongside meeting performance-based and aetiological indicators, yielded a lower rate of malnutrition diagnoses (36.51 %) compared with the PG-SGA assessment (55.56 %). This discrepancy underscores the distinctiveness of these two tools. This study's results align with previous cross-sectional studies that reported differences in malnutrition prevalence between the GLIM and PG-SGA assessments (14,16,17).

The higher malnutrition prevalence detected by the PG-SGA could be attributed to various factors. First, the two tools' differing perspectives and evaluation criteria play a crucial role. The PG-SGA evaluates patients with mild to moderate malnutrition, whereas the GLIM assessment is preceded by nutritional risk screening, which assesses both the presence and severity of malnutrition (15,18). In addition, the PG-SGA strongly emphasises the patients' subjective assessments of digestive symptoms and functional capacity, regardless of their weight loss percentage. Given that patients with hepatobiliary and pancreatic malignancies commonly experience reduced food intake and increased digestive tract reactions, the PG-SGA tends to yield higher malnutrition rates. Furthermore, the PG-SGA heavily relies

on patients' subjective assessments, which can introduce bias and data variability. Lastly, the GLIM assessment may encounter challenges in accurately assessing malnutrition in patients with ascites and oedema malignancies (19).

This study also demonstrated that combining the GLIM and PG-SGA diagnoses of malnutrition resulted in moderate sensitivity, which improved to good sensitivity when the PG-SGA diagnosed severe malnutrition. This suggests that the GLIM criteria are more sensitive in diagnosing severe malnutrition when severity ratings are not involved. However, including severity ratings led to a loss of consistency between the GLIM and PG-SGA assessments, indicating that not all patients with a PG-SGA grade C diagnosis were rated as severely malnourished by the GLIM. This discrepancy may be attributed to the presence of acute and chronic disease-associated inflammation in hospitalised patients, a factor not considered when introducing the aetiological criteria. This study suggests that incorporating acute and chronic disease-associated inflammation as an aetiological criterion, alongside c-reactive protein measurements as an objective indicator of inflammation, may enhance the validity of malnutrition assessments. Typically, the GLIM criteria exhibit better specificity than sensitivity due to the presence of acute and chronic infections in most oncology patients. While the PG-SGA lacks the inclusion of relevant inflammatory indicators, the GLIM's aetiological criteria consider acute and chronic disease-associated inflammation, potentially improving specificity while reducing sensitivity.

In nutrition research, there is a growing need for streamlined tools that offer simple yet comprehensive assessments of nutritional status, reducing the burden of extensive testing. This study demonstrated that the GLIM criteria exhibited superior correlations with individual nutritional indicators compared with the PG-SGA. Notably, the GLIM assessment's first nutritional risk screening component, BMI, emerged as a critical component, demonstrating direct correlations with two nutritional indicators. In contrast, the PG-SGA, developed specifically for oncology patients, provides a simple and easily synthesisable nutritional assessment without the need for extensive biochemical analysis. However, it focuses on assessing nutrient intake and body composition, overlooking intrinsic protein levels, which aligns with the absence of correlation with ALB (20).

To summarise, this study suggests that the GLIM criteria offer a more robust and comprehensive assessment of malnutrition, particularly in patients with hepatobiliary and pancreatic surgical malignancies. This echoes previous studies that have applied GLIM malnutrition assessment criteria in oncology patients.

It is essential to acknowledge the limitations of this research. The study's sample size was relatively small and lacked follow-up data to assess the long-term prognostic implications of the two assessment tools. Moreover, the distinction between malnutrition and cachexia was not explored. Further investigations involving larger cohorts of patients undergoing surgery for hepatobiliary-pancreatic malignancies are warranted to assess the prognostic value of these assessments and provide more comprehensive insights into their clinical utility.

CONCLUSION

In conclusion, this study revealed distinctions in the diagnostic capabilities of the GLIM and PG-SGA nutritional assessment instruments. The GLIM tool demonstrates superior correlation with individual nutritional parameters, although relying solely on conventional nutritional metrics for impartial malnutrition evaluation, as per the criteria of either tool, is deemed insufficient. Importantly, concurrently using both tools results in a heightened incidence of severe malnutrition diagnoses, underscoring the congruity in their assessments. This investigation posits the potential suitability of GLIM as an effective means for appraising the nutritional status of patients in this cohort. Furthermore, it underscores the imperative for subsequent investigations to substantiate and enhance the selection of nutritional assessment tools in this specific context while considering the constraints associated with the study's sample size and retrospective nature.

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Trabajo Original

Epidemiología y dietética

Attitudinal factors associated with protein sufficiency in Chilean vegan university students — A pilot study

Factores actitudinales asociados a la suficiencia proteica en estudiantes universitarios veganos chilenos. Estudio piloto

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Abstract

Introduction: vegan diets are currently an essential topic of discussion because they are recognized as a prototype of a healthy diet but are also associated with deficits in the intake of critical nutrients such as protein. Evaluating the factors that influence the deficit in their intake in vulnerable populations such as university students represents an important topic of interest, considering that this is one of the groups where veganism is most popular. Given this, the present study aimed to determine the degree of protein sufficiency and its associated factors in a sample of Chilean vegan university students.

Materials and methods: an exploratory cross-sectional study was conducted on 114 vegan university students who responded to an online survey on academic, attitudinal, clinical, dietary, and sociodemographic variables. Protein intake was calculated, and based on self-reported weight, daily protein adequacy was calculated according to the recommendation of 0.9 g/kg/day. Finally, the association between protein adequacy and previously consulted variables was calculated by determining the odds ratios.

Results: only 53.5 % had adequate daily protein intake, which was associated with the length of time respondents had been vegan (OR, 2.86; 95 % CI, 1.07 to 7.34; $p < 0.05$), use of supplements (OR, 5.24; 95 % CI, 1.17 to 25.2; $p < 0.05$), and the frequency with which they ate lunch at home (OR, 87.7; 95 % CI, 24.1 to 304; $p = 0.000$).

Conclusion: there needs to be more protein adequacy in the assessed sample. Protein adequacy is associated with the length of time on the vegan diet, frequency of eating lunch away from home, and use of supplements regularly.

Keywords:

Protein intake. Dietary protein. Vegan diets. Plant-based diet. University students.

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Resumen

Introducción: en la actualidad, las dietas veganas representan una importante temática de discusión debido a que son reconocidas como prototipo de régimen saludable pero también se encuentran asociadas a déficits en la ingesta de nutrientes críticos como las proteínas. La evaluación de los factores que influyen en el déficit de su ingesta en poblaciones vulnerables como los estudiantes universitarios representa un importante tema de interés, considerando que es uno de los grupos donde mayor popularidad presenta el veganismo. Frente a esto, el presente estudio tuvo como objetivo determinar el grado de suficiencia proteica y los factores asociados a esta en una muestra de estudiantes universitarios veganos chilenos.

Materiales y método: se realizó un estudio de alcance exploratorio de corte transversal en 114 estudiantes universitarios veganos que respondieron a una encuesta *online* sobre variables académicas, actitudinales, clínicas, dietarias y sociodemográficas. Se calculó la ingesta proteica y, en función del peso autorreportado, se calculó la adecuación proteica diaria de acuerdo con la recomendación de 0,9 g/kg/día. Finalmente se calculó la asociación entre la adecuación proteica y las variables anteriormente consultadas a partir de la determinación de los *odds ratios*.

Resultados: solo un 53,5 % presentaron una ingesta diaria adecuada de proteínas, la cual se asocia al tiempo de antigüedad del veganismo de los encuestados (OR: 2,86; IC 95 %: 1,07 a 7,34; $p < 0,05$), la utilización de suplementos (OR: 5,24; Il 95 %: 1,17 a 25,2; $p < 0,05$) y la frecuencia con la que almuerzan en el hogar (OR: 87,7; IC 95 %: 24,1 a 304; $p = 0,000$).

Conclusión: existe una importante falta de adecuación proteica en la presente muestra evaluada. La adecuación proteica se asocia con ~~el tiempo~~ del régimen vegano, la frecuencia de almuerzos fuera de casa y la utilización de suplementos de forma regular.

Palabras clave:

Ingesta proteica. Proteínas dietarias. Dietas veganas. Dieta basada en plantas. Estudiantes universitarios.

INTRODUCTION

Vegan diets correspond to diets based exclusively on the intake of plant-based foods, excluding ingredients of animal origin and their derivatives mainly for ethical, moral, environmental, and health reasons (1). In the current 21st century, the population adopting such diets has increased worldwide, with reports indicating a 350 % increase in the last decade (2), mainly popular with teenagers, young adults, and especially women (3).

It has been framed academically as a prototype of a healthy lifestyle as long as these diets are adequately planned (4) offering cardiovascular and metabolic health benefits, as it would correspond to a diet that improves clinical parameters of hypercholesterolemia, hypertension, coronary heart disease, type 2 diabetes *mellitus*, and obesity (5). However, evidence also reports critical nutritional deficiencies for the present regime, as indicated by a 2021 systematic review that included 36 cross-sectional studies, reporting that veganism is associated with low intakes of protein, vitamin B2, vitamin B3, vitamin B12, vitamin D, iodine, zinc, calcium, potassium, and selenium (6). Special attention is paid to protein as a critical macronutrient, as studies indicate that vegans not only ingest less protein than non-vegans but also have lower concentrations of essential amino acids in their blood (7). This is a risky situation considering that deficiencies lead to complications beyond their functions in skeletal muscle and other tissues, as they also disrupt different physiological systems, affecting growth and promoting vascular dysfunction and immune depletion (8).

While the main reason for lower intakes of this nutrient may be mainly due to the restriction of plant-based diets in contrast to the omnivorous Western dietary pattern, the main reason for lower intakes of this nutrient may be due to the restriction of plant-based diets in contrast to the omnivorous Western dietary pattern (9), the influence of attitudinal and sociodemographic factors may also be playing a critical and essential role as in the general population. For example, younger age, male sex, and regular meat intake are factors that reduce the risk of low protein intake (10). Along the same lines, high socioeconomic status has been associated with higher total protein intake, and low socioeconomic status has worse body protein depletion metrics (11,12). In particular, this could affect specific age groups such as university students, who represent a particular focus of attention as they are a population with a particular connection to animal welfare causes, are in transition to adulthood, and are making various independent decisions related to diet and lifestyle. These can be detrimental in terms of health, given the limited time they have to prepare food, the limited resources available to them, as well as the lack of access to sanitary devices due to their distance from them (13,14).

At the national level, information on this topic is still quite limited, as there is a report from 2013 that evaluated 53 vegan subjects, reporting that the primary motivation for following the diet was based on animalistic principles (75 %), and only 2 % considered the health benefits. It also reported that most respondents (27 %) used internet data as their primary source of information, and a significant percentage needed information on nutritional deficiencies in omega-3, vitamin D, and zinc, all critical nutrients in the vegan population (15). While this data strongly disagrees with a study published in 2020, which also asked about motivations and knowledge of deficiencies, the latter study did not specify the population opting for strict vegetarian diets. It was aimed exclusively at first-year university students at an institution that does not represent the socioeconomic reality of the country (16).

Considering the ethical and moral principles that underpin the choice of this type of diet and that do not consider health as the main focus, the lack of knowledge previously mentioned, and the fact that information on this subject is still quite limited at the national level, it is necessary to investigate how this type of diet is being carried out in the national university population in order to provide inputs that will allow us to improve the nutritional care aimed at this population group. Given this, this study aimed to determine the degree of protein sufficiency and its associated factors in a sample of Chilean vegan university students.

METHODS

A descriptive, cross-sectional, exploratory study was conducted on Chilean university students who declare themselves vegans and therefore follow a plant-based diet. The sample was calculated by cross-referencing the information declared by the Ministry of Education of the Government of Chile on the university population enrolled in the country (considering 1,194,311 enrolled students) (17) and the 4 % vegan population of the country according to projections by Chile's leading market research and public opinion company (18). From this, and using the Qualitrics® application, with 95 % confidence and a maximum of 5 % error, the figure of 384 people was obtained.

Recruitment was carried out online between October and December 2022 through a poster disseminated through the Facebook® profiles of all the student federations of the country's universities, both public and private. Influencers promoting plant-based diets on Instagram® were also contacted to publish the poster on their social networks. Interested individuals were able to click on a link that presented the poster, directing them to a survey on the Google Forms® platform where they had to give their informed consent to participate and then go on to complete the self-report survey. The survey asked about age, gender, weight, height, length of time on a plant-based diet, type of university, academic area, level of study, extracurricular activities, and coexistence. In addition, the time spent eating, budget, and eating occasions outside the home were asked about. Finally, a 24-Hour Reminder Survey (ER24H) was included, in which each subject presented his or her daily diet to determine the total protein intake per day and protein adequacy according to the indicated weight. To determine those mentioned above, an intake of at least 90 % of the daily protein requirement was considered adequate, calculated as 0.9 g per day/kg self-reported weight. Concerning the inclusion and exclusion criteria, only undergraduate university students who had been on the plant-based diet for at least one month were eligible to participate, and those on an evening diet or those on a second undergraduate course were excluded as these are variables that affect eating habits. Responses from ovo-lacto-vegetarians who demonstrated that they did not eat a strict vegetarian diet were also excluded.

All data obtained were processed in Microsoft Excel©, then exported and analyzed in GraphPad Prism v.9.3.1 for Windows (San Diego, California, USA). To determine the association between variables, each condition was dichotomized against the presence or absence of protein intake adequacy, calculating odds ratios (OR), 95 % confidence intervals (CI), and Fisher's test to estimate statistical significance ($p < 0.05$).

Finally, it is essential to mention that this work was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the Universidad Mayor campus in Temuco, Chile (Folio 0341).

RESULTS

A total of 223 responses from volunteers were recruited online, and 114 valid surveys were subsequently screened according to the exclusion criteria. Of these responses, the predominant population was under 27 years of age (85.9 %), women (83.4 %), students of biomedical, exact and natural sciences (57.8 %), four years or more of study (60.6 %), the primary extracurricular activity of physical activity (67.6 %) and predominantly cohabitation of two people or less (57.1 %) and with a family (65.7 %). Regarding the geographical area of the respondents and the financing of the institutions where they studied, there was heterogeneity between metropolitan (47.4 %) and non-metropolitan (52.6 %) regions, as well as public (53.5 %) and private (46.5 %) universities, respectively (Table I). Regarding the associated dietary and economic variables, the majority had a normal nutritional status (69.2 %), had been vegan for more than one year (78.9 %), spent more than 30 minutes at lunchtime (81.6 %), reported using supplements (92.2 %), and reported spending less than six and a half dollars per lunch when eating out (61.4 %), and no more than 125 dollars per month for food (76.3 %). Both dichotomous responses were homogeneous regarding state financial support for food and eating out more than three days per week. As for the primary variable evaluated, established by the degree of protein adequacy, only 53.5 % had an adequate macronutrient intake (Table I).

To determine the association between daily protein adequacy and each of the variables consulted, ORs were calculated as shown in table II. As for those enrolled in private institutions (60.7 %) as well as in humanities and social sciences degrees, they presented higher percentages of adequacy at the intra-group level (60.4 %), also aligning themselves with those who presented a normal nutritional status (50.7 %). However, the association does not reach an acceptable OR or statistical significance concerning the population enrolled in public institutions, natural and biomedical sciences students, and subjects with altered nutritional status.

Conversely, when considering the length of time respondents have been vegan, the magnitude more significant than one year is associated with protein adequacy in respondents, reaching nearly 60 % versus only 33 % of those who had been vegan for less than one year (OR, 2.86; 95 % CI, 1.07 to 7.34; $p < 0.05$), all aligned with supplementation (56.7 %) versus its negative counterpart (20 %), where the association found is higher (OR, 5.24; 95 % CI, 1.17 to 25.2; $p < 0.05$). More specifically, and with a higher significance, the variable of eating lunch less than three times a week outside the home stands out, where those who maintain this practice have a 90.3 % adequacy rate, a figure well above those who eat lunch outside the home more frequently, who do not exceed 10 % adequacy (OR, 87.7; 95 % CI, 24.1 to 30.4; $p = 0.000$).

The variables of age, sex, region of geographic origin, cohabitation, years of study, extracurricular activities, state financial support, money, and time spent on food did not influence the protein adequacy metrics in the present sample evaluated.

Table I. Sample characterization

	n (%)		*n* (%)
Age		*Nutritional status*	
18-26 years	98 (85.9 %)	Normal	79 (69.2 %)
27-35 years	16 (14.1 %)	Malnutrition	35 (30.8 %)
Sex		*Economic support*	
Female	95 (83.4 %)	Yes	63 (55.2 %)
Male	19 (16.6 %)	No	51 (44.7 %)
Region		*Vegan time*	
Metropolitan	54 (47.4 %)	< 1 year	24 (21.1 %)
Non metropolitan	60 (52.6 %)	> 1 year	90 (78.9 %)
University		*Time for lunch*	
Public	61 (53.5 %)	< 30 minutes	21 (18.4 %)
Private	53 (46.5 %)	> 30 minutes	93 (81.6 %)
Academic area		*Lunch away from home*	
Natural, biomedical, and exact sciences	66 (57.8 %)	< 3 times	62 (54.4 %)
Social sciences, humanities, and arts	48 (42.2 %)	> 3 times	52 (45.6 %)
Years of study		*Supplementation use*	
1-3 years	45 (39.4 %)	Yes	104 (91.2 %)
Four years or more	69 (60.6 %)	No	10 (8.7 %)
Extracurricular activity		*Monthly money for food*	
Physical activity	77 (67.6 %)	< 125 US Dollars	87 (76.3 %)
Work	38 (33.4 %)	> 125 US Dollars	27 (23.6 %)
Cohabitation		*Money for lunches away from home*	
Two persons or less	65 (57.1 %)	< 6.5 US Dollars	70 (61.4 %)
Three persons or more	49 (42.9 %)	> 6.5 US Dollars	44 (38.6 %)
Family cohabitation		*Protein intake*	
With family	75 (65.7 %)	Adequate	61 (53.5 %)
Without family	39 (34.2 %)	Inadequate	53 (46.5 %)

Table II. Association between protein intake and the study variables

	Adequate intake *n* (%)	Inadequate intake *n* (%)	OR	95 % CI
Age				
18-26 years	53 (54.1%)	45 (45.9%)	1.18	(0.39-3.53)
27-35 years	8 (50%)	8 (50%)	0.84	(0.28-2.55)
Sex				
Female	52 (54.7%)	43 (45.3)	1.34	(0.52-3.44)
Male	9 (47.4%)	10 (52.6)	0.74	(0.19-1.90)
Region				
Metropolitan	28 (51.9)	26 (48.2)	0.88	(0.43-1.79)
Non metropolitan	33 (55)	27 (45)	1.13	(0.55-2.31)
University				
Public	24 (45.3)	29 (54.7)	0.54	(0.25-1.11)
Private	37 (60.7)	24 (39.3)	1.86	(0.90-3.92)

(Continues on next page)

Table II (cont.). Association between protein intake and the study variables

	Adequate intake *n* (%)	Inadequate intake *n* (%)	OR	95 % CI
Academic area				
Natural, biomedical, and exact sciences	32 (48.5)	34 (51.5)	0.61	(0.28-1.27)
Social sciences, humanities, and arts	29 (60.4)	19 (39.6)	1.62	(0.78-3.49)
Years of study				
1-3 years	26 (57.8)	19 (42.2)	1.33	(0.63-2.86)
Four years or more	35 (50.7)	34 (49.3)	0.75	(0.34-1.57)
Extracurricular activity				
Physical activity	45 (58.4)	32 (41.6)	1.27	(0.56-2.82)
Work	20 (52.6)	18 (47.4)	0.79	(0.35-1.78)
Cohabitation				
Two persons or less	37 (56.9)	28 (43.1)	1.38	(0.67-2.86)
Three persons or more	24 (49)	25 (51)	0.72	(0.34-1.49)
Family cohabitation				
With family	39 (52)	36 (48)	0.83	(0.39-1.83)
Without family	22 (56.4)	17 (43.6)	1.19	(0.54-2.56)
Nutritional status				
Normal	45 (57)	34 (43)	1.57	(0.68-3.40)
Malnutrition	16 (45.7)	19 (54.3)	0.63	(0.29-1.46)
Economic support				
Yes	36 (57.1)	27 (42.9)	1.39	(0.68-2.87)
No	25 (49)	26 (51)	0.72	(0.34-1.47)
Vegan time				
< 1 year	8 (33.3)	16 (66.7)	0.34	(0.13-0.93)
> 1 year	53 (58.9)	37 (41.1)	2.86	(1.07-7.34)
Time for lunch				
< 30 minutes	11 (52.4)	10 (47.6)	0.94	(0.36-2.58)
> 30 minutes	50 (53.8)	43 (46.2)	1.06	(0.38-2.77)
Lunch away from home				
< 3 times****	56 (90.3)	6 (9.7)	87.7	(24.1-304)
> 3 times	5 (9.6)	47 (90.4)	0.01	(0.00-0.04)
Supplementation use				
Yes*	59 (56.7)	45 (43.3)	5.24	(1.17-25.2)
No	2 (20)	8 (80)	0.19	(0.03-0.8)
Monthly money for food				
< 125 US dollars	43 (49.4)	44 (50.6)	1.03	(0.47-2.27)
> 125 US dollars	18 (48.7)	9 (51.3)	0.96	(0.44-2.11)
Money for lunches away from home				
< 6.5 US dollars	38 (54.3)	32 (45.7)	1.19	(0.52-2.72)
> 6.5 US dollars	19 (50)	19 (50)	0.84	(0.36-1.92)

DISCUSSION

Protein intake in the vegan population is one of the leading nutritional issues facing people who opt for a plant-based diet. Studies indicate that their intake is significantly lower when compared to omnivores, pescetarians, and ovo-lacto-vegetarians ($p = 0.0001$), and there is a high dependence on the consumption of products containing soya-derived protein, accounting for as much as 3 % of total daily calorie intake (7). Although there are no published studies that refer to the degree of protein adequacy at the national level, a report by Agüero et al. indicated that the Chilean vegetarian-vegan population showed an increase in the consumption of legumes during the SARS-CoV-2 pandemic period and that they ate in a greater diversity of preparations compared to the omnivorous population (19). While this proves a better use of one of the primary protein sources of the plant-based

diet, it is essential to consider that integrating legumes alone is not enough to achieve a correct plant-based protein intake and could be mediated by different sociodemographic or attitudinal factors. In this line, our study is the first work to evaluate this type of variable in the Chilean vegan population, reporting a worrying figure of young adults who do not meet their protein requirements (46,5%), which could be the result of the population's lack of knowledge of their protein requirements due to a lack of access to competent professionals. (15), or conversely, they may have adequate knowledge of their requirements but do not have the means to acquire adequate food and portions (20). A recent qualitative report on Chilean vegans provided essential inputs to understand the reality faced by this population group, from (i) the constant reflection about their diet, which could be favorable for the acquisition of healthy eating habits, but which contrasts with (ii) the constant conflict when opting for a diet that is practical in their daily lives. From this, we can argue that the first idea aligns with our results, giving the length of time people have been vegan as a factor associated with a correct protein intake. This could be mediated by the animalistic and abolitionist motivational component of the regime itself, which would motivate its population to increase awareness of animal welfare but also human welfare to defend their position in front of society (21) if we add to this the environmental component, where individuals who have been vegan for longer can create links or networks with like-minded people who can educate them on better practices for eating well, as evidence has been reported in other minority groups (22). Regarding the second premise, the practicality of a vegan diet in the current context of the Chilean food industry does not seem to be a significant limitation considering the boom of products that have emerged in the last decade, where practically all supermarket chains in the country offer different protein products, from texturized soya to easy-to-prepare ready-made preparations such as croquettes and hamburgers. The development of these products has reached such a level that even a public domain report issued in 2021 by the National Institute of Industrial Property of Chile exposed the different technologies patented and used for the production of food for vegan and vegetarian diets in order to promote the national market (23). However, it is necessary to consider that the primary motivation for veganism is animal liberation, which is at odds with several brands offering plant-based protein options, as they have historically contributed to the meat industry (24,25). This offers an exciting debate and should establish that food's non-nutritive functions are more linked to ethical principles than strictly physiological ones (26).

About the other variables associated with protein adequacy, it was possible to identify the frequency of lunches at home and the use of supplements, which could implicitly inform cooking skills and concern for their nutritional status. This would be in line with the evidence, as several studies report that cooking skills and nutritional knowledge are directly related to the nutritional quality of the diet (27) and even predict adherence to a healthy diet (28).

On the other hand, and interestingly, food-related economic variables (state support for food, time and money spent on lunches, and monthly budget for meals) had no influence on protein adequacy in the present sample. These results are related to those published in the German vegan and omnivorous population, where it was concluded that financial constraints would not be a barrier to implementing plant-based diets. The present statement could be because food choice motivations differ from the general population, even turning towards healthier eating in some aspects, such as higher expenditure towards fruits (p = 0.0003), vegetables (p = 0.006), dairy alternatives (p = 0.0003) and legumes/nuts/seeds (p = 0.0003). It would be interesting to assess whether this motivation is at the expense of other typical expenditures that the university population might have (29,30).

As for the potential of this study, variables associated with protein adequacy were identified in a minority population group in the country, with statistically significant results. Based on these results, it would be interesting to confirm their influence in longitudinal studies or research considering a population beginning its vegan diet. This could elucidate and confirm whether these variables constitute factors to be considered in comprehensive nutritional care for the vegan population. In addition, a sample with a certain degree of homogeneity in terms of the socioeconomic level was obtained, considering the distribution between those who received state financial aid for food and the type of institution in which they studied (public and private). Regarding the study's main limitations, it is necessary to mention that the calculated sample size was not reached, in addition to the heterogeneity in the distribution of an essential number of variables that could be influencing the results. This should lead to caution in the extrapolation of the results, and it is necessary to replicate this type of initiative with a more extended recruitment and data collection period. On the other hand, and regarding the primary variable under evaluation, only a single nutritional indicator was used to establish protein sufficiency in the sample considered, being possible to complement this variable with the evaluation of the amino acid score and protein digestibility for more complex and complete analysis (31). It could also be interesting to add anthropometric indicators of muscular body composition that denote correct protein utilization (32).

Finally, it is essential to emphasize that although all nutritional care should be personalized and targeted for each individual, there are particular population groups, such as Chilean vegan university students, who present a cross-cutting context and needs. These should be identified to improve the role of health professionals in their care, promoting their health and preventing diseases based on the factors that nutrition and food research can report.

CONCLUSION

The present study reported that 46.5 % of the Chilean university vegan population surveyed had an inadequate daily protein intake. Concerning the subjects with an adequate intake, the length of time on the vegan diet, frequency of eating lunch away from home, and use of supplements were associated factors.

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ARÁN

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Trabajo Original

Epidemiología y dietética

Effect of sunlight on vitamin D and hemoglobin levels among the residents of Ningbo, China

Efecto de la luz solar sobre los niveles de vitamina D y hemoglobina entre los residentes de Ningbo, China

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Abstract

Objective: this study investigated the effect of sunlight on vitamin D and hemoglobin levels among the residents of Ningbo, China. The impact of gender, age, and season on vitamin D and hemoglobin levels was also explored.

Methods: a total of 8,481 research subjects, including 5,146 men and 3,335 women, who were permanent residents of Ningbo and received health checkups at Ningbo Second Hospital, were included in the study. Ningbo City climate bulletin data from 2019 to 2022 was also included.

Results: the study subjects received an average of 132.20 ± 40.05 h of sunlight exposure per month and had average vitamin D levels of 19.63 ± 6.61 ng/ml. Hemoglobin levels were adequate in 85.4 % of the participants and deficient in 14.6 %. Sunlight exposure correlated positively with vitamin D and negatively with hemoglobin levels. Regression analysis indicated that gender, age, and season affected vitamin D and hemoglobin levels to different degrees.

Conclusion: in Ningbo, vitamin D deficiency was common in adults while hemoglobin levels were mostly normal. The amount of sunlight exposure had a significant effect on vitamin D and hemoglobin levels and this relationship was impacted by gender, age, and season.

Keywords:

Vitamin D. Hemoglobin. Sunlight exposure. Gender. Age. Season.

Resumen

Objetivo: este estudio investigó el efecto de la luz solar sobre los niveles de vitamina D y hemoglobina entre los residentes de Ningbo, China. También se exploró el impacto del género, la edad y la estación del año en los niveles de vitamina D y hemoglobina.

Métodos: se incluyeron en el estudio un total de 8481 sujetos de investigación, incluidos 5146 hombres y 3335 mujeres, que eran residentes permanentes de Ningbo y recibieron controles médicos en el Segundo Hospital de Ningbo. También se incluyeron datos del boletín climático de la ciudad de Ningbo de 2019 a 2022.

Resultados: los sujetos del estudio recibieron un promedio de 132,20 ± 40,05 h de exposición solar al mes y tuvieron niveles promedio de vitamina D de 19,63 ± 6,61 ng/ml. Los niveles de hemoglobina fueron adecuados en el 85,4 % de los participantes y deficientes en el 14,6 %. La exposición a la luz solar se correlacionó positivamente con la vitamina D y negativamente con los niveles de hemoglobina. El análisis de regresión indicó que el género, la edad y la estación del año afectaron los niveles de vitamina D y hemoglobina en diferentes grados.

Conclusión: en Ningbo, la deficiencia de vitamina D era común en los adultos, mientras que los niveles de hemoglobina eran en su mayoría normales. La cantidad de exposición a la luz solar tuvo un efecto significativo sobre los niveles de vitamina D y hemoglobina y esta relación se vio afectada por el género, la edad y la estación del año.

Palabras clave:

Vitamina D. Hemoglobina. Exposición a la luz solar. Género. Edad. Estación del año.

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INTRODUCTION

Vitamin D, categorized as an indispensable fat-soluble vitamin (1), orchestrates pivotal roles in modulating calcium and phosphorus metabolism, along with facilitating bone morphogenesis (2). It governs bone accrual and physical maturation, interlinked profoundly with the cardiovascular, endocrine, and immune systems within the human anatomy (3). A staggering statistic reflects that over a billion children and adults globally grapple with vitamin D deficiency or insufficiency (4). Predominantly, the skin autonomously synthesizes this vitamin via exposure to ultraviolet light (UV) (5). This synthesis transpires when UV rays convert 7-dehydrocholesterol into vitamin D3, subsequently metabolized by the liver into 25-hydroxyvitamin D. Eventually, the kidneys convert this intermediary form to the biologically active variant of vitamin D, termed calcitriol. Sunlight exposure results in an augmentation of vitamin D levels in the integument (6). A diminution in levels of this vital vitamin can instigate conditions like osteochondrosis, osteoporosis, fractures, and rickets, besides escalating the risk of specific cancers.

Hemoglobin (Hb), a complex heterotetramer, primarily functions to ferry oxygen (O_2) from the respiratory organs to the peripheral tissues and reciprocally transports carbon dioxide (CO_2) from tissues to the lungs. The kinetics underlying Hb-O_2 interaction are meticulously calibrated to optimize this transfer, adapting to individual physiological growth, development, and metabolic fluctuations (7). Anemia's prevalence escalates with aging, afflicting approximately 6 % of individuals within the 50-64 years bracket and around 11 % of those aged 65 years and above (8). Both elevated and diminished hemoglobin concentrations correlate with augmented risks of cardiovascular diseases (CVD) (9,10). Concomitantly, anemia is related to escalated risks of cognitive impairment and instances of dementia in the elderly demographic (≥ 65 years) (11-13) and demonstrates a connection to increased occurrences of fractures (14), heart failure, and various other medical conditions.

The multifariousness in geographic locales, sunlight exposure durations, dietary habits, and attire preferences have manifested divergent prevalence rates of vitamin D deficiency across various regions in China (15). Consequently, a nuanced comprehension of the levels of vitamin D and hemoglobin across distinct regions can act as a linchpin for devising preventive strategies and therapeutic interventions for the contingent diseases. Ningbo, situated along the southern coast of China, typified by its subtropical monsoon climate, harbors a confluence of hills and plains, thereby providing a unique context for this study. The region, positioned at east longitude 120° 55'-122° 16' and north latitude 28° 51'-30° 33', witnesses an annual average temperature of 16.3 °C and amasses an annual sunlight exposure approximating 2,070 hours (16).

Embarking on a meticulous cross-sectional analysis, this study harnesses sunshine exposure and temperature data gleaned from the Ningbo region spanning a recent three-year trajectory, amalgamated with clinical data procured from its healthy denizens. The research endeavors to unravel the nexus between sunshine exposure and serum concentrations of vitamin D and hemoglobin, delving deeper to elucidate the influences of gender, age, and seasonal variations on these biochemical indices. The ensuing discussion seeks to proffer a holistic and nuanced perspective, intertwining multifarious elements to contribute a comprehensive understanding of the subject matter and advocate plausible preventative and remedial approaches.

MATERIAL AND METHODS

GENERAL INFORMATION

The foundational data for this intricate study originated from a meticulous cross-sectional population survey, operational from October 2019 to October 2022 in Ningbo, Zhejiang, China. The assembled cohort comprised 8,481 subjects, stratified into 5,146 men and 3,335 women, all enduring residents of Ningbo. The participative subjects underwent comprehensive physical examinations at the Health Examination Center located within the Second Hospital of Ningbo. Concurrently, climatic bulletins encapsulating the corresponding time frame were procured to enrich the dataset. The inclusion criteria meticulously omitted individuals afflicted with pathological states potentially skewing vitamin D or hemoglobin levels, such as hyperthyroidism, profound hepatic and renal maladies, malignant neoplasms, intensive infections, and leukemia.

METHODOLOGICAL FRAMEWORK

The acquisition process encompassed collection of indispensable parameters including the subjects' name, gender, age, month of examination, prevalent disease information, combined vitamin D (D2 + D3) concentrations (ng/mL) and hemoglobin levels (g/L) from the repositories of the Second Hospital of Ningbo. Corresponding average monthly temperature (°C) and sunlight exposure (h) metrics were extricated from Ningbo climatic bulletins. Chemiluminescence served as the predominant modality for quantifying total vitamin D (D2 + D3). Benchmarks established vitamin D sufficiency, insufficiency, and deficiency as 30-100 ng/mL, < 20 ng/mL, and 20-30 ng/mL, respectively. Hemoglobin quantification predominantly deployed the hemocytometer colorimetric method, with deficiency and sufficiency demarcated as < 130 g/L and ≥ 130 g/L, respectively. Stratification of subjects ensued according to age brackets and seasons, categorized according to the Gregorian calendar.

STATISTICAL ANALYSIS

Analytical processing was executed utilizing SPSS 26 software, with R and GraphPad deployed for graphical representations. Quantitative datasets were articulated as "$x \pm s$", and the interrelation, or lack thereof, between categorical variables was deciphered through Chi-square analysis, with count data delineated as the number and percentage of cases. Multiple logistic regression analyses were leveraged to scrutinize the influence of light duration on vitamin D and hemoglobin concentrations across diverse strata of gender, age, and seasonality. A p-value threshold of < 0.05 constituted the criterion for statistical significance, reinforcing the credibility and rigor of the analytical results.

RESULTS

DEMOGRAPHIC DISTRIBUTION

The evaluated cohort comprised a comprehensive total of 8,481 subjects, differentiated into 5,146 males (60.7 %) and 3,335 females (39.3 %). The seasonal distribution of subjects was strategically allocated, encompassing 1,197 subjects (14.1 %) in spring, 1,878 (22.1 %) in summer, 2,868 subjects (33.8 %) in autumn, and 2,720 subjects (32.1 %) in winter. The gender proportions remained steadfast across each seasonal phase.

AGE AND HEMOGLOBIN STRATIFICATION

Subjects were distributed across various age brackets, with most (7,245; 85.4 %) exhibiting a hemoglobin concentration of ≥ 130 g/L, contrasting with the remaining 1,236 (14.6 %) residing within the < 130 g/L hemoglobin concentration bracket. The mean vitamin D concentration was documented as 19.63 ± 6.61 ng/ml, juxtaposed with the mean monthly sunlight exposure of 132.20 ± 40.05 h, and a mean temperature of 19.01 ± 6.71 °C.

COMPARATIVE ANALYSIS OF VITAMIN D AND HEMOGLOBIN LEVELS

The analysis unveiled significant disparities in vitamin D concentrations, contingent on gender, age, and seasonal variation ($p < 0.001$). Women exhibited diminished serum vitamin D concentrations compared to men, and markedly elevated concentrations were discerned in individuals surpassing 55 years of age. Elevated vitamin D levels corresponded to summer and autumnal assessments compared to winter and spring, depicting the seasonal dependency (Table I).

Concurrently, hemoglobin concentrations revealed analogous variations, accentuated by gender, age, and seasonal progression ($p < 0.001$), with men exhibiting superior concentrations relative to women and subjects aged ≥ 65 years manifesting substantially reduced levels compared to their younger counterparts (Table II).

SUNLIGHT EXPOSURE AND CORRELATIONAL ANALYSIS

Sunlight exposure exhibited profound differences among subjects with diverse vitamin D statuses across gender, age, and seasons, save for spring. A pronounced positive correlation emerged between sunlight exposure and vitamin D concentrations ($r = 0.453$, $p < 0.001$) (Fig. 1).

Conversely, sunlight exposure depicted discernable variations between hemoglobin sufficient and deficient individuals, particularly among different genders ($p < 0.05$), but remained consistent across different ages and seasons, except within the 35-44 or ≥ 65 years age brackets. A noteworthy negative correlation materialized between sunlight exposure and hemoglobin concentrations ($r = 0.233$, $p < 0.001$) (Fig. 2).

Table I. Distribution of vitamin D level in groups

	Sufficiency		Deficiency		Insufficiency		χ^2	*p*-value
	Case	Percent	Case	Percent	Case	Percent		
Gender								
Male	394	7.66	2679	52.06	2073	40.28	186.755	< 0.001
Female	168	5.04	2236	67.05	931	27.92		
Age								
< 35	31	3.19	705	72.46	237	24.36	233.205	< 0.001
35-44	75	3.84	1247	63.85	631	32.31		
45-54	180	6.60	1575	57.71	974	35.69		
55-64	182	10.03	882	48.62	750	41.35		
≥ 65	94	9.29	506	50.00	412	40.71		
Season								
Spring	51	4.26	838	70.01	308	25.73	394.082	< 0.001
Summer	193	10.28	852	45.37	833	44.36		
Autumn	226	8.41	1366	50.86	1094	40.73		
Winter	92	3.38	1859	68.35	769	28.27		

Table II. Distribution of haemoglobin (Hb) level in groups

	< 130		≥ 130		χ^2	*p*-value
	Case	Percent	Case	Percent		
Gender						< 0.001
Male	127	2.47 %	5019	97.53 %	1540.446	
Female	1109	33.25 %	2226	66.75 %		
Age						< 0.001
< 35	155	15.93 %	818	84.07 %		
35-44	331	16.95 %	1622	83.05 %		
45-54	387	14.18 %	2342	85.82 %	50.850	
55-64	181	9.98 %	1633	90.02 %		
≥ 65	182	17.98 %	830	82.02 %		
Season						< 0.001
Spring	201	16.79 %	996	83.21 %		
Summer	336	17.89 %	1542	82.11 %	35.515	
Autumn	327	12.17 %	2359	87.83 %		
Winter	372	13.68 %	2348	86.32 %		

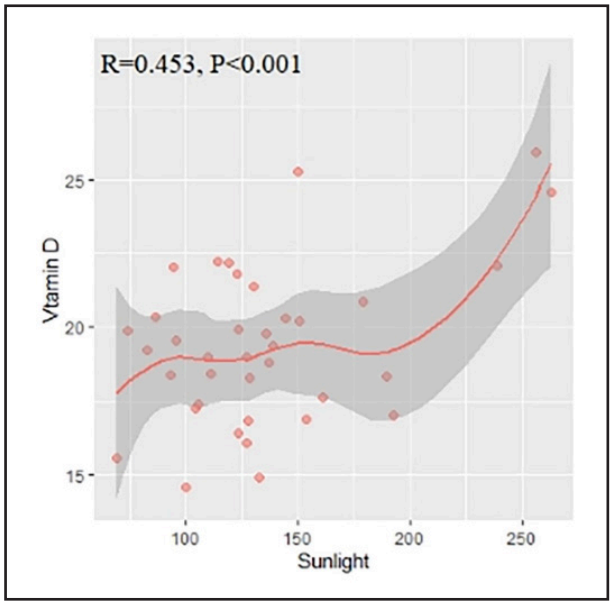

Figure 1.
The relationship between vitamin D level and sunlight (linear regression).

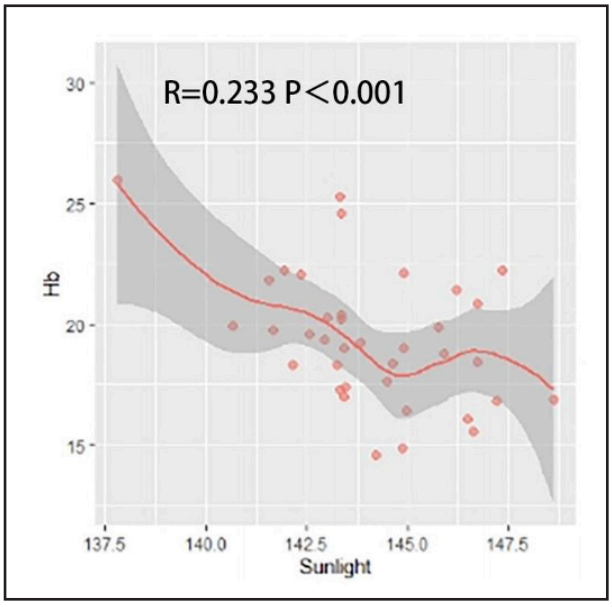

Figure 2.
The relationship between Hb level and sunlight (linear regression).

MULTIPLE LOGISTIC REGRESSION ANALYSIS

This multivariate analysis delineated the heightened susceptibility of women to vitamin D deficiency under constrained sunlight exposure relative to men (OR (female): OR (male) = 1.513). The proclivity for vitamin D deficiency attenuated with advancing age, reaching its zenith during winter. Surprisingly, temperature did not manifest as a decisive contributor to vitamin D synthesis ($p < 0.05$) (Table III). Similarly, women demonstrated elevated predisposition to hemoglobin deficiency at equivalent sunlight exposures (OR (female): OR (male) = 0.050). The impact of age and seasonal transition on hemoglobin concentrations was substantial, underscoring their influence (Table IV).

Table III. The impact of sunlight exposure on vitamin D

Variables	OR	Coefficient	SE	Wald χ^2	*p*-value	OR 95 % CI	
						Lower	Upper
Gender							
Male	Reference						
Female	1.513	0.414	0.097	18.217	< 0.001	1.251	1.830
Age group				77.933	< 0.001		
< 35	Reference						
35-44	0.865	-0.145	0.219	0.436	0.509	0.563	1.329
45-54	0.466	-0.764	0.200	14.622	< 0.001	0.315	0.689
55-64	0.305	-1.186	0.200	35.021	< 0.001	0.206	0.452
≥ 65	0.347	-1.057	0.215	24.106	< 0.001	0.228	0.530
Seasons				15.809	< 0.001		
Spring	Reference						
Summer	0.517	-0.660	0.248	7.066	0.008	0.318	0.841
Autumn	0.540	-0.617	0.178	12.048	0.001	0.381	0.765
Winter	1.091	0.087	0.207	0.177	0.674	0.727	1.638
Temperate	0.991	-0.009	0.019	0.212	0.645	0.954	1.029
Sunlight	0.994	-0.007	0.001	30.377	< 0.001	0.991	0.996
Constant	73.930	4.303	0.389	122.509	< 0.001	-	-

Table IV. The impact of sunlight exposure on Hb

Variables	OR	Coefficient	SE	Wald χ^2	*p*-value	OR 95 % CI	
						Lower	Upper
Gender							0.060
Male	Reference						
Female	0.050	-3.005	0.098	942.368	< 0.001	0.041	
Age group				62.361	< 0.001		
< 35	Reference						
35-44	1.725	0.545	0.136	16.029	< 0.001	1.321	2.252
45-54	1.393	0.332	0.118	7.864	0.005	1.105	1.756
55-64	1.76	0.565	0.114	24.489	< 0.001	1.407	2.201
≥ 65	2.584	0.949	0.129	54.495	< 0.001	2.008	3.324
Seasons				12.706	0.005		
Spring	Reference						
Summer	0.905	-0.1	0.106	0.879	0.348	0.735	1.115
Autumn	0.762	-0.272	0.099	7.625	0.006	0.628	0.924
Winter	1.061	0.059	0.092	0.419	0.517	0.887	1.270
Sunlight	0.998	-0.002	0.001	5.579	0.018	0.996	1.000
Constant	686.333	6.531	0.235	775.296	< 0.001	-	-

SYNTHESIS OF FINDINGS

The detailed analysis of results elucidates pivotal insights into the interdependence between vitamin D and hemoglobin concentrations, sunlight exposure, and various demographic and temporal parameters. These intricate interrelations and distinct patterns amplify the comprehensive understanding of the multifaceted interactions and their subsequent implications on physiological well-being and disease predisposition.

DISCUSSION

This study reveals that Ningbo receives less sunlight exposure compared to other regions of the country (17). However, the latitude of this region is influenced by the convergence of cold and warm air masses, and it is characterized by a notable presence of large mountains and oceans. Ningbo's geographical location and natural environment significantly affect the local weather patterns, leading to frequent catastrophic events and prevalent cloudy and rainy weather. The vitamin D levels are notably low among Ningbo residents, with merely 7.66 % and 5.04 % of men and women, respectively, having adequate levels. The current study shows that vitamin D deficiency was marginally more prevalent in women than in men. The Korean National Health and Nutrition Examination Survey (KNHANES), spanning from 2008 to 2014, revealed that 76.7 % of the female population had vitamin D deficiency (< 50 nmol/L) (18), contrasted with 54.6 % in Japan (19). Furthermore, the prevalence of vitamin D insufficiency and deficiency in Ningbo considerably surpasses the national average of 66.3 % (20). Ningbo's latitude, ranging between 28.51-30.33°, results in prolonged sunlight paths and diminished UV rays due to its oblique angle. Lifestyle-affected exposure to air pollution further restricts solar irradiation and impairs vitamin D synthesis in the skin. Although 85.4 % of the Ningbo population has sufficient hemoglobin levels, they are comparatively lower than those observed at different altitudes in China (21). A correlation exists between the variances in environmental oxygen levels at different altitudes and the dietary habits of the population.

This study identified a positive correlation between vitamin D and sunlight exposure. Although this vitamin can be partially obtained through diet, the majority is absorbed by the skin through ultraviolet B (UVB) radiation from the sun. Adequate UVB radiation triggers the conversion of 7-dehydrocholesterol (7-DHC) to pre-vitamin D3 (22), thereby enhancing vitamin D production. Given the same geographical conditions, climate, air quality, working environment, and health conditions, young Chinese women, who typically prioritize fair complexion, often use sunscreen and sunshade umbrellas to avoid direct sunlight. Consequently, a lack of sunlight exposure might be one of the reasons for diminished vitamin D synthesis in this demographic (23). Meanwhile, women of reproductive age (18-44 years) have high vitamin D consumption, but the intake levels of vitamin D remain relatively constant. Estrogen intensifies the function of vitamin D by promoting its accumulation and by amplifying the expression of vitamin D receptors. As middle-aged women in perimenopause and menopause exhibit lower levels of estrogen (24,25), it may elucidate why the overall serum vitamin D levels were lower in women than in men in this study. This observation aligns with previous studies (26-28).

Individuals > 55 years of age displayed significantly elevated levels of vitamin D compared to their middle-aged counterparts. This could be attributed to the fact that younger individuals, burdened with academic and professional pressures, predominantly stay indoors, while older, retired individuals tend to partake more in outdoor activities and thereby, receive increased sunlight exposure. This pattern correlates with the retirement ages of 60 for men and 55 for women. Vitamin D levels were significantly higher in summer and autumn compared to winter and spring, peaking in summer and reaching a nadir in winter — consistent with earlier studies (29-31). The summer months offer extended exposure to sunlight and high UV radiation, and the milder weather in autumn encourages outdoor activities. In contrast, winter, characterized by lower temperatures, necessitates wearing multiple layers of clothing and results in minimal skin exposure, and spring sees a greater number of rainy days, which together with reduced UV radiation exposure, constrain the synthesis of vitamin D (32).

Increased exposure to sunlight is associated with lower hemoglobin levels, potentially due to the damaging effect of UV irradiation on the red blood cell membrane (33). Additionally, irradiating red blood cells with light wavelengths that can induce skin diseases causes oxygen-dependent colloid-permeable hemolysis through the formation of peroxides (34).

Hemoglobin levels are significantly higher in men than in women, primarily because women have higher levels of estrogen and lower levels of androgens, hormones necessary for stimulating bone marrow and blood production. The decline in hemoglobin levels with age may be associated with decreased secretion and erythropoietic capability of the liver, kidneys, and other organs. A diminished hematopoietic capacity of bone marrow lowers the body's ability to absorb iron, and chronic blood loss can result from gastrointestinal diseases (35). Erythrocytosis is also more prevalent in men, possibly due to the higher smoking rate in this population (36). Hemoglobin levels were higher in autumn, a phenomenon potentially related to the local dietary habits of Ningbo residents.

The strength of this study lies in the data allowing for stratification by gender, age, and season. However, the study has several limitations. Firstly, its cross-sectional design prohibits the deduction of causality. Secondly, it does not offer extensive insights into the nutritional dietary intake and sunlight exposure in the population.

To address the findings of this study, health education should be extensively disseminated to encourage people to optimize natural conditions, advocate for the reasonable enhancement of outdoor activities, increase sunlight exposure, modify dietary structure, and augment the intake of vitamin D-rich foods. Women should be cautioned

against excessive sunscreen use. For those at high risk of vitamin D deficiency, or during the seasons when vitamin D levels are likely to be low, oral vitamin D supplements and fortified foods should be reasonably and timely promoted, based on individual's current vitamin levels. Utilizing lamps that produce UVB radiation is another alternative for promoting vitamin D production in some individuals (37). Vitamin D supplementation is crucial to avoid prolonged exposure to intense sunlight, capable of causing cellular damage. The effect of sunlight exposure on hemoglobin necessitates further exploration and analysis. Clinicians should monitor vitamin D status and hemoglobin levels to mitigate the adverse health impacts of their deficiencies.

CONCLUSION

This study underscores the significant vitamin D deficiency among residents of Ningbo, attributed to specific geographical, environmental, and lifestyle factors, with a pronounced prevalence in women. The constrained sunlight exposure in Ningbo, due to its unique geographical and atmospheric conditions, results in diminished vitamin D synthesis and variations in hemoglobin levels, reflecting the role of environmental elements in health outcomes. The conspicuous deficiency of vitamin D in Ningbo necessitates targeted health interventions and awareness campaigns. These interventions should encourage outdoor activities, balanced diets rich in vitamin D, and adequate sunlight exposure, considering its potential adverse effects.

In conclusion, the research sheds light on the distinct health challenges in Ningbo, highlighting the influence of localized factors on health indicators and urging for region-specific health strategies to ameliorate the overall well-being of the population in such unique environmental settings.

CONSENT FOR PUBLICATION

Not applicable. The study received an exemption from the Human Research Ethics Committee of Ningbo Second Hospital and did not require informed consent. Verify that all methods are implemented in accordance with relevant guidelines and regulations.

AUTHORS' CONTRIBUTIONS

Yi Yuan: formulation of overarching research goals and aims; Dongzhi Xu: data collection; Xuyue Hu: data curation and writing, original draft; Ruijie Zhang: data analysis and statistics; Ji Yang: English translation and polishing.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethics Committee of HwaMei Hospital, University of Chinese Academy of Sciences (Ningbo, China; approval code: SL-NBEY-KY-2023- 17-01).

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ARÁN

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Trabajo Original

Epidemiología y dietética

Association between the dietary inflammatory index and pelvic inflammatory disease – Findings from the NHANES data (2015-2018)

Asociación entre índice de inflamación dietética y enfermedad inflamatoria pélvica: hallazgos de los datos del NHANES (2015-2018)

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Abstract

Background: pelvic inflammatory disease (PID) is a common gynecological condition. The dietary inflammatory index (DII) scoring algorithm is a novel tool for evaluating the inflammatory potential of a diet. However, the association between DII and PID remains unexplored. This study aimed to evaluate and quantify the relationship between DII and the risk for PID.

Material and methods: the present study included two cycles of the National Health and Nutrition Examination Survey (NHANES) conducted between 2015 and 2018. A total of 2769 participants with complete information were enrolled. Weighted univariate and multivariate logistic regression analyses were performed to examine the association between DII and the risk for PID. Subsequently, the association was graphically represented using a restricted cubic spline (RCS).

Results: univariate and multivariate regression analyses revealed a strong correlation between DII and PID occurrence. After adjusting for all covariates, the odds ratio for the effect of DII on PID remained significant (OR = 1.220, 95 % CI: 1.024-1.452). The correlation analysis revealed a linear relationship between DII and the risk for PID.

Conclusions: this study unravels a significant positive correlation between DII and the risk for PID. This finding highlights the potential of anti-inflammatory diet therapy as a novel therapeutic intervention for PID. However, due to the limitations of the study design, further research is needed to explore this relationship in detail.

Keywords:

Dietary inflammatory index. Pelvic inflammatory disease. National Health and Nutrition Examination Survey. Cross-sectional study.

Resumen

Antecedentes: la inflamación pélvica es una enfermedad ginecológica común. El algoritmo de puntuación del índice de inflamación dietética (DII) es una nueva herramienta para evaluar el potencial inflamatorio de la dieta. Sin embargo, el vínculo entre la DII y la inflamación pélvica aún no se ha estudiado. El objetivo de este estudio fue evaluar y cuantificar la relación entre el riesgo de DII y PID.

Materiales y métodos: este estudio incluyó dos rondas de la Encuesta Nacional de Examen de Salud y Nutrición (NHANES) que se llevaron a cabo entre 2015 y 2018. Un total de 2769 participantes con información completa fueron incluidos en el estudio. Se realizaron análisis ponderados de regresión lógica univariable y multivariable para examinar las asociaciones entre el riesgo de DII y PID. Posteriormente, esta asociación se representa con una *spline* cúbica restringida (RCS).

Resultados: los análisis de regresión monovariable y multivariable mostraron una fuerte correlación entre la ocurrencia de DII y PID. Después de ajustar todas las covariables, la relación de ventaja de los efectos de DII sobre PID se mantuvo significativa (OR = 1,220, IC del 95 %: 1,024-1,452, $p = 0,029$). El análisis de correlación reveló una relación lineal entre el riesgo DII y PID.

Conclusiones: este estudio reveló una correlación positiva significativa entre el riesgo de DII y PID. Este hallazgo destaca el potencial de la dieta antiinflamatoria como una nueva intervención terapéutica PID. Sin embargo, debido a las limitaciones del diseño del estudio, se necesita más investigación para explorar esta relación en detalle.

Palabras clave:

Índice de inflamación alimentaria. Enfermedad pélvica. Encuesta Nacional de Salud y Nutrición. Estudios transversales.

Availability of data and materials: the data used in this study are publicly available (https://www.cdc.gov/nchs/nhanes).

Ethics approval and consent to participate: the National Center for Health Statistics Ethics Review Board approved all research (https://www.cdc.gov/nchs/nhanes/irba98.htm)

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BACKGROUND

Pelvic inflammatory disease (PID) is characterized by bacterial infection and inflammation of the upper genital tract (1). PID commonly leads to gynecological issues, including infertility and ectopic pregnancy. In the United States, approximately 1 million people are diagnosed with PID annually. Moreover, PID accounts for over 350,000 annual visits to the emergency department (2). PID can trigger various complications without proper treatment, thus imposing an enormous burden on individuals and healthcare systems (3). Currently, therapies for PID are based on combating the extent of infection and preventing inflammation relapses (4). While exposure to long-term overuse of antibiotics can lead to adverse health effects in patients and induce multidrug resistance in the pathogens. Therefore, strategies based on effective management of inflammation are still required for fighting against PID.

Diet has an important relationship with inflammatory processes in various diseases. Special diets have been demonstrated to have therapeutic potential in treating such diseases, highlighting the importance of studying the relationship between diet and inflammation (5). Excessive consumption of calcium-rich dairy products could increase inflammation and oxidative stress by increasing inflammatory factors TNF-α, reactive oxygen species, and IL-6 (6). Recently, a systematic assessment of the effect of diet on pain in rheumatoid arthritis suggests that anti-inflammatory diets could be effective in subsiding pain and symptoms, possibly via regulation of the inflammatory response (7). Supplementing the diet with foods enriched in vitamin D and trace elements (selenium, magnesium, zinc) is considered to be an effective adjunctive therapy in chronic pain management (8). As a novel disease management strategy, diet therapy is an effective way to counteract PID (9). Avoiding the ingestion of risky diets such as alcohol and coffee might help in alleviating the symptoms of PID (10).

DII is a recently developed assessment tool that allows quantification of the total inflammatory potential of a diet based on the properties of its components such as carbohydrates, proteins, vitamins, and trace elements (11). Based on its effect on inflammatory biomarkers, a diet could be characterized into categories ranging from maximally anti-inflammatory to pro-inflammatory (12). A previous study showed that DII was explicitly correlated with several indicators of inflammation such as increased leucocyte count, C-reactive protein level, interleukin (IL)-6 level, and tumor necrosis factor-α level (13). Several studies have suggested that DII is closely associated with tumor onset in cancers such as ovarian cancer and breast cancer, and higher DII correlates to a greater risk of cancer development (14,15). Moreover, DII might increase cardiovascular disease by enhancing systemic inflammation (16). Therapeutic options based on modulation of the inflammatory response such as decreasing the production of NO and IL-6 have been reported to be effective in treating PID (17). Strategies to effectively control inflammation remain ideal for devising therapeutic interventions for PID. However, few studies have attempted to evaluate the relationship between DII and PID. Hence, studies are necessary to examine the relationship between DII and PID, further quantifying the effect of DII on PID risk.

NHANES was started in the early 1960s to assess the health and nutritional status of the entire population of the United States (18). Taking advantage of the large sample size and comprehensive sampling design, the NHANES database has been widely recommended as a data source in many highly influential studies (19). Therefore, using weighted sampling of the NHANES, we aimed to conduct a systemic evaluation to elucidate the role of DII on the prevalence of PID, thereby providing new ideas for managing inflammation in patients with PID.

MATERIALS AND METHODS

STUDY POPULATION

For each of the surveys in NHANES, participants were interviewed in their homes to collect demographic and health data. This was followed by recording dietary intake recalls and physical measurements at a mobile health examination center (MEC). Data from 2015 to 2018 were used to ensure the objectivity and reliability of the study. According to the PID diagnostic questionnaire guidelines in NHANES, individuals equal to or over 18 years of age were selected as the candidate population. Data on exposure, outcome, and related covariates were collected from all participants, and individuals without complete information were not included in the study.

DIETARY INFLAMMATORY INDEX

Dietary intake information was accessed through face-to-face interviews in the MEC. Each participant was instructed to recall the types and quantities of foods and beverages consumed within 24 hours before the interview. DII reflects the global inflammatory potential of a diet based on the assessment of forty-five pro- and anti-inflammatory food parameters (20). For the intrinsic limitation of NHANES data, only 27 components were incorporated in the DII calculations including carbohydrates; protein; total fat; alcohol; fiber; cholesterol; saturated fat; monounsaturated and polyunsaturated fatty acids; *n*-3 and *n*-6 polyunsaturated fatty acids; niacin; vitamins A, B1, B2, B6, B12, C, D, E; iron; magnesium; zinc; selenium; folic acid; beta carotene; caffeine (21). By subtracting the estimated daily intake, z-scores were computed and transformed into centered proportions for each food parameter, and then summed up to acquire the overall DII scores for individual. Finally, to control for total energy intake, energy-adjusted DII scores were calculated based on the density of food components (intake per 1000 kcal) (22). Specifically, DII contained in the diet was obtained using an inbuilt function in the 'nhanesR' package and used in subsequent analyses. Based on the cut-offs defined by the tertile points, the DII scores were categorized into three groups (DII_Q): Q1, Q2, and Q3, representing anti-inflammatory, marginally pro-inflammatory, and highly pro-inflammatory diets, respectively (23).

PELVIC INFLAMMATORY DISEASE

Participants were screened using the 'rhq078' questionnaire to assess their PID status. Based on their responses to the question 'Ever treated for a pelvic infection/PID?', participants were divided into non-PID and PID groups.

ASSESSMENT OF COVARIATES

Age at menarche and regular menstruation were selected as potential covariates based on their previously reported correlation with the PID outcomes (24). Data for age at menarche were accessed from the responses to the 'Age when first menstrual period occurred?' in the 'rhq010' questionnaire (25). Data regarding the history of regular menstruation were accessed from the responses to the 'Had regular periods in past twelve months?' in the 'rhq031' questionnaire (26).

Data on age, education, marital status, poverty, and race were retrieved from responses to the demographic interview. Data for poverty level were divided into low, medium, and high according to the poverty income ratio (PIR) cut-offs: PIR < 1.35, $1.35 \leq$ PIR ≤ 1.85, and PIR > 1.85 (27). Body mass index (BMI) was measured at the mobile examination center. Based on BMI, participants were stratified into four categories, underweight (BMI < 18.5 kg/m^2), normal weight ($18.5 \leq$ BMI ≤ 24.9 kg/m^2), obese ($25 \leq$ BMI ≤ 29.9), and overweight (BMI ≥ 30) (28).

STATISTICAL ANALYSIS

Considering the complex and multistage sampling design of the NHANES, the data used in this study were weighted according to the sampling guidelines of the NHANES. Given the least common denominator approach, sample weights were calculated by the first-day dietary weight for each two-year cycle in NHANES (29). Descriptive statistics were performed to summarize the non-PID and PID data. For continuous variables, data were summarized using the mean and standard error of the mean (mean ± SE) for each group, and the differences were evaluated using a t-test. For categorical variables, data were expressed as percentages (%), and the differences in proportions were evaluated using the chi-square test.

To probe the relationship between DII and the prevalence of PID, a weighted univariate regression analysis was performed. Subsequently, multivariate regression analysis was conducted to assess the stability of the model. Multiple linear regression models were constructed using the 'svyglm' package in R. Four regression models were established guided by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology): the crude model was unadjusted; model I was adjusted for age and ethnicity; model 2 was adjusted for covariates that were statistically significant according to univariate regression analysis; model 3 was adjusted for all covariates. The relationship between DII and risk for PID was graphically represented using the 'rms' R package. Interactions test was performed on all variables within DII and other covariates in the multivariable model (model 3). Subgroup analyses were performed to evaluate the stability of these results. All analyses were performed using R (version 4.2.1) and RStudio (version 1.2.5042). Significance was determined using a two-tailed *p*-value threshold of 0.05.

RESULTS

CHARACTERISTICS OF INCLUDED PARTICIPANTS

Based on a detailed selection process, only those with complete information were enrolled in the study (Fig. 1). A total of 2769 participants were analyzed, representing 74,599,932 participants after survey weighting. Of these, 168 had PID and 2601 did not have PID. Participants in the PID group showed higher DII compared to those of the non-PID group, and the mean age of the PID group was older than that of the non-PID group. The covariates 'regular period', 'BMI', 'marital status', and 'PIR' showed significant statistical differences between the non-PID and PID groups (Table I).

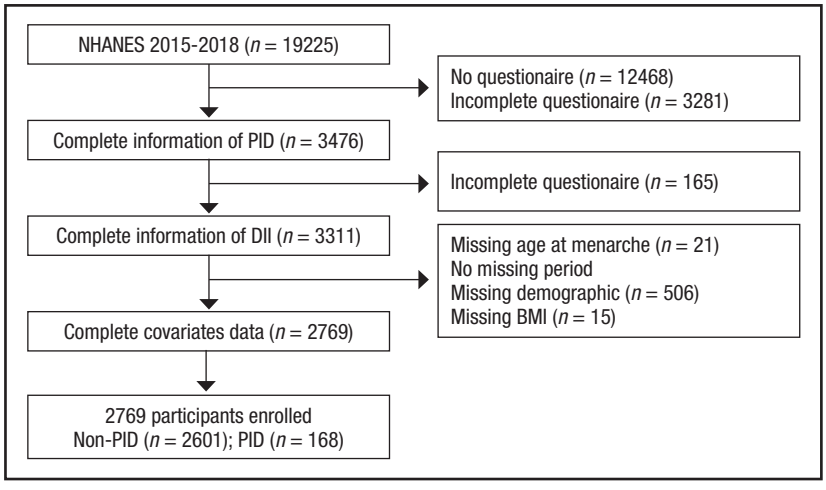

Figure 1.

Flow chart outlining the screening process (data from 2015-2018 NHANES).

Table I. Characteristics of participants (*n* = 2769)

Prevalence of PID	Total	Non-PID	PID	*p*-value
	(*n* = 2769)	**(*n* = 2601)**	**(*n* = 168)**	
DII n (%)	1.655 ± 0.094	1.605 ± 0.094	2.451 ± 0.202	< 0.001
Q1	923 (33.333)	883 (37.396)	40 (20.912)	0.002
Q2	923 (33.333)	869 (33.655)	54 (33.284)	
Q3	923 (33.333)	849 (28.949)	74 (45.804)	
Age, years	39.880 ± 0.391	39.683 ± 0.417	43.008 ± 1.133	0.011
Menarche age, years	12.624 (0.055)	12.642 (0.056)	12.338 (0.172)	0.098
Menstruation, n (%)				0.007
Regular	1900 (68.617)	1809 (65.847)	91 (51.998)	
Irregular	869 (31.383)	792 (34.153)	77 (48.002)	
BMI, n (%)				0.005
Underweight	55 (1.986)	54 (2.464)	1 (0.166)	
Normal weight	760 (27.447)	726 (30.562)	34 (12.585)	
Obese	1269 (45.829)	1178 (42.188)	91 (51.317)	
Overweight	685 (24.738)	643 (24.786)	42 (35.931)	
Education, n (%)				0.164
Less high school	415 (14.987)	386 (9.334)	29 (14.899)	
High school	577 (20.838)	536 (21.554)	41 (28.550)	
College	1777 (64.175)	1679 (69.112)	98 (56.551)	
Marital status, n (%)				0.023
Married	1624 (58.649)	1534 (63.001)	90 (55.794)	
Widowed	57 (2.059)	51 (1.987)	6 (5.247)	
Divorced/separated	426 (15.385)	384 (13.288)	42 (25.313)	
Single	662 (23.908)	632 (21.723)	30 (13.646)	
PIR, n (%)				< 0.001
Low	909 (32.828)	835 (24.132)	74 (42.302)	
Medium	880 (31.78)	821 (26.789)	59 (34.789)	
High	980 (35.392)	945 (49.079)	35 (22.909)	
Race, n (%)				0.371
Non-Hispanic white	900 (32.503)	843 (60.088)	57 (55.221)	
Mexican American	468 (16.901)	449 (10.489)	19 (6.813)	
Non-Hispanic black	635 (22.932)	582 (11.828)	53 (16.314)	
Other	766 (27.663)	727 (17.595)	39 (21.652)	

Significant variables are shown in bold. Continuous variables were presented as mean ± SE and evaluated by t-test. Categorical variables were presented as n *(%) and evaluated by the chi-square test. OR: odds ratio; CI: confidence interval; PID: pelvic inflammatory disease; BMI: body mass index.*

UNIVARIATE WEIGHTED LOGISTIC REGRESSION ANALYSIS

To determine whether DII could be used as a predictor of the occurrence of PID, we performed weighted univariate tests (Table II). For every unit increase in DII, the relative risk of PID increased by 31 % (OR = 1.310, 95 % CI: 1.124-1.527). In comparison with the reference group, univariate analyses of other covariates indicated that 'age' (OR = 1.025, 95 % CI: 1.005-1.045), 'irregular period' (OR = 1.780, 95 % CI: 1.176-2.693), 'divorced or separated' (OR = 2.151, 95 % CI: 1.122-4.123), and BMI were positively associated with the occurrence of PID. In contrast, 'high PIR' (OR = 0.266, 95 % CI: 0.118-0.602) was significantly negatively correlated with the occurrence of PID.

MULTIVARIATE WEIGHTED LOGISTIC REGRESSION ANALYSIS

After adjusting for age and race (model 1), the analysis revealed that a unit increase in the DII corresponds to a 1.307-fold

Table II. Univariate analysis for the prevalence of PID

Covariate	OR (95 % CI)	*p*-value
DII	1.310 (1.124,1.527)	0.001
Age, years	1.025 (1.005,1.045)	0.015
Menarche age, years	0.900 (0.790,1.024)	0.105
Menstruation, n (%)		0.008
Regular	Ref	
Irregular	1.780 (1.176,2.693)	
BMI, n (%)		
Underweight	Ref	
Normal weight	6.106 (0.791, 47.131)	0.08
Obese	18.036 (2.160,150.577)	0.009
Overweight	21.494 (2.722,169.741)	0.005
Education, n (%)		
Less high school	Ref	
High school	0.830 (0.316,2.181)	0.696
College	0.513 (0.223,1.180)	0.112
Marital status, n (%)		
Married	Ref	
Widowed	2.981 (0.614,14.462)	0.167
Divorced or separated	2.151 (1.122, 4.123)	0.023
Single	0.709 (0.417, 1.206)	0.195
PIR, n (%)		
Low	Ref	
Medium	0.741 (0.436,1.260)	0.257
High	0.266 (0.118,0.602)	0.003
Race, n (%)		
Non-Hispanic white	Ref	
Mexican American	0.707 (0.343,1.456)	0.333
Non-Hispanic black	1.501 (0.926,2.433)	0.096
Other	1.339 (0.564,3.178)	0.494

Significant variables are shown in bold. OR: odds ratio; CI: confidence interval; PID: pelvic inflammatory disease; BMI: body mass index.

increase in the risk for PID (OR = 1.307, 95 % CI: 1.116-1.532) (Table III). A similar positive correlation was observed in model 2 (OR = 1.224, 95 % CI: 1.041-1.439) and model 3 (OR = 1.220, 95 % CI: 1.024-1.452). Compared to the anti-inflammatory diets (Q1), the positive correlation between highly pro-inflammatory diets (Q3) and PID persisted in model 1 (OR = 2.797, 95 % CI: 1.573-4.976), model 2 (OR = 2.157, 95 % CI: 1.133-4.106) and model 3 (OR = 2.142, 95 % CI: 1.049-4.375). Moreover, the risk of PID showed a significant trend toward an increased grade of DII in all models ($p < 0.05$).

To present the relationships more intuitively, an RCS was plotted (Fig. 2). The association between DII and the risk for PID could be fitted by a straight line with a positive slope (non-linear *p*-value = 0.560 > 0.05), indicating that increasing DII was correlated with an increased risk of PID.

SUBGROUP ANALYSIS

To test for the robustness of the relationship, we performed a subgroup analysis (Fig. 3). DII values showed the highest odds ratio (OR) in the 'widowed marital' subgroup (OR = 3.004, 95 % CI: 0.602-14.994) and the lowest OR in the 'underweight BMI' subgroup (OR = 0.711, 95 % CI: 0.489-1.034). The test for interaction highlighted a significant interaction of DII with age (p for interaction = 0.011) and BMI (p = 0.009). To eliminate the heterogeneity, the age was then categorized into four subgroups: 20-29, 30-39, 40-49, and 50-59. The results showed that compared to those in other groups, individuals in 40-50 age (OR = 2.016, 95 % CI: 1.284-3.163) may be more sensitive to the DII, thus leading to a greater prevalence of PID. Compared to the 'underweight' group (OR = 0.711, 95 % CI: 0.489-1.034), the 'normal weight' (OR = 1.572, 95 % CI: 1.211-2.040), obese (OR = 1.096, 95 % CI: 0.934-1.287) and 'overweight' (OR = 1.562, 95 % CI: 1.149-2.122) groups had higher ORs. Overall, nearly all OR values in the subgroups were great than one, implying a stable positive association between DII and the prevalence of PID.

Table III. Association between DII and the risk for PID

	Crude	Model 1	Model 2	Model 3
	OR, 95 % CI *p*-value	OR, 95 % CI *p*-value	OR, 95 % CI *p*-value	OR, 95 % CI *p*-value
DII	1.31 (1.124, 1.527) 0.001	1.307 (1.116, 1.532) 0.002	1.224 (1.041, 1.439) 0.017	1.220 (1.024, 1.452) 0.029
Q1	Ref	Ref	Ref	Ref
Q2	1.768 (1.180, 2.651) 0.007	1.831 (1.211, 2.768) 0.006	1.648 (1.069, 2.542) 0.026	1.639 (1.039, 2.587) 0.036
Q3	2.829 (1.621, 4.940) < 0.001	2.797 (1.573, 4.976) 0.001	2.157 (1.133, 4.106) 0.022	2.142 (1.049, 4.375) 0.038
p for trend	0.001	0.002	0.029	0.048

Significant variables are shown in bold. OR: odds ratio; CI: confidence interval; PID: pelvic inflammatory disease; BMI: body mass index. Crude model was unadjusted, model I adjusted for age and ethnicity, model 2 adjusted for covariates found to be of statistical significance in univariate regression analysis, model 3 adjusted for all covariates (age, age at menarche, regular menstruation, BMI, education, marital status, PIR, race).

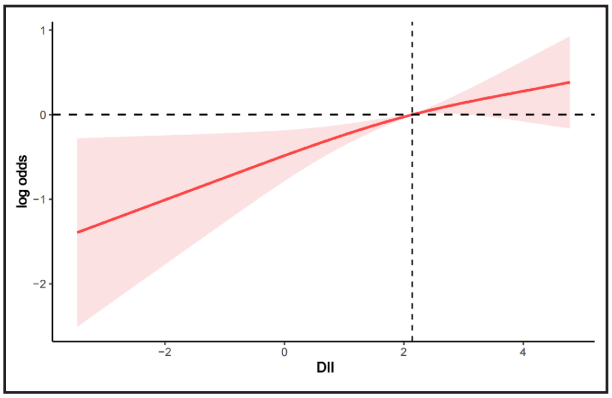

Figure 2.

Association between DII and the prevalence of PID (adjusted for age, age at menarche, regular menstruation, BMI, education, marital status, PIR, and race).

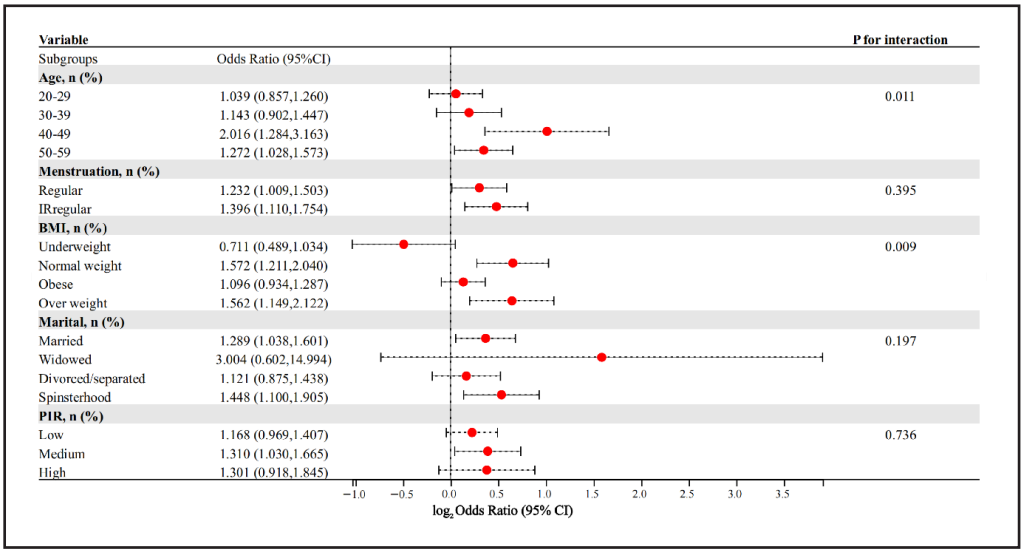

Figure 3.

Results of subgroup analyses of the associations between DII and the risk for PID.

DISCUSSION

In the present study, data from NHANES were processed using weighted approaches to increase the power to detect associations. The correlation between DII and the prevalence of PID was carefully assessed and verified through weighted univariate and multivariate linear regression analyses. The RCS further corroborated the positive linear association. This study confirms the relationship between DII and the risk for PID for the first time.

The overall prevalence of PID in our study was 6.07 %, which was similar to that reported in the prior research (30). While this could be an underestimation since the definitive diagnosis of PID mostly relies on the measurement of clinical symptoms (31). The diet pattern, predominately consisting of fruits and vegetables, can have anti-inflammatory effects by downregulating the immunomodulatory bioactivities in the periphery and in the central nervous system (32). Conversely, intake of high pro-inflammatory components such as processed meats and sugary beverages could induce levels of proinflammatory cytokines, thus increasing the adhesion of leukocytes to the endothelium (33). Regardless of the levels of covariate adjustment, DII consistently emerged as a risk factor for PID. Moreover, this relationship could be verified using the tertile trend of DII, and participants in the 'most pro-inflammatory diet' group had a higher risk for PID than those in the 'anti-inflammatory diet' group. Given the pathogenesis of PID and the regulatory role of DII, it is reasonable to conjecture that diet may affect the occurrence of PID through its effect on the inflammation process. With the help of RCS, this research was able to visualize the positive linear relationship between DII and PID, thus might elicit a preventive and therapeutic effect of DII against PID.

The present study also revealed that irregular menstruation might as a risk factor for PID, which was similar to a previous retrospective study (34). The uterine cavity is protected from bacteria by the cervix and its mucus barrier (35). While during menstrual disorders, the integrity barrier of the cervix was destroyed, thereby potentially assisting the vertical transmission of vaginal bacteria. Under the influence of a pro-inflammatory diet, the participants with irregular menstruation were prone to have a slightly increased prevalence of DII than those in the regular period. Poverty has been recognized as a risk factor for numerous diseases, and high PIR was demonstrated to be a protective factor for the

prevalence of PID. A retrospective clinical study indicated that less poverty condition may contribute to the alleviation of PID in white women (36). . Nevertheless, it's worth noting that the positive association between DII and PID persisted regardless of poverty status, highlighting the important pathogenic role of DII.

When fitting an interaction test for covariates, age, and BMI were the significant variations. The epidemiological analysis shows that the prevalence of PID increases with age (37). Similarly, in our study, age was positively related to the prevalence of PID, and participants in 40-49 years were more affected by DII than those in another age group, implying that more attention should be given and an anti-inflammatory diet was recommended to those participants. Being overweight and obese were identified to be a risk factor for PID, and higher BMI was associated with higher levels of inflammatory cytokines (38). After stratifying the data by BMI, positive correlations between DII and PID were observed in all groups except the underweight group. Notably, the positive correlation between DII and PID was seen in almost all subgroups, further emphasizing the consistency of this relationship.

Collectively, our study is the first to examine the correlation between DII and the risk for PID. With the advantage of the sampling design of NHANES, weighted approaches were used to achieve more definite results. Additionally, after adjustment for various covariates, the risk effects of DII on the prevalence of PID were evaluated and determined by multiple linear regression, thus providing solid evidence for this relationship. Yet, it is essential to note that the findings in this report are subject to several limitations. First, due to the questionnaire format of the 'rhq' and covariates, the analyses presented here might have a recall bias. Second, the sampling method could have introduced a selection bias. Third, the diagnostic criteria of PID were based on the questionnaire, which may have potential deviations. Finally, since this was a cross-sectional study, no causal relationship could be established between the DII and PID.

CONCLUSIONS

In conclusion, DII was tightly correlated with the prevalence of PID. After adjustment for all confounders, a positive linear relationship was presented between DII and the risk for PID. This study indicates that dietary interventions may have a therapeutic role in combating PID.

AUTHORS' CONTRIBUTIONS

Juan Juan Ma and Pan-Wei Hu have contributed equally in this article. MJ and HP collected the data, HP organized the data and wrote the manuscript, and ZQ and PJ designed the research plan. All authors agreed to the final version before submission. All authors read and approved the final manuscript. All authors agreed to the final version prior to submission. All authors read and approved the final manuscript.

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ARÁN

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Trabajo Original

Otros

Combined intervention strategy for reversing iron-deficiency anaemia and deficiency in psychomotor development in chronic malnutrition

Estrategia de intervención combinada para revertir la anemia ferropénica y la deficiencia en el desarrollo psicomotor en la desnutrición crónica

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Abstract

Background: chronic iron-deficiency anaemia in children has a negative impact on neuronal and cognitive development. Despite current knowledge on this subject, in Bolivia iron intake along the psychomotor development stimulation as part of a comprehensive rehabilitation process for children with severe chronic malnutrition is not yet used.

Objective: to evaluate the effect of a neurorestorative diet, consisting of iron supplements and other micronutrients, along with psychomotor stimulation in preschool children with chronic malnutrition, iron-deficiency anaemia and severe psychomotor delay.

Patients and methods: twenty-four children between 1 and 56 months of age admitted to the integral nutritional recovery centre (INRC), Paediatric Hospital of Cochabamba, Bolivia were included. A strategy of intervention was applied consisting of nutritional replenishment through the administration of elaborated meals prepared from local foods with high heme and non-heme iron concentration, added with vegetables plus the administration of micronutrient´s supplementation and the psychomotor stimulation. Anthropometric indices, psychomotor and biochemical parameters were measured at four times points, during the hospitalisation period.

Results: at the beginning, the anthropometric and psychomotor parameters were decreased (between -2 and -3 z score and below 50 % respectively). Combined strategy intervention with iron and other micronutrients together photons produced significant changes between the evaluated time points, both in anthropometric and psychomotor parameters, although these changes were less than expected.

Conclusions: the combined strategy used in this study allowed recovery from the anaemia and minimal growth due to the low birth weight or chronic malnutrition. However, the intervention was insufficient to achieve a complete recovery.

Keywords:

Anaemia. Iron replacement. Psychomotor development.

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Resumen

Antecedentes: la anemia ferropénica crónica en niños tiene un gran impacto negativo en el desarrollo neuronal y cognitivo. A pesar del conocimiento actual sobre el tema, en Bolivia aún no se utiliza la ingesta de hierro más estimulación del desarrollo psicomotor como parte de un proceso de rehabilitación integral de niños con desnutrición crónica severa.

Objetivo: evaluar el efecto de una dieta neuro reparadora, consistente en suplementos de hierro y otros micronutrientes, junto con estimulación psicomotora en niños preescolares con desnutrición crónica, anemia por deficiencia de hierro y retraso psicomotor severo.

Pacientes y métodos: se incluyeron veinticuatro niños entre 1 y 56 meses de edad ingresados en el centro de recuperación nutricional integral (CRIN), Hospital Pediátrico de Cochabamba, Bolivia. Se aplicó una estrategia de intervención consistente en la reposición nutricional mediante la administración de comidas elaboradas a partir de alimentos locales con alta concentración de hierro hemo y no hemo, adicionados con vegetales más la administración de suplementación con micronutrientes y la estimulación psicomotora. Se midieron índices antropométricos, parámetros psicomotores y bioquímicos en cuatro momentos del tiempo de hospitalización.

Resultados: al principio, los parámetros antropométricos y psicomotores estaban disminuidos (entre -2 y-3 puntuación z; y menor a 50 % respectivamente). La estrategia combinada de intervención con hierro y otros micronutrientes junto con fotones produjo cambios significativos entre los momentos evaluados, tanto en los parámetros antropométricos como psicomotores, aunque estos cambios fueron menores a lo esperado.

Conclusiones: la estrategia combinada utilizada en este estudio permitió la recuperación de la anemia y un crecimiento mínimo debido al bajo peso al nacer o la desnutrición crónica. Sin embargo, la intervención fue insuficiente para lograr una recuperación completa.

Palabras clave:

Anemia. Reposición de hierro. Desarrollo psicomotor.

INTRODUCTION

Iron-deficiency anaemia affects nearly half of preschool children and one-third of pregnant women worldwide, included Bolivia (1,2). Anaemia in children has a great physiological repercussions due to the lack of tissue oxygenation and therefore decreased energy production, contributing to the delayed growth and interfering in the development of vital tissues, including the brain, with a negative impact on neuronal, psychomotor and cognitive development, as it causes alterations in neurotransmitters and dopamine receptors, engaging the affective responses, cognitive function, GABA-receptors, as well as, movement coordination and memory patterns (3-10).

Chronic malnutrition and anaemia are determined by dietary deficiency of micronutrients and proteins primarily, and are also conditioned by social, economic, cultural factors, and/or the presence of underlying conditions that affect the ability to ingest, digest and absorb nutrients (11,12).

The acquisition of neuromotor, cognitive and psychosocial abilities occur around the first 2 - 3 years of life, that requires the maturation of the central nervous system and a pleasant psychoaffective environment with active intervention of the parents (13). There are multiple causes for deficiency in psychomotor development; different authors indicate the biological factors such as prematurity, neonatal anoxia, hereditary genetic factors, prenatal infections, and also the socio-environmental factors as conditioning to this, such as parental illiteracy, unemployment, social and geographical difficulties for accessibility to the health system (14-16). Despite actual knowledge of the neuroplasticity in children during the first years of life, supervised iron intake combined with psychomotor development stimulation as part of a comprehensive rehabilitation process for children with severe chronic malnutrition has not yet been considered in Bolivia. The purpose of this study was to evaluate the effect of a neurorestorative diet, based on iron and micronutrients supplementation along with psychomotor stimulation in preschool children with low birth weight and/or chronic malnutrition, iron deficiency anaemia and severe psychomotor delay.

METHODOLOGY

STUDY DESIGN AND POPULATION

An exploratory, descriptive, longitudinal study was conducted. Twenty-four children male and female between 1 to 56 months of age, were included in the study. They were admitted into Integral Nutritional Recovery Centre (INRC) at Manuel Ascencio Villarroel Paediatric hospital in Cochabamba, Bolivia according to the following criteria.

INCLUSION CRITERIA

Diagnosis of low birth weight (lower than 2500 g) and severe chronic malnutrition, defined thus, according WHO standards (17) [-3 z score Height/Age (≤ 3 SD) and -2 z score Weight/Height: (≥ -2 SD)]; evidence of severe delay in psychomotor development (Denver test: less than 50 %); presence of iron-deficiency anaemia (haemoglobin concentration: < 11 mg/dL); and absence of severe infectious process or serious complication. Informed consent signed by parents and mandatory hospitalisation period into INRC for 8 weeks. It was decided 2 weeks period between admission and the starting the combined intervention strategy for rutinary procedure to evaluate and monitoring for possible infections that need to be controlled. The next three post-assessments were conducted every 2 weeks after the first assessment. The values obtained in the previous assessment were used as comparison pattern.

EXCLUSION CRITERIA

Presence of one or more of the following criteria: Acute infectious disease; severe acute malnutrition defined thus, according WHO standards, (17) (-3 z score Weight/Height and ≥ -2 z score Height/Age); Anaemia due to deficiency of vitamin B9 and B12 (MCV > 100 fL); hypothyroidism; parental rejection; Children over 5 years old; premature discharge.

ASSESSMENTS

Anthropometry

Included the measurement of anthropometric indices Weight/Height; Weight/Age; Height/Age; Arm circumference/Age; Cephalic perimeter/Age and Triceps skinfold thickness/Age using WHO standards (17), at four time points, starting from the second week of admission to the INRC (first time); and ending at medical discharge (fourth time), corresponding to the week eight of hospitalization. The evaluations during intervention period were every 2 weeks, and the comparison of subsequent evaluations was made with the values of the first evaluation and also between them.

Haematology and biochemistry

Haemoglobin concentration, haematocrit, mean corpuscular volume and the biochemical parameters (glucose, albumin, total proteins, ferritin) were measured at two time points: the first measurement taken in the second week of admission and the second at medical discharge. Plasma concentration of TSH measurement was only performed upon admission to the INRC.

Psychomotor development

It included the measurement of Personal social area, Language, Gross motor area and Coordination through the Denver test at four time points, every 2 weeks, starting from the second week after admission to the INRC and concluding at medical discharge.

INTERVENTION STRATEGY

Nutritional supplementation

It starting in the 2nd week and involved the administration of meals prepared with selected local foods with high concentrations of hem and no-hem iron, combined with fruit and vegetables rich in vitamins A and C in children older than 4 months. The children younger than 4 months received an oligomeric milk formula. Additional micronutrients were administered as supplements, at the following doses: Iron sulphate: 5 mg/kg/weight, omega-3: 0,7 or 1,4 mg/day (18), prebiotics: 1 x 10^8 CFU *(Lactobacillus rhamnosus; acidophilic lactobacilli; streptococcus thermophilus)* as commercial formula; zinc: 2 mg/kg/weight; selenium: 5 µg/kg/weight; Cooper: 20 µg/kg/weight; B12 vitamin 2.4 mg/day and folic acid: 200 μg/day. The nutritional supplementation is summarised in figure 1.

During the two first weeks after admission, the children received standardized stabilizing diets (liquid and soft), either for infants or preschoolers. The liquid diets were dairy formulas that vary for each patient, because they had specific intolerances, so anti-reflux and/or lactose-free dairy formulas were used.

Nutritional stabilization and supplementation were carried out individually according to the children's admission to the INRC.

Psychomotor stimulation

The psychomotor stimulation was carried out twice session per day, and included the application of mechanical procedures to stimulate sensory, motor and language reflexes. The procedure was organised in three phases: a) environmental phase, assisted with intentional, epigenetic stimulation (mother-child relationship), environmental improvement and use of sound waves; b) management of psychomotor development delay based on an algorithm that considered sensory, sensorimotor and formal logic stimulation; and c) photon stimulation for 20 minutes using a light-emitting diodes (LED) (19,20) with a 6 w/0.5 ampere of electrical power by twice per day during 6 weeks, progressively in the patients individually, in pairs and also in groups. There were used a single colour, two colours, three colours and a range of colours with a great proportion of red-light pulsations, while avoiding excessive blue light. The psychomotor development progress was measured with the Denver test.

DATA COLLECTION

The relevant clinical information was collected by the clinical records at admission in the INRC. The anthropometric data collected included the ratios Weight-for-Height; Height-for-Age; Arm circumference-for-Age; Cephalic perimeter-for-Age; Triceps skinfold thickness-for-Age and Body Mass Index using WHO nutritional assessment tables for children under 5 years old, 2007 version (17). The collected psychomotor development data included Personal social area, Language, Gross motor area and Coordination expressed as an average in percentage (Denver test).

DATA ANALYSIS

The anthropometric data were processed using Anthro-2010 software (https://whonutrition.shinyapps.io/anthro), and the overall analysis of all variables was performed using SPSS software version 25.

The Student's t-test was used to evaluate the same variables at four time points measured every 2 weeks, from admission to the INRC to medical discharge.

ETHICAL PERMISSION

The study has been approved by the ethics committee of the Faculty of Medicine, Universidad Mayor de San Simón, Bolivia, number: C-BE-39/19. The parents of the children admitted to the

INRC and selected for the study signed written consent indicating their voluntary participation and the right to withdraw their children from the study at any time.

RESULTS

The twenty-four children who underwent nutritional replenishment and psychomotor stimulation showed average weight (SD) at birth of 1.9 (0.2) and 2.7 (1.4) kg (female and male respectively) and an Apgar score of 5.82 (0.19) and 6.37 (0.37) (female and male respectively). The anthropometric index, psychomotor and biochemist parameters taken 2 weeks following the hospitalisation (first time point assessment), were below. Only glycemia and total protein were within the normal reference range [87.41 (18.85) mg/dL and 6.07 (0.68) g/dL respectively] (Table I).

The nutritional intervention through iron supplementation, iron-fortified diet along the addition of other micronutrients (third phase) during the stay in the INRC (Fig. 1) produced significant changes between the evaluated time points, in anthropometric indices (Table II) and psychomotor parameters assessed (Fig. 2).

Between the anthropometric parameters evaluated, the index: Height/Age; Weight/Age and Arm circumference/Age, showed significant statistical differences (Student's t-test, $p < 0.05$) between the assessment time points: first vs. fourth; first vs. second and third vs. fourth. The skinfold thickness/Age showed significant statistical differences within the assessment time points: first vs. fourth and second vs. third. On the other parameters, it showed significant changes on the comparison first vs. fourth assessment (Table II).

The biochemical parameters: total protein, albumin, ferritin, haemoglobin, haematocrit and mean corpuscular volume within first and fourth-time points assessment (Table II), showed significant statistical changes (Student's t-test, $p < 0.05$).

Regarding the psychomotor parameters, they also had significant changes (Student's t-test, $p < 0.05$) between the four assessment time points for: Coordination, Personal social area and Language. Besides, the indoor Gross motor area has shown significant changes on the second vs- third and first vs. fourth assessment time points (Fig. 2).

Table I. Characteristics of Children at the time of starting combined intervention strategy in INRC

Characteristics of children		Values	Reference ranges
Gender[a]	Female (%)	10 (42)	
	Male (%)	14 (58)	
Age[b] (months)		16.75 (1-56)	
Anthropometric indices (z score)			
Weight/Height		-2.43 (2.03)	
Weight/Age		-3.65 (2.04)	
Height/Age		-3.39 (1.92)	
Arm circumference/Age		-2.99 (1.95)	
Cephalic perimeter /Age		-1.76 (2.40)	
Triceps skinfold thickness/Age		-2.18 (1.19)	
BMI		-2.64 (3.16)	
Psychomotricity (%)			
Personal social area		33.78 (18.67)	90-95
Language		43.60 (23.09)	
Gross motor area		35.97 (25.14)	
Coordination		44.83 (18.76)	
Biochemical parameters			
Thyroid stimulating hormone (TSH) (µUI/mL)		0.42 (0.06)	0.8-6
Glycaemia (mg/dL)		87.41 (18.85)	70-140
Total protein (g/dL)		6.07 (0.68)	6-8,3
Albumin (mg/dL)		2.77 (0.34)	3.2-3.5
Ferritin (ng/mL)		11.25 (8.86)	15-150
Haemoglobin (mg/dL)		9.30 (1.14)	11.25-12.75
Haematocrit (%)		28.02 (4.83)	34.5-37.5
Mean corpuscular volume (MCV) (fL)		77.66 (2.07)	80-100

Data are presented as mean (SD); n *= 24. INRC: integral nutritional recovery centre; SD: standard deviation. [a]Frequency (%); [b]Mean (range in months).*

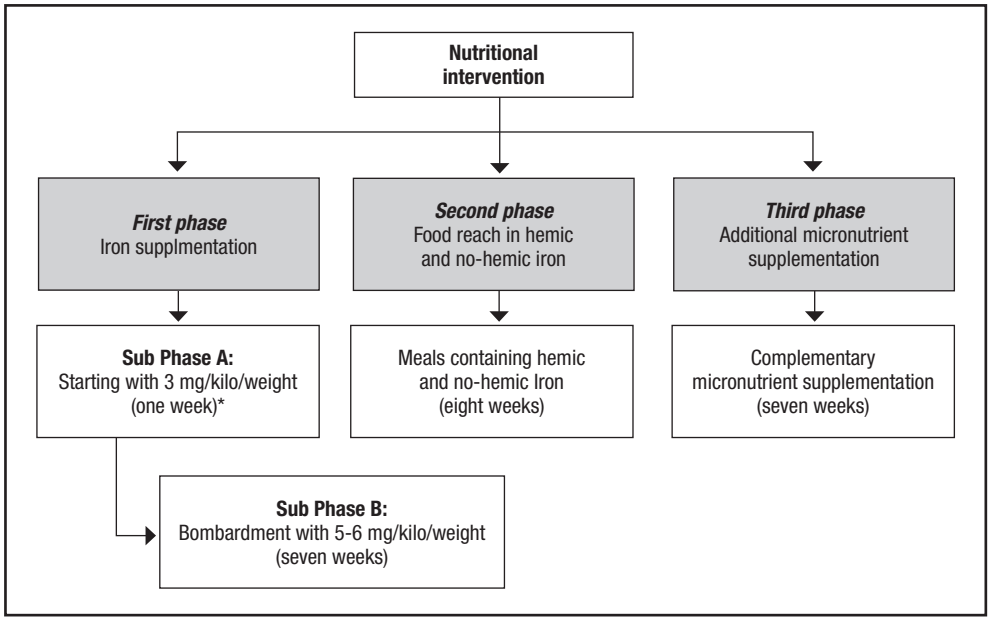

Figure 1.

Schematic representation of nutritional intervention performed in children admitted to INRC to revert the anaemia. The doses of Iron and other micronutrient supplementation are described in methodology. *Corresponds to the first week post admission.

Table II. Evolution of anthropometric and biochemical parameters during period of intervention (8 weeks), stating at second week of admission in INRC

Anthropometric indices (z score)	Evaluation times (n = 24)				
	First (2nd week)	Second (4th week)	Third (6th week)	Fourth (8th week)	*p* values
Height/Age	-3.39 (1.92)	-3.10 (1.89)	-2.88 (1.97)	-2.58 (1.92)	0.010 (1st/4th) 0.028 (1st/2nd) 0.010 (3rd/4th)
Weight/Height	-2.43 (2.03)	-1.69 (2.00)	-1.63 (2.17)	-1.58 (2.32)	0.066 (1st/4th)
Weight/Age	-3.65 (2.04)	-3.24 (1.99)	-2.99 (1.98)	-2.51 (1.85)	0.001 (1st/4th) 0.028 (1st/2nd) 0.010 (3rd/4th)
Cephalic perimeter/Age	-1.76 (2.40)	-1.75 (2.22)	-1.55 (2.22)	-1.36 (2.22)	0.197(1st/4th)
BMI	-2.64 (3.16)	-2.16 (2.13)	-1.94 (2.24)	-1.79 (1.71)	0.143 (1st/4th)
Arm circumference/Age	-2.99 (1.95)	-2.30 (1.77)	-1.95 (1.60)	-1.63 (1.62)	0.006 (1st/4th) 0.023(1st/2nd) 0.015 (3rd/4th)
Triceps skinfold thickness/Age	-2.18 (1.19)	-1.96 (0.98)	-1.68 (0.88)	-1.05 (2.39)	0.032 (1st/4th) 0.025 (2nd/3rd)
Biochemical parameters					
Glycaemia (mg/dL)	87.41 (18.85)			86.54(10.38)	0.083
Total protein (mg/dL)	6.07 (0.68)			7.99 (0.92)	0.001
Albumin (mg/dL)	2.77 (0.34)			3.96 (0.40)	0.001
Ferritin (µg/L)	11.25 (8.86)			20.05 (11.59)	0.002
Haemoglobin (g/dL)	9.30 (1.14)			12.28 (0.80)	0.001
Haematocrit (%)	28.02 (4.83)			37.10 (2.40)	0.001
Mean corpuscular volume (fL)	77.66 (2.07)			85.25 (1.56)	0.001

Data are presented as mean (SD); n = *24.*

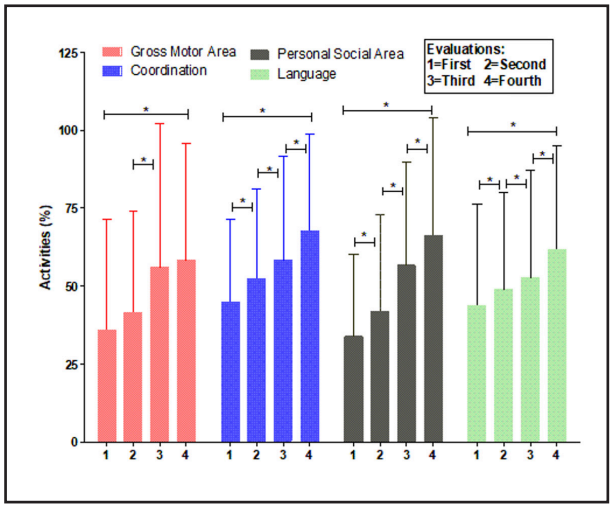

Figure 2.

Evaluation of four psychomotor parameters by Denver Test in four times. All parameters. Present differences statistically significant (Student's t-test). Gross motor area: first/fourth and second/third evaluation times, $p = 0.001$ and $p = 0.028$ respectively. Coordination, first/second, third/fourth and first/fourth evaluation times, $p = 0.001$ in all cases. Personal social area, first/second, and third/fourth evaluation times, $p = 0.001$ for both cases; second/third, and first/fourth evaluation times, $p = 0.002$ and $p = 0.029$ respectively. Language, first/second, $p = 0,044$; second/third, $p = 0,034$; third/fourth, $p = 0,002$ and first/fourth evaluation times, $p = 0.001$.

DISCUSSION

A suitable and stimulating environment, that includes conversation, full of images, light, music, interaction with toys, friendly treatment, as well as nutrition are important factors that take part in the growth and neural development stimulation of children (21,22). On this matter, the findings presented here have shown significant statistical changes on the anthropometric and psychomotor parameters measured between the fourth time points evaluated during application of combined intervention strategy. Nevertheless, the intervention, produced scant modifications on any of the measured parameters (anthropometric and psychomotor development), which reflects neuronal plasticity and its recovery capacity. This behaviour responds to the short intervention period (8 weeks) and it is expected that after hospital discharge the children will continue to recover growth until a measurable improvement is achieved. However, progressive changes are highlighted as result of the intervention with nutrient supplementation (minerals, vitamins and probiotics), not administering them as part of the therapy constitutes a risk factor because it makes possible the alteration of systemic metabolic homeostasis and the consequent cellular stress, including neuronal cells (23,24). Particularly, iron administration is essential for reversing anaemia and guaranteeing neuronal functioning (25), which enables development of neural, cognitive and psychosocial capabilities (6,25,26) achieved about the age of 2 to 3 in the suitable psychoaffective environment (13,26).

The brain becomes iron deficient before the onset of anaemia due to the prioritisation of iron available to red blood cells (RBCs) over other organs (27). Such deficiency will then lead to alterations in neurotransmitters and dopamine receptors that compromise affective responses, cognitive functioning and GABA receptors in children, before anaemia itself manifests (6,27). Even so, the use of photons through light of different colours of low intensity had a positive impact on the different areas of the child's psychomotor development due to its improvement on cognition and social and interpersonal skills, because it stimulates the brain tissue oxygenation, as previously was reported by others (20,28,29).

The increase in the values of different parameters evaluated, between different time points, with more evident differences between the first and the last points, reflect the positive effect of the combined intervention strategy applied to stop the deleterious effect of nutritional iron and other micronutrients deficiencies on neurodevelopment and its biological and social consequences (4,8,30).

The iron deficiency anaemia must be assessed within the concept of supply and demand, in which the demands are created by erythropoiesis, tissue oxygenation, erythrocyte turnover, and erythrocyte loss from haemorrhage and erythrocyte half-life from anaemia are decreased (31). Small-for-gestational-age (SGA) new-borns have low iron stores, which increases the risk of anaemia in the offspring, and its support the findings of this research, and also developmental delay (32), as was found here, characterised by a history of low birth weight and low APGAR score, which indicates the probability of "some problems during birth" that reduced oxygen in the blood (32).

Additionally, as previously reported by others, chronic malnutrition and anaemia have as a determining factor the dietary deficiency of basic nutrients, in addition to being conditioned by social, economic and cultural factors and/or by the presence of base pathologies that determine the ability to ingest, digest food or absorb nutrients (11,12).

The limited progress in the nutritional recovery and psychomotor improvement, probably respond to the confluence of factors such as the low birth weight (Table I) and the unstimulating household environments, low purchasing power of the families, low level of parental education (33,34) and in the present study as additional characteristic the rurality of the families (35).

The children discharged post-intervention were followed for a year in the outpatient clinic to promote recovery of growth and information, education and communication sessions with their parents.

In conclusion, the first years of life are the ones with the biggest neuronal maturation, where the first neural connections are established and the nervous tissue network becomes more complex. The possibility of recovery in these first years will have a great impact on an appropriate intervention. Unfortunately, chronic malnutrition in such people were so severe that the combined strategies used in this study, despite the progress in the recovery (reversion of anaemia and improvement of psychomotor parameters), was not enough to achieve complete recovery.

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ARÁN

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Trabajo Original

Otros

Roles dentro de los entornos domésticos en Chile: la "portera alimentaria"

Roles within domestic environments in Chile: the "food gatekeeper"

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Resumen

Introducción: se estudiaron los roles en el ciclo alimentario dentro del entorno doméstico, revisitando el concepto de "portera alimentaria".

Métodos: la información se obtuvo de 10 etnografías y 24 entrevistas en profundidad a personas responsables de las tareas alimentarias en hogares de ingresos bajos en Santiago, Chile, durante la pandemia. Se realizó un análisis temático desde el marco de entornos alimentarios y género.

Resultados: los resultados mostraron que el tiempo destinado al ciclo alimentario es altamente desigual entre los géneros y se responsabiliza a las mujeres del bienestar nutricional de las familias. Este rol conlleva anteponer la alimentación de los/as otros/as a la propia.

Conclusión: la discusión subraya la necesidad de considerar la distribución de roles en las intervenciones de salud nutricional, evitando reproducir prácticas riesgosas para la salud y calidad de vida las porteras alimentarias, al sobreexigirlas bajo la justificación de la eficacia en la transmisión de hábitos saludables a las familias.

Palabras clave:

Ambiente. Dieta. Mujeres.

Abstract

Introduction: this project studied the roles played in the food cycle within the domestic environment, revisiting the concept of the "food gatekeeper".

Methods: information was obtained from 10 ethnographies and 24 in-depth interviews with people responsible for food tasks in low-income households in Santiago, Chile, during the pandemic. A thematic analysis was conducted from the framework of food environments and gender.

Results: the results showed that the time allocated to the food cycle is highly unequal between genders and women are held responsible for the nutritional well-being of families. This role entails putting the feeding of others before their own.

Conclusions: in conclusion, the need to consider the distribution of roles in nutritional health interventions is emphasized, avoiding reproducing risky practices for health and quality of life of food gatekeepers, by overexerting them under the justification of effectiveness in the transmission of healthy habits to families.

Keywords:

Environment. Food. Women.

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INTRODUCCIÓN

El concepto de "portera alimentaria" se remonta a los trabajos de psicología de Kurt Lewin (1), quien desarrolla la noción de "*gatekeeper*" para identificar las maneras y razones en las que un alimento determinado podía o no llegar a la mesa. En él evidencia un rol decisivo de la mujer en la cadena alimentaria. En sus observaciones de las primeras décadas del siglo pasado, ya se constataba cómo las madres y esposas ocupan una posición específica dentro del sistema alimentario, teniendo responsabilidad y poder, al decidir sobre la admisión o rechazo de los productos que ingresan en los hogares.

Posteriormente, la definición de portera alimentaria es señalada por Poulain en sus estudios sobre sociología de la alimentación para graficar las dinámicas de organización de los hogares (desde el ingreso de alimentos hasta el conjunto de elecciones y acciones vinculadas a su preparación y consumo), que legitiman que ese alimento sea comestible (2). La expansión de este concepto refiere actualmente a la persona responsable de la mayor parte de las tareas relacionadas con la alimentación dentro del hogar (3,4).

En nuestro país, los estudios interdisciplinarios sobre alimentación de las últimas décadas han establecido que son las mujeres las que de manera tradicional e histórica han ocupado el rol de porteras alimentarias, a pesar de importantes transformaciones socioculturales como el ingreso masivo de las mujeres al mercado laboral (5,6). Esta lógica continúa operando en las generaciones más jóvenes e independientemente de su clase social (7-12).

Retomar el concepto de portera alimentaria como categoría social permite observar la desigual distribución de responsabilidades en el ciclo alimentario en los entornos domésticos, focalizando una de las tantas brechas que frenan la igualdad sustantiva, no solo en las relaciones sociales y de poder sino también en términos de salud y bienestar entre hombres y mujeres, así como entre los sectores de altos y bajos ingresos.

La cocina es una labor productiva, reproductiva, social y política que sobrepasa la dimensión de la preparación y el consumo (13-15).

El objetivo de esta investigación fue estudiar y caracterizar el rol de la portera alimentaria en entornos domésticos de nivel socioeconómico bajo.

MATERIAL Y MÉTODOS

Este fue un estudio cualitativo basado en la propuesta metodológica para investigar los entornos alimentarios domésticos validada en una investigación anterior (16). Se realizaron entrevistas en profundidad, observación etnográfica y toma de fotografías de las conductas alimentarias y de los espacios y tiempos de comidas para comprender las maneras en que el ciclo alimentario se lleva a cabo en los entornos domésticos.

Estas técnicas se aplicaron en 24 hogares con al menos un niño/a menor de 6 años y mayor de 6 meses de edad, pertenecientes a una comuna vulnerable (17) de Santiago de Chile. El estudio fue liderado por un equipo multidisciplinario de investigadoras en colaboración con la Municipalidad de la Comuna de San Joaquín, entre diciembre de 2019 y julio de 2022, durante el confinamiento por COVID-19.

CONTEXTO

La comuna de San Joaquín es un territorio relevante para este estudio puesto que su población depende mayoritariamente del sistema público de salud (90,2 %), presenta un grado relativamente alto de vulnerabilidad económica (17) y prevalencias importantes de desnutrición por exceso (18). A diciembre de 2018 tenía un 12,8 % de hogares sin acceso a servicios básicos y un 18,2 % de hogares hacinados, ambos indicadores por sobre el promedio nacional (17). Los datos obtenidos de los controles de salud de la población y de la Encuesta Nacional de Salud (2017) (18) revelaron que el 32 % de los niños/as menores de 6 años presentan obesidad y que entre la población de 15 y más años hay un 66,7 % de desnutrición por exceso. Lo anterior evidencia que en esta comuna los problemas vinculados a la mala alimentación son de alta prevalencia desde las primeras etapas de la vida y se intensifican con la edad.

MUESTRA

Se realizó un muestreo estratégico de tipo estructural. En el contexto de una comuna con alta vulnerabilidad se seleccionaron hogares inscritos en el sistema público de salud por ser la población mayoritariamente receptora de las intervenciones nutricionales. Adicionalmente, se incluyó a familias con hijos/as que inician su alimentación para observar dinámicas alimentarias en las que existen sujetos en total dependencia de sus personas cuidadoras. El contacto con los hogares se hizo directamente desde la Municipalidad de San Joaquín (órgano territorial administrativo).

LEVANTAMIENTO DE LA INFORMACIÓN

Entrevistas en profundidad

Se entrevistó a la persona a cargo de los cuidados del/la menor en cada uno de los 24 hogares seleccionados. Como esta etapa fue desarrollada durante la cuarentena por COVID-19, las entrevistas debieron realizarse telefónicamente y ser audiograbadas. Cada entrevista tuvo una duración de entre una y tres llamadas telefónicas, de aprox. un hora cada una.

Etnografías

Una vez que la cuarentena fue levantada y las medidas de distanciamiento social flexibilizadas, se realizó la etnografía a 10 familias. Debido al contexto sanitario, se hicieron etnografías

en modalidad hibrida. Se iniciaron con una visita al hogar (con medidas sanitarias estrictas), para completarse mediante el contacto telefónico/virtual posterior: se solicitó a las personas cuidadoras fotografiar los momentos alimentarios de preparación, consumo, limpieza y orden en sus hogares.

CONSIDERACIONES ÉTICAS

El protocolo de investigación fue aprobado por los comités de ética de la Facultad de Ciencias Sociales de la Universidad de Chile y el Servicio de Salud Metropolitano Sur.

Los consentimientos informados fueron compartidos virtualmente y leídos en la primera llamada telefónica. Su aceptación fue grabada en el mismo contacto. Todos los datos de las personas participantes fueron anonimizados para asegurar su confidencialidad.

ANÁLISIS

Las transcripciones de las entrevistas, las fotografías, etnografías y notas de campo fueron el corpus para el análisis temático deductivo. A partir de los objetivos del estudio y experiencia anterior de las investigadoras se definió un libro de códigos. Con estos 48 códigos cuatro investigadoras independientes codificaron las 24 entrevistas. Posteriormente, gracias a la codificación axial y selectiva realizadas a partir del enfoque de los entornos alimentarios y de la teoría de género, se elaboraron dos categorías principales en torno al rol de portera alimentaria. Se utilizó el software Atlas ti.9.

RESULTADOS

Nuestro primer hallazgo fue que, a pesar de dos décadas de avances durante el nuevo milenio, las mujeres siguen afrontando la mayoría de las tareas domésticas independientemente de si trabajan remuneradamente, fuera o no, de sus casas. Como consecuencia cargan con una responsabilidad desmedida frente a las otras personas que habitan sus hogares, sobre todo en función de las actividades asociadas a la alimentación cotidiana del grupo familiar.

Del total de los hogares participantes, las personas encargadas de todas las labores del ciclo alimentario fueron únicamente mujeres, de entre 28 y 61 años, en general las mujeres-madres, pero también se identificó la participación de abuelas y tías.

Lo anterior nos otorga un perfil icónico configurado por madres que trabajan remuneradamente que, en general, se apoyan en otras pares cercanas para poder sobrellevar las labores del hogar en complementariedad con sus trabajos asalariados. De esta manera, abuelas, tías, vecinas, amigas, suegras, pero siempre mujeres, se adosan al circuito de las responsabilidades domésticas y de crianza/cuidado.

Lo observado no deja dudas, las mujeres son las principales responsables de diseñar, estructurar y ejecutar lo que se come y también de listar lo imprescindible de comprar en la feria, almacén o en el supermercado. Además, son las encargadas de realizar dicha compra, del almacenaje de esos alimentos, de su preparación, servicio de la mesa, recogida de los utensilios ocupados, del orden, limpieza y desecho. En definitiva, la mujer se torna en lo que llamamos la "portera alimentaria", cubriendo con su desempeño lo que otros/as miembros del hogar no realizan (a pesar de la condición de autonomía e incluso adultez).

Estas "porteras alimentarias" se atan a la consagración de ser constantes prestadoras de servicio, construyendo una identidad femenina que se define, asienta y legitima en función del bienestar/cuidado y preocupación por los demás antes que el suyo propio (19,20). Es decir, este tipo de identidad o mandato sexo-genérico permite que las "porteras alimentarias" ejecuten acciones recurrentes, naturalizadas y normalizadas, incluso en desmedro de su propia salud y calidad de vida.

Lo anterior pudo ser constatado de manera directa en los patrones y dinámicas que las mujeres desarrollan al interior de sus hogares para la ejecución del ciclo alimentario. Al respecto, en este artículo nos detenemos en dos aspectos centrales: 1) la consolidación de un uso y definición del tiempo que evita que este recurso sea algo que las porteras alimentarias piensan para sí mismas, y 2) la descripción de un tipo de conducta y consumo diario por parte de las "porteras" que apela en extremo a su desvalorización como sujeto.

EL TIEMPO PARA OTROS DE LAS "PORTERAS ALIMENTARIAS"

En los relatos de las porteras alimentarias el argumento principal para ser las únicas encargadas de la casa y la cocina es que sus parejas o maridos no disponen de tiempo al trabajar remuneradamente fuera del hogar. Esta sería la gran justificación de un arreglo tradicional que implica que ellos, en tanto hombres trabajadores, se encuentran eximidos de la responsabilidad de la alimentación de su persona y del resto de los/as integrantes del hogar.

"Ahhh claro, si él también cocina, pero como no tiene tiempo, cocino yo" (Malva).

"Bueno si, él trabaja mucho, y si, él trabaja mucho, por ende… yo estoy las 24/7 con los niños, tampoco tengo mucho tiempo, pero la que cocina soy yo" (Carmen).

De esta manera, el mundo laboral es un ámbito que se valora por sobre lo doméstico y así la dedicación del tiempo de los hombres se reserva para un uso que los dispensa totalmente de los quehaceres de la mantención del hogar. M.ª Jesús Izquierdo (21) afirma que varones y mujeres se pueden diferenciar en el sentido y el uso que le dan al tiempo. Las investigaciones feministas han utilizado el "tiempo" como instrumento habitual en los últimos años para graficar las desigualdades de género (22) y corroborar los privilegios de los hombres y las desventajas de las mujeres (23). Desde la Cuarta Conferencia Mundial sobre las Mujeres (1995), los países se comprometieron a vi-

sibilizar la distribución y contribución de las mujeres al trabajo no remunerado y desde entonces por medio de encuestas de uso del tiempo visibilizar cuánto de este recurso destinan tanto hombres como mujeres a las actividades no remuneradas, como cuidados y alimentación de personas al interior de sus hogares. Las cifras muestran que las mujeres dedican entre 1 hora y 3 horas más que los hombres a las labores domésticas; 2 a 10 veces más de tiempo diario al cuidado de hijos, hijas, personas mayores y enfermas, mientras que los hombres destinan por día más tiempo al ocio (24).

"A los dos nos gusta cocinar, a él le gusta cocinar, pero no lo hace mucho por tiempo, y porque claro en la semana trabaja, y el tiempo no sé, por ejemplo. El tiempo que nosotros llevamos juntos, los primeros años de matrimonio, él trabajaba y estudiaba, entonces yo también trabajaba, pero llegaba de mi trabajo y llegaba a cocinar en la noche, para llevar almuerzo yo al otro día. Él comía por lo general en su trabajo, tenían almuerzo casi siempre en los trabajos que tuvo, entonces él comía en su trabajo, pero yo tenía que dejar comida para mí, uno de mis hijos y para mí, para llevar a mi trabajo, entonces yo llegaba y yo preparaba la comida en la semana, siempre era lo mismo" (Rosario).

Este relato da cuenta de lo radical de esta estructura, pues a pesar de que en algún momento ambos trabajan fuera del hogar, es ella la que debe organizar su tiempo para preparar su comida y la de su hijo, sin que la pareja asuma esta labor como una responsabilidad conjunta.

Las mujeres, cuando realizan trabajo fuera del hogar, llevan lo que se ha denominado la doble jornada o doble carga (25-27), situación que devela la flagrante debilidad de un sistema mayor de sobrecargas, pues son ellas las que deben armonizar los tiempos que les permitan asumir y responder tanto a las labores de la casa como a las que ejecutan para la consecución de su salario. Se constata así una nueva desigualdad entre los dos sexos en función de los usos del tiempo. En este sentido, las pautas temporales como pistas sobre lo que está ocurriendo en los procesos de la formación de los roles de género (28) es todavía la demostración de la rígida distribución sexual del trabajo entre hombres y mujeres, sobre todo en los espacios íntimos de las casas y de la alimentación.

El "tiempo de las mujeres" (29) se define como polisémico, en tanto alberga todas las instancias y labores que el tiempo dominante (tiempo de producción, laboral y remunerado) invisibiliza. Ese tiempo de las mujeres es aquel espacio y momento que incluye una enormidad de quehaceres de la vida (fuera del trabajo productivo) pero que, paradójicamente, lo hacen posible. Es justamente ese trabajo oculto, él que es totalmente necesario y hasta imprescindible para mantener el ámbito productivo (30). Mucho del tiempo de las mujeres se dedica para que el resto de su familia pueda desarrollarse de manera adecuada en sus otros espacios y esferas.

La constatación de un patrón de uso del tiempo de las mujeres como "tiempo mientras" fue la manera que escogimos para nombrar y visibilizar que las mujeres no poseen un espacio temporal claro y reservado para ellas mismas, para realizar actividades propias de descanso, ocio y entretención. Lo que más bien observamos, es que sus rutinas diarias, laborales renumeradas y no remuneradas, tratan de ser congeniadas con las actividades y temporalidades de los/as otros/as integrantes de la familia. Por ejemplo, "mientras" sus hijos/as están en el colegio hay que limpiar, ordenar y planchar, y eventualmente ellas ven alguna telenovela, el matinal de tv, escuchan la radio, y llaman por teléfono. "Mientras" sus hijos/as juegan en el vecindario, ellas pueden tomarse un café y ver sus celulares. "Mientras" van a la feria, pasan a buscar a los/as hijos/as al colegio, o aprovechan de vitrinear o "copuchar" con una vecina o familiar que vive en una residencia cercana.

Pero esos tiempos no poseen una dimensión exclusiva y garantizada, son espacios y momentos que surgen de acuerdo con un acontecer nunca establecido y periódico, sin estructura. Los momentos de esparcimiento y relajo de las mujeres, son más bien prácticas que emergen como una casualidad y que pocas veces se manifiesten en actividades que escapan de su rutina laboral y doméstica. Esto es un punto no menor a la hora de identificar barreras para las recomendaciones de los equipos de salud. Por ejemplo, en cuanto a la necesidad de realizar actividad física, pero también para asistir a los centros asistenciales.

Adscribimos a las palabras de Setién, quien señala: "*los tiempos de obligaciones condicionan los tiempos libremente elegidos, por lo cual la libre elección sólo puede ejercerse dentro del intervalo de tiempo residual que resta una vez terminadas todas las restantes actividades"* (31).

INGESTA DE LAS "PORTERAS ALIMENTARIAS"

Con respecto al tipo de conducta y consumo de alimentos de las "porteras alimentarias" se reafirman los hallazgos de investigaciones anteriores (9), que muestran que en el momento de la comensalidad las mujeres-madres están constantemente de pie, yendo y viniendo de la mesa a la cocina, sirviendo y retirando platos, recogiendo las basuras, buscando los bebestibles, trayendo de la cocina a la mesa lo que se olvidó o le falta a alguien, etc. En esa dinámica de ires y venires se produce una instancia discontinua de consumo donde la comida casi nunca se come en calma, de una sola vez y en compañía. Es decir, para las mujeres, su dinámica cotidiana de comensalidad les dificulta disfrutar de un plato de comida caliente y junto al resto de los/as comensales. Más complejo aún, han desarrollado un patrón de ingesta en que su alimento se constituye no por preparaciones, sino por productos al paso (del tipo *snacking* o picoteo) y el juntar las sobras y restos de los/as demás. La experiencia registrada es que se trasladan elementos de los otros platos de algún integrante de la familia, generalmente el de un hijo/a que dejó comida, provocando un vaciado complementario y sumatorio, teniendo como resultado que las porteras alimentarias comen lo que dejan otros/as, comen el desecho, mostrando un consumo de los rastrojos, o lo que también hemos denominado como ingesta de vertedero (32). Esta ingesta no necesariamente es frugal, al contrario, puede constituir un consumo excesivo de calorías dañando la salud nutricional de las mujeres.

En definitiva, el tiempo y la ingesta de las "porteras alimentarias" es la metáfora de la desvalorización de las mujeres como las principales encargadas de lo doméstico en una cultura que naturaliza dicha función y que configura un ordenamiento social jerárquico entre hombres y mujeres, sosteniendo labores, cargas y responsabilidades desiguales. Esta investigación, corrobora que, al interior de los entornos domésticos, se reproduce el establecimiento iniciático y diario de una transmisión que no solo revela un tipo de alimentación sino también de conductas y prácticas que identifican y localizan en un nivel secundario a las mujeres. Ello a pesar de que fueron las responsables, ejecutoras y coordinadoras de todo el ciclo alimentario, haciendo factible que el resto de sus integrantes coman y –en el mejor de los casos– se nutran, mientras que ellas quedan en una situación alimentaria y nutricional desmejorada que puede redundar en sobrepeso y obesidad, pero con falta de nutrientes esenciales.

Lo que debiésemos pensar en comunidad, profesionales de las salud, academia y ciudadanía en general, es de qué manera aseguramos que los núcleos familiares se alimenten del modo más saludable posible, sin sobrecargar de responsabilidad a las mujeres. Lo que se quiere destacar aquí es que el objetivo debiese ser que las tareas requeridas para sostener una adecuada alimentación se realicen, pero no por ello exigir a las mujeres que sean las únicas que las lleven a cabo, ni tampoco culparlas de los fracasos de las estrategias para lograrlo. Esto implica necesariamente comenzar a proponer con decisión la distribución de las tareas como una política del buen vivir en las políticas, programas, recomendaciones y hacerlo visible en las atenciones de salud.

DISCUSIÓN

La transformación de los ambientes alimentarios ha modificado el modo en que nos relacionamos con los alimentos, favoreciendo el desarrollo de enfermedades nutricionales como la obesidad. Las políticas públicas como estrategia para enfrentar el problema no son genéricamente neutras y pueden robustecer dinámicas segregacionistas e incluso sexistas, manteniendo la alimentación como un reducto esquivo en la generación hacia oportunidades de cooperación e igualdad de género.

La "portera alimentaria" es la traducción de una dinámica sexo-genérica de distribución desigual, que se anuda en un sistema-estructura binaria donde las mujeres siguen siendo las encargadas casi únicas de alimentar y cuidar al grupo familiar. En este sentido, la portera alimentaria es la traducción de una continuidad sobre la organización del ciclo alimentario y de la verificación de una resistencia cultural sobre la incorporación de nuevos/as integrantes como sujetos que se hacen parte permanente y sistemáticamente de la función nutricia de las/los integrantes del hogar.

Lo anterior es la constatación más evidente, de que aún no poseemos nuevos arreglos al interior de los entornos domésticos que potencien una transformación hacia la igualdad sustantiva y permitan un bienestar colectivo.

El análisis desde la categoría "portera alimentaria", retoma una discusión de larga data, que propuso el feminismo para mostrar como las sociedades occidentales establecen una división segmentada de los espacios, y que dicotomiza valoraciones y reconocimientos, incluso garantías y derechos.

La esfera de lo doméstico además de ser entendida como labores rutinarias y pasivas (33-35), se encarna en lo femenino (36), reproduciendo la noción de que no es propiamente un trabajo. De este modo cuando las mujeres salen a lo público, desde el ingreso al mercado laboral, lo hacen con el imperativo de continuar como encargadas de las tareas del hogar.

Los tiempos dedicados a las labores asociadas a lo alimenticio son enormes; y si estas labores no son redistribuidas entre los/as integrantes del grupo, es claro que las personas responsables (mujeres), tendrán una descompensación y sobrecarga de tareas y un mayor perjuicio de su salud y bienestar.

En continuidad con lo anterior, los hallazgos de nuestro estudio no fueron alentadores en función de identificar patrones de reorganización más igualitarios y colaborativos entre los/as integrantes de un mismo hogar. Por el contrario, se constató que las mujeres disponen de su tiempo para que otros no pierdan (inviertan) el suyo en cuidados y en el ciclo de la alimentación (salvo el consumo); y por lo mismo, para que esos otros/as, principalmente hombres, puedan orientar energías en actividades como el trabajo fuera del hogar, el descanso y el ocio.

Identificar aristas menos visibles, pero igualmente determinantes, como las lógicas de género y su incidencia en la cultura alimentaria de los entornos domésticos, puede ser un aporte en generar recomendaciones pertinentes y transformadoras, otorgando insumos para que los gestores de políticas públicas y los equipos de salud, al contemplar tales aristas, readecúen sus metas comprendiendo que solicitar cambios en la dieta es mucho más que la simple decisión de qué se come y de qué alimentos traspasarán, o no, el umbral (las "puertas") de una casa.

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ARÁN

Nutrición Hospitalaria

Trabajo Original

Otros

Impact of a 6-week dietary and lifestyle modification intervention on food cravings and eating behaviors in women

Impacto de una intervención dietética y de modificación del estilo de vida de 6 semanas de duración sobre los antojos de alimentos y las conductas alimentarıas en mujeres

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Abstract

Introduction: the multifaceted nature of food craving mirrors the complexity underlying the development of eating disorders.

Objectives: the study aimed to investigate the impact of a 6-week dietary and lifestyle intervention on food cravings, eating behaviors, and changes in physical and biochemical measures among women.

Methods: this study constitutes a behavior modification investigation involving a cohort of 35 female participants who sought consultation at a private nutrition counseling facility. At first, anthropometric and biochemical data were recorded; Information Form, Food Craving Questionnaire-Trait Scale (FCQ-T), Three-Factor Eating Scale (TFEQ-R21) were applied and 3-Day Food Consumption Records were taken. After 6 weeks of dietitian follow-up, the data collection tools were repeated and the individuals were compared with the baseline.

Results: after 6-week follow-up, according to the examination of the food consumption records, differences in daily energy, fat, monounsaturated fatty acid, fibre, vitamin E, potassium, magnesium, iron intake levels were found significant ($p < 0.05$). Differences in body weight, body mass index (BMI), waist/height ratio, fat mass, fat ratio and fasting glucose, HbA1c, total cholesterol, triglyceride, LDL, AST, TSH, free T3, free T4 levels were found significant ($p < 0.05$). According to the FCQ-T evaluation; differences in total and nine sub-dimension scores of the scale were found significant ($p < 0.001$). According to the TFEQ-R21 evaluation; differences in cognitive restraint, emotional eating and uncontrolled eating scores were found significant ($p < 0.05$).

Conclusions: a successful 6-week dietary and lifestyle intervention with improvement in anthropometric measurements and biochemical parameters is effective in reducing food cravings and regulating eating behaviours.

Keywords:

Feeding behavior. Feeding and eating disorders. Dietary management. Follow-up studies.

Authors´ contributions: PH was responsible for all stages of the article; writing process designing the review protocol and screening potentially eligible studies. She contributed to writing the report, interpreting results and creating ´Summary of findings´ tables, extracting and analysing data and interpreting results and provided feedback on the report. SB was responsible for writing the protocol and report, conducting the search, screening potentially eligible studies, extracting data, updating reference lists.

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Data availability: the datasets generated during the current study are available from the corresponding author on reasonable request.

Ethics approval: numbered 61351342/2022-54 and dated 26.04.2022 was obtained from Uskudar University Non-Interventional Research Ethics Committee.

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Resumen

Introducción: la compleja relación entre el deseo de alimentos y los trastornos alimentarios es el foco de este estudio.

Objetivos: ınvestigamos el efecto de una intervención de 6 semanas en la dieta y el estilo de vida sobre los antojos, los comportamientos alimentarios y las mediciones físicas y bioquímicas en mujeres.

Métodos: este estudio involucró a 35 mujeres que buscaban asesoramiento nutricional privado. Inicialmente, se recopilaron datos antropométricos y bioquímicos, se aplicó el Formulario de Información, el Cuestionario de Ansia Alimentaria-Escala de Rasgos (FCQ-T), la Escala de Tres Factores Alimentarios (TFEQ-R21) y se registró la ingesta de alimentos durante 3 días. Tras 6 semanas de seguimiento por un dietista, se repitieron las evaluaciones y se compararon con los datos iniciales.

Resultados: tras 6 semanas se observaron diferencias significativas ($p < 0.05$) en la ingesta diaria de energía, grasas, ácidos grasos monoinsaturados, fibra, vitamina E, potasio, magnesio y hierro. También se encontraron diferencias significativas en el peso corporal, el índice de masa corporal (IMC), la relación cintura/altura, la masa grasa, la proporción de grasa y los niveles de glucosa en ayunas, HbA1c, colesterol total, triglicéridos, LDL, AST, TSH, T3 libre y T4 libre ($p < 0,05$). En cuanto al FCQ-T, las puntuaciones totales y de las nueve subdimensiones mostraron diferencias significativas ($p < 0,001$). Además, según el TFEQ-R21, las puntuaciones de restricción cognitiva, alimentación emocional y alimentación incontrolada fueron significativamente diferentes ($p < 0,05$).

Conclusiones: una intervención dietética y de estilo de vida de 6 semanas, que mejora las medidas antropométricas y los parámetros bioquímicos, resulta eficaz en la reducción del deseo por la comida y la regulación de los comportamientos alimentarios en mujeres.

Palabras clave: Conducta alimentaria. Trastornos de la alimentación y la ingestión. Manejo dietético. Estudios de seguimiento.

INTRODUCTION

Obesity is a multifactorial and intricate medical condition characterized by excessive adiposity, and it is strongly associated with an elevated risk of numerous non-communicable diseases. The report from the World Health Organization (WHO) in May 2022 revealed that the prevalence of overweight and obesity has reached epidemic proportions in the European Region, impacting almost three out of every five adults and one out of every three children —a staggering 138 % increase over the past half-century. Notably, Turkey stands out as the nation with the highest prevalence of overweight individuals, with 66.8 % of its adult population being overweight and 32.1 % falling into the obese category. This weight-related condition stands as a primary contributor to mortality due to afflictions such as thirteen distinct forms of cancer, cardiovascular disorders, and type 2 diabetes *mellitus*. Significantly, the sobering reality is that none of the 53 countries composing the European region are currently on course to achieve their 2025 objectives aimed at curbing the escalating obesity rates. The report contends that the underlying causes of obesity exhibit a complexity that surpasses the mere amalgamation of an unhealthy diet and physical inactivity (1). This intricate situation is exacerbated by the widespread availability of food products, which consequently fosters a propensity for unrestrained food consumption and the consequent development of numerous maladies associated with eating disorders. While the perpetuation of distorted cognitions about food undeniably contributes to the surge in food intake, the formulation of strategies to mitigate these cognitions unveils a fundamental aspect –namely, the desire to consume food (2).

Food craving constitutes a concept characterized by the compelling urge to indulge in delectable foods, even in the absence of physiological hunger (3). The desire to eat encompasses a remarkably comprehensive spectrum of dimensions (4). This entails cognitive facets, including contemplations of eating; emotional dimensions, manifesting as food cravings or fluctuations in mood (5); physiological elements, exemplified by heightened salivation; behavioral components, evident through the pursuit and consumption of food (6); and pleasurable aspects, involving the activation of the body´s reward center (7). The intricate multidimensional structure characterizing the food craving parallels the intricate origin of eating disorders. The development of these disorders, influenced by biological, psychological, and social factors (8), underscores the criticality of delving into the biopsychosocial underpinnings, including the exploration of precarious eating behaviors (9).

Van Strien, Frijters, Bergers, and Defares (1986) delineate three distinct categories of eating behaviors: *external eating,* rooted in the externality theory, denotes an escalation in food consumption prompted by external food cues, rather than by internal sensations of hunger or satiety; *restrained eating,* aligned with the cognitive restraint theory, encompasses a deliberate endeavor to attain or sustain a desired weight through reduced caloric intake; and *emotional eating,* drawing from the psychosomatic theory, is characterized by heightened food intake as a reaction to internal emotional states, such as anger, fear, sadness, or happiness (10). The interplay of food intake and subsequent craving manifests with emotional ambivalence, particularly evident among individuals meeting the criteria for food addiction. In these cases, there exists a duality of "wanting" and "liking" food, despite the acknowledgment that its consumption won´t yield emotional improvement and will instead lead to negative emotions and feelings of guilt (11).

The extensive examination of attitudes within the field of psychology underscores the predictive relationship between attitudes and behaviors, while emphasizing the need to assess attitudes and behaviors as distinct entities (12). In this context, an individual´s sentiments, cognitions, and actions concerning eating collectively shape their eating attitude (13). Simultaneously, an individual forges an emotional eating attitude amid negative emotion, while also holding the expectation that weight loss can be achieved through conscious reduction of food intake in the cognitive realm (14). Underpinning this anticipation, the individual, rather than gravitating towards foods aligned with physiological requirements, adopts

a behavior that diminishes the allure of desired foods (15). For those who find themselves unable to counteract the restrictive messages originating within their psyche regarding eating, the eventual outcome of this process is an escalated desire to eat coupled with an inability to regulate their restrictive disposition, ultimately leading to overconsumption. In this context, the theory of restraint, as formulated by Lowe and Butryn posits that the excessive desire for overeating may stem from the cognitive restraints instituted in response to this very desire (16). Within the relevant body of literature, an exploration reveals studies suggesting that restrictive eating attitudes can indeed bolster the desire for food consumption (17,18).

Taking all these factors into consideration, the objective of this study was to investigate the impacts of 6-week interventions involving dietary and lifestyle modifications on various aspects including anthropometric measurements, body composition, biochemical parameters, levels of cravings, and eating behaviors among women.

MATERIALS AND METHODS

PARTICIPANTS

This study was conducted as a behavior modification study with the objective of investigating the effects of a 6-week medical nutrition therapy (MNT) and intensive lifestyle modification interventions (ILMIs) –dietary and lifestyle intervention– on anthropometric measurements, biochemical parameters, food craving levels, and eating behaviors among women who were suffering from overweight or obesity. The study´s population consisted of 50 women who sought assistance at a private nutrition counseling office during the period of April to June 2022. The sample size determination involved using the random sampling method with a 90 % confidence interval and ± 10 % margin of error. A sample size of 35 was achieved, exceeding the initially calculated minimum of 33, based on a population of 50, using the formula:

$$n = \frac{(N \times t^2 \times p \times q)}{(d^2 \times (N-1)) + (t^2 \times p \times q)}$$

The "Ethics Committee Approval" bearing the reference number 61351342/2022-54 and dated 26.04.2022 was obtained from Uskudar University´s Non-Interventional Research Ethics Committee for the purpose of this research. The participants were provided with a comprehensive explanation of the study´s objectives and scope, and their participation was contingent upon providing informed and voluntary consent. This research was conducted in strict adherence to the principles outlined in the "Helsinki Declaration" and guidelines for "Research and Publication Ethics".

STUDY DESIGN

At the commencement of the study, participants were provided with the Information Form, the Food Cravings Questionnaire-Trait (FCQ-T), and the Three-Factor Eating Questionnaire-R21 (TFEQ-R21). Furthermore, the women underwent assessments for anthropometric measurements and body composition, with recorded within the last 3 months biochemical parameters and the acquisition of 3-Day Food Consumption Records.

Utilizing this information, MNT plans was individually prescribed based on patients´ specific characteristics, encompassing food preferences, dietary habits, physical activity levels, working conditions, sociocultural contexts, and lifestyles. The dietary plans were crafted to ensure that 45-65 % of daily energy derived from carbohydrates, emphasizing complex carbohydrates with low- and medium-grade glycemic index and glycemic load values to meet daily fiber needs. Protein intake was set at 15-20 %, with half sourced from high-value animal products, and fats were targeted at 25-35 %, aligning with the directives of TÜBER (Dietary Guidelines for Turkey) (19) and the principles of the Mediterranean diet (20). These tailored plans took into consideration the distinctive characteristics of each woman. Subsequently, the participants underwent a 6-week monitoring phase led by a dietitian, which encompassed nutritional education and guidance for cultivating a health-conscious lifestyle. This intervention was classified as ILMIs. During weekly consultations with the dietitian, comprehensive analyses were conducted on the 3-Day Food Consumption Records, while the ILMIs recommendations were integrated to ensure the continuity of the training and the seamless integration of MNT into participants´ lifestyles.

Upon the culmination of the 6-week period of dietary and lifestyle intervention, the FCQ-T and TFEQ-R21 assessments were re-administered. Furthermore, anthropometric measurements, body composition evaluations, and biochemical parameter recordings were conducted anew on the female participants.

The study´s inclusion criteria encompassed women aged 18 years or older who were classified as overweight or obese (with a BMI > 25 kg/m²). These individuals were required to be free from health conditions that could hinder their ability to comprehend written material. Conversely, individuals failing to meet the predefined inclusion criteria, along with those under specific circumstances such as pregnancy or lactation, were deemed to meet the exclusion criteria.

DATA COLLECTION

Information form comprises a set of 12 questions designed to gather insights into the general characteristics of the women participating in the study. These questions encompass details such as age, educational background, current employ-

ment status, smoking and alcohol consumption habits, as well as eating patterns.

Food Craving Questionnaire-Trait (FCQ-T), developed by Cepeda-Benito et al. in 2000, serves as an assessment tool aimed at gauging individuals´ inclinations toward eating in relation to various timeframes and situations. Comprising 39 items, the FCQ-T employs a 6-point scale for scoring (ranging from 1: never to 6: always). This questionnaire encompasses nine distinct subscales that gauge different aspects of food cravings, including intentions to consume food, anticipation of positive reinforcement, relief from negative emotional states, perceived lack of control over eating, preoccupation with food, hunger, emotional triggers, cues prompting cravings, and feelings of guilt. Higher scores attained from both the overall scale and its individual sub-dimensions indicate a heightened propensity for desiring food consumption. The FCQ-T underwent a validation and reliability study specific to the Turkish context in 2019, carried out by Akkurt et al. (21).

Three-Factor Eating Questionnaire-R21 (TFEQ-R21), devised by Cappelleri et al. in 2009, serves as a tool for exploring individuals´ eating behaviors. This questionnaire comprises 21 items that are distributed across three distinct sub-dimensions: uncontrolled eating, cognitive restraint, and emotional eating. Participants provide responses to these items using a four-point Likert-type scale (ranging from 1: definitely false to 4: definitely true). Elevated scores in any of the TFEQ-R21´s sub-dimensions indicate a heightened propensity for exhibiting eating behaviors related to that particular factor. The TFEQ-R21´s Turkish validity and reliability evaluation was conducted by Karakuş et al. in 2016 (22).

Anthropometric measurements and body composition, evaluations were conducted following specific protocols. The height of the participants was determined using the Mesilife Portable Height Gauge, following the guidelines of the frankfort horizontal plane. To assess body composition, the bioelectrical impedance analysis method was employed, facilitated by the Tanita MC-780 MA model.

To ensure accuracy and consistency, several precautions were taken during the measurements. Participants were required to have fasted for a minimum of 4 hours, abstained from consuming caffeinated beverages for at least 4 hours prior, refrained from intensive exercise for 12 hours before the measurements, and avoided using diuretics for at least the last 6 hours. Measurements were performed at room temperature and the subjects were asked to remove metal jewellery (23).

Biochemical parameters, were assessed through a comprehensive array of analyses, providing insights into various aspects of participants´ health. The following parameters were examined: fasting blood glucose, HOMA-IR, HbA1c, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, ALT, AST, TSH, free T3, free T4, and ferritin levels.

Distinct timeframes were established to categorize these analyses. Parameters evaluated within the 3 months prior to the study were designated as pre-study biochemical parameters. Conversely, analyses conducted subsequent to within 5 days after termination of the 6-week period of dietary and lifestyle intervention were classified as post-study biochemical parameters. This approach facilitated a comparative understanding of participants´ biochemical profiles before and after the intervention.

Three-Day Food Consumption Record played a crucial role in the study´s dietary assessment. The "3-Day Food Consumption Records" recorded over two weekdays and one weekend day, were explained in detail to the participants by the dietitian (SB) before the study commenced. Both before the study commenced and throughout the 6-week intervention period, these records were meticulously evaluated in face-to-face interviews between the participants and the dietitian. To ensure the accuracy of the records, resources including the "Food and Food Photo Catalogue: Measurements and Quantities", "Food Atlas" and replicas were employed. These tools aided in verifying the precision of the recorded dietary information (24). The dietary energy and nutrient intake on a daily basis were subjected to thorough analysis. This analysis was conducted using the "Computer Assisted Nutrition Programme, Nutrition Information System - BeBIS 7.2," a specialized software developed for Turkey (25).

STATISTICAL ANALYSIS

Descriptive statistics were employed to provide a clear overview of the demographic characteristics. The frequency and percentage distributions were utilized for this purpose. For assessing the normal distribution of numerical variables, the Shapiro-Wilk test was executed. In instances where data exhibited normal distribution, the results were summarized using mean ($\bar{x}$) and standard deviation (SD) values. Conversely, non-normally distributed data were presented with median values along with their corresponding range (min-max). To analyze paired data with normal distribution, the Dependent Sample T Test was applied. For paired data that did not conform to normal distribution, the Wilcoxon Signed Rank Test was employed. These tests enabled the comparison of two dependent groups under different conditions. Statistical analysis was conducted utilizing the SPSS v26 software (IBM Inc., Chicago, IL, USA), a renowned statistical package program. This software facilitated the robust examination of the collected data, yielding valuable insights for the study´s analysis.

RESULTS

A total of 35 female participants, with a mean age of 36.49 ± 11.90 years and 40 % had been diagnosed with various medical conditions by a physician. The most prevalent conditions were thyroid diseases, accounting for 14.3 %, followed by hypertension at 11.4 %, followed by gynecological diseases and menstrual irregularitiesat 8.6 % and followed by cardiovascular diseases at 5.7 %. When participants were

requested to assess their appetite on a scale ranging from 1 to 10, the obtained mean score was 5.37 ± 1.24 (Table I).

The estimates of energy, macro, and micronutrient intake, based on the three-day food consumption records collected both baseline and after the 6-week dietary and lifestyle intervention are presented in table II. The variations in participants´ daily intake levels of energy ($p = 0.042$), fat (g) ($p = 0.045$), monounsaturated fatty acid (g) ($p = 0.012$), dietary fiber (g) ($p = 0.001$), water-soluble fiber (g) ($p < 0.001$), water-insoluble fiber (g) ($p = 0.008$), vitamin E ($p = 0.016$), potassium ($p = 0.031$), magnesium ($p = 0.006$), and iron ($p = 0.001$) were found to be statistically significant.

Table III provides the anthropometric measurements, body composition, and biochemical parameters of the female participants both before and after the 6-week dietary and lifestyle intervention. Statistically significant differences were observed in the following parameters: body weight ($p < 0.001$), BMI ($p < 0.001$), waist/height ratio ($p < 0.001$), fat mass (g) ($p < 0.001$), and fat percentage (%) ($p < 0.001$). Moreover, the analysis revealed statistically significant differences in fasting glucose ($p < 0.001$), HbA1c ($p = 0.001$), total cholesterol ($p < 0.001$), triglycerides ($p = 0.001$), LDL ($p = 0.001$), AST ($p = 0.045$), TSH ($p < 0.001$), free T3 ($p = 0.013$), and free T4 ($p < 0.001$) levels between the pre-intervention and post-intervention periods.

The baseline and post-6-week dietary and lifestyle intervention FCQ-T and TFEQ-R21 scores for the female participants were detailed in table IV. Notably, there were notable reductions observed in the FCQ-T´s total score and all its sub-dimension scores among the women, and these reductions were statistically significant ($p < 0.001$). Upon analyzing the eating behaviors of the women, notable differences emerged in the levels of cognitive restraint ($p = 0.016$), emotional eating ($p < 0.001$), and uncontrolled eating ($p < 0.001$), all of which were determined to be statistically significant.

Table I. Baseline characteristics of study participants

	n	%
Age (mean ± SD)	36.49 ± 11.90	
Marital status		
Married	25	71,4
Single	10	28,6
Educational background		
High School and below	12	34,3
University and above	23	65,7
Employment status		
Not working	14	40,0
Working	21	60,0
Diagnosis of chronic disease		
Yes	14	40,0
No	21	60,0
*> 150 min/week physical activity status**		
Yes	8	22,9
No	15	42,9
Sometimes	12	34,3
Smoking status		
Smoker	5	14,3
Non-smoker	30	85,7
Alcohol consumption status		
Yes	4	11,4
No	31	88,6
Average daily sleep duration (mean ± SD)	7.20 ± 1.55	
Appetite assessment level (mean ± SD)	5.37 ± 1.24	

**WHO suggestion.*

Table II. Effect of 6-week dietary and lifestyle intervention on intake of energy, macro and micronutrients

	Baseline	**After**		
	Mean ± SD / Median (min-max)	**Mean ± SD / Median (min-max)**	**t / W**	***p***
Energy and macronutrients				
Energy (kcal)	810.31 ± 183.45	895.62 ± 150.97	*-2.111*	*0.042*
Protein (%)	21.91 ± 2.68	21.34 ± 4.19	0.651	0.519
Protein (g)	42.86 ± 10.79	46.38 ± 11.30	-1.353	0.185
CHO (%)	34.09 ± 7.11	32.43 ± 6.69	0.985	0.332
CHO (g)	65.62 ± 15.98	69.77 ± 15.05	-1.146	0.260
Fat (%)	44.09 ± 6.85	46.26 ± 5.72	-1.146	0.166

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Table II (cont.). Effect of 6-week dietary and lifestyle intervention on intake of energy, macro and micro nutrients

	Baseline	After		
	Mean ± SD / Median (min-max)	**Mean ± SD / Median (min-max)**	**t / W**	***p***
Fat (g)	40.64 ± 12.90	46.76 ± 11.40	*-2.078*	*0.045*
Saturated fat (g)	11.91 ± 4.20	12.19 ± 3.02	-0.335	0.740
Monounsaturated fat (g)	15.37 ± 5.77	19.09 ± 6.06	*-2.659*	*0.012*
Polyunsaturated fat (g)	10.43 ± 4.87	12.10 ± 4.75	-1.503	0.142
Cholesterol (mg)	198.13 ± 86.96	235.40 ± 98.31	-1.934	0.061
Fiber (g)	12.74 ± 2.74	15.28 ± 3.27	*-3.563*	*0.001*
Water soluble fiber (g)	3.93 ± 0.94	5.10 ± 1.50	*-4.027*	*< 0.001*
Water ınsoluble fiber (g)	*8.3 (4.6-11.4)*	*9.41 (6.4-13.2)*	*-2.653*	*0.008*
Vitamins				
Vitamin A (µg)	*632.34 (225.27-1852.11)*	*854.5 (368.63-2984.16)*	-1.769	0.077
Vitamin E (mg)	*10.85 (3.09-26.67)*	*13.04 (5.1-24.32)*	*-2.408*	*0.016*
Vitamin B1 (mg)	*0.57 (0.28-0.68)*	*0.55 (0.39-0.81)*	-1.738	0.082
Vitamin B2 (mg)	1.01 ± 0.27	1.04 ± 0.16	-0.547	0.588
Vitamin B6 (mg)	0.86 ± 0.21	0.93 ± 0.18	-1.579	0.124
Folate (µg)	*183.93 (85.26-285.98)*	*206.58 (136.79-347.27)*	-1.425	0.154
Vitamin C (mg)	*93.56 (22.84-160.74)*	*87.13 (29.48-176.51)*	-0.655	0.512
Minerals				
Sodium (mg)	1817.16 ± 550.74	2007.32 ± 571.99	-1.436	0.160
Potassium (mg)	1664.31 ± 323.95	1840.73 ± 293.76	*-2.252*	*0.031*
Calcium (mg)	580.28 ± 169.90	597.10 ± 111.7	-0.491	0.627
Magnesium (mg)	188.70 ± 44.91	217.16 ± 37.01	*-2.940*	*0.006*
Phosphorus (mg)	793.59 ± 197.73	846.091 ± 31.92	-1.298	0.203
Iron (mg)	7.07 ± 1.38	8.29 ± 1.55	*-3.594*	*0.001*
Zinc (mg)	5.77 ± 1.46	6.00 ± 1.11	-0.701	0.488

t: dependent sample t test; W: Wilcoxon Signed Rank Test.

Table III. Effect of 6-week dietary and lifestyle intervention on anthropometry, body composition and biochemical profiles

	Before	After		
	Mean ± SD / Median (min-max)	**Mean ± SD / Median (min-max)**	**t / W**	***p***
Anthropometric measurements				
Body weight (kg)	73.38 ± 14.09	69.91 ± 13.40	*11.888*	*< 0.001*
BMI (kg/m^2)	26.99 ± 4.34	25.67 ± 4.11	*11.428*	*< 0.001*
Waist circumference (cm)	83.37 ± 17.68	82.37 ± 12.59	0.345	0.732
Waist/height ratio	0.52 ± 0.07	0.50 ± 0.07	*12.423*	*< 0.001*
Fat (kg)	22.96 ± 8.25	20.21 ± 7.54	*9.424*	*< 0.001*
Fat (%)	30.28 ± 6.13	27.93 ± 6.33	*7.637*	*< 0.001*
Muscle (kg)	47.53 ± 7.14	47.70 ± 7.26	-0.353	0.726

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Table III (cont.). Effect of 6-week dietary and lifestyle intervention on anthropometry, body composition and biochemical profiles

	Before	After		
	Mean ± SD / Median (min-max)	**Mean ± SD / Median (min-max)**	**t / W**	***p***
Biochemical parameters				
Glucose	88.00 ± 12.95	82.86 ± 8.70	*3.877*	*< 0.001*
HbA1c	*5.5 (2.4-8.4)*	*5.4 (4.5-6.2)*	*-3.348*	*0.001*
Total cholesterol	*196 (126-355)*	*170 (120-362)*	*-4.917*	*< 0.001*
Triglyceride	120.97 ± 60.79	102.69 ± 45.92	*3.589*	*0.001*
LDL	118.53 ± 40.88	107.54 ± 40.84	*3.619*	*0.001*
HDL	58.32 ± 15.06	62.31 ± 21.36	-1.492	0.145
ALT	21.16 ± 17.93	16.96 ± 7.99	1.642	0.110
AST	18.25 ± 8.14	15.80 ± 4.75	*2.081*	*0.045*
TSH	*1.8 (0.7-5.5)*	*1.5 (0.6-5)*	*-4.281*	< 0.001
FT3	2.82 ± 0.77	2.58 ± 0.75	*2.703*	0.013
FT4	0.99 ± 0.17	0.90 ± 0.18	*4.797*	*< 0.001*
Ferittin	*20.3 (3-95.5)*	*22 (5-98)*	-1.669	0.095

BMI: body mass index; t: dependent sample t test; W: Wilcoxon Signed Rank Test.

Table IV. Effect of 6-week dietary and lifestyle intervention on FCQ-T and TFEQ-R21 levels

	Baseline	After		
	Mean ± SD / Median (min-max)	**Mean ± SD / Median (min-max)**	**t / W**	***p***
FCQ-T total	3.24 ± 1.16	2.49 ± 0.89	*7.015*	*< 0.001*
Intentions to consume food	*3.33 (1-5.67)*	*2.67 (1-4.33)*	*-4.214*	*< 0.001*
Anticipation of positive reinforcement	*3.4 (1-6)*	*2.4 (1-4.8)*	*-4.571*	*< 0.001*
Relief from negative states	*3.33 (1-5.67)*	*2 (1-5.67)*	*-4.014*	*< 0.001*
Perceived lack of control over eating	*3 (1-6)*	*2 (1-4.5)*	*-3.985*	*< 0.001*
Preoccupation with food	*2.43 (1-5.57)*	*1.86 (1-4.14)*	*-3.717*	*< 0.001*
Hunger	3.68 ± 1.35	2.75 ± 0.98	*5.954*	*< 0.001*
Emotional triggers	*2.75 (1-6)*	*2 (1-5.75)*	*-4.128*	*< 0.001*
Cues prompting cravings	*3 (1-6)*	*2.25 (1-4.75)*	*-3.787*	*< 0.001*
Feelings of guilt	3.56 ± 1.54	2.93 ± 1.21	*4.331*	*< 0.001*
TFEQ-R21				
Cognitive restraint	15.83 ± 3.98	17.31 ± 3.98	*-2.535*	*0.016*
Emotional eating	*12 (6-24)*	*10 (6-24)*	*-4.035*	*< 0.001*
Uncontrolled eating	*20 (9-36)*	*17 (9-33)*	*-3.989*	*< 0.001*

TFEQ-R21: Three-Factor Eating Questionnaire-R21; FCQ-T: Food Craving Questionnaire-Trait; t: dependent sample t test; W: Wilcoxon Signed Rank Test.

DISCUSSION

In this investigation, a comprehensive assessment of participants´ nutritional status following the 6-week dietary and lifestyle intervention unveiled noteworthy outcomes. A substantial rise in daily energy intake was observed, along with a notable increase in total fat attributed to heightened consumption of monounsaturated fats. Furthermore, a marked augmentation in total fiber intake, contributed by amplified consumption of both water-soluble and water-insoluble fibers, was evident. This dietary modulation correspondingly led to statistically significant elevations in the intake of key micronutrients, namely vitamin E, potassium, magnesium, and iron. Scrutinizing the anthropometric measurements and body composition of the female participants yielded compelling results. A significant reduction was observed across body weight, fat mass, fat ratio, BMI, and waist/height ratio, col-

lectively underscoring the effectiveness of the intervention on shaping these parameters. The intricate interplay between diet and physiological profiles was further substantiated through the analysis of biochemical parameters. The intervention prompted noteworthy declines in fasting blood glucose, HbA1c, total cholesterol, LDL cholesterol, triglyceride levels, as well as AST, TSH, free T3, and free T4 levels. These findings collectively underscore the success of the 6-week medical nutrition therapy (MNT) and ıntensive lifestyle modification interventions (ILMIs) –dietary and lifestyle intervention– in generating functional and constructive outcomes across anthropometric, compositional, and biochemical profiles, thus highlighting its potential for positive transformation within this cohort.

Through the 6-week dietary and lifestyle intervention undertaken in this study, notable transformations were observed in participants´ food cravings and eating behaviors. A compelling reduction was identified in the participants´ inclinations across all sub-dimensions of food cravings, underpinning the efficacy of the intervention. In a parallel manner, a notable elevation in cognitive restraint tendencies, coupled with marked decreases in the tendencies for uncontrolled eating and emotional eating, both integral sub-dimensions of eating behavior, were noted and established as statistically significant outcomes of the intervention. These findings resonate with Meule´s (2020) proposition that food deprivation can contribute to the fading of conditioned food craving responses (26). Additionally, they align with Rogers and Smit´s (2000) (27) assertion that ambivalence towards specific foods, such as chocolate, may prompt deliberate attempts to restrict, evade, or eliminate consumption of these foods. This alignment is particularly evident given a study´s outcome indicating that individuals predisposed to food overconsumption tend to exhibit lower executive control and reduced motor inhibition of food cravings compared to those who practice eating restraint (28). However, the current study´s findings diverge from Hill´s (2007) proposition that heightened avoidance, driven by physiological or cognitive mechanisms, may amplify the desire for certain foods (29). Affirming this notion, it´s noteworthy that an individual´s craving for food can persist even in scenarios where the food is merely imagined (30) or when they are subjected to deprivation, as in the case of restricted intake (31). These findings underscore the intricate interplay of both physical and psychological deprivation as pivotal factors influencing food craving dynamics (18).

In the broader literature, a spectrum of insights and perspectives emerges on the intricate relationship between cognitive restraint, dietary interventions, and food craving. While some studies resonate with the findings of this study, suggesting that interventions can indeed lead to decreased food cravings, others present contrasting viewpoints. A study involving the assessment of 7-day food diaries among 129 female dieters and non-dieters unveiled that dieters manifested heightened cravings for foods they intentionally restricted, compared to non-dieters (32). Likewise, another study highlighted that individuals instructed to abstain from consuming a favored food for a span of 5 days exhibited an increase in preoccupation with the restricted food and a concurrent escalation in food cravings (29). Similarly, akin to the complex dynamics in cognitive restraint, the literature presents a lack of consensus concerning the correlation between calorie restriction and food cravings. There are studies in the literature showing that 12 weeks of low-calorie dietary intervention decreases food craving (33) and 16 weeks of low-calorie dietary intervention may increases food cravings, possibly due to alterations in appetite-regulating hormones (34). Furthermore, it´s noteworthy that emotional and psychological factors can play a significant role in shaping cravings. For instance, a study by Van Strien et al. (2013) highlighted that certain personality traits, such as external eating and emotional eating, could mediate the relationship between dietary restraint and food cravings (35). These divergent findings underscore the intricate and multifaceted nature of the relationship between dietary interventions and the complex phenomenon of food cravings. The interplay of physiological, psychological, and contextual factors within these interventions necessitates a holistic approach for a comprehensive understanding of the underlying dynamics.

The intricate interplay between food restriction, encompassing cognitive restraint and calorie restriction, and the phenomenon of cravings introduces a realm of complexity and ambiguity. A comprehensive view emerges when considering findings from a 2017 systematic review and meta-analysis, which revealed that extended energy-restricted diets exhibited the capacity to diminish both overall food cravings and desires for high-energy-dense foods (36). The triggers behind diet-induced cravings can be rooted in either physiological factors, such as an insufficiency of food or nutrients, or psychological factors, which can manifest as the ironic consequence of attempting to suppress the innate desire to consume. Supporting this intricate relationship, research conducted by Boswell and Kober (2016) demonstrated that food craving could elucidate up to 11 % of the variance in both eating behavior and weight gain (37). Intriguingly, certain studies delve into the correlation between lack of control over eating and the subsequent surge in the urge to consume (food craving), highlighting a linkage with heightened levels of anxiety and a negative mood (38,39). This heightened sensitivity may be underpinned by the challenge of inhibiting intrusive thoughts related to food —a hallmark characteristic of food craving (40). The intricate dynamics encompassing food restriction, cravings, psychological factors, and mood underscore the need for a holistic perspective in interpreting the interrelationships at play.

In the context of the current study, the inclusion of lifestyle change education alongside a prescribed calorie-restricted dietary intervention yielded a reduction in food cravings. This reduction corresponded with an increase in cognitive restraint —a tendency to regulate food intake to maintain body weight and shape. Additionally, there was a decrease in uncontrolled eating —a tendency characterized by a loss of control over food in response to hunger or external stimuli. Moreover, a decrease in emotional eating —a tendency to overconsume in the presence of negative emotions like loneliness, anxiety, or demoralization— was observed. These changes in eating behaviors are pivotal, as they contribute to the amelioration of eating disorders, obesity, and obesity-related disorders. By fostering cognitive restraint,

curbing uncontrolled eating, and mitigating emotional eating tendencies, the intervention equips individuals with valuable tools to counteract the emergence of these complex issues.

In essence, the study´s findings contribute to the evolving discourse surrounding effective strategies to promote healthier eating behaviors and mitigate the adverse consequences of obesity-related disorders. The integration of dietary modifications with comprehensive lifestyle education emerges as a potent approach to not only curb food cravings but also foster sustainable habits that promote overall well-being.

CONCLUSION

In summation, the findings of this study substantiate the profound impact that a well-structured nutrition plan, coupled with comprehensive nutrition education, can exert on a multitude of health dimensions. Beyond its discernible effects on anthropometric measurements, body composition, and biochemical parameters, such interventions demonstrate a remarkable potential to mitigate the emergence of obesity-related ailments in the future. By fostering favorable shifts in food selectivity within eating behaviors and attitudes, these interventions serve as a preventative measure against potential health complications associated with obesity.

Building upon this framework, the significance of addressing food cravings and cultivating healthful eating behaviors is evident. To this end, the establishment of structured training programs and counseling services, guided by a collaborative approach involving dietitians and psychologists, emerges as an imperative. This multidisciplinary perspective underscores the need to approach food cravings and eating behaviors holistically, recognizing the intricate interplay of psychological, emotional, and physiological factors.

In light of the study´s outcomes, it becomes evident that fostering a synergistic partnership between dietary interventions, nutrition education, and psychological support holds the key to promoting resilient eating habits and preventing the onset of obesity-related diseases.

STRENGTHS AND LIMITATIONS OF THE STUDY

This study is very important as it is the first behaviour modification study in Turkey to evaluate the effects of dietary and lifestyle intervention on both food cravings and eating behaviour. Despite our meticulous approach, it is important to acknowledge the limitations inherent in this study. Primarily, the sample size, could be expanded to encompass a more diverse demographic, thereby bolstering the generalizability of the conclusions drawn. Secondarily, it´s crucial to note that the study exclusively focused on female participants. Inclusive research that incorporates male participants and encompasses a wider spectrum of individuals would undoubtedly enrich the comprehensiveness of future studies. Furthermore, our evaluation was conducted within a relatively concise timeframe of 6 weeks. To more comprehensively discern the lasting implications of lifestyle changes, an extended follow-up period could prove invaluable. The pursuit of prolonged investigations is warranted to ascertain the enduring sustainability of the observed effects.

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Revisión

Evidence on the benefits of probiotics for preterm infants

Evidencia sobre los beneficios del uso de probióticos en niños prematuros

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Abstract

This article reviews the evidence for the use of different strains of probiotics in the prevention of prevalent pathologies in premature neonates.

A systematic review was conducted of the use of probiotics in neonates with less than 37 weeks of gestational age, based on a search for systematic reviews and observational and experimental studies performed during the period from January 2014 to February 2021. For this purpose, the PubMed, MEDLINE and Cochrane Library databases were consulted. The aim of this article was to review the existing data on the relationship between the administration of probiotics (with different strains and doses) and the risk of necrotising enterocolitis, mortality, late sepsis and other disease parameters in premature infants.

The literature search obtained 240 articles, of which we selected 16, representing a total sample of over 200,000 premature infants. Analysis of the data obtained reveals statistical evidence that the combined administration of probiotics (especially of *Lactobacillus* and *Bifidobacterium* strains) reduces the incidence of grade II or higher necrotising enterocolitis, all-cause mortality, late sepsis, length of hospital stay and time until complete enteral nutrition is achieved. However, no benefits were apparent with respect to alleviating bronchopulmonary dysplasia, retinopathy of prematurity or intraventricular haemorrhage.

Further research is needed to determine the most appropriate strains, doses and treatment duration for preterm infants to achieve the health benefits identified.

Keywords:

Probiotics. Premature infants. Low birth weight infants. Morbidity. Necrotising enterocolitis.

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Resumen

En este artículo se revisa la evidencia del uso de las diferentes cepas de probióticos en la prevención de diversas patologías prevalentes en recién nacidos prematuros.

Se ha realizado una revisión sistemática sobre el uso de probióticos en recién nacidos de menos de 37 semanas de edad gestacional, realizando una búsqueda de revisiones sistemáticas, estudios observacionales y experimentales desde enero de 2014 hasta febrero de 2021. Para ello se han utlizado motores de búsqueda como PubMed, MEDLINE y la biblioteca Cochrane. El objetivo de este artículo fue revisar los datos existentes sobre la relación entre la administración de probióticos (con diferentes cepas y dosis) y el riesgo de enterocolitis necrotizante, mortalidad, sepsis tardía, y otros parámetros de enfermedad en prematuros.

En la búsqueda se obtuvieron 240 artículos, de los que seleccionamos 16, obteniendo más de 200.000 recién nacidos prematuros como muestra. En esta revisión se muestra con evidencia estadística, que la administración combinada de probióticos (espcialmente cepas de *Lactobacillus* y *Bifidobacterium*) reducen la incidencia de NEC en grado II o mayor, mortalidad por todas las causas, sepsis tardía, días de estancia hospitalaria y tiempo en lograr nutrición enteral completa. No se han podido evidenciar beneficios en cuanto a la displasia broncopulmonar, retinopatía de la prematuridad y hemorragia intraventricular.

Se precisan nuevos estudios para conocer las cepas, dosis y tiempo de tratamiento más adecuados en neonatos prematuros para lograr beneficios en salud.

Palabras clave:

Probióticos. Prematuros. Neonatos muy bajo peso. Morbilidad. Enterocolitis necrotizante.

INTRODUCTION

Probiotics were first described in the 1960s, but perhaps the definitive expression was offered in 2014, when the World Health Organisation defined probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" (1).

After childbirth, the maternal flora predominates over environmental flora, playing an essential role in the development of the infant's systemic and mucosal immunity. Bacteria promoting oxidative metabolism, such as *Enterobacteriaceae, Streptococci* and *Staphylococci*, are the first to proliferate in the gut.

It is widely accepted that breast milk should be the first feeding option for neonates, infants and, of course, premature infants. Breast milk is a complete food, from the nutritional, immunological and microbiological standpoint, and is a source of commensal or probiotic bacteria for the newborn's intestine. Probiotic supplementation is considered a promising alternative means of simulating the microbiological characteristics of breast milk and thus achieving its associated beneficial effects. However, this belief must be based on solid scientific evidence of specific beneficial effects, obtained in properly designed clinical studies, in which the appropriate strain, dose and administration route are selected for the therapeutic goals addressed (2).

According to several recent studies, the composition of the neonate's gut microbiota may be affected by gestational age and birth weight. Any alteration in this respect is an important risk factor for the development of necrotising enterocolitis (NEC), sepsis and increased mortality. Studies have also considered whether the appropriate supply of probiotics to premature infants reduces hospital stay and the time required to achieve complete enteral nutrition.

The aim of the present study is to compile evidence on the use of probiotics in preterm infants, and the impact on NEC, mortality, sepsis, and time to achieve complete enteral nutrition.

METHODS

This systematic review was performed via a search of websites presenting data on relevant clinical practice: the Cochrane Library, PubMed and MEDLINE databases. In PubMed, the MeSH terms used were "Infant, Premature"(Mesh) AND ("Infant, Very Low Birth Weight"(Mesh) OR "Infant, Premature/classification"(Mesh) OR "Infant, Premature/growth and development"(Mesh) OR "Infant, Premature/mortality"(Mesh) AND 2014(PDAT): 2021(PDAT) AND (English(lang) OR Spanish(lang)) AND (Clinical Trial(ptyp) OR Meta-Analysis (ptyp) OR Practice Guideline (ptyp) OR Randomized Controlled Trial (ptyp) OR Review (ptyp)) AND "Infant"(Mesh) AND "Probiotics"(Mesh).

Ethics committee approval was not required for this study.

The following selection criteria were applied: a) premature infants with less than 37 weeks' gestational age or less than 2500 g birth weight; b) studies published during the period 2014 to 2021; c) studies focused on diagnosis or treatment; and d) comparison between intervention groups, with placebo or negative control.

The exclusion criteria were: a) articles in which there were no interventions with probiotics; b) articles in languages other than Spanish or English; c) studies dealing exclusively with animals; d) articles that presented insufficient data; and e) articles that did not differentiate between premature infants and other age groups.

The probiotics identified in this review were various strains of *Lactobacillus, Bifidobacterium, Saccharomyces, Streptococcus, Bacillus* and others, used either in combination or in monotherapy, and compared with the administration of a placebo. The flow chart for the source selection process is shown in figure 1.

RESULTS

The literature search initially yielded 240 articles. After discarding duplicates and excluding unrelated articles (according to the document title and abstract), 25 papers remained, for which the full texts were obtained. Following application of the inclusion/exclusion criteria described, nine of these papers were excluded, leaving sixteen for the final analysis (Fig. 1).

The main results presented in these papers concerned the relation between the consumption of probiotics and the incidence of NEC, late sepsis, mortality, length of hospital stay and the time required to achieve complete enteral nutrition. The details of each study are summarised in table I.

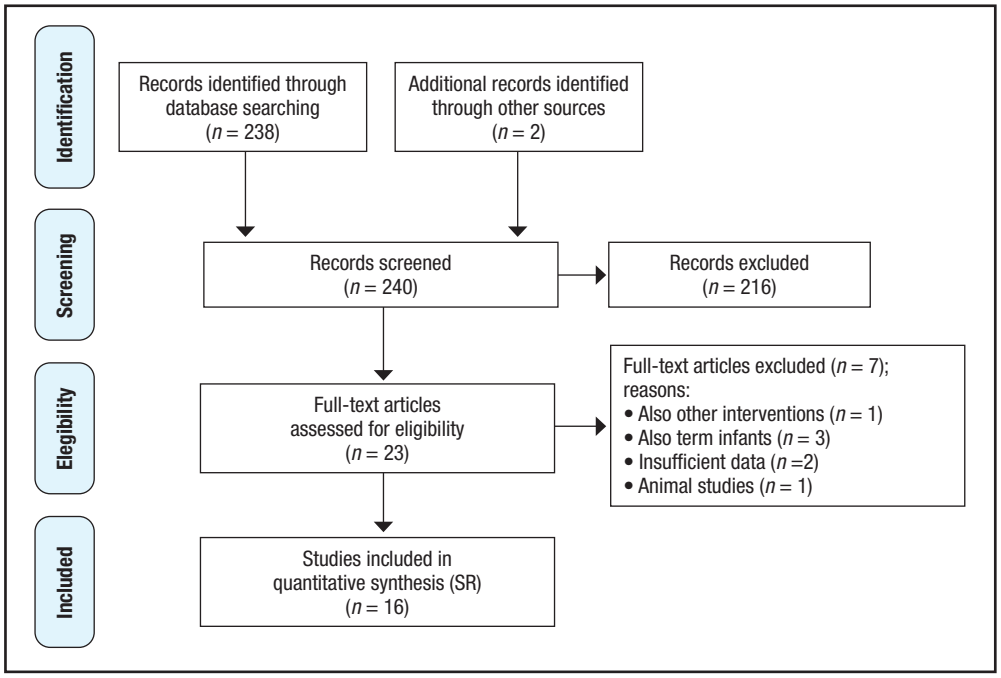

Figure 1.

Flow diagram (PRISMA) of the studies selected for analysis.

The meta-analyses reported by Chris et al. in 2018 (3) and Chi et al. in 2020 (4) described 96 studies and analysed the following variables: mortality, NEC, late sepsis and time to achieve complete enteral nutrition. Chris et al. (3) analysed 51 studies. In four of these (representing a total study population of 830 premature infants), mortality decreased following the use of different strains of *Bifidobacterium, Lactobacillus* and *S. thermophilus*, with a relative risk (RR) of 0.17. The presence of grade II or higher NEC was reduced, with a RR that was significantly lower for seven treatments in which different strains of *Lactobacillus* and *Bifidobacterium* were combined. The RR for late sepsis was significantly lower with the *Lactobacillus* + *Bifidobacterium* combination, compared to placebo treatment. Similarly, the time required to achieve complete enteral nutrition was reduced when the following probiotics were supplied: *L. reuteri*; the combination of *B. bifidum*, *B. infantis*, *B. longum* and *L. acidophilus*; and the combination of *B. longum* and *L. rhamnosus GG*.

In 2020, Chi et al. (4) conducted a meta-analysis of 45 trials conducted between 2002 and 2018, with a total population composed of 12,320 premature infants with less than 37 weeks' gestational age or less than 2500 g birth weight. The administration of *Bifidobacterium* and *Lactobacillus* reduced mortality rates (RR 0.56) and NEC (RR 0.47) compared to the placebo treatment.

The reviews by Bi et al. (5) and Jin et al. (6) both evaluated the impact on NEC in preterm infants given probiotics. The first of these reviews analysed 34 studies with a total population of 9,161 patients and reported that the risks of NEC (OR 0.38, 95 % CI 0.27-0.54), gastro-intestinal sepsis (OR 0.82, 95 % CI 0.69-0.98) and mortality (OR 0.54, 95 % CI: 0.42-0.71) were all significantly reduced after the administration of a combination of probiotics, especially those with *Lactobacillus* and/or *Bifidobacterium*, versus placebo treatment. Furthermore, there was a significant decrease in mortality in the preterm infants who received a combination of probiotics, compared to placebo treatment (OR 0.49, 95 % CI 0.32-0.69). In the second of these reviews, Jin et al. (6) examined various experimental studies, with a total population of 10,520 infants, and observed great variability in terms of the probiotic strains, doses and administration times described. These authors concluded that the combination of *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb-12/B94 was effective in reducing NEC. Despite clinical heterogeneity, the conclusion of this cumulative meta-analysis was that probiotic treatment decreased the incidence of NEC (RR 0.53; 95 % CI 0.42-0.66). However, one of the trials in this review, focused on premature infants with less than 28 weeks gestational age, concluded that the routine use of "Infloran®" was associated with an increase in grade II or higher NEC (13.3 % vs 5.9 %, $p = 0.010$).

Baldasarre et al. (7) conducted an extensive literature search concerning the management of intestinal dysbiosis with probiotics, and the resulting impact on NEC. The results obtained indicate that the use of probiotics (*Lactobacillus* + *Bifidobacerium*) reduces the incidence of NEC in premature infants with less than 34 weeks' gestational age or less than 1500 g birth weight, and also reduces the time to achieve complete enteral nutrition, as well as the incidence of late sepsis.

Another study, by Robertson et al. (8), examined the results obtained for a sample of 982 infants during a ten-year period (five before the routine use of probiotics in preterm infants, and five after their introduction), for NEC, late sepsis and mortality. The rate of NEC fell from 7.5 % (35/469 neonates) in the first period to 3.1 % (16/513 neonates) in the second (HR = 0.44, 95 % CI 0.23 to 0.85, $p = 0.014$), regardless of any other covariates, including breastfeeding. Similar, the rate of late sepsis

decreased from 22.6 % to 11.5 % ($p < 0.0001$). With the introduction of routine probiotic administration, mortality (all causes) also fell, from 14.3 % to 9.2 %. Finally, the NEC-reducing effect was most pronounced during the two weeks of postnatal life.

In 2018, Underwood et al. (9) reviewed nine meta-analyses of controlled trials, from which they concluded that the use of probiotics reduced the incidence of NEC and mortality, but had no beneficial effect in preventing intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD) or retinopathy of prematurity (ROP). They also reported that in a subgroup of 4,683 extremely low birth weight neonates (< 1000 g), the administration of probiotics produced a significant reduction in NEC, mortality and late sepsis (HR for NEC 0.48, death 0.59, late sepsis 0.83). Similar findings were reported by Xiong et al. (10), who reviewed 98 articles in this context and observed a moderate decrease in the incidence of NEC (stage II or greater) and mortality after the administration of a combination of probiotics.

Bi et al. (11) analysed 34 studies with a total population of 9,161 patients. These authors found that different strains of *Lactobacilli, Bifidobacteria, Bacillus, Saccharomyces* and a combination of probiotics significantly reduced the incidence of NEC after the administration of probiotics, compared to placebo treatment (from 6.23 % to 3.54 %) (RR = 0.58, 95 % CI 0.48-0.69, $p < 0.05$).

For the probiotic combination group, the incidence of NEC (2.48 %) was approximately 40 % that of the placebo group (6.33 %) (RR = 0.40). *Lactobacilli* and *Bifidobacteria*, administered separately, also reduced the incidence of NEC compared to the placebo. In addition, the risk of sepsis was significantly reduced (probiotics group 15.59 %; placebo group 17.95 %), as was mortality (5.23 % and 7.41 %, respectively) (RR = 0.72, 95 % CI 0.61 to 0.85).

A meta-analysis by Sun et al. (12) of studies of preterm infants with less than 1500 g birth weight or less than 32 weeks' gestational age reported that infants given probiotics achieved a 37 % reduction in NEC, 37 % in late sepsis and 20 % in mortality, as well as 3.8 days' reduction in the length of hospital stay. These authors also reported that probiotics were more effective when taken with breast milk, when they were consumed for at least six weeks, when a dose of less than 10^9 CFU was administered, and when multiple strains were administered.

In 2020, Morgan et al. (13) reviewed 63 clinical trials of probiotic supplementation versus placebo treatment, finding that the combination of one or more strains of *Lactobacillus* spp. and *Bifidobacterium* spp. reduced all-cause mortality (OR 0.56, 95 % CI 0.39 to 0.80). Combinations of one or more strains of *Lactobacillus* spp. and one or more strains of *Bifidobacterium* spp., *Bifidobacterium animalis* subspecies *lactis*, *Lactobacillus reuteri* or *Lactobacillus rhamnosus* significantly reduced severe NEC. It was also observed that combinations of *Lactobacillus* spp. and *Bifidobacterium* spp and *Saccharomyces boulardii* reduced the number of days required to achieve full enteral nutrition (mean reduction: 3.30 days). The review found moderate or high-quality evidence that, compared to placebo, a single strain of B. *animalis* subspecies *lactis* or *L. reuteri* significantly reduced the length of hospital stay (mean reductions: 13 days, 95 % CI, 22.7 to 3.3 days; and: 7.9 days, 95 % CI 11.6 to 4.2 days, respectively).

In 2017, Aceti et al. (14) analysed the relationship between type of diet (breast milk or artificial milk) and probiotic supplementation, evaluating data from 5,868 neonates. Regardless of the type of diet, fewer cases of late sepsis were observed in the probiotic group (13.6 %) than in the placebo group (17.24 %) (RR 0.79). Moreover, the breastfed neonates who received one of the probiotic combinations showed fewer cases of late sepsis. In this review, the following probiotics were considered: *Lactobacillus rhamnosus, Lactobacillus reuteri, Lactobacillus sporogenes*.

Also, in 2017, Dermyshi et al. (15) reviewed 30 clinical trials and 14 observational studies and concluded that the administration of probiotics in premature infants reduced rates of NEC (grade II or higher) and all-cause mortality. In addition, the risk of sepsis fell by 12 % in the experimental studies and by 19 % reduction in the observational studies. By probiotic groups, the following results were obtained: *Lactobacillus GG* and *Bifidobacterium lactis* significantly reduced the incidence of severe NEC stage II-III; however, neither *L. reuteri, B. breve* nor *Saccharomyces boulardii* alone achieved a significant reduction in severe NEC. Subgroup analysis showed that combinations of two or more strains of probiotics were most beneficial in reducing the risk of NEC.

In 2020, Sharif presented a systematic review (16) of the use of probiotics to prevent NEC in very low birth weight preterm infants. This review examined 56 trials with a total population of over 10,000 infants. The most widely used probiotics were combinations of *Bifidobacterium* spp., *Lactobacillus* spp., *Saccharomyces* spp. and *Streptococcus* spp. The administration of probiotics reduced the risk of NEC, although at least 33 patients had to be treated for this beneficial effect to become apparent (NNTB 33, 95 % CI 25 to 50). On the other hand, this analysis concluded that probiotics may have little or no effect on severe neurodevelopmental impairment.

In 2018, in a related study, Grev et al. (17) conducted a review of probiotic supplementation for mothers aimed at preventing morbidity and mortality in preterm infants. The studies included in this review considered populations of pregnant women who received probiotics supplements from 36 weeks of gestation, or earlier, until delivery. The probiotics examined belonged to the *Lactobacillus*, *Bifidobacterium* and *Saccharomyces* genera. No significant differences were observed in the incidence of NEC or mortality, but in this case the quality of the scientific evidence generated was very low.

In 2017, our research group published a quasi-experimental study (18) on the use of probiotics in premature infants with less than 32 weeks of gestational age. The study aim was to determine whether routine supplementation with probiotics -*L. rhamnosus* GG (LGG) or *L. acidophilus* + *B. bifidum*- was associated with a reduced risk of severe NEC, in preterm infants with less than 32 weeks' gestation. The results obtained showed that routine supplementation with LGG or *L. acidophillus* + *B. bifidum* was associated with a reduced risk of severe NEC, late-onset sepsis and mortality in preterm infants with less than 32 weeks' gestation.

Table I. Characteristics of the studies included in the systematic review

Authors. Study design and number of articles analysed	Characteristics of patients	Sample size	Intervention	Results
Chris et al. (2018) (3) NMA (51)	37 GA < 2500 g	*n:* 11231	*Bacillus Bifidobacterium Enterococcus Lactobacillus Saccharomyces, Streptococcus*	Some strains or combinations of probiotics are effective in reducing mortality and morbidity due to NEC. No recommended dose or duration of treatment established
Chi et al. (2021) (4) NMA (45)	< 37 GA < 2500 g	*n:* 13230 (intervention*n:* 6577; placebo: 5743)	*Lactobacillus, Prebiotic + Bifidobacterium*	Used alone, probiotics are of limited effectiveness. Mortality is reduced with the Bifidobacterium + prebiotic combination. Morbidity from NEC is lower in the Lactobacillus + prebiotic association. In all cases, the probiotic results are better than those of placebo treatment
Bi et al. (2019) (5) NMA (34)	< 37 GA < 2500 g	*n:* 9161	*Lactobacillus, Bifidobacterium, Bacillus, Saccharomyces, Lactobacillus + Bifidobacterium*	The combination of probiotics + Bifidobacterium presents advantages when used in premature infants. Further research is needed before other probiotics can be recommended, as no reduction in the incidence of NEC, sepsis or mortality was observed
Jin et al. (2019) (4) SR (23)	< 37 GA < 2500 g	*n:* 10520	*Lactobacillus + Bifidobacterium*	The use of probiotics reduced the incidence of NEC, although further studies to determine the quality of probiotic preparations, their safety, optimal dose and treatment duration are needed before routine use can be recommended. It cannot be concluded that the use of a single probiotic is less useful than that of a combination. The incidence of NEC was higher in preterm infants < 27 weeks' GA who received Infloran
Baldassarre et al. (2019) (7) NMA	< 34 GA or < 1500 g	*n:* not stated	*Lactobacillus + Bifidobacterium*	The incidence of NEC was lower in the patients who received probiotics, as was the time to achieve complete enteral nutrition, the length of hospital stay and all-cause mortality. No differences were found in the risk of developing ROP, in the appearance of IVH or in the alleviation of BPD
Robertson et al. (2020) (8) SR	< 36 GA + < 1500 g	*n:* 982	*Lactobacillus + Bifidobacterium*	The incidence of NEC and late sepsis was reduced with the administration of *Lactobacillus* and *Bifidobacterium*
Underwood (2018) (9) MA (23)	< 37 GA < 28 GA < 1000 g	*n:* 85596 *n:* 4683	*Lactobacillus + Bifidobacterium*	The use of probiotics reduced the risk of NEC, and of all causes of mortality. There were no changes in the incidence of ROP, HIV or BPD. However, no predetermined dosage can be recommended. In preterm infants <28 weeks' GA and <1000 g birth weight, NEC, late sepsis and mortality were all lower in the group that received probiotics
Xiong et al. (2019) (10) SR (98)	< 37 GA < 2500 g	*n:* unknown	*Lactobacillus, Bifidobacterium* and/or *Saccharomyces*	The combined use of probiotics reduced the risk of grade II or higher NEC, and all causes of neonatal mortality

(Continues on next page)

Table I (cont.). Characteristics of the studies included in the systematic review

Authors. Study design and number of articles analysed	Characteristics of patients	Sample size	Intervention	Results
Bi et al. (2019) (11) MA (34)	< 37 GA < 2500 g	*n:* 9161 (intervention*n:* 4648; control: 4523	*Lactobacillus + Bifidobacterium*	In premature infants, the combined administration of probiotics reduced the risk of NEC, sepsis of the intestinal tract and mortality, compared to the use of probiotics alone or placebo. The exact dose of probiotics and duration of treatment cannot be concluded
Sun et al. (2017) (12) MA (32)	< 32 GA or < 1500 g	*n:* 8604	*Lactobacillus, Bifidobacterium, Enterococcus, Streptococcus*	The combined administration of low-dose probiotics (< 10^9 CFU) in preterm infants reduces the incidence of NEC, sepsis, mortality and length of hospital stay, if administered for < 6 weeks. No effects on weight gain or IVH were observed
Morgan et al. (2020) (13) MA (63)	< 37 GA < 2500 g	*n:* 15712	*Lactobacillus + Bifidobacterium. Bacillus + Enterococcus. Bifidocbacterium + Streptoccus* isolate	The combined administration of *Lactobacillus + Bifidobacterium* reduces the incidence of NEC and all causes of mortality. The combined administration of *Lactobacillus + Bifidobacterium + S. boulardii* reduces the number of days to complete enteral nutrition, compared to other combinations and placebo
Aceti et al. (2017) (14) MA (37)	< 37 GA	*n:* 5868 (intervention*n:* 2934; control: 2934)		The combined administration of probiotics with breast milk reduced the incidence of late sepsis in preterm infants. No specific treatment duration or dose could be established
Dermyshi et al. (2017) (15) MA (44)	< 34 GA < 1500 g	*n:* 26855	*Lactobacillus + Bifidobacterium*	The combined administration of incidence of NEC and all causes of mortality. No effects on late onset sepsis
Sharif et al. (2020) (16) MA (56)	< 32 GA < 1500 g	*n:* 10812	*Lactobacillus, Bifidocacterium, Saccharomyces, Streptococcus*	Probiotics in very low brith weight infants can reduce the risk oz NEC, sepsis and detah. No effects on neurodevelopment
Grev et al. (2018) (17) MA (12)	< 37 GA	*n:* 1204	*Lactobacillus, Bifidobacterium, Saccharomyces*	The administration of probiotics to mothers of premature infants appears to reduce the time to achieve enteral nutrition, but does not reduce the risk of NEC, surgery for NEC or mortalityin premature infants
Uberos et al. (2017) (18) CT	< 32 GA < 1500 g	*n:* 261	*Lactobacillus + Bifidobacterium (Bivos* or *Infloran)*	The administration of probiotics in premature infants between 27-32 w GA decreases the incidence of NEC, late sepsis and mortality. In patients under 27 w GA, more studies are requiered for its routine recommendation

NMA: network meta-analysis. SR: systematic review. MA: meta-analysis. CT: clinical trial. GA: gestational age (weeks). NEC: necrotising enterocolitis. IVH: intraventricular haemorrhage. ROP: retinopathy of prematurity. BPD: bronchopulmonary dysplasia.

DISCUSSION

Current scientific evidence confirms the utility of different combinations of probiotics in the prevention of NEC and late neonatal sepsis in very low birth weight preterm infants. Achieving a good balance in intestinal microbiota can inhibit intestinal dysbiosis and regulate the immune response (19). The fact that preterm infants have a less developed immune system increases the risk of infections, NEC and morbidity-mortality (20).

Breast milk is the best nutrition for neonates, especially premature infants (21), protecting them against NEC and sepsis, and this effect is increased with probiotic supplementation. Very low-weight preterm infants may be immunologically more vulnerable, and so information regarding the efficacy, safety and possible side effects of the different strains used must be available before their routine use. However, the use of lactobacillus and bifidobacteria does not cause concern, because these strains normally reside in the gastrointestinal tract of healthy infants (2). Careful selection of the strain or strains used in probiotic supplementation will minimise the risk of side effects.

Evidence suggests that rates of NEC, late sepsis and mortality, and length of hospital stay and time required to achieve complete enteral nutrition all decrease with the use of probiotics. However, other variables such as IVH, ROP and BPD are not affected by this supplementation (7,9,12).

The meta-analysis by Chris et al., in 2018 (3), examined the use of different types of strains of *Bacillus, Bifidobacterium, Enterococcus, Lactobacillus, Saccharomyces* and *Streptococcus*, but was unable to establish the most suitable combinations or doses to reduce the incidence of NEC, mortality, length of hospital stay or time to achieve enteral nutrition. However, these authors did observe that the most commonly used probiotics were combinations of *Lactobacillus* and *Bifidobacterium*. Another meta-analysis, by Bi (5), concluded that although a combination of probiotics with *Bifidobacterium* seems to reduce the incidence of NEC, more studies are needed to determine which probiotic strain is ideal in preterm infants, as was also concluded by Jin (6). The use of *Lactobacillus* and *Bifidobacterium* during the first two weeks of postnatal life is a safe and inexpensive option, which also reduces the incidence of NEC (8). Studies have shown that 10^9 CFU seems to be a sufficient dose to achieve a beneficial effect (12), and that the combination of several strains of probiotics is the most effective means of reducing the risk of late sepsis and NEC (13,15-17).

The main limitation of the present study is the lack of detailed information regarding the analysis of each gestational age group, beyond the inclusion of premature infants with less than 37 weeks' gestational age or less than 2,500 g birth weight. Without more extensive data, it is hard to determine the real benefit obtained from the use of probiotics in extremely low-weight newborns.

Nevertheless, it can be concluded that the administration of probiotics is safe and effective in reducing the risk of NEC, late sepsis and mortality, as well as the length of hospital stay and the time required to achieve complete enteral nutrition in premature infants. Furthermore, combinations of several strains of probiotics seem to be more effective than the administration of single strains. Those most commonly used are *Lactobacillus* and *Bifidobacterium*. At present, there is no clear evidence as to which strains should most appropriately be administered, nor for how long or at what doses.

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Revisión

Relationship between food insecurity and malnutrition in schoolchildren from low- and middle-income countries — A systematic review

Relación entre inseguridad alimentaria y desnutrición en escolares de países de bajos y medianos ingresos: revisión sistemática

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Abstract

The objective of this review is to study the relationship between food insecurity (FI) and malnutrition in schoolchildren from low-and middle-income countries (LMIC). The review was conducted using the databases PubMed, MEDLINE, CENTRAL, LILACS and SCiELO during the months of March to April 2022 without language or publication date restrictions. The search strategy consisted of combinations of text words and controlled vocabulary (MeSH terms and DeCS) related to "schoolchildren", "low- and middle-income countries" and "food insecurity". Fifteen studies were included in this review. Studies assessing FI and undernutrition in LMIC schoolchildren have indicated that FI is associated with lower height-for-age and higher prevalence of undernutrition overall. Only two studies identified a positive risk association between FI and overweight and obesity, the remaining studies suggested that schoolchildren with FI have a lower risk of overweight and obesity than those without FI. The review suggests a link between FI and undernutrition in schoolchildren from LMIC, with controversial results on overweight and obesity. Comprehensive public health policies should consider contextual and population-specific factors in addressing FI's impact on nutritional status.

Keywords:

Food insecurity. Children. Malnutrition. Vulnerable populations. Low- and middle-income countries.

Resumen

El objetivo de esta revisión fue estudiar la relación entre la inseguridad alimentaria (IA) y la desnutrición en escolares de países de bajos y medianos ingresos (PBMI). La revisión se realizó utilizando las bases de datos PubMed, MEDLINE, CENTRAL, LILACS y SciELO durante los meses de marzo a abril de 2022 sin restricciones de idioma o fecha de publicación. La estrategia de búsqueda consistió en combinaciones de palabras y vocabulario controlado (términos MeSH y DeCS) relacionados con "escolares", "países de bajos y medianos ingresos" e "inseguridad alimentaria". Quince estudios se incluyeron en esta revisión. Los estudios que evaluaron la IA y la desnutrición en escolares de PBMI mostraron que la IA está asociada con una menor talla para la edad y una mayor prevalencia de desnutrición en general. Solo dos estudios encontraron una asociación de riesgo positiva entre la IA y el sobrepeso y la obesidad; el resto de los estudios sugieren que los escolares con IA tienen menor riesgo de sobrepeso y obesidad que aquellos sin IA. La revisión sugiere una asociación entre la IA y la desnutrición en escolares de PBMI, con resultados contradictorios en el sobrepeso y la obesidad. Las políticas de salud pública deberían considerar factores contextuales y específicos de la población al abordar el impacto de la IA en el estado nutricional.

Palabras clave:

Inseguridad alimentaria. Escolares. Desnutrición. Poblaciones vulnerables. Países de bajos y medianos ingresos.

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INTRODUCTION

Malnutrition affects physical, mental and social development, especially in children (1). The World Health Organization (WHO) defines malnutrition as the product of "deficiencies, excesses and imbalances in a person's caloric and/or nutrient intake", this definition includes both undernutrition and overweight and obesity (1). Multiple studies have documented that children with undernutrition have a higher risk of dying from any cause, an increased risk of infectious and respiratory diseases, diarrhea, anemia, as well as poor physical and cognitive development (1,2). On the other hand, overweight and obesity in children are associated with lower self-esteem and an increased risk of skin and orthopedic diseases, as well as a higher risk of developing lipid abnormalities, sleep apnea, cardiovascular disease, type 2 diabetes, and some types of cancer in adulthood (1,2).

The children with the highest risk of malnutrition are those who are in vulnerable environments, that is, they live in rural communities or in low-income households or belong to an indigenous community or ethnic minority (3). Globally, 18.4 % of children between the ages of 5 and 19 were overweight and obese in 2016 (4). Although developed countries have the highest prevalence, low- and middle-income countries (LMICs) have seen a significant increase in their rates of obesity and overweight in the last decade (4). Undernutrition in schoolchildren is rarely reported worldwide, but several local studies have shown that rural and indigenous communities in LMICs are the most affected (2). Malnutrition can occur due to limited access to nutritious food as in food insecurity (FI).

The Food and Agriculture Organization (FAO) defines FI as "the limited or uncertain availability of nutritionally adequate and safe foods, or limited or uncertain ability to acquire acceptable foods in socially acceptable ways" (5). FI is associated with multiple health problems, including a higher risk of asthma, anemia, cognitive problems, anxiety and depression, than people who are food secure (6-8). In the world, 29.3 % of people were moderately or severely food insecure in 2021, with LMICs, such as Africa (57.9 %) and Latin America and the Caribbean (40.6 %), having the highest prevalence (2).

Multiple studies have evaluated the relationship between FI and malnutrition. In the case of adults and adolescents, a higher level of FI is associated with a higher prevalence of overweight and obesity, particularly in women (9,10). In contrast, in preschool children (< 5 years), higher levels of FI are associated with an increased risk of developing undernutrition (10,11). In relation to schoolchildren (5 to 12 years), higher levels of FI have been associated with lower diet quality (12). Schoolchildren with FI have a lower consumption of fruits, vegetables, fiber, legumes, as well as a higher intake of calories, mainly from saturated fats and added sugars than their peers without FI (13-16). This indicates that schoolchildren with FI have a greater risk of malnutrition than those without FI.

A century ago, being overweight and obese was associated with wealth, but not anymore. In developed countries, poor children are often the most likely to be overweight or obese (17). Children who are overweight often come from socioeconomically disadvantaged families. In the United States, for example, the rate of overweight in children decreases as educational level and family income increase (18). Sopoede et al. conducted a systematic review whose objective was to evaluate the relationship between FI and malnutrition in children aged 2 to 19 years in the US (19). The authors concluded that there is no evidence showing a relationship between FI and undernutrition. In relation to FI and overweight and obesity, the results were not consistent, but there seems to be a trend towards a higher risk of obesity. For schoolchildren (5-12 years) in LMICs, little is known about the relationship between FI and malnutrition. The purpose of this review is to study the relationship between FI and nutritional status in schoolchildren with characteristics of vulnerability from LMICs.

METHODS

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All study designs were considered for inclusion in this review.

Participants

The population was schoolchildren (5 to 12 years) in conditions of vulnerability from LMICs. Vulnerability was considered when they lived in a rural community, had a low socioeconomic level and/or belonged to an Indigenous community or ethnic minority. Studies in which the majority of participants (more than 80 %) are in this age range or present separate data for this age range were included.

Exposure

The review included studies that assessed FI using a validated survey tool.

Comparisons

Schoolchildren from the same environment without FI were considered as a comparison.

Outcome measures

Primary outcomes were BMI-for-age Z-score (BMI-Z), odds ratio (OR)/relative risk (RR) for undernutrition, and OR/RR for overweight and obesity. Other anthropometric measures such as weight, waist circumference, skinfolds, height-for-age Z-score (HAZ), weight-for-

age Z-score (WAZ), weight-for-height Z-score (WHZ) as well as the prevalence/incidence of malnutrition and prevalence/incidence of overweight and obesity were considered secondary outcomes.

SEARCH STRATEGY

The search for articles was performed using the databases PubMed (interface National Library of Medicine), MEDLINE (OVID interface), The Cochrane Library – CENTRAL (OVID interface), LILACS (Virtual Health Library) and SciELO (Scientific Electronic Library Online). The search was conducted during the months of March to April 2022 without language or publication date restrictions. The search strategy consisted of combinations of text words and controlled vocabulary (MeSH terms and DeCS) related to "schoolchildren", "low- and middle-income countries" and "food insecurity" considering the search platform. The PubMed search strategy can be found in the supplementary material (Supplementary Table I). Following the recommendations of the Cochrane handbook, the bibliographical references of systematic reviews and included studies were considered as additional search sources (20).

SELECTION OF STUDIES

For the article selection process, the Mendeley version 1.19.8 software was used, to which the results of the searches in the different databases were imported for subsequent processing. In the first stage, duplicate results were removed. In the second stage, titles and abstracts were reviewed eliminating articles that clearly did not meet the inclusion criteria. If the inclusion criteria were not well defined in the abstract, the article went to the third stage. In the third stage, the full text was reviewed to assess whether it met the inclusion criteria. The study selection process is described in the PRISMA flowchart (Fig. 1).

DATA EXTRACTION AND SYNTHESIS

For data extraction, an electronic format (Excel sheet) was used, which collected the title of the article, author, year of publication, type of study, study population, number of participants, measurement tools and cut-off points for FI and malnutrition, in addition to the main results. The information collected from the included studies is presented through a narrative synthesis.

RESULTS

CHARACTERISTICS OF INCLUDED STUDIES

Of the 36 full-text articles that were evaluated, nine did not evaluate the relationship between FI and malnutrition, five did not meet the age criteria, and seven were not conducted in LMICs (Fig. 1). The 15 studies included in the review had a cross-sectional design and were published between 2007 and 2021 (6,21,30-34,22-29). These studies analyzed populations from Brazil (21,31), Ethiopia (23,30), the Philippines (24), Malaysia (25), Venezuela (27), Nicaragua (6), Colombia (34), Bolivia (22), Mexico (26,28,29,33) and Jamaica (32). The sample size ranged from 61 to 7181 schoolchildren, and all studies had vulnerability characteristics.

Nine different tools were used to assess FI, eight of which assessed FI at the household level and one at the personal level. The tools used were Brazilian Food Insecurity Scale (EBIA) (21,31),

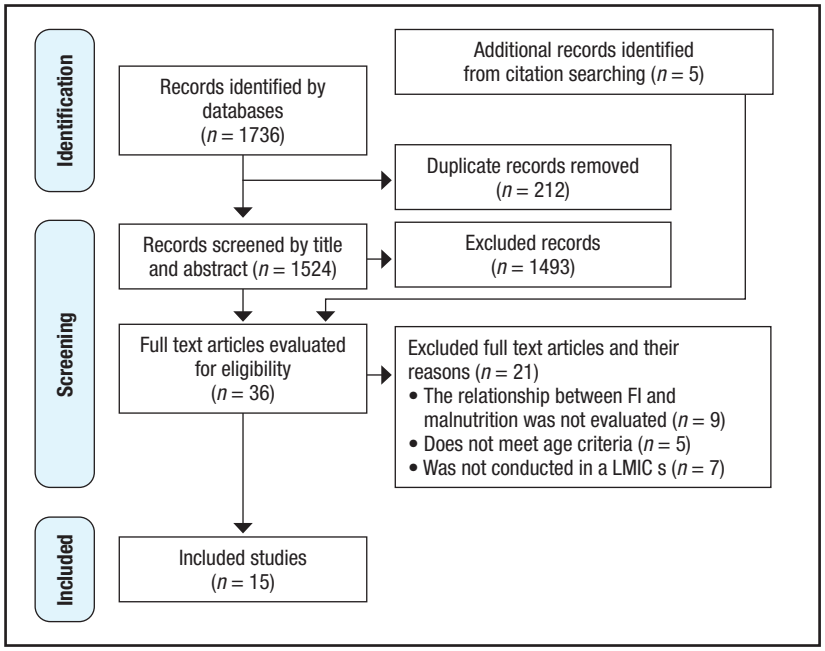

Figure 1.

Flowchart of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Household Food Insecurity Access Scale (HFIAS) (22,23), Food Insecurity Experience Scale (FIES) (24), Radimer/Cornell Hunger and Food Insecurity Instrument (25), USDA Household Food Security Survey Module (HFSSM) (34) and its version short (27), Latin American and Caribbean Food Security Questionnaire (ELCSA) (6,29), Food and Nutrition Technical Assistance (FANTA) (30), Mexican Food Safety Scale (EMSA) (26,28) and 2-items Hunger Vital Sign (HVS) (32,33).

To assess nutritional status, BMI-Z, HAZ, WAZ and WHZ were used. To classify children, 12 studies used the WHO 2007 cut-off points (21,22,31,34,23-30), one the CDC 2000 cut-off points (33), one the Frisancho 2008 cut-off points (6), and one the Cole references specific for sex and age (32).

FOOD INSECURITY AND UNDERNUTRITION

Eight articles evaluated the relationship between FI and undernutrition, the summary of results is shown in table I. Three studies found that higher levels of FI were associated with an increased risk (OR, 1.34 to 2.79) of stunted (measurement by HAZ) in schoolchildren (6,23,27). However, leiri *et al.* could not find a significant association between FI and HAZ, but did find a significant association between FI and lower WAZ (24). In agreement, two studies showed that schoolchildren with FI have a higher risk of low WAZ (OR, 3.0 to 4.8) compared to children without FI (30,34). Two studies found no significant association between FI and anthropometric indices (21,25).

Table I. Summary of studies that evaluated food insecurity and undernutrition

Population (authors, year)	Study design	FI evaluation	Malnutrition assessment	Outcomes
61 Brazilian children aged 5-10 years (Bueno *et al.*, 2021)	Cross-sectional	Brazilian Food Insecurity Scale (EBIA)	BMI-Z and HAZ Cut-off points WHO 2007	No significant association was found between nutritional status and familial FI
671 Ethiopian children aged 10.9 ± 2.67 years (Geletaw *et al.*, 2021)	Institution-based quantitative cross-sectional study	Household Food Insecurity Access Scale (HFIAS)	BMI-Z and HAZ Cut-off points WHO 2007	Children from food-insecure households were 2.79 times [AOR. 2.79; 95 % CI: 1.81, 4.31] more likely to be stunted than children from food-secure households
327 Philippine children aged 6-12 years (leiri *et al.*, 2021)	Community-based, cross-sectional study	Food Insecurity Experience Scale (FIES)	HAZ and WAZ Cut-off points WHO 2007	There was no association between the experience of household FI and HAZ Household income, household size, parental BMI, and the experience of household severe FI were significantly associated with lower WAZ in the adjusted model
167 Malaysian children aged 7-11 (Teh *et al.*, 2020)	Cross-sectional	Radimer/Cornell Hunger and Food Insecurity Instrument	BMI-Z and HAZ Cut-off points WHO 2007	There were no associations between the food security index and anthropometric indices
1730 Venezuelan children aged 7-12 years (Herrera-Cuenca *et al.*, 2019)	Cross-sectional	6-item short USDA Household Food Security Survey Module (HFSSM)	BMI-Z and HAZ Cut-off points WHO 2007	We found a significant association between FI and short height in children ($X^2 = 8.205$. 2 df; $p = 0.017$)
431 Nicaraguan children aged 3-11 years (Schmeer *et al.*, 2017)	Cross-sectional	Latin American and Caribbean Food Security Questionnaire (ELCSA)	HAZ Cut-off points Frisancho 2008	Children in mildly food insecure households had 34% higher odds of low height-for-age compared with children living in food secure households
450 Ethiopia children aged 7-14 years (Wolde *et al.*, 2015)	Cross-sectional survey	Food and Nutrition Technical Assistance (FANTA)	BMI-Z, HAZ and WAZ Cut-off points WHO 2007	Children live in food insecure households are more likely to be stunted, under-weight and wasted than children live in food secure households (AOR = 2.5; 95 %, 1-5.6; AOR = 3.9; 95 % CI, 1.2-12.0; AOR = 4.8; 95 % CI, 1.7-13.6)
2526 Colombian children aged 5-12 years (Isanaka *et al.*, 2007)	Cross-sectional survey	USDA Household Food Security Survey Module (HFSSM)	HAZ, WAZ and WHZ Cut-off points WHO 2007	FI children were almost 3 times more likely to be underweight compared with food-secure children ($p = 0.0007$)

FI: food insecurity; BMI-Z: body mass index for age Z-score; HAZ: height-for-age Z-score; WAZ: weight-for-age Z-score; WHZ: weight-for-height Z-score; WHO: World Health Organization.

FOOD INSECURITY AND OVERWEIGHT OR OBESITY

Nine articles evaluated the relationship between FI and overweight or obesity, the summary of results is shown in table II. Two studies conducted in Mexican schoolchildren found that higher levels of FI were associated with an increased risk of overweight and obesity (OR, 2.3) (28,33). However, Murillo-Castillo et al. and Shamah-Levy et al. found that higher levels of FI were associated with lower prevalence of overweight and obesity in Mexican schoolchildren (26,29). Similarly, two studies conducted in schoolchildren in Brazil and Jamaica found the same negative association between FI and lower risk of overweight and obesity (OR, 0.78 and OR, 0.65, respectively) (31,32). Bethancourt et al. found that FI and hair cortisol concentration were associated with a lower BMI-Z, in turn, FI was associated with a higher percentage of body fat in Bolivian schoolchildren (22).

Table II. Summary of studies that evaluated food insecurity and overweight or obesity

Population (authors, year)	Study design	FI evaluation	Malnutrition assessment	Outcomes
61 Brazilian children aged 5-10 years (Bueno *et al.*, 2021)	Cross-sectional	Brazilian Food Insecurity Scale (EBIA)	BMI-Z and HAZ Cut-off points WHO 2007	No significant association was found between nutritional status and familial FI
167 Bolivian children aged 6-16 years (Bethancourt *et al.*, 2021)	Cross-sectional	Household Food Insecurity Access Scale (HFIAS)	BMI-Z Cut-off points WHO 2007	There was a significant positive association between HFIAS score and % body fat (Model 1 $\beta = 0.44$, SE = 0.22, $p = 0.04$) Although neither HFIAS nor hair cortisol concentration were independently associated with BMI-Z, they had a significant negative linear joint effect on BMI-Z ($\beta = -0.08$; SE = 0.04, $p = 0.04$)
167 Malaysian hildren aged 7-11 (Teh *et al.*, 2020)	Cross-sectional	Radimer/Cornell Hunger and Food Insecurity Instrument	BMI-Z and HAZ Cut-off points WHO 2007	There were no associations between the food security index and anthropometric indices
100 Mexican children aged 6-12 years (Murillo-Castillo *et al.*, 2020)	Cross-sectional	Mexican Food Safety Scale (EMSA)	BMI-Z Cut-off points WHO 2007	Adjusted analysis showed a negatively association between food insecurity and overweight and obesity, both in boys and girls (p for trend in logit < 0.01)
105 Mexican children aged 6-12 years (Rosas *et al.*, 2017)	Descriptive cross-sectional	Mexican Food Safety Scale (EMSA)	BMI-Z Cut-off points WHO 2007	49.4 % of households present FI; among these, 51.61 % of schoolchildren show obesity; 29.03 % overweight; 19.35 % risk of overweight, and 64.52 % cardiometabolic risk
7181 mother-schoolchild (5-11 years) pairs Mexicans (Shamah-Levy *et al.*, 2017)	Cross-sectional survey	Latin American and Caribbean Food Security Scale (ELCSA)	HAZ, WAZ and WHZ Cut-off points WHO 2007	The logistic regression model revealed a significantly lower prevalence of overweight and obesity among those with mild, moderate, or severe FI ($p < 0.05$)
782 Brazilian children aged 6.9 ± 0.6 years (Vicenzi *et al.*, 2015)	Cross-sectional school-based	Brazilian Food Insecurity Scale (EBIA)	BMI-Z Cut-off points WHO 2007	After controlling for potential confounders, children with food insecurity had 22 % lower odds of overweight
1674 Jamaican children aged 10-11 years (Dubois *et al.*, 2011)	Cross-sectional	2-items Hunger Vital Sign (HVS)	BMI-Z Overweight was defined using Cole's age- and sex-specific criteria	Children in FI households had odds of 0.65 (95 %, CI: 0.4-0.9) for being overweight or obese in comparison to those in food-secure households
768 Mexican children aged 9-15 years (Ortiz-Hernández *et al.*, 2007)	Cross-sectional	2-2-items Hunger Vital Sign (HVS)	BMI-Z Cut-off points CDC 2000 references	Children with severe FI were 2.53 times more likely to be overweight than children without FI ($p = 0.002$)

FI: food insecurity; BMI-Z: body mass index for age Z-score; HAZ: height-for-age Z-score; WAZ: weight-for-age Z-score; WHZ: weight-for-height Z-score; WHO: World Health Organization.

DISCUSSION

LMICs are the most affected by FI and malnutrition. Children with FI and malnutrition have less physical, mental and social development in addition to more health problems(1,2,6,8). Knowing the relationship between FI and malnutrition, as well as its determinants, can allow the development of better strategies for its approach. However, evaluating the association between FI and malnutrition in schoolchildren is complicated because both problems are multifactorial.

There are many validated tools to assess FI and nutritional status, further complicating the association between FI and malnutrition. FI can be assessed at a household or personal level. In this review, nine different tools for assessing FI were identified, with eight at the household level and one at the personal level. Household-level surveys include a section to capture children's experience, however, when answered by the head of the household, they identify FI globally (35). Various authors have suggested that parents' perceptions of their children's FI could be imprecise or incomplete (36,37). This may be because not all members of the same household deal with FI in the same way (38). Parents may not be fully aware of their children's experiences or the actions they take to reduce the severity of FI (39). Research suggests that this discrepancy may be due to different ways of reasoning and response styles (36-39).

Studies evaluating the reliability of schoolchildren reporting their own experiences of FI concluded that those aged between 6 and 16 years are capable of doing so (37,40). In the USA, Connell et al. developed the Children Food Security Survey (CFSS), which adapted 9 questions from the HFSSM for use with children aged between 12 and 17 years (40). The CFSS demonstrated acceptable reliability and apparent internal validity (40). A study comparing the diet quality with FI levels, using both the HFSSM and CFSS for measurement, concluded that both surveys concurred in classifying FI as long as the child was ≥ 6 years old (41). However, the author suggested that the CFSS might be more sensitive in detecting differences in micronutrient intake (41).

The studies included in this review used the BMI-Z, HAZ, WAZ and WHZ indices to define malnutrition. Two of the studies included in this review did not find a significant association between FI and anthropometric indices (21,25). Nutritional status is normally defined by anthropometric indices, however, there are other tools that can aid in a more comprehensive evaluation. Nutritional status is defined as the physical condition resulting from the relationship between individual requirements and the consumption, absorption and use of energy and nutrients (1). Therefore, for a comprehensive nutritional assessment, one must consider not only anthropometric parameters, but also macro and micronutrient intake, as well as physical activity levels and the child's medical history. Some studies suggest that the lack of association between FI and malnutrition may be attributed to potential confounding variables, including the child's sex and age, household income level, parents' nutritional status, and ethnicity (42-44).

Of the eight articles in this review that evaluated the association between FI and undernutrition, six of them showed significant associations between higher FI and greater risk of stunted and undernutrition in general. Various theories have been proposed as possible causes of lower HAZ in schoolchildren with FI, such as delayed introduction of supplemental foods, or the introduction of poorly nutritious foods rich in starch and low in protein, vitamin A, iron and zinc (16). On the other hand, an analysis of eating habits in relation to FI levels showed that diet quality decreases with increasing FI. Children with FI have a higher intake of calories from saturated fats and added sugars, as well as a lower intake of fruits, vegetables, and dairy products (12-15,45). These eating patterns suggest an increased risk of obesity in children with FI.

Examining the intriguing relationship between FI and a reduced risk of excess weight, particularly overweight and obesity, reveals a noteworthy pattern in our reviewed studies. Five out of the nine studies investigating the FI-overweight/obesity link reported a lower prevalence of these conditions, as indicated by a lower BMI-Z, among children experiencing FI. This trend, observed predominantly in developing countries, contrasts with patterns in developed nations, where higher FI levels often correlate with increased prevalence of overweight and obesity. The variations observed across different socio-economic contexts, food availability, accessibility, and levels of physical activity might account for these disparities (42-44).

In the global issue of overweight and obesity, it is noteworthy that, while developed countries exhibit the highest rates of these conditions, LMICs have experienced a significant increase in their rates over the past decade (4). This phenomenon is intertwined with the complex relationship between FI and overweight or obesity, as revealed by nine studies analyzed in this review. Of these, five demonstrate that children facing FI have lower prevalences of overweight and obesity. However, these same studies agree that the quality of the diet is compromised, reflected in reduced consumption of fruits and vegetables, as well as increased intake of simple carbohydrates and saturated fats, which over time could contribute to the development of overweight or obesity (22,26,29,31,32).

It is important to note that the apparent lack of association between FI and a higher prevalence of overweight and obesity can be explained by the nutritional transition phase these countries are undergoing, where a dual burden of malnutrition is observed in the same household. One study highlights that FI is associated with stunting in preschoolers only if the mother does not suffer from obesity (29). The disparity in the relationship between FI and overweight or obesity between developed and developing LMICs may be due to divergent trajectories. While in developed countries, available social support services are associated with an increase in overweight/obesity, in developing countries, limited assistance in the form of food subsidies contributes to children from poorer families with FI consuming fewer total calories, thereby decreasing the chances of developing overweight or obesity (32,46,47).

However, it is crucial to note that the association between FI and excess body fat was highlighted in the study by Bethancourt et al., demonstrating a higher percentage of body fat in schoolchildren experiencing FI (22). Similarly, the studies

conducted by Rosas et al. and Ortiz-Hernández et al. found a higher risk of overweight and obesity among schoolchildren facing FI (28,33). The complexities of the relationship between FI and obesity are multifaceted and encompass factors such as the consumption of cheaper and more energy-dense foods, periods of insufficient food leading to overeating when available, and fluctuations in eating habits within families experiencing FI (48).

Schoolchildren living in vulnerable environments are at higher risk of experiencing a high prevalence of FI and malnutrition (2,3). Knowing the social determinants associated with FI and malnutrition will allow the creation of better approach strategies. As a strength, this review shows how FI may be related to malnutrition in schoolchildren (5 to 12 years) from LMICs. A limitation of this review is that the included studies had a cross-sectional design that precludes establishing causal relationships, so more research is recommended to explain how FI is related to malnutrition in schoolchildren through stronger epidemiological designs. Additional investigations may also be conducted to determine if there are other social determinants associated with these factors. These social determinants may include family structure, socioeconomic and educational level, access to resources, among others.

CONCLUSION

The present systematic review addressed the complex relationship between FI and malnutrition in schoolchildren from low- and middle-income countries. Analyzing 15 cross-sectional studies revealed significant variability in the findings. Concerning undernutrition, the majority of studies indicate an association between elevated levels of FI and an increased risk of low HAZ or low WAZ. However, discrepancies surfaced, with certain studies failing to establish a significant link between FI and anthropometric indices. Regarding overweight and obesity, the evidence presented conflicting results, with studies suggesting both positive and negative associations between FI and these health issues. The diverse outcomes underscore the necessity of considering contextual and population-specific factors when interpreting the relationship between FI and nutritional status.

These findings highlight the complexity of the relationship between FI and malnutrition in schoolchildren, suggesting that socioeconomic, cultural, and regional factors may significantly shape this association. The emphasis is placed on comprehensively addressing FI in public health policies, considering the various dimensions of nutritional status in school populations across diverse contexts.

Supplemental Table I. Search strategy in PubMed

Search number	Query	Results
12	#5 and #8 and #11	1,139
11	#9 or #10	14,520
10	Food insecur*[Title/Abstract] or Food secur*[Title/Abstract]	14,395
9	"Food Insecurity"[Mesh:NoExp] or "Food Security"[Mesh:NoExp]	1,254
8	#6 or #7	250,603
7	(((((“Poverty”[Mesh:NoExp]) OR “Child Poverty”[Mesh:NoExp]) OR “Poverty Areas”[Mesh:NoExp]) OR “Indigenous Peoples”[Mesh:NoExp]) OR “Rural Population”[Mesh:NoExp]) OR “Ethnic and Racial Minorities”[Mesh:NoExp]	113,585
6	developing countr*[Title/Abstract] OR developing nation*[Title/Abstract] OR developing population*[Title/Abstract] OR “developing world”[Title/Abstract] OR less developed countr*[Title/Abstract] OR “underdeveloped world”[Title/Abstract] OR middle income countr*[Title/Abstract] OR middle-income nation*[Title/Abstract] OR middle-income population*[Title/Abstract] OR low-income countr*[Title/Abstract] OR low-income nation*[Title/Abstract] OR low-income population*[Title/Abstract] OR lower income countr*[Title/Abstract] OR lower income nation*[Title/Abstract] OR lower income population*[Title/Abstract] OR underserved countr*[Title/Abstract] OR underserved nation*[Title/Abstract] OR underserved population*[Title/Abstract] OR underserved world[Title/Abstract] OR under served countr*[Title/Abstract]	148,889
5	#1 or #2 or #3 or #4	2,491,586
4	Elementary school[Title/Abstract]	8,346
3	school children[Title/Abstract]	24,911
2	Child*[Title/Abstract]	1,579,931
1	“Child”[Mesh:NoExp]	1,840,224

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ARÁN

Nutrición Hospitalaria

Revisión

La importancia de la alimentación en la prevención de la endometriosis: revisión sistemática

The importance of nutrition in the prevention of endometriosis – Systematic review

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Resumen

Antecedentes y objetivo: la endometriosis es un trastorno dependiente de hormonas que se caracteriza por la presencia de tejido similar al endometrial en sitios extrauterinos, lo que puede desencadenar una reacción inflamatoria crónica. Esta enfermedad afecta principalmente a mujeres en edad fértil y puede tener un impacto negativo en su bienestar físico, mental y social. Existen patrones alimentarios considerados antiinflamatorios, como el de dieta mediterránea, que podrían ayudar en la prevención y el tratamiento de la endometriosis. El objetivo de esta revisión fue conocer la relación entre el consumo de diferentes grupos de alimentos y la prevención de la endometriosis.

Materiales y métodos: se realizó una revisión sistemática siguiendo la metodología PRISMA. Se consultaron las bases de datos PubMed, Scopus, Cochrane Library y Web of Science. Se seleccionaron estudios publicados entre 2013 y 2023, que fueran accesibles en texto completo, escritos en inglés y español y que incluyeran una muestra de mujeres con endometriosis y/o mujeres sanas, además de evaluar la relación entre la alimentación y la endometriosis. Se excluyeron artículos no relacionados, revisiones sistemáticas o metaanálisis y estudios piloto y realizados en animales.

Resultados: se incluyeron diez estudios en total. El consumo de frutas, verduras (no crucíferas), lácteos, pescados, patatas, legumbres, vitaminas (A, C, D y B12), ácidos grasos monoinsaturados y poliinsaturados y minerales (calcio, potasio y magnesio) parece reducir el riesgo de endometriosis.

Conclusiones: se necesitan más estudios que investiguen la relación entre el consumo de los diferentes grupos de alimentos y el riesgo de endometriosis.

Palabras clave:

Endometriosis. Dieta mediterránea. Dieta antiinflamatoria. Adherencia. Mujeres en edad fértil.

Abstract

Background and objective: endometriosis is a hormone-dependent disorder characterized by the presence of endometrial-like tissue in extra-uterine sites, which can trigger a chronic inflammatory reaction. This disease mainly affects women of childbearing age and can have a negative impact on their physical, mental and social well-being. There are eating patterns considered as anti-inflammatory, such as the Mediterranean diet, which could help in the prevention and treatment of endometriosis. The objective of this review was to know the relationship between the consumption of different food groups and the prevention of endometriosis.

Materials and methods: a systematic review was carried out following the PRISMA methodology. PubMed, Scopus, Cochrane Library and Web of Science databases were consulted. Studies published between 2013 and 2023 were selected, accessible in full text, written in English and Spanish and including a sample of women with endometriosis and/or healthy women, in addition to evaluating the relationship between diet and endometriosis. Unrelated articles, systematic reviews or meta-analyses, pilot studies and studies conducted in animals were excluded.

Results: a total of ten studies were included. The consumption of fruits, vegetables (not cruciferous), dairy products, fish, potatoes, legumes, vitamins (A, C, D and B12), monounsaturated and polyunsaturated fatty acids and minerals (calcium, potassium and magnesium) seems to reduce the risk of endometriosis.

Conclusions: further studies investigating the relationship between consumption of different food groups and risk of endometriosis are needed.

Keywords:

Endometriosis. Mediterranean diet. Anti-inflammatory diet. Adherence. Women of childbearing age.

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INTRODUCCIÓN

La endometriosis es un trastorno dependiente de hormonas que se caracteriza por la presencia de tejido similar al endometrial en sitios extrauterinos, lo que puede desencadenar a menudo una reacción inflamatoria crónica (1). Se estima que la prevalencia de la endometriosis es aproximadamente del 10-15 % en mujeres en edad reproductiva, lo que se extrapola a alrededor de 190 millones de mujeres en todo el mundo (2,3). Se trata de uno de los trastornos del sistema reproductivo femenino más comúnmente diagnosticados y tratados (4). Sin embargo, se sospecha que estos datos podrían subestimar el número real de mujeres afectadas, pues muchas de ellas son diagnosticadas accidentalmente tras ser intervenidas quirúrgicamente para el tratamiento de otras patologías (5), ya que no existe un método no invasivo para diagnosticarla como *gold standard*. No obstante, sí existen otros métodos de diagnóstico como pueden ser una ecografía transvaginal realizada por especialistas expertos o la resonancia magnética, que muestra más de un 90 % de especificad y sensibilidad (5). Se estima que la endometriosis está presente en el 2-22 % de las mujeres sin ninguna manifestación clínica de la afección, en el 40-80 % de las pacientes con dolor abdominal bajo y en el 13-48 % de las mujeres con infertilidad (6,7).

En cuanto al efecto de la enfermedad sobre la calidad de vida relacionada con la salud, su presencia puede afectar al bienestar físico, mental y social de la mujer (8,9). Es una enfermedad debilitante caracterizada por dismenorrea (dolor durante el periodo menstrual), dispareunia (dolor durante las relaciones sexuales), disquecia (dificultad al defecar), disuria (dolor o molestia al orinar) e infertilidad, pero puede haber también muchas quejas inespecíficas como dolor pélvico, fatiga, hinchazón y dolor de espalda (10). Además de ser uno de los principales síntomas en mujeres con endometriosis, se sabe que la dismenorrea tiene un alto impacto social, ya que a menudo se asocia con el absentismo escolar o laboral (11). Para manejar los síntomas existen diferentes opciones, que incluyen analgésicos, terapias hormonales o métodos quirúrgicos (12). Respecto al tratamiento farmacológico, este se basa en bloquear la secreción de estrógeno de los ovarios, para lo que se utilizan medicamentos de primera línea tales como anticonceptivos orales y los progestágenos, por su capacidad para disminuir el dolor y las recidivas y presentar menos efectos secundarios. También existen otros tratamientos como el danazol o los agonistas de la hormona liberadora de gonadotropina (GnRH-a), pero son considerados tratamientos de tercera línea por presentar un gran número de efectos secundarios (13). Sin embargo, el manejo de estos síntomas no está estandarizado, y la enfermedad puede reaparecer incluso después de un adecuado manejo quirúrgico o farmacológico (14).

Aparte de las intervenciones médicas, los hábitos alimentarios y los estilos de vida han recibido cada vez más atención en los últimos años, no solo como un factor de riesgo modificable sino también como un nuevo enfoque terapéutico (12). Los factores dietéticos pueden influir en el riesgo de endometriosis a través de vías hormonales o inflamatorias. Atendiendo a las vías hormonales, se sabe que la endometriosis depende del estrógeno para su crecimiento y mantenimiento, y se ha encontrado una asociación entre la dieta y las enfermedades dependientes de estrógenos (similares al cáncer de mama o de endometrio). Muchas modificaciones dietéticas y de estilo de vida pueden jugar un papel considerable en la minimización de los síntomas y pueden influir en la gravedad o progresión de la enfermedad (14,15). En cuanto a las vías inflamatorias, los hábitos alimentarios parecen tener una influencia moderada en algunos marcadores inflamatorios que aumentan en la endometriosis (por ejemplo, interleuquina 6 [IL-6], interleuquina 1 beta [IL-1β], factor de necrosis tumoral [TNF-α], proteína C reactiva [PCR]), los cuales están elevados en el líquido peritoneal y en la sangre de mujeres con endometriosis (16,17).

Por lo tanto, se sabe que la alimentación, como factor de riesgo modificable, puede tener efectos sobre la inflamación y, de hecho, actualmente se conoce que existen alimentos específicos que ejercen efectos sobre las vías inflamatorias del cuerpo (18,19). En general, el patrón de alimentación antiinflamatoria se enfoca en comer alimentos integrales, de origen vegetal, ricos en grasas saludables, con fitonutrientes y de bajo índice glucémico, de manera que no elevan la glucosa en sangre rápidamente (20). En efecto, la literatura científica indica que ciertos patrones de alimentación antiinflamatorios se asocian con una reducción de los marcadores de inflamación como son la PCR, la IL-6 y el TNF-α (21-23).

Dados sus efectos protectores en la reducción de procesos inflamatorios, una dieta antiinflamatoria también podría ser de gran ayuda en la prevención y el tratamiento de la endometriosis, que es precisamente una enfermedad inflamatoria crónica. Por todo ello, el objetivo de este estudio fue realizar una revisión sistemática de la literatura para evaluar la relación entre el consumo de alimentos, nutrientes y patrones alimentarios con el riesgo de padecer endometriosis.

MATERIAL Y MÉTODOS

Se realizó una revisión sistemática de la literatura, siguiendo como referencia la metodología PRISMA (24). La calidad de cada uno de los estudios se evaluó con la herramienta Cochrane Collaboration Risk of Bias (ROB) (25), que incluye siete ítems que cubren seis dominios de sesgo. Se considera que cada elemento tiene un ROB alto, bajo o poco claro.

Esta revisión fue registrada en la base de datos PROSPERO con el código CRD42023440338.

FUENTES DE DATOS

Para la obtención de los documentos, se realizaron búsquedas electrónicas en las bases de datos internacionales PubMed, Scopus, Cochrane Library y Web of Science. Se identificaron artículos adicionales mediante la búsqueda de las referencias de otros artículos.

ESTRATEGIA DE BÚSQUEDA

La estrategia de búsqueda tuvo como objetivo identificar los estudios publicados disponibles en texto completo. Se utilizó una estrategia de búsqueda masiva, utilizando tanto los descriptores MeSH como los términos título y *abstract*. Se utilizaron las siguientes palabras clave transformadas en términos MESH *(medical subject heading): "Nutritional Status", "Feeding Behavior", "Mediterranean diet", "Diet"* (dieta), *"Endometriosis", "Women", "Women of childbearing age, "Women of reproductive age"* y *"Women of fertile age",* unidos por los operadores booleanos OR y AND. La tabla I muestra la estrategia de búsqueda utilizada en la base de datos PubMed.

SELECCIÓN DE LOS ARTÍCULOS

La selección de los artículos se realizó mediante la lectura del título y el resumen de todos los artículos resultantes de la búsqueda en PubMed, Scopus, Cochrane Library y Web of Science. Los artículos fueron evaluados de forma independiente por dos autores para confirmar los criterios de inclusión/exclusión. La calidad de cada estudio fue evaluada de forma independiente por dos autores, utilizando los criterios de Crombie adaptados por Petticrew y Roberts. Los desacuerdos fueron resueltos por un tercer autor.

Tanto la calidad de los estudios de cohortes como la de los estudios de casos y controles se evaluaron con la escala de Newcastle-Ottawa (25) (Tabla II).

El primer autor (A.Z.M) y el segundo autor (K.C.G) del estudio calificaron cada artículo incluido de forma independiente y las discrepancias se resolvieron mediante acuerdo con el tercer autor (L.M.M). La estadística Cohen's kappa se calculó para evaluar la fiabilidad entre evaluadores para el ROB sin elementos que evaluaran el cegamiento de los participantes o evaluadores, ya que todos los estudios fueron calificados como ROB altos por los dos evaluadores cuando se analizaron todos los elementos. Se analizó la fiabilidad interevaluadores mediante el estadístico Cohen's kappa obteniendo un valor de ICC = 0,8.

Tabla I. Estrategia de búsqueda en la base de datos

Estrategia de búsqueda
#1 ("Endometriosis" [Title/Abstract] OR "Endometriosis" [MeSH Terms])
#2 ("Nutritional Status" [Title/Abstract] OR "Nutritional Status" [MeSH Terms]) OR ("Feeding Behavior" [Title/Abstract] OR "Feeding Behavior" [MeSH Terms]) OR ("Mediterranean diet" [Title/Abstract] OR "Diet, Mediterranean" [MeSH Terms]) OR ("Diet" [Title/Abstract] OR "Diet" [MeSH Terms])
#3 ("Women" [Title/Abstract] OR "Women" [MeSH Terms]) OR ("Women of childbearing age" [Title/Abstract]) OR ("Women of reproductive age" [Title/Abstract]) OR ("Women of fertile age" [Title/Abstract])
#4 #1 AND #2 AND #3

Tabla II. Herramienta preguntas Newcastle-Ottawa

Referencias	1	2	3	4	5	6	7	8
Estudios de cohortes								
Harris HR y cols. (1)	*	*	*	*	**	*	*	*
Yamamoto A y cols. (26)	*	*	*	*	**	*	*	*
Nodler JL y cols. (2)	*	*	*	*	**	*	*	*
Schwartz NRM y cols. (16)	*	*	*	*	**	*	*	*
Liu P y cols. (28)	*	*	*	*	**	*	*	*
Harris HR y cols. (18)	*	*	*	*	**	*	*	*
Estudios de casos y controles								
Ashrafi M y cols. (15)	-	*	-	*	**	*	*	*
Schink M y cols. (12)	-	*	*	*	**	*	*	*
Roshanzadeh G y cols. (29)	*	*	*	*	**	*	-	-
Samaneh Y y cols. (6)	-	*	*	*	**	*	*	*

Ítems de la Escala Newcastle-Ottawa para estudios de cohortes y e*studios de casos y controles: 1: representatividad; 2: cohorte no expuesta; 3: determinación de la exposición; 4: resultado; 5: comparabilidad de las cohortes; 6: evaluación del resultado; 7: seguimiento; 8: adecuación del seguimiento. Se asigna un máximo de una estrella para cada dominio dentro de las categorías "Selección" y "Resultado"* y se asigna un máximo de dos estrellas a *"Comparabilidad".*

CRITERIOS DE INCLUSIÓN Y EXCLUSIÓN

Los criterios de inclusión, según los cuales se seleccionaron los artículos, fueron: a) artículos accesibles en texto completo, escritos en inglés o español; b) artículos publicados en los últimos diez años (publicados entre 2013 y 2023); c) que incluyeran una muestra de mujeres con endometriosis y/o una muestra de mujeres sanas; y d) que evaluaran la relación entre la alimentación y el riesgo y/o prevención de la endometriosis.

Se excluyeron artículos no relacionados con el tema del estudio, revisiones sistemáticas o metaanálisis, estudios piloto y estudios realizados en animales.

DATOS EXTRAÍDOS

La extracción de datos se llevó a cabo por el primer y segundo autor y se realizó teniendo en cuenta el año de publicación (2013-2023), el objetivo del estudio, el tamaño muestra, el tipo de estudio, la edad media de las participantes, los resultados, las fortalezas y las limitaciones.

SÍNTESIS DE LOS RESULTADOS

Una vez completada la extracción de datos, los resultados se agruparon en dos bloques: a) según los instrumentos y las pruebas diagnósticas utilizados para realizar la evaluación dietética y ginecóloga; y b) según los resultados encontrados entre la ingesta de alimentos, los nutrientes y el riesgo de endometriosis.

RESULTADOS

Se identificaron 102 artículos en total. Tras aplicar los filtros "2013-2023", "inglés" y "español", se eliminaron 37 artículos. A continuación, se leyeron los títulos y resúmenes y se eliminaron otros 53 artículos, según los criterios de inclusión y exclusión. Por lo tanto, en esta revisión se incluyó finalmente un total de diez artículos (Fig. 1).

La tabla III muestra las características de los estudios incluidos. Toda la muestra incluida fueron mujeres con una edad media de 32,9 ± 6,81 años. El número total de sujetos analizados por todos los artículos incluidos fue de 342.884, de los cuales 338.082 (98,77 %) eran mujeres sanas al principio del estudio y 4.802 (1,43 %) eran mujeres con endometriosis. Atendiendo al país de origen, seis estudios fueron realizados en Estados Unidos (1,2,16,18,26,28), tres se realizaron en Irán (6,15,29) y uno, en Alemania (12). En cuanto al diseño de los estudios incluidos, seis fueron de cohortes (1,2,18,16,26,28) y cuatro, de casos y controles (6,12,15,29).

Por otro lado, en la tabla III también se analizó la calidad de la evidencia de los estudios incluidos en base al modelo Grading of Recommendations, Assessment, Development and Evaluation (GRADE), ya que presenta un gran interés en la medicina basada en la evidencia (27). En dicha tabla se aprecia que todos los estudios incluidos se encontraban entre un nivel de calidad de la evidencia muy baja y baja, ya que todos eran estudios observacionales y presentaban algunos sesgos.

EVALUACIÓN DIETÉTICA Y GINECOLÓGICA

La evaluación dietética se realizó mediante cuestionarios de frecuencia de consumo de alimentos validados (FFQ) en ocho estudios (1,2,6,12,18,26,28,29). En uno de estos ocho estudios (2), se les pidió a las participantes que completaran un cuestionario de frecuencia de consumo de alimentos sobre su dieta en la escuela secundaria (HS-FFQ). Por último, en un estudio se recopiló información dietética a través de un cuestionario estructurado sobre hábitos dietéticos (15) y en otro, a través de un recordatorio de 24 horas (28).

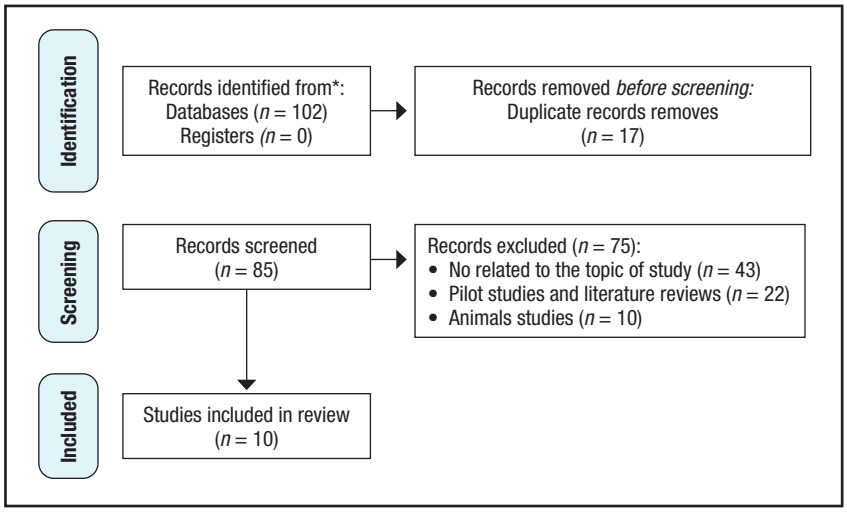

Figura 1.
Selección de estudios.

Tabla III. Características de los estudios incluidos

Autores	País	Año	Edad media	Muestra *(n)*	Objetivo	Tipo de estudio	Fortalezas y limitaciones	Calidad de la evidencia (GRADE)
Harris HR y cols. (1)	Estados Unidos	2018	33,5	70.835 mujeres sanas	Investigar si la ingesta de frutas y verduras, nutrientes concentrados en estos alimentos o equivalentes de actividad de retinol se asociaron con endometriosis confirmada por laparoscopia	Cohortes	Altas tasas de seguimiento; modelos rigurosos para ajustar la ingesta calórica total y cuantificar la asociación con frutas y verduras independientes de otros componentes de la dieta; examen de asociaciones por subtipo de caso y exploración de la modificación del efecto por fumar Error en el autoinforme de la ingesta dietética	Baja ⊕⊕⊖⊖
Yamamoto A y cols. (26)	Estados Unidos	2018	34	81.908 mujeres sanas	Determinar si una mayor ingesta de carnes rojas, aves, pescados y mariscos se asocia con el riesgo de endometriosis confirmada por laparoscopia	Cohortes	Diseño prospectivo; ajuste por calorías totales, minimizando los errores correlacionados La cohorte utilizó información autoinformada; el cuestionario de frecuencia de consumo de alimentos (FFQ) puede clasificar erróneamente a las personas con dietas inusuales y puede introducir error sistemático; posible confusión por factores que se asocian con los hábitos dietéticos y el diagnóstico laparoscópico de endometriosis	Baja ⊕⊕⊖⊖
Nodler JL y cols. (2)	Estados Unidos	2020	33,5	32.868 mujeres sanas	Evaluar la asociación entre el consumo de lácteos en la adolescencia y el riesgo de endometriosis confirmada por laparoscopia	Cohortes	En el análisis primario solo se incluyeron aquellos casos que fueron diagnosticados por laparoscopia; se realizó el ajuste de múltiples factores de confusión El estudio depende del retiro a largo plazo de las participantes; posible clasificación errónea, en ausencia de datos prospectivos recopilados durante la adolescencia seguida de décadas de seguimiento	Muy baja ⊕⊖⊖⊖
Harris HR y cols. (18)	Estados Unidos	2013	33,5	70.556 mujeres sanas	Investigar si la ingesta de alimentos lácteos, los nutrientes concentrados en los alimentos lácteos (calcio, vitamina D, magnesio, y fósforo) y los niveles plasmáticos previstos de 25-hidroxivitamina D (25[OH]D) se asocian con la endometriosis confirmada por laparoscopia	Cohortes	Utilización de los niveles plasmáticos previstos antes del diagnóstico de endometriosis, que puede representar el nivel promedio a largo plazo de 25(OH)D de un individuo mejor que una única medición de plasma; alta tasa de seguimiento; casos confirmados por laparoscopia Posible clasificación errónea de los niveles plasmáticos de 25(OH)D previstos en los datos; confusión por otros factores dietéticos o de estilo de vida	Baja ⊕⊕⊖⊖
Ashrafi M y cols. (15)	Irán	2020	30,9 ± 5,74	413 mujeres (206 controles y 207 casos)	Evaluar el papel de la dieta en el riesgo de endometriosis entre mujeres iraníes	Casos y controles	Todas las participantes completaron el cuestionario Riesgo de sesgo de recuerdo; como aproximadamente el 90 % de la población de estudio en ambos grupos era infértil, esto podría limitar la generalización de resultados a todas las mujeres con endometriosis; no se usó un FFQ validado	Muy baja ⊕⊖⊖⊖

(Continúa en página siguiente)

Tabla III (cont.). Características de los estudios incluidos

Autores	País	Año	Edad media	Muestra (n)	Objetivo	Tipo de estudio	Fortalezas y limitaciones	Calidad de la evidencia (GRADE)
Schink M y cols. (12)	Alemania	2019	34,7 ± 7,9	208 mujeres (52 controles y 156 casos)	Examinar la ingesta real de nutrientes y los posibles factores de influencia en pacientes con endometriosis	Casos y controles	Análisis detallado y diferenciado de la ingesta de nutrientes; como posibles factores que influyen en la ingesta de nutrientes, también se determinó y comparó la prevalencia de comorbilidades y síntomas gastrointestinales en los dos grupos de pacientes No se examinó la ingesta de frutas y verduras	Baja ⊕⊕⊖⊖
Samaneh Y y cols. (6)	Irán	2019	30,2 ± 6,8	156 mujeres (78 controles y 78 casos)	Evaluar la relación entre el consumo de alimentos y la ingesta de nutrientes con el riesgo de endometriosis	Casos y controles	Utilización de un FFQ validado Problema de persuadir a los sujetos para que respondan muchas preguntas; posibilidad de sesgo de selección y sesgo de recuerdo, incluido el informe insuficiente o excesivo de los elementos dietéticos específicos, que podría haber afectado los resultados	Baja ⊕⊕⊖⊖
Liu P y cols. (28)	Estados Unidos	2023	40 ± 9,8	3.410 (265 con endometriosis y 3.145 sin endometriosis)	Investigar la asociación entre el índice inflamatorio de la dieta (DII) y el riesgo de endometriosis	Cohortes	Gran tamaño muestral, lo que permite generalizar los resultados; además, se ajustó por un gran número de factores de confusión La limitación es que no fue posible encontrar la causa y el efecto de la asociación entre las puntuaciones del DII y la endometriosis Otra limitación es que el diagnóstico de la endometriosis fue autoinformado y no todos se confirmaron laparoscópicamente	Baja ⊕⊕⊖⊖
Schwartz NRM y cols. (16)	Estados Unidos	2022	36	81.961	Investigar la asociación entre el consumo de hidratos de carbono de calidad y la ingesta de fibra y gluten con el riesgo de endometriosis	Cohortes	El principal sesgo es que los datos fueron autoinformados, pero al ser un estudio longitudinal se pudieron controlar dichas variables	Baja ⊕⊕⊖⊖
Roshanzadeh G y cols. (29)	Irán	2023	30,54 ± 6,75	156 (78 con endometriosis y 78 sin endometriosis)	Investigar la relación entre la ingesta de micronutrientes y el riesgo de endometriosis	Casos y controles	La principal limitación es que no tuvieran muestras sanguíneas	Baja ⊕⊕⊖⊖

GRADE: grados de recomendación de la evidencia. ⊕⊕⊕⊕: calidad alta, ensayos clínicos aleatorizados con escasas limitaciones y fuertes asociaciones. La investigación futura es poco probable que cambie nuestra confianza en la estimación del efecto. ⊕⊕⊕⊖: calidad moderada, ensayos clínicos aleatorizados con algunas inconsistencias y/o gradiente dosis-respuesta presente. La investigación futura es probable que cambie nuestra confianza en la estimación del efecto. ⊕⊕⊖⊖: calidad baja, ensayos clínicos aleatorizados con incertidumbre muy importante y/o múltiples factores de confusión y estudios observacionales. Es muy probable que la investigación futura tenga un impacto en nuestra confianza de estimación del efecto. ⊕⊖⊖⊖: calidad muy baja, estudios observacionales con múltiples sesgos. Cualquier estimación en el efecto es muy incierta.

El diagnóstico de endometriosis se llevó a cabo mediante laparoscopia en ocho estudios incluidos (1,2,6,12,15,18,26,29) y en dos estudios (16,28) se utilizaron cuestionaros autoinformados como método de diagnóstico de la endometriosis. Además, en el estudio de Ashrafi M y cols. (15), el estadio de la enfermedad fue definido de acuerdo con el sistema de clasificación de la versión revisada de la Sociedad Americana de Medicina Reproductiva (ASRM) como estadio I (mínimo), estadio II (leve), estadio III (moderado) y estadio IV (grave). Por último, en el estudio de Schink M y cols. (12), se recogió información sobre la historia ginecológica a través de un cuestionario estandarizado que incluyó preguntas sobre antecedentes de embarazo, parto, uso previo de anticonceptivos hormonales, antecedentes ginecológicos (enfermedades preexistentes, diagnóstico de endometriosis, histerectomía, ovariectomía, ligadura de trompas, otras cirugías y cirugías relacionadas con

la endometriosis, familiares de primer grado con enfermedad ginecológica, medicamentos relacionados con la endometriosis y otros enfoques terapéuticos), así como los síntomas relacionados con la endometriosis y las limitaciones físicas.

RELACIÓN ENTRE GRUPOS DE ALIMENTOS Y RIESGO DE ENDOMETRIOSIS

En el estudio de Harris HR y cols. (1) se hallaron efectos beneficiosos en el consumo de frutas cítricas, indicando que las mujeres que consumían una mayor cantidad de frutas cítricas tenían un 22 % menos de riesgo de sufrir endometriosis (IC 95 % = 0,69-0,89; $p = 0,004$). Por otro lado, el consumo de vegetales crucíferos se relacionó con un mayor riesgo de sufrir endometriosis (RR = 1,3; IC 95 % = 0,95-1,34; $p = 0,03$).

Según los resultados del estudio de Yamamoto A y cols. (26), las mujeres con un mayor consumo de carne roja tenían un 56 % más de riesgo de sufrir endometriosis (IC 95 % = 1,22-1,99; $p < 0,0001$). Esta asociación fue más fuerte para las carnes rojas no procesadas (RR = 1,57; IC 95 % = 1,35-1,83 para ≥ 2 porciones/día *versus* ≤ 1 porciones/semana; $p < 0,0001$). La ingesta de pollo, pescado y huevos no se relacionó con el riesgo de endometriosis. Por el contrario, el estudio de Samaneh Y y cols. (6) encontró una asociación entre una mayor ingesta de proteínas, especialmente proteínas animales (carne roja, lácteos, pescado), y un menor riesgo de endometriosis ($p < 0,05$). También se asoció con un menor riesgo de endometriosis un alto consumo de verduras, frutas, patatas, legumbres, lácteos y aceite líquido, y la baja ingesta de patatas fritas ($p < 0,05$).

En los estudios llevados a cabo por Nodler JL y cols. y Harris HR y cols. (2,18) se encontraron efectos positivos del consumo de lácteos en la reducción del riesgo de endometriosis. En el estudio de Nodler JL y cols. (2) se analizó la ingesta de lácteos de las participantes durante la adolescencia y se halló que las mujeres que consumieron más productos lácteos durante la adolescencia tuvieron un 32 % menos de riesgo de endometriosis en la edad adulta (IC 95 % = 0,47-0,96; $p = 0,04$). En el estudio de Harris y cols. (18) se halló que las participantes que consumían tres o más raciones de lácteos al día presentan un 18 % menos de riesgo de sufrir endometriosis (OR = 0,82; IC 95 % = 0,71-0,95; $p = 0,03$).

En el estudio de Ashrafi M y cols. (15) se encontraron efectos positivos del consumo de varios alimentos en la reducción del riesgo de endometriosis: verduras (OR = 0.39; IC 95 % = 0,21-0,74; $p = 0,004$), fruta fresca (OR = 0,68; IC 95 % = 0,50-0,93; $p = 0,015$), lácteos (leche: OR = 0,65, IC 95 % = 0,47-0,92, $p = 0,014$; y queso: OR = 0,53, IC 95 % = 0,37-0,76, $p < 0,001$), carne roja (OR = 0,61; IC 95 % = 0,41-0,91; $p = 0,015$) y leguminosas de grano (OR = 0,59; IC 95 % = 0,47-0,77; $p < 0,001$).

RELACIÓN ENTRE INGESTA DE NUTRIENTES Y RIESGO DE ENDOMETRIOSIS

En el estudio de Schink M y cols. (12) se analizaron micronutrientes específicos para determinar su influencia en el riesgo de endometriosis. Las participantes con endometriosis mostraron una menor ingesta de vitamina C ($p = 0,031$), vitamina B12 ($p = 0,008$) y magnesio ($p = 0,043$) en comparación con los controles. También mostraron una menor ingesta de ácidos orgánicos ($p = 0,006$), maltosa ($p = 0,0,16$), glucógeno ($p = 0,035$), ácido mirístico ($p = 0,041$), metionina ($p = 0,046$), lisina ($p = 0,048$), treonina ($p = 0,046$) e histidina ($p = 0,049$). Además, la ingesta total de proteínas animales fue significativamente menor en el grupo con endometriosis en comparación con los controles ($p = 0,047$). Roshanzadeh G y cols. (29) demostraron que mayores ingestas de potasio (OR = 0,74; IC 95 % = 0,56-0,99; $p = 0,01$), calcio (OR = 0,74; IC 95 % = 0,56-0,99; $p = 0,01$), vitamina C (OR = 0,70; IC 95 % = 0,52-0,94; $p = 0,02$), vitamina B2 (OR = 0,73; IC 95 % = 0,55-0,98; $p = 0,01$) y B12 (OR = 0,71; IC 95 % = 0,53-0,95; $p = 0,02$) se correlacionaban con un menor riesgo de sufrir endometriosis.

En el estudio llevado a cabo por Samaneh Y y cols. (6) encontraron que las mujeres con una mayor ingesta de ácidos grasos monoinsaturados, fibra soluble e insoluble, ácido oleico, ácido eicosapentaenoico y ácido docosahexaenoico presentaron una menor prevalencia de endometriosis ($p < 0,05$).

Harris HR y cols. (18) evaluaron la relación entre los niveles de vitamina D y el riesgo de endometriosis y hallaron que las mujeres situadas en el quintil más alto de niveles de vitamina D presentaron un 24 % menos de riesgo de sufrir endometriosis (OR = 0,76; IC 95 % = 0,60-0,97; $p = 0,004$).

Por último, en el estudio llevado a cabo por Schwartz NRM y cols. (16) se evaluó la relación entre la ingesta de fibra y el riesgo de endometriosis. Los resultados mostraron que la ingesta de fibra procedente de las frutas se asoció con un menor riesgo de endometriosis, sin que dicha asociación fuese significativa. La ingesta de gluten se asoció de manera significativa con un menor riesgo de endometriosis (RR = 0,91; IC 95 % = 0,8-1,02; $p = 0,01$). Por el contrario, la ingesta de fibra procedente de las verduras y, en concreto, de las crucíferas se asoció con un mayor riesgo de sufrir endometriosis (RR = 1,31; IC 95 % = 1,02-1,24; $p = 0,004$).

RELACIÓN ENTRE PATRONES ALIMENTARIOS Y RIESGO DE ENDOMETRIOSIS

De los diez estudios incluidos, solo uno evaluó la relación entre un patrón alimentario y el riesgo de endometriosis. En concreto, el estudio de Liu P y cols. (28) evaluó la relación entre el índice inflamatorio de la dieta (DII) y su relación con el riesgo de sufrir endometriosis. Los resultados mostraron que las participantes situadas en el tercil más alto en el DII presentaron de manera significativa un mayor riesgo de sufrir endometriosis (OR = 1,57; IC 95 % = 1,14-2,17; $p = 0,007$).

En la tabla IV se muestra un resumen de los grupos de alimentos analizados en los estudios incluidos y su influencia en el riesgo de desarrollar endometriosis.

Tabla IV. Influencia de diferentes grupos de alimentos, patrones dietéticos y nutrientes en el riesgo de desarrollar endometriosis

	Grupos de alimentos						
Autor	**Frutas**	**Verduras**	**Tubérculos**	**Legumbres**	**Carnes rojas**	**Pescados**	**Lácteos**
Harris HR y cols. (1)	Frutas cítricas ↓	Vegetales crucíferos ↑	-	-	-	-	-
Yamamoto A y cols. (26)	-	-	-	-	↑	-	-
Nodler JL y cols. (2)	-	-	-	-	-	-	↓
Harris HR y cols. (18)	-	-	-	-	-	-	↓
Ashrafi M y cols. (15)	↓	↓	-	↓	↓	-	↓
Schink M y cols. (12)	-	-	-	-	↓	↓	↓
Samaneh Y y cols. (6)	↓	↓	↓	-	↓	↓	↓
Liu P y cols. (28)	↓				↑	↓	↓
Schwartz NRM y cols. (16)	↓	↓	-	-	-	-	-
	Vitaminas y minerales						
Autor	**Vit. C**	**Vit. B12**	**Vit. B2**	**Vit. D**	**Mg**	**Ca**	**K**
Schink M y cols. (12)	↓	↓	-	-	↓	-	-
Roshanzadeh G y cols. (29)	↓	↓	↓	-	-	↓	↓
Harris HR y cols. (1)	-	-	-	↓	-	-	-
	Nutrientes						
Autor	**AO**	**Maltosa**	**Gluten**	**AAS**	**AGM**	**Fibra**	**W-3**
Schink M y cols. (12)	↓	↓	-	↓			
Samaneh Y y cols. (6)	-	-	-	-	↓	↓	↓
Schwartz NRM y cols. (16)	-	-	↓	-	-	Fibra de crucíferos ↑	-
	Patrones dietéticos						
Autor	**Índice inflamatorio de la dieta**						
Liu P y cols. (28)	↑						

↑: aumento del riesgo de endometriosis; ↓: disminución del riesgo de endometriosis; Vit.: vitamina; Mg: magnesio; Ca: calcio; K: potasio; AO: ácidos orgánicos; AAS: aminoácidos; AGM: ácidos grasos monoinsaturados; W-3: omega-3.

DISCUSIÓN

Los resultados de esta revisión sugieren que la ingesta de alimentos como frutas, vegetales (no crucíferos), productos lácteos, pescados, patatas y legumbres, y de nutrientes como las vitaminas antioxidantes, las vitaminas del grupo B, la vitamina D, el calcio, el potasio, el magnesio y los ácidos grasos monoinsaturados y poliinsaturados, se asocia con menor riesgo de desarrollar endometriosis. Además, patrones de dietas antiinflamatorias se relacionan de manera clara con una importante reducción del riesgo de sufrir endometriosis. De igual manera, se han atribuido efectos beneficiosos en la prevención de esta patología a nutrientes como los ácidos grasos de la serie omega-3, los ácidos orgánicos, algunos aminoácidos, la maltosa y el gluten, pero la investigación al respecto es muy escasa.

En relación al consumo de carnes rojas, los resultados obtenidos han sido contradictorios. Yamamoto A y cols. (26) indican que una elevada ingesta de carne roja se asocia con un mayor riesgo de sufrir endometriosis, mientras que los estudios de Samaneh Y y cols. (6) y Ashrafi M y cols. (15) muestran lo contrario. Esta discrepancia puede ser debida a la calidad metodológica de los estudios, que tienen tamaños muestrales muy dispares y son estudios de diferentes países en los cuales el tipo de carne puede ser diferente. La carne de res y la de cordero son las más consumidas en Irán, mientras que en la mayoría de los demás países la carne de cerdo es una de las más consumidas (15).

Respecto a la ingesta de vegetales crucíferos, los estudios incluidos en esta revisión los asocian con un mayor riesgo de endometriosis, lo cual, en principio, parece no ser coherente, considerando que estos vegetales contienen varios fitoquímicos y nutrientes que han demostrado tener beneficios para la salud, además de ser una buena fuente de fibra dietética (1). Sin embargo, las verduras crucíferas pueden no ser tan fácilmente absorbidas o digeridas, y algunas tienen un alto contenido de oligo, di y monosacáridos y polioles fermentables (FODMAP), que se ha informado que pueden exacerbar los síntomas del síndrome del intestino irritable (30). Los síntomas gastrointestinales son casi tan comunes como los síntomas ginecológicos en mujeres con endometriosis, y presentar estos síntomas suele ser el primer paso para obtener una confirmación quirúrgica de la endometriosis (31).

En el caso de las frutas y las vitaminas, en el estudio incluido en esta revisión de Harris HR y cols. (1) los resultados señalan que las frutas se asocian con un menor riesgo de endometriosis. Los cítricos, que son ricos en vitaminas A y C, fueron los más fuertemente asociados con la reducción del riesgo de endometriosis. En el estudio de Mier-Cabrera y cols. (32) se comparó la ingesta de antioxidantes en 83 mujeres infértiles con endometriosis con la de 80 mujeres con hijos que se sometieron a ligadura de trompas y se observó una menor ingesta de vitaminas A, C y E entre las mujeres con endometriosis, datos coincidentes con los encontrados en este estudio. Esto puede deberse a que el crecimiento y la adherencia de las células endometriales en la cavidad peritoneal pueden verse influenciados por los radicales libres y las especies reactivas de oxígeno (ERO), y las vitaminas C y E pueden contrarrestar el efecto de los radicales libres y las ERO (33).

En todos los estudios incluidos en esta revisión en los que se evaluó la relación entre la ingesta de lácteos y el riesgo de endometriosis (2,6,12,15,18), los resultados sugirieron que el consumo de lácteos disminuyó el riesgo de desarrollar endometriosis. Hay varias hipótesis sobre el posible impacto bioquímico y fisiológico que tienen los productos lácteos, la vitamina D y el calcio, que puede suponer un menor riesgo de endometriosis. Se ha postulado que los lácteos y el calcio pueden reducir el estrés oxidativo e inflamatorio (18). En el estudio de Zemel y cols. (34) se ha demostrado que los factores inflamatorios como las ERO, el TNF-α y la IL-6 estaban disminuidos por dietas ricas en calcio y lácteos. De manera similar, se han observado relaciones inversas entre la vitamina D y los niveles de PCR en varias afecciones, como la diabetes *mellitus* y la enfermedad vascular aterosclerótica (35). El mecanismo biológico a través del cual la vitamina D puede afectar el riesgo de endometriosis aún no se conoce completamente, aunque se supone que involucra la regulación del sistema inmunitario, ya que existe una fuerte evidencia de que la endometriosis depende no solo de los niveles hormonales de esteroides circulantes sino también de la respuesta inmunológica (36). Además, se ha demostrado que las mujeres con endometriosis tienen un sistema inmunitario alterado (37), y la vitamina D puede influir en la endometriosis a través de la supresión de los procesos proinflamatorios.

En relación con los procesos inflamatorios, según indican los resultados de esta revisión, dietas proinflamatorias ricas en hidratos de carbono refinados y grasas saturadas y trans se asocian con un mayor riesgo de sufrir endometriosis. El mecanismo de acción se basa en que las dietas proinflamatorias producen mayores niveles de inflamación sistémica, aumentando los valores de PCR, IL-6, TNF-α, leucocitos, así como los neutrófilos, lo que provoca una mayor implantación, crecimiento e invasión de tejido endometrial y, en consecuencia, aumenta el riesgo de sufrir endometriosis (10-13,31,34-36). A su vez, esto podría explicar el efecto beneficioso de compuestos antiinflamatorios como los ácidos grasos omega-3, los antioxidantes, las vitaminas del complejo B, la vitamina D, el magnesio y los fitoquímicos presentes en frutas y verduras. Adoptar una dieta equilibrada, que incluya una gran variedad de alimentos antiinflamatorios, puede fortalecer la capacidad del organismo para controlar la inflamación y, de este modo, prevenir y reducir la progresión de la endometriosis. Esto remarca la importancia de un abordaje integral de esta patología mediante un enfoque multidisciplinario que incluya el tratamiento dietético-nutricional.

Esta revisión sistemática presenta varias limitaciones que deben ser consideradas. En primer lugar, puede haber pérdida de evidencia, ya que se analizaron únicamente artículos en español e inglés y la búsqueda fue realizada en bases de datos como PubMed, Scopus, Cochrane Library y Web of Science. También se ha de tener en cuenta que los estudios incluidos eran observacionales y no se han incluido ensayos clínicos aleatorizados, dado que hasta la fecha no existen ensayos clínicos que evalúen este objetivo de estudio. Otra limitación es la heterogeneidad entre los estudios incluidos en cuanto al origen geográfico, lo cual puede haber afectado a los resultados. No obstante, la principal fortaleza de esta revisión sistemática es su diseño de investigación, ya que la integración de diversos estudios incrementa el poder estadístico de los resultados y la validez externa. Además, se realizó una evaluación crítica y exhaustiva de la calidad de los estudios incluidos mediante el uso de herramientas estandarizadas de calidad.

Esta revisión proporciona información relevante, aplicable a la práctica clínica.

CONCLUSIONES

Esta es una de las primeras revisiones que relacionan la ingesta de diferentes grupos de alimentos, nutrientes y patrones alimentarios con el riesgo de desarrollar endometriosis. Nuestros resultados muestran que los hábitos alimentarios pueden ejercer un rol importante en la prevención de la enfermedad. En este sentido, se requieren futuros estudios de calidad que profundicen en esta línea de investigación con el objetivo de diseñar estrategias de prevención y promoción de la salud centradas en la mejora de los hábitos dietéticos en las mujeres con el objetivo de ayudar a prevenir la aparición de la endometriosis.

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ARÁN

Nutrición Hospitalaria

Revisión

Revisión de la nutrición e hidratación con relación al ejercicio físico en el embarazo

Review of nutrition and hydration in relation to physical exercise during pregnancy

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Resumen

Los estudios sobre recomendaciones nutricionales para la embarazada que realiza ejercicio físico son escasos. El objetivo de este artículo no es centrarnos en la dieta de la embarazada de forma global, sino revisar aquellos aspectos de la misma que pueden tener relación con el ejercicio físico. Para ello, se recogen las recomendaciones nutricionales y sobre hidratación contenidas en las principales guías de práctica clínica sobre ejercicio físico durante el embarazo, incluyendo las primeras guías españolas.

Así mismo, se abordan los requerimientos energéticos que precisan las gestantes que realizan ejercicio físico durante el embarazo para una ganancia de peso gestacional adecuada, aspectos relacionados con los macronutrientes en el citado grupo de población, y dos temas específicos, como son las necesidades nutricionales en la adolescente que practica ejercicio físico durante su embarazo y los trastornos de la conducta alimentaria en deportistas embarazadas.

Se concluye afirmando que las embarazadas que realizan ejercicio físico de forma regular deben llevar una dieta variada y equilibrada, como es la dieta mediterránea, eludir períodos largos de ayuno para evitar la aparición de hipoglucemias y mantener una adecuada ingesta de líquidos antes, durante y después del ejercicio físico. Las adolescentes embarazadas que realizan ejercicio físico requieren una supervisión nutricional para que alcancen una ganancia de peso gestacional adecuada. La deportista embarazada con un trastorno de la conducta alimentaria tiene un mayor riesgo de complicaciones durante el embarazo y parto, ginecológicas, fetales y neonatales, y, por tanto, requiere un estrecho seguimiento por especialistas en medicina maternofetal.

Palabras clave:

Nutrición. Hidratación. Ejercicio físico. Embarazo. Adolescencia. Trastornos de la conducta alimentaria.

Abstract

Studies on nutritional recommendations for pregnant women who exercise are scarce. The objective of this article is not to focus on the diet of pregnant women as a whole, but to review those aspects of it that may be related to physical exercise. To this end, the nutritional and hydration recommendations contained in the main clinical practice guides on physical exercise during pregnancy are collected, including the first Spanish guides.

Likewise, the energy requirements required by pregnant women who perform physical exercise during pregnancy for adequate gestational weight gain are addressed, aspects related to macronutrients in the aforementioned population group, and two specific topics, such as nutritional needs in the adolescent who practices physical exercise during pregnancy and eating disorders in pregnant athletes

It is concluded by stating that pregnant women who exercise regularly should eat a varied and balanced diet, such as the Mediterranean diet, avoid long periods of fasting to avoid the appearance of hypoglycemia and maintain adequate fluid intake before, during and after physical exercise. Pregnant adolescents who engage in physical exercise require nutritional supervision to achieve adequate gestational weight gain. The pregnant athlete with an eating disorder has a higher risk of complications during pregnancy and childbirth, gynecological, fetal and neonatal, and, therefore, requires close monitoring by specialists in maternal-fetal medicine.

Keywords:

Nutrition. Hydration. Physical exercise. Pregnancy. Adolescence. Eating disorders.

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INTRODUCCIÓN

El embarazo es un período de gran trascendencia para la madre y el feto, caracterizado por un aumento de los requerimientos energéticos (1), en el cual se debe prestar especial atención a una adecuada ingesta de macro y micronutrientes. Una dieta saludable antes y durante el embarazo es extremadamente importante, tanto para el desarrollo del feto, como para la salud materna (2). Tanto si practica ejercicio físico de forma regular, como si no, la embarazada debe llevar una dieta variada y equilibrada, como es la dieta mediterránea (DM), y a la vez mantener un ritmo de ganancia de peso adecuado (3).

La DM y la adherencia a la pirámide alimenticia saludable se consideran como el estándar para una alimentación saludable (4). La DM, caracterizada por una ingesta elevada de aceite de oliva y alimentos vegetales (frutas, verduras, legumbres, frutos secos y cereales no refinados), ingesta baja a moderada de productos lácteos, pescado y aves, ingesta moderada de alcohol y baja ingesta de carnes rojas y dulces (5), puede aportar los requerimientos nutricionales del embarazo y proteger del desarrollo de patologías obstétricas (1).

Se ha reportado que la interacción entre el ejercicio físico y una mayor adherencia a la DM durante el embarazo se asoció con menos síntomas depresivos y un menor riesgo de depresión posparto (6), y que un programa de ejercicio, más una adherencia óptima a la DM durante el embarazo, podría ser una estrategia útil para promover una composición corporal más saludable en el período posparto (7).

A pesar de sus grandes beneficios, los resultados de un estudio mostraron que la adherencia a la DM fue de baja a moderada entre las mujeres embarazadas, observándose la mayor adherencia entre las mujeres con más poder adquisitivo, con opciones de estilo de vida generalmente más saludables (8). En otro realizado en nuestro país la adherencia fue identificada como media (9).

Por otra parte, la actividad física durante el embarazo promueve la salud materna, fetal y neonatal. Los beneficios para la salud de la actividad física prenatal incluyen un riesgo reducido de aumento de peso gestacional excesivo, diabetes gestacional, preeclampsia, hipertensión gestacional, complicaciones del parto, cesárea, parto instrumental, parto prematuro, complicaciones del recién nacido, incontinencia urinaria, depresión posparto y dolor lumbopélvico No se asocia con el aborto espontáneo, muerte fetal, muerte neonatal, amenaza de parto prematuro, ruptura prematura de membranas, hipoglucemia neonatal, bajo peso al nacer, defectos de nacimiento e inducción del parto (10).

Las principales guías de actividad física/ejercicio durante el embarazo recomiendan que todas las mujeres embarazadas, sin contraindicaciones médicas u obstétricas, se mantengan activas físicamente durante la gestación con el objetivo de conseguir beneficios para su salud y, al mismo tiempo, reducir la posibilidad de complicaciones durante el embarazo (11). Tanto la Guía de la Sociedad Canadiense de Obstetricia y Ginecología (SOGC) (12), como la de la Sociedad Española de Ginecología y Obstetricia (SEGO) (13), coinciden en la recomendación de al menos 150 minutos semanales de ejercicio físico de intensidad moderada para las embarazadas (SOGC: Grado de la recomendación: fuerte. Calidad de la evidencia: moderada; SEGO: Grado de la recomendación: fuerte. Calidad de la evidencia: alta).

Por otra parte, la evidencia actual respalda que el ejercicio realizado durante la gestación tiene un efecto beneficioso sobre la prevención de diabetes *mellitus* gestacional y trastornos hipertensivos del embarazo (14,15).

Diferentes investigaciones han estudiado la asociación entre la actividad física y la dieta durante el embarazo (2,16-24), y dieta, actividad física en el embarazo y la salud cardiovascular de la descendencia (25). Se ha documentado que las mujeres embarazadas que siguen una dieta balanceada suelen practicar actividad física regularmente (26), y que las intervenciones basadas en la dieta y la actividad física en el embarazo tienen el potencial de alterar los resultados maternos e infantiles (24,27,28).

Pero los estudios sobre recomendaciones nutricionales para la embarazada que realiza ejercicio físico son escasos.

El objetivo de este artículo no es centrarnos en la dieta de la embarazada de forma global, sino revisar aquellos aspectos de la misma que pueden tener relación con el ejercicio físico.

MATERIAL Y MÉTODOS

Se ha realizado una revisión narrativa a partir de una búsqueda bibliográfica, sin límite de tiempo, utilizando motores de búsqueda de sitios web y bases de datos como PubMed y Scielo. Las palabras clave fueron: “nutrition”, “hydration”, “physical exercise”, “pregnancy”, “adolescence”, “eating disorders”.

Se anotaron las fechas de todas las publicaciones y se comprobaron si estaban disponibles. Los criterios de inclusión fueron: artículos sobre nutrición e hidratación en la embarazada que realiza ejercicio físico. Como criterios de exclusión se utilizaron los siguientes: artículos escritos en un idioma diferente al inglés o español y *blogs*. Los apartados abordados en esta revisión fueron consensuados por todos los autores.

RECOMENDACIONES NUTRICIONALES Y SOBRE HIDRATACIÓN RECOGIDAS EN LAS PRINCIPALES GUÍAS SOBRE EJERCICIO FÍSICO DURANTE EMBARAZO

Las recomendaciones nutricionales y sobre hidratación recogidas en las guías de práctica clínica sobre ejercicio físico en el embarazo de tres sociedades internacionales de obstetricia y ginecología de reconocido prestigio y gran influencia internacional en este tema —dos de ellas pioneras en la elaboración de este tipo de recomendaciones: el Colegio Americano de Obstetricia y Ginecología (ACOG) (29) y la SOGC (12); y el Real Colegio de Obstetras y Ginecólogos de Australia y Nueva Zelanda (RANZCOG) (30)—, son mínimas, por no decir testimoniales, en un tema tan importante como es la nutrición de la embarazada que realiza ejercicio físico. En la tabla I se exponen las recomendaciones que figuran en estas guías, junto con las que aparecen en las primeras guías españolas para el ejercicio durante el embarazo de la SEGO (13).

Tabla I. Recomendaciones sobre nutrición e hidratación para la embarazada que realiza ejercicio físico que figuran en las principales guías de práctica clínica sobre ejercicio físico en el embarazo

	Sociedad Canadiense de Obstetricia y Ginecología (SOGC) (12)	**Sociedad Española de Ginecología y Obstetricia (SEGO) (13)**	**Colegio Americano de Obstetricia y Ginecología (ACOG) (29)**	**Real Colegio de Obstetras y Ginecólogos de Australia y Nueva Zelanda (RANZCOG) (30)**
País	Canadá	España	Estados Unidos	Australia y Nueva Zelanda
Fecha de publicación	2019	2019	Marzo 2020	Marzo 2020 / Revisada en marzo 2023
Título	*Guía canadiense 2019 de actividad física durante el embarazo*	*Guías clínicas para el ejercicio físico durante el embarazo*	*Actividad física y ejercicio durante el embarazo y el posparto*	*Ejercicio durante el embarazo*
Idioma de las guías	Inglés	Español	Inglés	Inglés
Páginas	8	8	11	16 (2 en la revisión)
Referencias	40	31	78	31
Recomendaciones nutricionales y sobre hidratación para las embarazadas que realizan ejercicio físico				
1. Mantener una nutrición e hidratación adecuadas	Sí	Sí	Sí	Sí
2. Adecuada ingesta de líquidos (antes, durante y después del ejercicio físico)	Sí	Sí	--	--
3. Ingesta calórica adecuada para evitar la pérdida de peso (puede afectar negativamente al crecimiento fetal)	--	--	Sí	--
4. Evitar hacer ejercicio físico con altas temperaturas y humedad (evitar el sobrecalentamiento)	--	--	Sí	Sí

En la tabla II figuran las recomendaciones sobre nutrición e hidratación para la embarazada que realiza ejercicio físico del Centro Federal de Nutrición del Ministerio Federal de Alimentación y Agricultura de Alemania (31), del Departamento de Salud del Gobierno de Australia (32) y de la Sociedad Perinatal de Singapur (33).

Por último, reseñar que un grupo de dieciséis expertos del Comité Olímpico Internacional (COI), representantes de diferentes países, sistemas de salud y disciplinas, tras realizar unas revisiones sistemáticas basadas en la evidencia sobre ejercicio físico y embarazo en las deportistas recreacionales y de élite con embarazos sin complicaciones, elaboró unas recomendaciones de ejercicio durante el embarazo y después del parto. En lo que respecta a la nutrición, aconsejaban a las mujeres embarazadas que siguieran las recomendaciones específicas de su país y buscaran asesoramiento de sus proveedores de atención prenatal con respecto a la suplementación de nutrientes, antes y durante el embarazo. Y que las deportistas de élite embarazadas prestaran especial atención a la ingesta energética adecuada para lograr el aumento de peso gestacional recomendado (34).

EVALUACIÓN AGREE II

Se aplica el instrumento para la Evaluación de Guías de Práctica Clínica (AGREE II) (35) como herramienta para valorar la calidad de las guías (rigor metodológico, presentación de la información, aplicabilidad e independencia editorial, entre otras) de práctica clínica sobre ejercicio físico en el embarazo, que tratan aspectos de nutrición e hidratación. En la tabla III se muestran las puntaciones obtenidas en cada dominio de las guías y su puntuación final expresada en porcentaje. La evaluación de las principales guías fue realizada por dos revisores, reduciendo de esa forma un posible sesgo en los resultados obtenidos.

Las guías del Departamento de Salud del Gobierno de Australia (32) y del RANZCOG (30) obtuvieron las puntuaciones más altas (91,6 % y 79,16 %, respectivamente). Destaca el hecho de que la elaborada por el Departamento de Salud del Gobierno de Australia (32) presenta los mejores resultados medios de los dominios (media de todos los dominios del 81,85 %, con una desviación estándar de 8,39, indicando que los resultados de cada dominio son parecidos). El resto de las guías tienen una media de dominios superior al 50 %, excepto la elaborada por la Sociedad Perinatal de Singapur (33), que fue la peor valorada.

Tabla II. Recomendaciones sobre nutrición e hidratación para la embarazada que realiza ejercicio físico que figuran en otras guías de organismos internacionales

	Centro Federal de Nutrición del Ministerio Federal de Alimentación y Agricultura de Alemania (31)	Departamento de Salud del Gobierno de Australia (32)	Sociedad Perinatal de Singapur (33)
País	Alemania	Australia	Singapur
Fecha de publicación	2018	2020	2020
Título	*Dieta y estilo de vida antes y durante el embarazo: recomendaciones prácticas de la Red de Familias Jóvenes - Comienzo Saludable*	*Guías de actividad física para las mujeres embarazadas basadas en la evidencia*	*Guía sobre actividad física y ejercicio en el embarazo*
Idioma de las guías	Alemán	Inglés	Inglés
Páginas	21	78	16
Referencias	272	201	29
Recomendaciones nutricionales y sobre hidratación para las embarazadas que realizan ejercicio físico	Las embarazadas que realicen actividad física intensa o en ambientes calurosos requieren una mayor cantidad de agua	Las mujeres gestantes deben evitar la deshidratación y la nutrición inadecuada, mantenerse bien hidratadas y tratar de asegurarse de que la ingesta de energía esté en línea con la ganancia de peso gestacional recomendada	Las mujeres embarazadas deben tratar de mantenerse bien hidratadas antes y después del ejercicio La actividad física de alta intensidad o la actividad física prolongada de más de 45 minutos de duración puede provocar hipoglucemia y/o deshidratación, por lo que se deben tomar precauciones como una hidratación adecuada, aporte calórico previo al ejercicio, reducción de la duración de la sesión de ejercicio y realización de la actividad física en un ambiente fresco

Tabla III. Calidad de las guías principales según la herramienta AGREE II

Guías	Dominio 1 (%)	Dominio 2 (%)	Dominio 3 (%)	Dominio 4 (%)	Dominio 5 (%)	Dominio 6 (%)	Media de los dominios y desviación típica (%) (±)	Resultado final (%)
Sociedad Canadiense de Obstetricia y Ginecología (SOGC) (12)	91,66	88,8	80,20	91,66	62,5	58,3	78,85 ± 14,95	33,3
Sociedad Española de Ginecología y Obstetricia (SEGO) (13)	80,50	80,50	59,37	83,33	50	50	67,28 ±15,91	70,83
Colegio Americano de Obstetricia y Ginecología (ACOG) (29)	91,66	50	37,5	91,66	37,40	75	63,86 ± 25,50	66,6

(Continues on next page)

Tabla III (cont.). Calidad de las guías principales según la herramienta AGREE II

Guías	Dominio 1 (%)	Dominio 2 (%)	Dominio 3 (%)	Dominio 4 (%)	Dominio 5 (%)	Dominio 6 (%)	Media de los dominios y desviación típica (%) (±)	Resultado final (%)
Real Colegio de Obstetras y Ginecólogos de Australia y Nueva Zelanda (RANZCOG) (30)	91,66	80,55	62,5	91,66	54,16	79,16	76,61 ± 15,35	79,16
Centro Federal de Nutrición del Ministerio Federal de Alimentación y Agricultura de Alemania (31)	83,33	75	57,29	83,3	33,33	75	67,86 ± 19,41	58,3
Departamento de Salud del Gobierno de Australia (32)	91,6	86,1	80,20	83,3	66,6	83,3	81,85 ± 8,39	91,6
Sociedad Perinatal de Singapur (33)	27,7	22,2	33,3	72,22	20,83	54,1	38,39 ± 20,53	37,5

INGESTA DE CALORÍAS EN LA EMBARAZADA QUE REALIZA EJERCICIO FÍSICO Y GANANCIA DE PESO GESTACIONAL ADECUADA

La ingesta adecuada de calorías es fundamental durante el embarazo. Hay que tener en cuenta que se requiere un aporte extra de energía para asegurar el buen crecimiento del feto (3). Durante el embarazo debe producirse un aumento paulatino de la ingesta energética total (36). Se calcula que, sobre los requerimientos previos al embarazo, si se mantiene el mismo ejercicio físico, es necesario un incremento de 300 kcal/día durante el segundo y tercer trimestres (200 kcal/día de media durante todo el embarazo). Debemos conseguir que la dieta de la embarazada contenga la energía necesaria y las cantidades mínimas de nutrientes que aseguren el mantenimiento de la salud materna y un crecimiento y desarrollo fetales óptimos (3).

Sin embargo, una atleta o deportista embarazada que continúe entrenando durante el embarazo puede tener un gasto total de energía bastante alto, dependiendo del tipo, intensidad, frecuencia y duración de la actividad realizada (37) (Fig. 1).

La práctica excesiva de ejercicio físico, acompañada de una inadecuada ingesta de calorías, afectará de manera negativa tanto a la madre como al feto, impidiendo una correcta ganancia de peso materno y, por tanto, afectando al crecimiento fetal, pudiendo causar crecimiento intrauterino retardado (CIR) (3). El indicador de primera línea de una ingesta energética suficiente para el crecimiento y desarrollo del feto debe ser una ganancia de peso gestacional adecuada. Sin embargo, un incremento de peso adecuado indica que la ingesta calórica es correcta, pero no garantiza el aporte adecuado de los distintos nutrientes (38).

Al contrario que el déficit energético, que cursa con adelgazamiento o escasa ganancia ponderal y se puede detectar con facilidad, las deficiencias de micronutrientes durante el embarazo, al cursar con un período asintomático, son difíciles de cuantificar específicamente, por lo que esta circunstancia puede ser peligrosa para el desarrollo fetal, sobre todo si sucede en las primeras etapas de la gestación (40). Así, una alimentación deficiente en micronutrientes está relacionada con la preeclampsia, partos prematuros, CIR, bajo peso al nacer y malformaciones congénitas (41).

En las deportistas de élite embarazadas, la evaluación por ecografía se debería utilizar con más frecuencia para valorar el adecuado crecimiento fetal, y máxime en el contexto de un crecimiento de la altura uterina persistentemente menor que el esperado, o ante una ganancia materna de peso escasa (34).

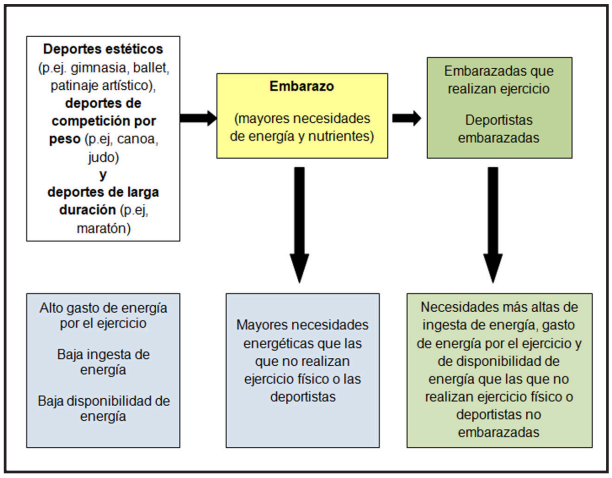

Figura 1.

Aumento de las necesidades energéticas de las deportistas embarazadas en comparación con las no deportistas (extraída y modificada de: G. Silva MR et al.) (39).

MACRONUTRIENTES EN LA MUJER EMBARAZADA QUE REALIZA EJERCICIO FÍSICO

RIESGOS DEL EJERCICIO FÍSICO EN LA MUJER EMBARAZADA Y EN EL FETO RELACIONADOS CON LOS HIDRATOS DE CARBONO

La utilización de los hidratos de carbono (HC) por los músculos esqueléticos en movimiento en las gestantes aumenta significativamente durante el ejercicio extenuante, pudiendo producir en la madre una hipoglucemia. Una bajada de los niveles de glucosa en sangre puede limitar el consumo de la glucosa por parte del feto. Durante el ejercicio agudo hay una hipoxia fetal transitoria, reduciéndose la utilización de la glucosa por el feto. Si la hipoglucemia se repite de forma crónica puede repercutir en el feto conllevando problemas de desnutrición, bajo peso al nacer o alteraciones en el crecimiento de los órganos o tejidos (42). Es primordial también no realizar períodos largos de ayuno para evitar la aparición de hipoglucemias, siendo aplicable también a las gestantes no deportistas (3).

Se ha demostrado que el ejercicio prenatal agudo y crónico reduce las concentraciones de glucosa sanguínea materna circulante, con un efecto mayor en mujeres con diabetes (43), y que el ejercicio físico de alta intensidad (29,44,45) o el ejercicio prolongado de más de 45 minutos pueden provocar hipoglucemia en el embarazo. Por lo tanto, la ingesta calórica adecuada antes del ejercicio, o limitar la intensidad o la duración de la sesión de ejercicio, son esenciales para minimizar este riesgo (29,44). Además, los niveles de glucosa en sangre de las mujeres embarazadas en su tercer trimestre de gestación disminuyen a un ritmo más rápido y a un nivel significativamente más bajo después del ejercicio, que en las mujeres no embarazadas (44).

Por otra parte, se ha reportado que el acondicionamiento aeróbico previene la hipoglucemia inducida por el ejercicio y preserva la capacidad de utilizar carbohidratos y producir lactato durante el ejercicio intenso al final de la gestación (46).

En general, el ejercicio al principio y en la mitad del embarazo estimula el crecimiento de la placenta, mientras que la cantidad relativa de ejercicio al final del embarazo determina su efecto sobre el crecimiento fetal tardío. Las fuentes de alimentos de bajo índice glucémico en la dieta disminuyen la tasa de crecimiento y el tamaño al nacer, mientras que las de alto índice glucémico lo aumentan. Por consiguiente, puede ser posible mejorar los resultados del embarazo, tanto en mujeres sanas de bajo riesgo como en una variedad de poblaciones de alto riesgo, simplemente modificando la actividad física materna y la ingesta de carbohidratos en la dieta durante el embarazo (47).

PROTEÍNAS Y EJERCICIO FÍSICO EN EL EMBARAZO

La influencia de la proteína dietética materna durante el embarazo sobre el fenotipo y la salud de la descendencia es un tema que ha suscitado gran interés para la investigación (48-50).

Se ha informado que, en mujeres desnutridas durante el embarazo, la suplementación equilibrada de energía y proteínas puede aumentar el peso al nacer, mientras que la suplementación rica en proteínas podría tener efectos adversos sobre el crecimiento fetal (51). Una revisión Cochrane de 12 ensayos aleatorios informó un aumento de peso al nacer y una disminución del riesgo de muerte fetal y de recién nacidos pequeños para la edad gestacional después de una suplementación equilibrada de energía/proteína (< 25 % de energía proveniente de proteínas), sin cambios en el aumento de peso gestacional. El asesoramiento nutricional prenatal, con el objetivo de moderar la energía y optimizar la ingesta de proteínas, ha sido eficaz para reducir el riesgo de parto prematuro y muerte fetal (52).

Un estudio mencionó el porcentaje del total de las kilocalorías que deben aportar las proteínas en la dieta de las embarazadas que realizan ejercicio físico. En el mismo participaron 242 mujeres mayores de 18 años a las 12-17 semanas de gestación. Después de las medidas de referencia, las participantes se asignaron al azar a un programa estructurado y supervisado de nutrición + ejercicio (intervención), o atención habitual (control) durante la duración de su embarazo. La mayoría de aquellas que siguieron al principio del embarazo un programa estructurado y supervisado de nutrición (dieta con un alto contenido en proteínas, que aportaba un 25 % de la energía diaria, proporcionado principalmente por productos lácteos) y ejercicio, lograron una ganancia de peso gestacional adecuada (53).

NECESIDADES NUTRICIONALES DE LAS ADOLESCENTES EMBARAZADAS QUE REALIZAN EJERCICIO FÍSICO

Uno de los grupos de embarazadas que realizan ejercicio físico y requiere una supervisión cuidadosa es el de las adolescentes. Las necesidades totales de nutrientes son mayores durante la adolescencia que en cualquier otro período, y también lo son los requerimientos de nutrientes por kilogramos de peso corporal. La adolescencia es un periodo de la vida en el cual es probable que la dieta sea inadecuada para las ingestas dietéticas, especialmente para el aporte energético y algunos micronutrientes, como el hierro, calcio, zinc, ácido fólico, riboflavina y vitaminas A, D y B6. Además, estas jóvenes se hallan en un periodo muy exigente de su propio crecimiento y desarrollo, asociado ahora con las mayores necesidades energéticas para el crecimiento y desarrollo del feto (39,54).

Por lo tanto, es recomendable que las adolescentes embarazadas que realicen ejercicio físico se esfuercen por alcanzar ganancias de peso hacia el extremo superior de los rangos para mujeres con pesos similares para la altura (39).

TRASTORNOS DE LA CONDUCTA ALIMENTARIA, EMBARAZO Y DEPORTISTAS

Los trastornos de la conducta alimentaria (TCA) más frecuentes, especialmente entre la población femenina, son la anorexia

nerviosa (AN) y la bulimia nerviosa (BN). Los TCA representan situaciones de alto riesgo durante el embarazo (40,55), ya que pueden ocasionar anomalías durante el embarazo y parto (hemorragia posparto, diabetes gestacional, preeclampsia, aumento de la tasa de abortos espontáneos, parto inducido, hipertensión inducida por el embarazo y mayor duración de la primera y segunda etapa del parto), complicaciones ginecológicas (síndrome de ovario poliquístico), fetales (restricción del crecimiento intrauterino y malformaciones) y neonatales (bajo peso al nacer y puntuación APGAR baja al minuto 1) (55-58). También se ha descrito que los hijos de madres que han presentado TCA durante el embarazo son niños que, sin presentar ningún déficit mental, desarrollan con lentitud sus habilidades físicas y mentales. Además, son emocionalmente más dependientes y en muchas ocasiones necesitarán apoyo psicológico para su relación social (40).

Se ha reportado una prevalencia de los TCA de un 5,5 % (59) y un 7,5 % (60) en mujeres embarazadas. Una revisión sistemática recientemente publicada reportó una prevalencia del 4,3 %, observándose el ejercicio excesivo en el 0,7 % de las mujeres embarazadas (61). Sin embargo, los datos sobre la prevalencia de TCA en deportistas embarazadas son escasos. Un estudio, realizado en mujeres deportistas de élite noruegas, reportó que el 26 % de ellas tenían TCA, y el 12 % informaron haber tenido un trastorno alimentario, antes o durante el embarazo, no especificando el porcentaje exacto durante el embarazo (62).

Existe evidencia de que la frecuencia de TCA es más alta entre los deportistas que entre los no deportistas. En una investigación realizada para estudiar la prevalencia de AN, BN, anorexia atlética y trastornos de la alimentación no especificados de otra manera, en deportistas de élite noruegos, masculinos y femeninos, el 13,5 % de los deportistas, incluidos hombres y mujeres, tenían trastornos alimentarios, frente a un 4,6 % de los controles. La prevalencia de TCA fue mayor en las deportistas que en los deportistas, y entre las deportistas que competían en deportes estéticos, dependientes de la delgadez y del peso, fue mayor (42 %) que la observada en deportes de resistencia (24 %), técnicos (17 %) y deportes con balón (16 %) (63).

Las deportistas competitivas están constantemente bajo el estrés de mejorar sus resultados y adaptarse al ideal específico de su deporte. Dentro de los factores de riesgo importantes para casos graves de TCA se incluyen la presión para perder peso, el comienzo temprano del entrenamiento deportivo específico, sobreentrenamiento, lesiones, restricción de la ingesta alimentaria y la vulnerabilidad individual (37,64). Además, el entorno deportivo y el comportamiento inadecuado de los entrenadores pueden exacerbar el problema (64).

Las deportistas embarazadas con un TCA y su descendencia corren un especial riesgo, ya que compiten por una cantidad limitada de recursos nutricionales (37,39). Se debe considerar que la deportista embarazada con un TCA, pasado o actual, tiene un mayor riesgo de complicaciones del embarazo como las mencionadas con anterioridad, y requiere un estrecho seguimiento obstétrico desde el inicio de la gestación para detectar, en el momento más precoz posible, aquellos trastornos que, debidos a una situación carencial, puedan comportar un grave riesgo para el feto. Si una deportista embarazada presentara síntomas o fuera considerada en riesgo de presentar un comportamiento alimentario anormal por parte del personal médico, entrenadores u otros miembros de su equipo, el primer paso sería la identificación del trastorno alimentario (37). El empleo de cuestionarios de *screening* ayudará a identificar y detectar precozmente estos trastornos (65).

Hay que recordar que algunas mujeres ocultan su condición, y además, la mayoría de los sanitarios no preguntan sobre los desórdenes alimentarios. Es importante registrar los datos antropométricos (talla y peso) en la primera visita y la evolución ponderal en las visitas sucesivas. También preguntar específicamente por las costumbres alimentarias o el uso de laxantes, diuréticos o la inducción del vómito, pudiendo usarse cuestionarios, diarios de alimentos, o cualquier otro sistema (40).

Posteriormente, se derivará a un nutricionista, psicólogo o psiquiatra y, para optimizar los resultados maternos y fetales, se le debería realizar un seguimiento muy estrecho por especialistas en medicina maternofetal, nutrición y psicología, para la planificación de las comidas, el tratamiento de los síntomas y la evaluación de las consecuencias de la desnutrición, tanto para la madre, como para el feto. Además, su entrenador debería realizar ajustes en su entrenamiento. En casos graves, el tratamiento puede requerir hospitalización (37).

CONCLUSIONES

Las embarazadas que practican ejercicio físico de forma regular deben llevar una dieta variada y equilibrada, como es la dieta mediterránea. Es fundamental que no realicen períodos largos de ayuno para evitar la aparición de hipoglucemias y se hidraten de forma adecuada, antes, durante y después del ejercicio físico.

La ingesta adecuada de calorías es fundamental durante el embarazo. Se requiere un aporte extra de energía para asegurar el buen crecimiento del feto. La práctica excesiva de ejercicio físico, acompañada de una inadecuada ingesta de calorías afectará de manera negativa tanto a la madre como al feto, impidiendo una correcta ganancia de peso materno y, por tanto, afectando al crecimiento fetal, pudiendo causar CIR. El indicador de primera línea de una ingesta energética suficiente para el crecimiento y desarrollo del feto debe ser una ganancia de peso gestacional adecuada, pero no garantiza el aporte adecuado de los distintos nutrientes.

Las adolescentes embarazadas que realizan ejercicio físico requieren una supervisión nutricional para que alcancen una ganancia de peso gestacional adecuada, ya que se hallan en un periodo muy exigente de su propio crecimiento y desarrollo, asociado ahora con las mayores necesidades energéticas para el crecimiento y desarrollo del feto, y para la realización de ejercicio físico.

Se debe considerar que la deportista embarazada con un TCA pasado o actual tiene un mayor riesgo de complicaciones del embarazo y parto, ginecológicas, fetales y neonatales, y, por tanto, requiere un estrecho seguimiento obstétrico. Es fundamental el reconocimiento temprano del trastorno, así como un seguimiento muy estrecho por especialistas en medicina maternofe-

tal, nutrición y psicología para la planificación de las comidas, el tratamiento de los síntomas y la evaluación de las consecuencias de la desnutrición, tanto para la madre, como para el feto.

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NUTRITIONAL STATUS, COVID-19 PROGNOSIS AND HEMODIALYSIS PATIENTS

Dear Editor,

We would like to discuss "Nutritional status and its relationship with COVID-19 prognosis in hemodialysis patients (1)". The purpose of this study was to characterize the nutritional status of COVID-19 patients receiving long-term hemodialysis (HD) treatment and to investigate any possible prognostic relationships. The research employed a retrospective observational design, encompassing all COVID-19 instances among patients receiving long-term care at a particular Spanish hospital unit. Of the 189 individuals who were investigated, 22 patients (12 %) received a COVID-19 diagnosis during the study period. The patients had a mean age of 71 years, were mostly male, and had concomitant conditions like diabetes *mellitus*.

The study's findings demonstrated that the serum levels of ferritin and triglycerides in the survivors and the dead patients differed significantly. It is necessary to recognize the limitations of the study, though. First off, the results may not have been as broadly applicable due to the tiny sample size. Furthermore, bias and confounding variables that were not taken into consideration during the analysis might have been introduced by the study's retrospective methodology. Moreover, the research failed to include possible modifications in dietary status or therapeutic approaches throughout the COVID-19 infection, which would have affected the results.

Larger, prospective studies that are better able to determine the relationship between nutritional state and prognosis in COVID-19 patients on chronic HD treatment should be the main emphasis of future research in this field. The significance of diet in treating COVID-19 in this patient population would be better understood by longitudinal studies that monitor changes in nutritional indicators over time and their effect on outcomes. Studies should also take into account other variables that may also affect the prognosis of COVID-19 in individuals receiving long-term HD treatment, such as socioeconomic status, access to healthcare, and adherence to treatment regimens.

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COMPLEMENTANDO LA EVIDENCIA SOBRE LA IMPORTANCIA DEL EJERCICIO FÍSICO SUPERVISADO EN LA REDUCCIÓN DE LA FATIGA EN PACIENTES CON CÁNCER DE MAMA

Sr. Editor:

Hemos leído con mucho interés el artículo titulado "Intervenciones con actividad física supervisada en el manejo de la fatiga relacionada con el cáncer: una revisión sistemática" (1), que resalta la importancia del ejercicio supervisado en el alivio de la fatiga en pacientes con cáncer. Aunque el documento establece una base sólida, consideramos crucial ampliar el debate centrándonos en la diversificación de las modalidades de ejercicio y la personalización de los programas para pacientes con cáncer de mama (BC, del inglés *breast cancer*).

Para enriquecer esta discusión, nos referimos al reciente resumen de revisiones sistemáticas u *overview* titulado "Efectos de las intervenciones de ejercicio en la fatiga relacionada con el cáncer en pacientes con cáncer de mama: una revisión general de revisiones sistemáticas" (2). Este estudio ofrece una visión completa de la efectividad del ejercicio físico en la reducción de la fatiga en pacientes con BC, consolidando los hallazgos de diversas revisiones sistemáticas y metaanálisis. Su objetivo es proporcionar a clínicos, formuladores de políticas e investigadores una síntesis clara de la evidencia disponible para facilitar la toma de decisiones clínicas basadas en un conjunto unificado de información (3-5).

Los hallazgos resaltan que prácticas como el yoga y el ejercicio aeróbico no solo son viables, sino también efectivas en la reducción de la fatiga relacionada con el cáncer (2). Cabe mencionar que estas conclusiones se respaldan con resultados específicos de estudios clínicos aleatorizados (ECA), donde se ha observado una mejora significativa en la fatiga de los pacientes que participaron en estos tipos de ejercicios. Además, se ha informado que el yoga y el ejercicio aeróbico pueden contribuir positivamente a la calidad de vida de los pacientes (2).

Es innegable la importancia de la supervisión profesional durante el ejercicio, ya que garantiza la seguridad y la efectividad de las actividades, al mismo tiempo que proporciona un estímulo motivacional esencial (1,6). Esto se basa en evidencia acumulada de numerosos estudios, los cuales destacan la necesidad de la supervisión profesional para adaptar las rutinas de ejercicio a las condiciones individuales de los pacientes y minimizar riesgos (1,6).

Abogamos firmemente por la integración sistemática de estas intervenciones de ejercicio supervisado en el tratamiento estándar para pacientes con BC, lo que podría suponer una mejora notable en la reducción de la fatiga. Esta recomendación se apoya en múltiples ECA que demuestran consistentemente los beneficios del ejercicio supervisado en la fatiga relacionada con el cáncer y en la calidad de vida de los pacientes (7).

Para concluir, expresamos nuestro agradecimiento a *Nutrición Hospitalaria* por brindar un espacio de reflexión sobre el papel del ejercicio físico supervisado y reafirmar, con una evidencia más sólida y respaldada por ECA, sus beneficios en este campo.

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MÁS ALLÁ DE LA FUNCIÓN PULMONAR: IMPACTO DE LA OBESIDAD EN EL LINFEDEMA RELACIONADO CON EL CÁNCER DE MAMA

Sr. Editor:

Con gran interés, me dirijo a usted para abordar un aspecto poco explorado en la interacción entre el cáncer de mama (BC, del inglés *breast cancer*), la desnutrición por exceso y el riesgo de desarrollar linfedema secundario a cáncer de mama (BRCL). En este manuscrito, buscamos ilustrar no solo la influencia del exceso de peso y la obesidad en los volúmenes pulmonares de pacientes con BC, como se describe en el estudio previo (1), sino también cómo estas condiciones pueden incrementar la probabilidad de BRCL en dichos pacientes.

El estudio mencionado indica que las pacientes con BC y peso normal tienen volúmenes pulmonares significativamente más altos en comparación con las que tienen sobrepeso u obesidad (1). Este hallazgo es crucial, ya que subraya cómo la desnutrición por exceso puede exacerbar la disminución de la función pulmonar en este grupo de pacientes (1).

No obstante, lo que realmente requiere un análisis detallado es cómo estos descubrimientos influyen en el riesgo de desarrollar BRCL (2-5), una afección que impacta de manera considerable en la calidad de vida de las pacientes con BC (6,7). El BRCL se caracteriza por la acumulación de líquido linfático en los tejidos y a menudo surge como complicación del tratamiento del BC. Se asocia con diversos factores, incluyendo la mastectomía total, la disección de los ganglios linfáticos axilares, la radioterapia, el uso de taxanos y, especialmente, la obesidad (8). Esta última ha sido identificada como un factor de riesgo significativo para el BRCL, debido a la presión intersticial aumentada en los tejidos que obstaculiza el drenaje linfático eficiente (2-5,9).

La relación entre obesidad, disminución de la capacidad pulmonar y BRCL en pacientes con BC plantea un gran desafío para el tratamiento médico. La obesidad no solo amenaza la función pulmonar, como se muestra en el estudio (1), sino que también puede aumentar el riesgo de BRCL, creando un ciclo de morbilidad que afecta la recuperación y la calidad de vida de las pacientes (6,7).

Es fundamental que los clínicos e investigadores comprendan la interconexión entre el BC y comorbilidades como la obesidad, y adopten un enfoque multidisciplinario en su manejo. Esto incluye tratar no solo el tumor, sino también las comorbilidades asociadas. Los programas de control de peso y ejercicio físico supervisado deberían ser un componente clave del plan de tratamiento, para mejorar la función pulmonar y reducir el riesgo de complicaciones como el BRCL.

Agradecemos la oportunidad de abordar este tema tan relevante y esperamos que fomente una mayor investigación y discusión sobre la importancia de abordar la obesidad y sus efectos secundarios en pacientes con BC.

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