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Prevalencia de la desnutrición en pacientes con enfermedad de Alzheimer: una revisión sistemática. La necesidad de métodos consistentes para la evaluación nutricional

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ABSTRACT

Objectives: epidemiological data show growing numbers of patients with Alzheimer´s disease. Cognitive decline and progressive swallowing impairment lead to a significant deterioration of the nutrition status in this population. Early detection and treatment of malnutrition is important for the prognosis of the disease.

Method: a systematic review was conducted. Four databases such as Cochrane, PubMed, Embase and Web of Science were searched by two independent researchers. The inclusion criteria encompass adult patients with diagnosed Alzheimer's disease, studies with screening tools for nutritional assessment such as Mini-Nutritional Assessment and body mass index. Patients without diagnosis or with possible or probable Alzheimer's disease were excluded. Finally, 36 studies with 5293 participants were included to the systematic review. PRISMA protocol was followed when writing this article. Critical Appraisal tools for use in JBI Systematic Reviews were used for quality assessment.

Results: 36 studies were included in this systematic review. More than half of the respondents were from Europe. According to MNA 33.97 % of participants were at risk of malnutrition, 3.74 % malnourished and more than 62 % had proper nutritional status. According to the BMI, nearly 50 % of patients were overweight or obese, 4.22 % had BMI < BMI < 18,49 kg/m^2. Risk of malnutrition and malnutrition was diagnosed in 53.8 % and 8.2 % of patients assessed with Mini-Nutritional Assessment - short form.

Conclusion: the risk of malnutrition in AD is high, however, significant differences between studies can be observed due to methodological differences. Large epidemiological studies are needed with unified nutritional assessment methods for patients with Alzheimer's disease.

Keywords: Malnutrition. Alzheimer´s disease. Prevalence. Systematic review.

RESUMEN

Objetivos: los datos epidemiológicos muestran un número creciente de pacientes con enfermedad de Alzheimer. El deterioro cognitivo y el

deterioro progresivo de la deglución conducen a un deterioro significativo del estado nutricional en esta población. La detección temprana y el tratamiento de la desnutrición son importantes para el pronóstico de la enfermedad.

Métodos: se realizó una revisión sistemática. Dos investigadores independientes buscaron en cuatro bases de datos: Cochrane, PubMed, Embase y Web of Science. Los criterios de inclusión abarcaron pacientes adultos con enfermedad de Alzheimer diagnosticada, estudios con herramientas de evaluación nutricional, como la *Mini-Nutritional Assessment* y el índice de masa corporal. Se excluyeron los pacientes sin diagnóstico o con enfermedad de Alzheimer posible o probable. Finalmente, se incluyeron 36 estudios con 5293 participantes en la revisión sistemática. Se siguió el protocolo PRISMA al redactar este artículo. Se utilizaron herramientas de evaluación crítica del JBI para la evaluación de la calidad de los estudios.

Resultados: se incluyeron 36 estudios en esta revisión sistemática. Más de la mitad de los participantes eran de Europa. Según el MNA, el 33,97 % de los participantes estaban en riesgo de desnutrición, el 3,74 % estaban desnutridos y más del 62 % tenían un estado nutricional adecuado. Según el IMC, casi el 50 % de los pacientes tenían sobrepeso u obesidad, mientras que el 4,22 % tenían un IMC inferior a 18,49 kg/m^2. Se diagnosticó riesgo de desnutrición y desnutrición en el 53,8 % y el 8,2 % de los pacientes evaluados con la *Mini-Nutritional Assessment - short form.*

Conclusión: el riesgo de desnutrición en la EA es alto; sin embargo, se pueden observar diferencias significativas entre los estudios debido a diferencias metodológicas. Se necesitan estudios epidemiológicos amplios con métodos unificados de evaluación nutricional para pacientes con enfermedad de Alzheimer.

Palabras clave: Desnutrición. Enfermedad de Alzheimer. Revisión sistemática.

INTRODUCTION

The buildup of amyloid plaques and neurofibrillary tangles in the brain characterizes Alzheimer’s disease, a progressive neurodegenerative condition. Alzheimer’s disease causes most cases of dementia (1,2). Currently, all over the world, there are approximately 50 million people living with this disease (3). Because of the aging population databases show that in the United States this number will probably escalate by 35 % by 2030 and probably triple by 2050 (4).

At present, there aren’t any unambiguous proven methods of therapy and treatment for Alzheimer’s disease (5). Experimental studies on new treatment strategies have made little progress. These two factors with the growing number of Alzheimer’s patients may have economic and social implications (6) such as direct and indirect costs. Age and family history are currently the two most important risk factors of Alzheimer’s disease. However, lifestyle, diet and physical activity are also mentioned (7).

There are numerous nutritional issues seen among patients with Alzheimer's disease, these include weight loss, a lower body mass index compared to people without the disease, a loss of appetite and swallowing problems. Patients with AD can present a several problems such as mobility problems which make it impossible to properly shop, prepare and eat a meal. Memory problems can also result in skipping meals. All of these may promote disease progression, malnutrition and lower quality of life (8).

According to studies, up to 50 % of patients with AD may be malnourished. Furthermore, barely one-fifth of senior caregivers noticed dietary deficiencies in their relatives (9). There is often the endless problem that Alzheimer's disease causes malnutrition and malnutrition exacerbate Alzheimer's dementia leading to the worsening of malnutrition. For this reason, nutritional screening methods should be used in all patients with Alzheimer’s disease. A serious problem often highlighted in AD patients is swallowing problems, which further affect the progression of malnutrition. Effective nutritional treatment using a texture-modified diet or artificial nutrition such as enteral or parenteral nutrition can significantly influence patient prognosis (8).

Validated methods of nutritional status assessment exist and should be used in the screening of all patients. Identifying the percentage of

malnourished people is key to developing an effective strategy for the detection and treatment of nutritional disorders in patients with AD. These findings suggest that innovative theories about risk factors, as well as techniques for preventing and delaying disease progression are highly needed.

This review analyzes data on the prevalence of malnutrition in patients with Alzheimer's disease to discuss the relationship between the disease and nutritional status assessment results.

MATERIALS AND METHODS

Protocol and registration

PRISMA the recommended reporting items for systematic reviews and meta-analyses, was followed when writing this review. The study was not registered.

Eligibility criteria

The PICOS framework was adopted to specify qualifying requirements (Suppl. Table I). Adult patients made up the population of interest (P). Screening tools such as Mini-Nutritional Assessment and body mass index was the exposure under consideration (I), there were no comparison (C), and the outcome of interest (O) was the prevalence of malnutrition or risk of malnutrition. Regarding the study's methodology: cross-sectional, cohort, case-control and randomized were acceptable and were divided by type. We included studies published from 2000 to 2022. The exclusion included case reports, comments, meta-analyses, retracted publications, retraction of publications, systematic reviews, reviews, editorials, letters, clinical cases and posters. Language wasn't a restriction on searching for articles.

Information sources and search strategy

From October 2021 to June 2022, we were researching four databases including Cochrane, PubMed, Embase and Web of Science. Software called Ryann was used to manage all articles (https://rayyan.ai/reviews/349032). We included studies using MeSH terms (Medical Science Heading) shown in supplementary table II. We contacted with authors (with corresponding e-

mail addresses and other e-mail addresses found in the internet) for additional information (Fig. 1).

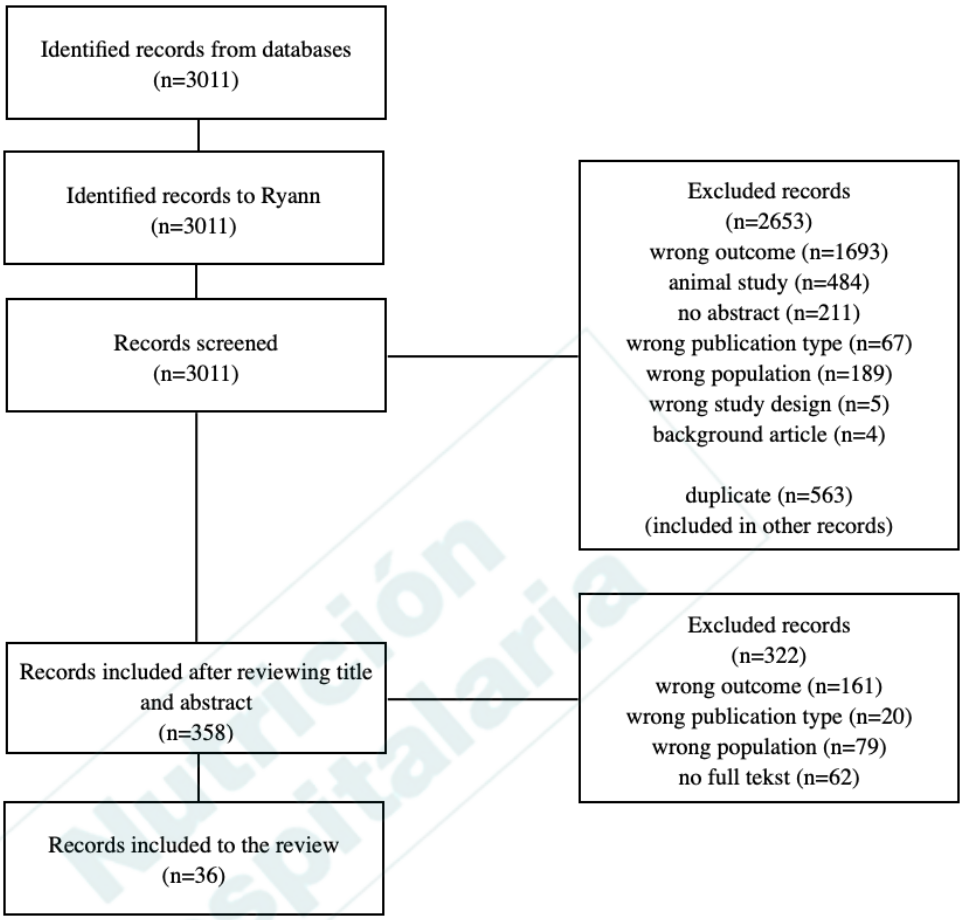

Figure 1. Flowchart.

Study selection

The *inclusion criteria* encompassed:

- Adult patients,
- Diagnosed Alzheimer's disease,
- Study had to contain information about screening tools for assessing nutritional status such as Body Mass Index, result of screening nutritional status assessment (Mini-Nutritional Assessment or Subjective Global Assessment).

The *exclusion criteria* encompassed:

- Animal research including animals such as mouse, rat, rabbit and rodent,
- Studies on cells or *in vitro,*
- Studies on patients with dementia and other neurodegenerative diseases without confirmed diagnosis,
- Studies on patients with a diagnosis of possible or probable Alzheimer's disease,
- Lack of response from the authors for 14 days to the request for additional information. We contacted with authors. In case of no answer for 14 days we wrote "nd" that means "no data" or excluded the record. Ethnicity was not a reason for exclusion.

Data collection process

Four investigators completed literature searches and data extraction. Initially studies were included or excluded based on title or abstract. If there were any doubt, full texts were checked. Each record received two independent analyses (AZ, GR). In case of disagreements consensus has been reached after discussing the given issue or an independent researcher was asked to settle the matter (MM, KK).

The retrieved information was kept in an MS Excel spreadsheet with column titles: author, title, year of the study, population/country, type of study, number of participants (*n*), age (mean), age (standard deviation), maximum age, minimum age, number of men (*n*), number of men (%), number of women (*n*), number of women (%), the severity of the disease (scale), method (MNA, SGA, BMI, other), number of points (average), number of points (standard deviation), minimum number of points, maximum number of points, number of patients at risk of malnutrition (*n*), number of patients at risk of malnutrition (%), number of malnourished patients (*n*), number of malnourished patients (%), number of patients with proper nutritional status (*n*), number of patients with proper nutritional status (%), number of overweight or obese patients (*n*), number of overweight or obese patients (%), OR, minimum CI, maximum CI.

Data items

PICOS structure's criteria for study inclusion was shown in table I.

There were some discrepancies in interpretation of body mass index. Because of that we took the interpretation:

1. BMI < 18,49 kg/m^2-malnutrition.
2. 18,5 < BMI < 24,99 kg/m^2-normal weight.
3. BMI ≥ 25 kg/m^2-overweight or obese.

Quality assessment and statistical analysis

Quality assessment in this review was made with Critical Appraisal tools for use in JBI Systematic Reviews. The purpose of this is to evaluate a study's methodology and ascertain how well it has assessed the possibility of bias in its planning, execution and analysis. The analysis includes studies with quality scores greater than 50 %. The final score for each study was determined based on agreement from at least two authors. All assessments are shown in Supplementary figures 1- 4.

Occurs of patients with malnutrition, risk of malnutrition, proper nutritional status and overweight or obese was estimated after combined data from included studies. Results were reported with standard deviation (SD). Data was compiled and analyzed with MS Excel program.

RESULTS

Group characteristic

In total, 5293 respondents were assessed including 46.72 % women and 33.40 % men. Gender was not provided for almost 20 % of participants. Respondents came from 4 continents, over 50 % of them were from Europe. Detailed characteristics of participants in terms of sex, age and origin were shown in table I.

Table I. Study group characteristics

Variable	Number *n* (%)
Total number of participants	5293
Sex	
Male	1768 (33.4 %)
Female	2473 (46.7 %)
Not given	1050 (19.8 %)
Age (years)	
Minimum age	30
Maximum age	105
Origin	
Europe	2826 (53.4 %)
Asia	959 (18.1 %)
North America	1381 (26.1 %)
South America	127 (2.4 %)
Africa	0 (0 %)

Nutritional status - Mini-Nutritional Assessment

Mini-Nutritional Assessment was used in 15 studies. From 1846 respondents, 627 (33.97 %) were at risk of malnutrition, 69 (3.74 %) were malnourished and 1150 (62.3 %) had proper nutritional status. The MNA score of 347 (15.82 %) individuals was not given. The minimum mean MNA result reported in studies was 8.64 and the maximum was 26.5. Prevalence of malnutrition according to MNA range from 0 % to 18.90 %. Figures and percentages are shown in table II. The detailed results from every study are shown in table III.

Table II. Number of patients with different nutritional status according to MNA score

Nutritional status	**Number *n* (%)**
At risk of malnutrition	627 (33.97)
Malnourished	69 (3.74)
Proper nutritional status	1150 (62.3)
Not given	347 (15.82)

Table III. MNA score and number of patients malnourished, with risk of malnutrition and proper nutritional status

Study	**Participants**	**Age ± SD (min, max)**	**Gender**		**Mean MNA score ± SD**	**Risk of malnutrition**		**Malnourished**		**Proper nutritional status**	
			Male *n* (%)	**Female *n* (%)**		***n***	**%**	***n***	**%**	***n***	**%**
Marino et al. 2015 (10)	36	74,2±10.1 (54,90)	10 (27.8)	26 (72.2)	21.1 ± 2.6	nd	55.5	nd	11.1	nd	nd
Delgado et al. 2020 (11)	127	80 ± 5.9 (55,91)	35 (27.6)	92 (72.4)	25.5	35	27.6	3	1.7	89	70.1
Brocker et al. 2003 (12)	479	77.4 ± 7.1 (nd)	127 (26.5)	352 (73.5)	23.4 ± 3.2	166	34.7	22	4.6	291	60.8
Salas-	53	84.8 ± 6	9	44	15.8 ±	nd	nd	nd	nd	nd	nd

Study	Participants	Age ± SD (min, max)	Gender		Mean MNA score ± SD	Risk of malnutrition		Malnourished		Proper nutritional status	
			Male *n* (%)	Female *n* (%)		*n*	%	*n*	%	*n*	%
Salvado et al. 2005 (13)		.8 (nd)	(17)	(83)	4.2						
Pelazza et al. 2020 (14)	22	nd (60,nd)	nd	nd	22.1 ± 3.2	1	4.5	0	0	21	95.5
Sousa et al. 2020 (15)	79	nd (65,90)	32 (40)	47 (60)	nd	69	87	10	13	0	0
Zekry et al. 2008 (16)	61	86.1 ± 6 (nd)	10 (16.4)	51 (83.6)	8.6 ± 2.4	nd	nd	nd	nd	nd	nd
Droogsma et al. 2012 (17)	312	77.6 ± 5.7 (nd)	119 (38.1)	193 (61.9)	26.5	44	14.1	0	0	268	85.9
Ivanski et al. 2018 (18)	35	78.9 ± 8.72 (nd)	13 (37.1)	22 (62.9)	17.6	25	71.4	5	14.3	5	14.3
Rocapsana-Garcia et	111	78.5 ± 6.3	40 (36)	71 (64)	nd	75	67.6	21	18.9	15	13.5

Study	Participants	Age ± SD (min, max)	Gender		Mean MNA score ± SD	Risk of malnutrition		Malnourished		Proper nutritional status	
			Male *n* (%)	Female *n* (%)		*n*	%	*n*	%	*n*	%
al. 2018 (19)		(nd)									
Saragat et al. 2012 (20)	83	79.5 ± 3.8 (66,96)	29 (34.9)	54 (65.1)	24.6 ± 3.6	35	42.1	3	3.6	45	54.2
Tang et al. 2017 (21)	103	73 ± 3.2 (nd)	nd	nd	18.2 ± 1	nd	nd	nd	nd	nd	nd
Verhaar et al. 2020 (22)	129	68 ± 7.8 (nd)	67 (51.9)	62 (48.1)	25	nd	nd	nd	nd	nd	nd
Suominen et al. 2015 (23)	40	78.2 ± 5.5 (64,nd)	21 (53)	19 (47)	nd	17	43	0	0	23	57
Vellas et al. 2005 (24)	523	76.3 ± 6.3 (nd)	nd	nd	nd	135	25.8	0	0	388	74.2

SD: standard deviation; nd: no data.

Nutritional status - body mass index

We included 32 studies with 1731 respondents that took into account body mass index in assessing nutritional status. The minimum BMI score was 12 kg/m^2 and maximum 47 kg/m^2. Seventy-three (4.22 %) subjects were malnourished, 46.04 % had proper BMI and the most respondents were overweight (49.74 %). In two studies, the mean BMI results was not reported. The division into groups depending on the nutritional status was not given in 22 studies. Minimum mean BMI result reported in studies was 21.5 kg/m^2 and maximum was 28.2 kg/m^2. Prevalence of malnutrition according to BMI ranged from 0 % to 43.7 %. The results from each study are summarized in table IV.

Table IV. BMI results and number of patients malnourished, with proper nutritional status and overweight or obese

Study	**Numer of participants**	**Age ± SD (min, max)**	**Gender**		**Mean BMI result ± SD**	**Malnourished**		**Proper nutritional status**		**Overweight or obese**	
			Male *n* (%)	**Female *n* (%)**		***n***	**%**	***n***	**%**	***n***	**%**
Marino et al. 2015 (10)	36	74.2 ± 10.1 (54,90)	20 (27.8)	26 (72.2)	24.7 ± 4.4	16	43.7	12	34.3	8	21.9
Pelazza et al. 2020 (14)	22	nd (60,nd)	nd	nd	27.5 ± 5.2	nd	nd	nd	nd	nd	nd
Sousa et al. 2020 (15)	79	nd (65,90)	32 (40)	47 (60)	nd	13	17	35	44	31	39

Study	Numer of participants	Age ± SD (min, max)	Gender		Mean BMI result ± SD	Malnourished		Proper nutritional status		Overweight or obese	
			Male *n* (%)	Female *n* (%)		*n*	%	*n*	%	*n*	%
Zekry et al. 2008 (16)	61	86.1 ± 6 (nd)	10 (16.4)	51 (83.6)	23.2 ± 4.4	nd	nd	nd	nd	nd	nd
Droogsma et al. 2012 (17)	312	77.6 ± 5.7 (nd)	119 (38.1)	193 (61.9)	26.2 ± 4.4	nd	nd	nd	nd	nd	nd
Ivanski et al. 2018 (18)	35	78.9 ± 8.7 (nd)	13 (37.1)	22 (62.9)	26.2	0	0	8	22.9	28	80
Rocaspana-Garcia et al. 2018 (19)	111	78.5 ± 6.4 (nd)	40 (36)	71 (64)	26.4 ± 3.7	nd	nd	nd	nd	nd	nd
Kimura et al. 2019 (25)	318	78.3 ± 5.6 (nd)	nd	nd	21.9 ± 3.3	nd	nd	nd	nd	nd	nd
Saragat et al.	83	79.5 ± 3.8	29 (34.9)	54 (65.1)	26.5 ± 4.5	4	5.7	31	37.3	48	57.8

Study	Numer of partic ipants	Age ± S D (min, max)	Gender		Mean BMI result ± SD	Malnou rished		Proper nutrition al status		Overwei ght or obese	
			Male *n* (%)	Femal e *n* (%)		*n*	%	*n*	%	*n*	%
2012 (20)		(66,96)									
Wu et al. 2020 (26)	157	79.4 ± 7. 9 (nd)	52 (33.1)	105 (66.9)	24.1 ± 3.7	nd	nd	nd	nd	nd	nd
Mathys a et al. 2017 (27)	16	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
Martin et al. 2018 (28)	71	77.5 ± 7. 7 (nd)	18 (25.4)	53 (74.6)	27.5 ± 3.9	nd	nd	nd	nd	nd	nd
Faxen-Irving et al. 2005 (29)	93	80.5 ± 6. 8 (nd)	26 (28)	67 (72)	23 ± 4. 4	nd	nd	nd	nd	nd	nd
Verhaar et al. 2020 (22)	129	68 ± 7.8 (nd)	67 (51.9)	62 (48.1)	25 ± 3. 7	nd	nd	nd	nd	nd	nd
Droogs ma et	303	79.4 ± 5. 5	112	191	26.5 ±	nd	nd	nd	nd	nd	nd

Study	Numer of partic ipants	Age ± S D (min, max)	Gender		Mean BMI result ± SD	Malnou rished		Proper nutrition al status		Overwei ght or obese	
			Male *n* (%)	Femal e *n* (%)		*n*	%	*n*	%	*n*	%
al. 2013 (30)		(nd)	(37)	(63)	4						
Kimura et al. 2018 (31)	205	77.2 ± 5. 1 (nd)	75 (36.6)	130 (63.4)	21.9 ± 3.1	nd	nd	nd	nd	nd	nd
Weiner et al. 2009 (32)	11	71 (61.89)	6 (54.5)	5 (45.5)	27.3	nd	nd	nd	nd	nd	nd
Burns et al. 2011 (33)	70	74.9 ± 6. 7 (nd)	nd	nd	25 ± 3. 9	nd	nd	nd	nd	nd	nd
Lee et al. 2020 (34)	125	79.5 ± 7. 9 (65,89)	40 (32)	85 (68)	24.1 ± 3.7	nd	nd	nd	nd	nd	nd
Suomin en et al. 2015 (23)	40	78.2 ± 5. 5 (64,nd)	21 (53)	19 (47)	26.3 ± 3.6	nd	nd	nd	nd	nd	nd
Alosco	986	76.1 ± 1	547	439	25.4 ±	38	3.9	406	41.	542	55

Study	Numer of participants	Age ± SD (min, max)	Gender		Mean BMI result ± SD	Malnourished		Proper nutritional status		Overweight or obese	
			Male *n* (%)	Female *n* (%)		*n*	%	*n*	%	*n*	%
et al. 2017 (35)		0.8 (30,105)	(55.5)	(44.5)	4.5				2		
Vidoni et al. 2011 (36)	100	75 ± 7.9 (nd)	58 (58)	42 (42)	25.6 ± 3.7	2	2	41	41	57	57
Intebi et al. 2002 (37)	15	71.3 ± 7.4 (55,82)	6 (40)	9 (60)	25.5 ± 5.1	0	0	10	66.7	5	33.3
Venturelli et al. 2016 (38)	85	76 ± 4 (nd)	27 (32)	58 (68)	23 ± 4	nd	nd	nd	nd	nd	nd
Theodoropoulou et al. 2012 (39)	27	72.6 ± 4.7 (nd)	10 (37)	17 (63)	27.2 ± 7.3	nd	nd	nd	nd	nd	nd
Wang et al. 2004 (40)	51	76.2 ± 7.4 (nd)	29 (56.9)	22 (43.1)	21.5 ± 3.6	nd	nd	nd	nd	nd	nd
Noreik	6	69.2 ± 7.	2	4	23.8 ±	0	0	5	83.	1	16.

Study	Numer of partic ipants	Age ± S D (min, max)	Gender		Mean BMI result ± SD	Malnou rished		Proper nutrition al status		Overwei ght or obese	
			Male *n* (%)	Femal e *n* (%)		*n*	%	*n*	%	*n*	%
et al. 2015 (41)		5 (57,78)	(33.3)	(66.7)	2.6				3		7
Vellas et al. 2005 (24)	523	76.3 ± 6. 3 (nd)	nd	nd	23.8 ± 3.8	nd	nd	nd	nd	nd	nd
Peguer oles et al. 2018 (42)	162	73.3 ± 6 (56,89)	82 (50.6)	80 (49.4)	27.4 ± 4	0	0	52	32. 1	110	67. 9
Moody et al. 2021 (43)	52	71.9 ± 7. 4 (nd)	31 (59.6)	21 (40.4)	27.9 ± 6.1	nd	nd	nd	nd	nd	nd
Astrup et al. 2008 (44)	228	69.8 ± 1 0.1 (38,92)	125 (55)	103 (45)	25.7 ± 4.2	0	0	197	86. 4	31	13. 6
Cezar et al. 2021 (45)	19	79 ± 5.4 (65,nd)	10 (52.6)	9 (47.4)	26.2 ± 3.6	nd	nd	nd	nd	nd	nd

SD: standard deviation; nd: no data.

Nutritional status - other screening tools

In addition to Mini-Nutritional Assessment and Body Mass Index, two questionnaires were used to assess the nutritional status - Mini-Nutritional Assessment - short form (MNA-SF) and modified-Mini-Nutritional Assessment.

According to MNA-SF most of the respondents (53.8 %) were at risk of malnutrition, 8.2 % were malnourished and 38.1 % had proper nutritional status. Results are shown in table V. There was only one study in which m-MNA was used (41) and it resulted in all respondents having proper nutritional status. Detailed data from this study was shown in table VI.

Table V. MNA-SF score and number of patients malnourished, with risk of malnutrition and proper nutritional status

Study	**Participants**	**Age ± SD (min, max)**	**Gender**		**Mean MNA-SF score ± SD**	**Risk of malnutrition**		**Malnourished**		**Proper nutritional status**	
			Male *n* (%)	**Female *n* (%)**		***n***	**%**	***n***	**%**	***n***	**%**
Kimura et al. 2019 (25)	318	78.3 ± 5.6 (nd)	nd	nd	10.7 ± 2.1	171	53.8	26	8.2	121	38.1
Kimura et al. 2018 (31)	205	77.2 ± 5.1 (65,89)	75 (36.6)	130 (63.4)	11.7 ± 1.9	nd	nd	nd	nd	nd	nd

SD: standard deviation; nd: no data.

Table VI. m-MNA score and number of patients malnourished, with risk of malnutrition and proper nutritional status

Study	Participants	Age ± SD (min, max)	Gender		Mean MNA-SF score ± SD	Risk of malnutrition		Malnourished		Proper nutritional status	
			Male *n* (%)	Female *n* (%)		*n*	%	*n*	%	*n*	%
Noreik et al. 2015 (41)	6	69.2 ± 7.5 (57,78)	2 (33.3)	4 (66.7)	13.2 ± 1.2	0	0	0	0	6	100

SD: standard deviation; nd: no data.

DISCUSSION

The prevalence of dementia is rising and it is not a part of healthy aging. Nutritional deficiencies are a frequent problem in patients with Alzheimer's disease (46) and can lead to reduced consumption and malnutrition. At each stage of the disease, these problems may be different, but they overlap with the progression. We can observe changes in eating habits such as reduced food intake due to problems with eating (both due to motor disorders and lack of awareness of supporting techniques) and the effects of certain medications that reduce appetite and consumption (8). Navrátilová et al. (47) study shown that even with normal voluntary calorie intake, AD patients were undernourished. It is worth emphasizing that patients may also have difficulties with shopping or preparing meals.

Swallowing disorders are a common and serious disorder in AD patients. It is estimated that it may affect 13-57 % (8) of patients and significantly influence the progression of the disease and the development of malnutrition. For this reason, all patients with AD should be screened for dysphagia with questionnaires and if necessary in-depth investigations. If

swallowing disorders are diagnosed, nutritional intervention should be instituted immediately. It may consist of texture modified diet (depending on the results of the test, a safe consistency should be selected for the patient). If the consistency selected for the patient is not able to ensure an adequate energy supply, additional Food for Special Medical Purposes (FSMP) should be interpolated. If the texture-modified diet is not effective and the patient nutritional status is worsening, artificial nutrition treatments such as enteral or parenteral nutrition should be considered.

Adequate intake of energy and nutrients is crucial in the development of dementia, contributing to inflammation, oxidative stress, and vascular damage. Key ingredient deficiencies may contribute to cognitive impairment and the progression of existing dysfunction.

Due to the complex nature of Alzheimer's disease, treatment and all therapeutic methods used should be discussed and agreed in an interdisciplinary team consisting of a doctor, nurse, dietitian, psychologist, speech therapist, neurologist, and physiotherapist (8,48,49).

Malnutrition can be observed prior to the symptoms of dementia (46) and it could have a negative influence on the progression of the disease (11). All these elements contribute to the importance of the topic and increasing knowledge of malnutrition in AD patients. This review aimed to assess the prevalence of malnutrition in patients diagnosed with AD.

Prevalence of malnutrition in patients with Alzheimer’s disease is a poorly understood issue and this review showed that there are few studies focusing on this area. To our knowledge this a first qualitative review on the prevalence of malnutrition in patents with AD. The strong point of this review is the satisfactory bias assessment for the included studies. This study reported several key observations.

First, most of the studies included in this review did not look directly at prevalence of malnutrition but we extracted information about nutritional status from studies on other topics. That could be a reason for incomplete data in many studies. In studies with Mini-Nutritional Assessment, we could not evaluate nutritional status of almost 16 % of respondents because the lack of data. In studies with BMI the same problem was observed in more than 61 % of respondents.

Prevalence of malnutrition according to MNA ranged from 0 % (14,17,23,24) to 18.9 % (19). Maximum percentage of patients with risk of malnutrition was 87 % (15) and minimum was 4.5 % (14). Rocapsana- Garcia et al. (19) study showed the highest sum of patients who were malnourished or at risk of malnutrition (86.48 %). What is worth mentioning there was one study (15) with 0 % patients with proper nutritional status. On the other hand, there were four studies (14,17,23,24) that claimed none of the patients were malnourished and that patients with proper nutritional status represent 57 % to 95.5 % of respondents.

Second, when it comes to nutritional assessment based on Body Mass Index we perceived a problem with discrepancies in the interpretations, and therefore reference values were suggested in the Materials and Methods section. Currently, the GLIM (Global Leadership Initiative on Malnutrition) criteria should be used to assess the nutritional status (50), however, due to the lack of use of this method by authors in the included studies, we were not able to use it for the systematic review. The highest rate of patients with malnutrition was 43.70 % (10) but in majority of studies it was less than 5.70 % (35,36,37,41,42,44). Interestingly, some studies indicated patients with excess of body mass. The highest percentage was 80 % (18) and the lowest 16.70 % (41). However, it is not possible to interpret this data without detailed information about body composition, unintentional weight loss, reduced food consumption etc. What is worth mentioning BMI carries a high risk of underestimation, especially in the elderly so it should be used as a part of broader nutritional status assessment such as Global Leadership Initiative on Malnutrition (GLIM).

When we compared the results from studies that measured nutritional status with both tools (MNA and BMI) occurrence of malnutrition is higher according to MNA than to BMI (18). It shows that there is a need for other tools for the evaluation of the prevalence of malnutrition in patients with Alzheimer’s disease. Also, a standardized method of nutritional status assessment for a group of patients with Alzheimer’s disease is required. There was a problem comparing the results with the MNA-SF due to the small number of studies using the tool included. We mentioned only two studies that evaluated nutritional status according to MNA-SF (5,25)

and the prevalence of malnutrition was 8.2 %. Modified - Mini-Nutritional Assessment is a modified form of the Mini-Nutritional Assessment used in one study (41). This questionnaire consists of BMI, weight change in the last 3 months, mobility, dependence on food intake, number of main meals consumed per day, fluid intake and subjective assessment of overall health compared to healthy peers. Patients were categorized as well-nourished, at risk of malnutrition, or malnourished. According to a study using this tool, all participants were in a normal nutritional state (41). Due to only some common elements, it is impossible to clearly compare the results of modifed-MNA with MNA-SF, therefore these methods can be treated as a supplement to the screening assessment of nutritional status.

This systematic review shows a high prevalence of malnutrition in patients with Alzheimer's disease. However, large diversity of used methodology and assessment methods resulted in significant differences in observed epidemiology. There is a need for a wide-spread use of unified methods for nutritional status assessment suggested by scientific societies to present real prevalence data in epidemiological studies.

Limitations

Several major limitations were noted in the development of this systematic review. There were a lot of studies that took into consideration patients without diagnosis or with possible or probable Alzheimer's disease. This group is not a representative sample of the population of patients with AD. Likewise, frequently there wasn't clear information about the diagnosis of the disease. Also, there was a lack of direct research aimed to indicate the prevalence of malnutrition in patients with Alzheimer's disease. The data about nutritional status were rather supplementary than essential in included studies. Another problem that appears is discrepancies in the interpretation of the Body Mass Index, which is implicated in difficulties in data interpretation, especially in the context of the current malnutrition diagnosis proposed by the Global Leadership Initiative on Malnutrition. Finally, discrepancies in the presentation of nutritional assessment data, different outcomes indicated by the researchers, and lack of a control group

in many studies indisposed to performing a meta-analysis of presented results.

One of the weak points of every review is the poor author’s response indicator, which had a great impact on the decision about the exclusion study for further analysis.

CONCLUSION

In conclusion, it is difficult to clearly indicate the scale of malnutrition among patients with Alzheimer's disease, because the data range from 0 % to 43.7 % depending on the applied methods. The wide range of results illustrated how the current understanding of routine nutritional assessment is limited. There is an urgent need for a standardized protocol for the diagnosis of AD taking into account nutritional status. Due to the high prevalence and associated primary and secondary consequences of malnutrition, it seems that systematic screening of at-risk populations should be crucial to healthcare strategies especially based on the recommended current methods of nutritional assessment (e.g. GLIM) which were not used in the studies included in the review. This review also identified the gap in current research on malnutrition in Alzheimer’s disease and the need for further high-quality research.

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