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Undernutrition, serum vitamin B12, folic acid and depressive symptoms in older adults

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Abstract

Background: **the question on whether undernutrition remains linked to depressive symptoms, considering the effect of deficiencies of vitamin B12 and folate, is of practical relevance because they are potentially preventable and treatable. This study aims to evaluate whether undernutrition is linked to depressive symptoms, considering the effect of vitamin B12 and folate plasma levels.**

Method: **a cross-sectional study was conducted in a sample of 84 older adults living in care homes. Data about nutritional status using Mini-Nutritional Assessment, serum folic acid and Vitamin B12 levels, cognitive ability, functional dependency, symptoms and /or depressive behaviour was obtained. Depression symptoms were measured using the 20-item version of the Center for Epidemiologic Studies Depression scale.**

Results: **fifty three older adults were at depression risk (63.1%). Of those, 34% were at undernutrition risk. Although a high frequency of older adults with low plasma levels of vitamin B12 (42.9%) and lower levels of folic acid (5.9%) was found, no significant differences concerning the existence of depressive symptoms were found. In the multivariable analysis, an increase in depression risk was observed amongst participants nutritionally at risk OR = 3.47 (1.05-11.46), whereas having low levels of folic acid and Vitamins B12 were not associated with depression risk.**

Conclusion: **amongst undernourished older adults, an increase in risk of depression was observed independently of folic acid and vitamin B12 status. These results highlight the need to implement preventive strategies, particularly directed at older adults living in care home.**

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DESNUTRICIÓN, VITAMINA B12 SÉRICA, ÁCIDO FÓLICO Y SÍNTOMAS DEPRESIVOS EN LOS ADULTOS MAYORES

Resumen

Antecedentes: **la cuestión del posible vínculo entre la desnutrición y los síntomas depresivos, considerando el efecto de las deficiencias de vitamina B12 y de folato, es de importancia práctica porque estas son potencialmente prevenibles y tratables. Este estudio tiene como objetivo evaluar si la desnutrición está relacionada con los síntomas depresivos, teniendo en cuenta el efecto de los niveles plasmáticos de vitamina B12 y de folato.**

Método: **un estudio transversal se llevó a cabo en una muestra de 84 adultos mayores que viven en hogares de cuidado. Se obtuvieron datos sobre el estado nutricional utilizando *Mini-Nutritional Assessment,* los niveles séricos de ácido fólico y vitamina B12, la capacidad cognitiva, la dependencia funcional, y/o los síntomas de comportamiento depresivo. Los síntomas de depresión se midieron utilizando la versión de 20 ítems de la Escala de Depresión del Centro de Estudios Epidemiológicos.**

Resultados: **cincuenta y tres adultos mayores estaban en riesgo de depresión (63,1%). De ellos, el 34% estaban en riesgo de desnutrición. Aunque se encontró una alta frecuencia de adultos mayores con bajos niveles plasmáticos de vitamina B12 (42,9%) y niveles más bajos de ácido fólico (5,9%), no se encontraron diferencias significativas en relación con la existencia de síntomas depresivos. En el análisis multivariable se observó un aumento en el riesgo de depresión entre los participantes con riesgo nutricional OR = 3,47 (1,05 a 11,46), mientras tener bajos niveles de ácido fólico y vitamina B12 no se asociaron con el riesgo de depresión.**

Conclusión: **entre los adultos mayores desnutridos se observó un aumento en el riesgo de depresión, independientemente del ácido fólico y del estado de la vitamina B12. Estos resultados ponen de manifiesto la necesidad de implementar estrategias preventivas, especialmente dirigidas a los adultos mayores que viven en hogares de cuidado.**

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Palabras clave: *Desnutrición. Depresión. Ancianos. Ácido fólico. Vitamina B12.*

Abreviations

AMTS: Abbreviated Mental Test Score.
BMI: Body Mass Index.
CES-D: Epidemiologic Studies Depression Scale.
ESPEN: European Society for Clinical Nutrition and Metabolism.
HGS: Handgrip Strength.
MNA: Mini Nutritional Assessment.

Introduction

According to the World Health Organization, the number of people aged 80 years or older will almost quadruple to 395 million between now and 2050, leading to increased attention of health professionals on this age group[1]. Depressive disorders are amongst the most common mental health problems in older adults with a serious burden[2-4] affecting circa one quarter of care homes non-demented residents[5].

Undernutrition is also a common problem in the elderly. A multinational pooled analysis using the Mini Nutritional Assessment (MNA) tool showed a prevalence of undernutrition of 39% in hospitals, 14% in older adults living in nursing homes and approximately 6% of those who reside in the community[6]. The prevalence of undernutrition risk reported in this analysis is even higher, being 47% in hospitals, 54% in nursing homes and 32% in the community[6]. Undernutrition is related to unfavourable outcomes such as a decline in functional status, immune dysfunction, higher hospital and readmission rates, as well as with a poor quality of life and higher mortality[7].

Through multivariate cross-sectional analyses, it has been shown that undernutrition identified by the MNA was independently associated with depressive symptoms amongst community dwelling older adults[8,9]. On the other hand, depressive symptoms have been also linked to an increased undernutrition risk[7,8,10,11].

Moreover, undernutrition and depression, share some common risk factors. The deterioration of nutritional status and the appearance of depressive symptoms in older adults are related to decreased food intake, disease, polypharmacy, and social problems[7]. Ageing related disturbances on appetite and nutrient absorption, transport, and metabolism are contributing factors for nutrient deficiencies, namely for vitamin B12 and folate[12,13]. Low vitamin B12 and folate levels have been associated with increased melancholic depressive symptoms in older adults[14,15].

The available evidence linking undernutrition and depression in older adults is based on nutritional status assessment using the MNA[7-9,11] or relying specifically on anthropometry[16]. Although MNA is a validated and widely recognized scale for nutritional assessment, micronutrient low levels and deficiencies such as of vitamin B12 and of folic acid may go undetected unless serum levels are measured. The question on whether undernutrition remains linked to depressive symptoms, considering the effect of these deficiencies, is of practical relevance because they are potentially preventable and treatable. This study aims to further increase the knowledge about the association between undernutrition and depression amongst institutionalized older adults while taking into consideration vitamin B12 and folate plasma levels.

Methods

Study design and population

A cross-sectional study was conducted in a convenience sample of 84 older adults, residing in care homes in northern, central and rural Portugal, who volunteered for this study.

Two interviewers worked on data collection during the same period. In order to improve intra and inter interviewer agreement, all the procedures were previously trained.

The Abbreviated Mental Test Score (AMTS)[17] was used to assess cognitive function. It consists of 10 questions and each question correctly answered scores one point. Inclusion criterion was having a score higher than 7 assuring there was not cognitive impairment. Participants were asked about demographics and life style. Functional status was assessed and anthropometric data were collected. Nutritional status and depressive symptoms were assessed with questionnaires. Laboratory levels of vitamin B12 and folic acid were measured.

General, life-style and functional characteristics

Demographical and social information which include sex, age, marital status and education level (number of completed years of schooling) was collected. Participants were asked if they were current smokers, ex-smokers or never smoked, and whether they were current alcohol users or not. The practice of programmed physical activity during the week was also asked, as well as the type of activity, duration and frequency. Participants were asked about the number of drugs and this information was checked by the caregiver.

Functional characteristics such as activities of daily life were assessed with Barthel Index[11]. It is scored out of 100 points with 10 different activities. In the original version, a patient who scores 100 is continent, independent in feeding, bathing, dressing, getting in and out of bed, can walk at least one block and can ascend and descend stairs without help. A score of 0-20 suggests a total dependence, 21-60 severe dependence, 61-90 moderate dependence and 91-99 slight dependence. Independent and slight dependent participants were grouped into a single class (“independence”) and participants with severe or total dependence were

grouped into another single class ("severe dependence").

The handgrip strength (HGS) was measured by a previously calibrated Jamar mechanical handgrip dynamometer according to procedures described by American Society of Hand Therapists[18]. As HGS is higher among men, sex-specific tertiles were determined. High strength was defined as above 16.0 KgF in female and 25.0 KgF in male. Intermediate strength was considered between 12.0 and 16.0 KgF in female and between 19.5 and 25.0 KgF in male.

Anthropometric measurements and nutritional status

Anthropometric data were collected applying standard procedures[19]. Patients were weighed wearing light clothes, using a mechanical scale to the nearest 0.1 kg. Height was measured with a fixed tape to the nearest 0.1 cm. If height was impossible to obtain, it was estimated by knee height through formulas[20]. Weight and height were used to calculate body mass index (BMI), (BMI = weight [kg] / (height [m])^2), and it was categorized according to the recommendations of World Health Organization[21]. For patients with oedema (n = 12, 14.3%), weight and BMI data were not considered. Knee height, mid-arm circumference and calf circumference were measured with a tape to the nearest 0.1 cm.

Nutritional status was evaluated with the MNA, a validated questionnaire for older adults[6], recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN)[22]. The questionnaire consists of 18 questions about anthropometric and dietary assessment, weight loss, health status, mobility and living situation. A score below 17 points indicates undernutrition, a score between 17 and 23.5 points indicates a risk of undernutrition and a score of 24 or higher indicates a normal nutritional status.

Laboratory parameters

Blood samples were collected from participants following an overnight fast. Measurement of laboratory parameters was performed using chemiluminescence (Immulite® 2000, Siemens), according to the cut-offs defined for serum vitamin B12 (deficiency: <400 pg/ml) and folic acid (deficiency: <3 ng/ml).

Depressive symptoms

The Epidemiologic Studies Depression Scale (CES-D) was used to measure depressive symptoms[23]. CES-D has been shown to be a valid and reliable measure of current symptoms in Caucasian and African-American populations[24]. It assesses the frequency of depressive symptoms in the past week on a scale from 0 (rarely) to 3 (most or all of the time). Responses to the 20 items are summed for a total score ranging from 0 to 60. CES-D scores of 16 or higher indicate a high and clinically significant level of depressive symptoms.

Data analyses

Categorical variables were summarized as counts and proportions, and compared using the chi-square test. Means and their standard deviation values were presented for normal distributed data and were compared with Student's t-test. Undernourished and at undernutrition risk older adults were grouped into a single class. All analyses were stratified according to the risk of depression. Logistic regression model was used to quantify the association between undernutrition and other variables with the presence of a high level of depressive symptoms. Odds ratios and respective confidence intervals at 95% were calculated. P value < 0.05 was considered significant. All analyses were carried out using SPSS® software, version 20.0 for Windows® XP.

Ethics

This study was approved by the Ethics Committee for Health of the Centro Hospitalar S. João, EPE, Porto, Portugal and by the institutional boards of care homes. It was conducted according to the Declaration of Helsinki[19].

Results

Age of participants ranged from 65 to 101 years with a mean (standard deviation) of 82.1 (6.3) years. Fifty three older adults were at depression risk (63.1%), with the majority being females (75.5%) and 71.7% being widows (Table I). Regarding life-style characteristics, 16.7% of the study participants used to undertake programmed physical activity during the week. Among these, 50% used to walk on foot, 35.7% went to the gym and 14.3% participated in dance sessions. On average, they used to walk for 90 minutes, 6 times per week; gym was practiced during 45 minutes, twice a week, and the dance lasted 90 minutes, once a week. Among participants who undertook programmed physical activity, approximately 57% did not present or presented a low level of depressive symptoms. According to Barthel Index, 78.6% of practitioners were totally independent and 21.4% had a slight dependence, and half of them showed high hand grip strength.

Considering BMI categories classification, 2.4% of the participants were classified as being underweight and 26.2% were obese. According to MNA, 3.6% were undernourished, 22.6% were at risk of undernutrition; 81.8% of participants at risk of undernutrition/undernutrition were classified with depression risk.

Table I
General, life-style and functional characteristics of the sample according to the risk of depression (CES – D ≥ 16)

	Center for Epidemiologic Studies Depression Scale (CES – D)		*p*
	Without depression risk n = 31 (36.9%)	*With depression risk n = 53 (63.1%)*	
General characteristics			
Gender, n (%)			
Female	13 (41.9)	40 (75.5)	0.002*
Male	18 (58.1)	13 (24.5)	
Age, mean (standard deviation)	81.4 (5.2)	82.5 (6.9)	0.485
Country area, n (%)			
North coast	8 (25.8)	22 (41.5)	0.209
Central coast	15 (48.4)	24 (45.3)	
Countryside	8 (25.8)	7 (13.2)	
Marital status, n (%)			
Single	3 (9.7)	8 (15.1)	0.048*
Married	11 (35.5)	7 (13.2)	
Divorced	1 (3.2)	0 (0.0)	
Widowed	16 (51.6)	38 (71.7)	
Education (completed years), n (%)			
0 years	8 (25.8)	11 (20.8)	0.559
1 a 4 years	15 (48.4)	32 (60.4)	
≥ 5 years	8 (25.8)	10 (18.9)	
Life-style characteristics			
Smoking, n (%)			
Never smoked	22 (71.0)	46 (86.8)	0.200
Ex-smoker	8 (25.8)	6 (11.3)	
Current smoker	1 (3.2)	1 (1.9)	
Alcohol use (current), n (%)			
No	17 (54.8)	29 (54.7)	0.991
Yes	14 (45.2)	24 (45.3)	
Practice of physical activity (at week), n (%)			
Yes	8 (25.8)	6 (11.3)	0.086
No	23 (74.2)	47 (88.7)	
Functional characteristics			
Barthel Index, n (%)			
Independence	18 (58.1)	24 (45.3)	0.636
Moderate dependence	13 (41.9)	28 (52.8)	
Severe dependence	0 (0.0)	1 (1.9)	
Handgrip strength (KgF) **, n (%)			
Female: high	7 (53.8)	16 (40.0)	0.682
intermediate	3 (23.1)	12 (30.0)	
low	3 (23.1)	12 (30.0)	
Male: high	7 (38.9)	4 (30.8)	0.809
intermediate	6 (33.3)	4 (30.8)	
low	5 (27.8)	5 (38.5)	

* $p < 0.05$; ** High strength was defined as above 16.0 KgF in female and 25.0 KgF in male. Intermediate strength was considered between 12.0 and 16.0 KgF in female and between 19.5 and 25.0 KgF in male.

Although a high frequency of older adults with low plasma levels of vitamin B12 (42.9%) and lower of folic acid (5.9%) was found no significant differences concerning depressive symptoms were identified (Table II).

In the logistic regression analysis, being male was associated with a lower risk of having depressive symptoms, whereas not being married was related with a significant increase of this risk (Table III). Amongst undernourished participants and participants in risk of

Table II
Nutritional status parameters according to the risk of depression (CES – D ≥ 16)

	Center for Epidemiologic Studies Depression Scale (CES – D)		*p*
	Without depression risk n = 31 (36.9%)	*With depression risk n = 53 (63.1%)*	
Weight (Kg) **, mean (s.d.)			
Female	66.3 (15.1)	63.6 (11.7)	0.227
Male	75.1 (10.6)	65.9 (10.4)	0.663
Height (m), mean (s.d.)			
Female	1.54 (0.04)	1.51 (0.05)	0.113
Male	1.64 (0.08)	1.67 (0.09)	0.959
Mid-arm circumference (cm), mean (s.d.)			
Female	28.9 (3.8)	28.4 (3.1)	0.587
Male	29.1 (2.9)	28.4 (3.1)	0.878
Calf circumference (cm), mean (s.d.)			
Female	35.6 (4.3)	34.6 (3.2)	0.227
Male	35.6 (3.9)	34.5 (3.5)	0.946
BMI (Kg/m^2) **, n (%)			
Underweight	0 (0.0)	2 (4.3)	0.051
Normal weight	9 (36.0)	11 (23.4)	
Overweight	5 (20.0)	23 (48.9)	
Obesity	11 (44.0)	11 (23.4)	
MNA, n (%)			
Normal nutritional status	27 (87.1)	35 (66.0)	0.034*
Risk of undernutrition/ undernutrition	4 (12.9)	18 (34.0)	
Vitamin B12, n (%)			
< 400 pg/ml	13 (41.9)	23 (43.4)	0.896
≥ 400 pg/ml	18 (58.1)	30 (56.6)	
Folic Acid, n (%)			
< 3 ng/ml	1 (3.2)	4 (7.5)	0.419
≥ 3 ng/ml	30 (96.8)	49 (92.5)	

Abbreviations: BMI, body mass index; MNA, Mini-Nutritional Assessment; s.d., standard deviation
* p < 0.05, ** (n= 72, 85.7%)

undernutrition more than 3-fold increase in risk of depression was observed whereas having low levels of folic acid and Vitamins B12 was not associated with risk of depression. (Table III).

Discussion

Present study results shows that nutritional status is related to depressive symptoms in institutionalized older adults, accounting for the effect of gender, marital status, folic acid and vitamin B12 serum levels.

According to our results, 26.2% of older adults were at risk of undernutrition/undernourished. Multimorbidity, reduction of some physiological abilities and a disadvantaged socio-economic situation also contribute to a high prevalence of undernutrition in older adults[7]. According to a recent revision, approximately 20% of nursing home residents had some form of undernutrition, with prevalences ranging from 1.5 to 66.5%[25]. Serrano-Urrea, R *et al*. reported a higher prevalence of undernutrition and risk of undernutrition of 40.1% in institutionalized older adults[26]. As our sample was restricted to those older adults who volunteered to participate in the study and without cognitive impairment, undernutrition frequency reported here may be lower than in other samples including non-collaborating elders, who are more likely to be undernourished.

A very high proportion of our participants, circa two thirds (63%), had a high and clinically significant level of depressive symptoms risk of depression in the preceding week. These results were similar to those reported by Pérez Cruz E *et al*. (63.9%), despite the different scales used to measure depressive symptoms[27]. Depression and cognitive impairment are two common mental health problems among older adults[2-4]. In a representative sample of residential and nursing care home residents, high prevalence of depressive and/or behavioural symptoms and psychotropic use suggested significant unmet need[28]. These results highlight the need to implement preventive strategies.

Depressive symptoms have a relevant impact on health and consequently on nutritional status. Depression is the most commonly diagnosed cause of pa-

Table III
Logistic regression model for the association between general characteristics, nutritional status parameters and the risk of depression (CES – D ≥ 16)

	Risk of depression (CES – D) Odds ratio (95% CI)
Gender	
Female	1
Male	0.235 (0.091-0.606)*
Marital status	
Married	1
Not married	3.614 (1.223-10.678)*
MNA	
Normal nutritional status	1
Risk of undernutrition / undernutrition	3.471 (1.052-11.457)*
Vitamin B12	
≥ 400 pg/ml	1
< 400 pg/ml	1.062 (0.433-2.602)
Folic Acid	
≥ 3 ng/ml	1
< 3 ng/ml	2.449 (0.261-22.956)

Abbreviations: *CES-D, Center for Epidemiologic Studies Depression Scale;* CI, confidence intervals; MNA, Mini-Nutritional Assessment
* statistical significance

thologic weight loss in older adults, accelerating the development of sarcopenia and frailty[27,29]. Akin, S *et al*. reported depression as a determinant of poor nutrition leading to weight loss and loss of appetite[30]. In our sample, a very high proportion of participants at risk of undernutrition or undernourished were classified with a moderate/high risk of depression (81.8%), regardless of depression may be a cause or a consequence of a poor nutritional status. Among undernourished participants and participants at risk of undernutrition according to MNA, a 3-fold increase in risk of depression was observed, confirming previous results[8,9]. In the van Bokhorst-de van der Schueren MA *et al*. study and according to our results, patients with undernutrition had more depressive symptoms ($p<0.01$)[7]. Pérez Cruz E *et al*. also reported that undernourished people had more depressive symptoms than people without undernutrition risk ($p<0.01$)[27]. These studies also used MNA as tool for assessment nutritional status.

On the other hand, significant differences between functional characteristics and risk of depression were not found, as well as between anthropometric characteristics, such as weight, height, mid-arm circumference, calf circumference and BMI, and risk of depression. In fact, MNA was the nutritional status indicator that best predicted the risk of depression. The MNA test is a simple, non-invasive, well-validated and recommended screening tool for undernutrition in older adults[6,22]. It contains geriatric specific assessment questions related to nutritional and health conditions, cognition, independence and quality of life[6]. In community-dwelling elderly persons, the MNA detects risk of undernutrition and life-style characteristics associated with nutritional risk while albumin levels and the BMI are still in the normal range[31]. In home care patients and nursing home residents, this tool is related to living conditions, meal patterns, and chronic medical conditions and allows targeted interventions[10].

Contrary to the present study results, lower vitamin B12[14] and folate levels[15] have been found to be associated with depression. There are also some previous results which did not find an association between vitamin B12 levels and depressive disorders[32,33]. In addition, vitamin B12 level, *per se*, was not associated with length of hospital stay, contrary to poor nutritional status assessed by MNA, which was related to a lengthened hospital stay[34]. Nevertheless, we cannot exclude the possibility that our negative results are a consequence of the cross-sectional design. Vitamin B12 low levels can be recent and thus not related to depressive symptoms.

Regarding to general and life-style characteristics, among participants who undertook programmed physical activity, approximately 57% did not present or presented a low risk of depression. It is known that depression in people over sixty is associated with low levels of physical activity[35]. However, present results showed that only gender and marital status were associated with the risk of depression. Marital status is a robust predictor of health outcomes in Western populations[36]. According to a previous study, divorced and widowed men reported higher rates of depressive symptoms than married men[36]. In this context, depression has a relevant impact on social life, reducing the ability to purchase and prepare food, for instance.

It was previously shown that depression and nutritional status were strongly correlated in young-old but not in old-old community-dwelling older adults[9], revealing that not only the factors correlated with but also the symptoms of depression may vary among different older adults age groups. Due to the advanced age in our sample, with only 13.1% of the participants aged between 65 and 75 years, we were not able to explore the relation of undernutrition with depression by age groups.

The limitations of this study are mainly related to the cross-sectional design that does not allow the establishment of causal relationship between nutritional status and depression risk. The restriction of this sample to those who volunteered to participate in this study and without cognitive impairment limits the ability of assessing factors related to depression in those older adults who were more likely to have poor mental health and to be undernourished and also the generalization of present results to other samples with different profiles. Further longitudinal research is needed in order to evaluate this association amongst these groups.

This study results confirm the previously reported association between undernutrition and the presence of depressive symptoms in older adults residing in care

homes[25] and shows that these results are not modified by vitamin B12 and folate serum levels.

In conclusion, MNA score was significantly associated to the risk of depression, independently of folic acid and vitamin B12 status. Amongst undernourished and at risk of undernutrition older adults, more than threefold increase in risk of depression was observed. As undernutrition is potentially preventable and treatable these results highlight the need to implement preventive strategies, particularly directed to older adults living in care homes.

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