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NUTRITIONAL ASSESSMENT OF PATIENTS WITH PRIMARY PROGRESSIVE DEMENTIA AT THE TIME OF DIAGNOSIS

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SUMMARY

Background: *patients with different types of dementia may experience changes in nutritional status, which are manifested by specific eating habits. The aim of this study was to determine the nutritional status and eating habits of patients at the time of confirmed diagnosis of primary progressive dementia.*

Subject and methods: *The study included 40 outpatients (63% women) diagnosed with either form of dementia. The mean age at diagnosis was 77±6 years and the mean time between the onset of first symptoms of the disease and diagnosis was 3-36 months. Nutritional assessment was determined at the time of confirmed diagnoses and included dietary habits (non-quantitative modified food frequency questionnaire (FFQ)), anthropometric (body weight and height and body mass index-BMI) and biochemical parameters (serum concentrations of vitamin B12, folic acid and 25-hydroxy vitamin D). Dietary habits were collected over a 12-month period with the help of a spouse or close family member.*

Results: *The results showed that none of the outpatients were malnourished, the largest number of outpatients (43%) were in the normal body mass category followed by 33% in the overweight category. The results of this study confirmed previous findings of higher preference for sweet foods observed in 53% of patients with dementia. Low status of vitamin B12 was observed in 57% of outpatients, folic acid in 24% and 25 (OH) D in 75% of outpatients. Lower frequency of consumption of dark green leafy vegetables and lower consumption of poultry meat, fish and eggs could have an impact on nutrient deficiency.*

Conclusions: *The poor nutritional status of outpatients with primary progressive dementia is associated with unhealthy dietary habits that may lead to micronutrient deficiencies. Dietary monitoring and intervention should be initiated immediately after the diagnosis of primary progressive dementia with the goal of reducing nutritional deficiencies and preventing further and more severe impairment of cognitive function.*

Key words: *primary progressive dementia - nutritional status - eating habits - vitamin deficit - malnutrition*

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INTRODUCTION

Nutritional status has been defined as the health status of an individual as it is affected by the intake and utilization of nutrients (Todhunter 1970). Due to impaired cognitive function, individuals with dementia may develop various difficulties with food intake and changes in eating and nutritional habits over time (Cipriani et al. 2016). Changes in eating habits can reduce dietary variety and lead to imbalanced nutrient intake and malnutrition. In addition to impaired cognitive function, it has been recognized that such patients have specific eating habits that include increased or decreased appetite, dysphagia (difficulty swallowing), hyperphagia (an abnormally strong sense of hunger or desire to eat), a preference for sweet and carbohydrate foods, and consumption of non-food items (Trinkle et al. 1992, Cullen et al. 1997, Kai et al. 2015, Formiga et al. 2015, Cipriani et al. 2016), which may affect nutritional status. Considering their cognitive impairment, especially memory loss, one of the first symptoms of dementia is that patients have difficulty remembering whether they have eaten a meal or not. Therefore, nutritional status in patients with dementia is usually affected by unintentional weight loss, which increases during the stages of dementia (Albanese et al. 2013). However, weight gain as a result of hyperphagia in patients with dementia has also been documented (Ikeda et al. 2002).

Nutritional status in patients with dementia may also be affected by severe deficiencies in various micronutrients such as folate, vitamin B12 or thiamine (Mikkelsean et al. 2016, Lopes Da Silva et al. 2014)). Low levels of these vitamins may predict cognitive decline, but according to (Behrens et al. 2020), taking oral vitamin B supplementation may not prevent cognitive decline.

Nutritional deficiencies can begin in the early stages of the disease, which if not addressed, can increase the rate of deterioration as well as increase the risk of falls, infections, and pressure ulcers (Cipriani et al. 2016, Volkert et al. 2015, Ahmed et al. 2016a, Shunichiro, 2015). Changes in dietary or eating behaviors may not be evident at the initial presentation of patients with dementia, so our aim was to determine the nutritional status and eating habits of newly diagnosed patients.

SUBJECTS AND METHODS

Study design and participants

This was a retrospective study. Medical records of patients diagnosed with dementia were extracted from the Neurological Polyclinic in the Dementia Clinic and General Neurology Clinic from November 2018 to February 2020. The sample included a total of 40 patients. The extracted data included demographic characteristics, medical history, symptoms on admission, laboratory tests and nutritional assessment. The presence of diabetes, hypertension, hyperlipidemia, depression and other psychiatric disorders such as schizophrenia and anxiety disorder were also considered.

Methods

Assessment of cognitive status

Assessment of cognitive status on arrival at the clinic was performed by a specially trained psychologist. The established final diagnosis of psychological assessment was no evidence of significant cognitive impairment, the presence of mild cognitive impairment (MCI), and confirmed severe cognitive impairment consistent with expectations and criteria for the diagnosis of dementia. Other routine investigations included ultrasound of the head and neck vessels (carotid ultrasound), EEG (Electro Encephalogram), CT (Computed Tomography) or brain NMR (Nuclear Magnetic Resonance). In this study, the specific mapping tool Brain SPECT (single photon emission computed tomography) was used in patients with clinically proven dementia, but where it was unclear what type it was.

Clinical and psychological treatments were performed to define the type of dementia. Alzheimer's dementia (AD) was diagnosed if the person showed progressive cognitive impairment characteristic of AD, a striking positive effect on antidementia drugs over a period of time, and if SPECT showed cerebral blood flow distribution specific to this type of dementia.

Frontotemporal dementia (FTD) was diagnosed if the person had clinically progressive cognitive impairment characteristic of this dementia type, poor to no response to antidementia drugs, and SPECT results indicated this dementia type.

Similarly, two other dementia types, Lewis body and vascular dementia, were defined based on monitoring of clinical condition, specific patterns of progressive cognitive impairment, response to antidementives, and SPECT findings.

Nutritional assessment

Nutritional assessment included assessment of dietary, anthropometric, and biochemical parameters and was performed prior to any intervention at baseline to gain better insight into the patient's nutritional status.

Dietary methods

Patients' dietary habits during the past 12 months were assessed using a modified non-quantitative food frequency questionnaire (FFQ, NHANES Questionnaire 2003-2004). The spouse or a close family member helped to complete the questionnaire. The FFQ consisted of 18 general questions, including the number of meals, composition, timing, and variety of those meals. The frequency of consumption of meat, certain liquids (alcohol, juices), sweets and spices was also examined. General questions about the composition of a breakfast, lunch, and dinner were also included. In addition, patients answered questions about how they ate, whether they ate with their hands and in the same order, and whether there was an increased preference for certain foods, with an emphasis on sweets. Further questions were divided into 8 groups in which the intake of individual food groups was examined in more detail: 1. liquids, 2. breads, biscuits and cakes, 3. vegetables (green leaves, cooked legumes) and fruits (fresh, wild fruits), 4. Meat (chicken, red meat, processed meat, fast food) and fish, 5. dairy products, 6. fats (butter, margarine, some vegetable oils for food preparation), 7. nuts, fruits, 8. additional sugars (sugar, honey or sweeteners, dressings for salads, ketchup). Any change in intake of specific food groups during the last 12 months was also recorded.

Anthropometric assessment

Anthropometric assessment included height, body weight and body mass index. Body weight was measured with a scale (Digitron JIK-6CAB) in current clothing and without shoes, with arms extended to the body with an accuracy of 100 g. Body height was measured with a stadiometer (M130, TTM Zagreb), without shoes, on a flat and firm surface with an accuracy of 0.5 cm. Patients' legs had to stand side by side while the heels touched the measurement scale, the body was upright, the shoulders relaxed, and the head was in the so-called Frankfurt horizontal (Lee & Nieman 2003). BMI (kg/m^2) is defined according to the World Health Organization (WHO) and was calculated as the patient's body mass expressed in kilograms (kg) divided by the square of the patient's height expressed in square meters (m^2) (WHO 2004).

Biochemical parameters

Biochemical parameters were obtained from the patient's medical record. All blood samples were analyzed by the Clinical Department for Laboratory Diagnostics University Hospital Dubrava, Zagreb. Serum concentrations of vitamins: Cobalamin (vitamin B12), Folic acid (vitamin B9) and 25-hydroxy vitamin D (25 (OH) D) were determined by standard laboratory procedures.

Statistical analysis

Statistical analysis was performed using SPSS Statistics v. 22 (SPSS Inc., Chicago, IL, USA). Anthropometric and other general parameters (age, body mass, BMI and age of patients with first symptoms) are presented in the form of mean ± standard deviation (SD) and frequency of consumption in the form of absolute frequency.

RESULTS

At the beginning of the study, the outpatients were identified according to clinical criteria and nutritional status, anthropometric parameters and biochemical tests were performed (Tables 1 and 2).

The sample studied included a total of 40 outpatients, 25 women and 15 men. The average age at the time of diagnosis was 77±6 years and the average time between the onset of the first symptoms of the disease and diagnosis was 3-36 months.

Twenty-one outpatients were diagnosed with Alzheimer's disease (AD) and two outpatients were diagnosed with frontotemporal dementia (FTD), one of whom had a combination with AD and the other had a vascular form of dementia. In the remaining outpatients, the type of dementia was not defined. After subsequent data collection, five outpatients died, four of whom were diagnosed as AD and one as vascular dementia.

When the first dementia symptoms appeared, there was almost no difference in who noticed them first. The outpatients themselves (47.5%) noticed the symptoms about the same time as their family (50%). The results in Table 1. showed that in all 40 outpatients the first symptoms observed were memory problems, a combination of memory and thinking problems, especially disorientation in time and space. The presence of dementia in the family was evident in seven outpatients.

Regarding the level of education, more than one third of the patients reported the lowest level of education, primary education (36.5%), while the majority (40%) had higher education (Table 1).

When it comes to the presence of comorbidities, the largest number of outpatients (45%) had hypertension, while hyperlipidemia was the second most common (25%). Hypothyroidism was present in 15%, while 12.5% of outpatients had type 2 diabetes. 35% of the outpatients had symptoms of depression or a diagnosis of depression.

Anthropometric parameters were used to determine body mass (BM) and body mass index (BMI). Our sample showed that an average BMI of 27.3±5.4 kg/m^2 indicated an overweight status among outpatients.

The results in Table 1. showed that the largest number of outpatients (43%) were in the normal body mass category (18.5-24.99 kg/m^2), followed by 33% in the overweight category (25.0-29.99 kg/m^2). None of the outpatients were malnourished (18.50 kg/m^2) and only one was in the extreme obesity class III (≥40.00 kg/m^2).

An inverse association was observed between serum vitamin B12 levels and BMI. Serum vitamin B12 concentrations were lower (177.90±73.45 pmol/L) in outpatients with BMI (25.0 kg/m^2), compared with higher vitamin B12 concentrations (293.18±174.21 pmol/L) in outpatients with normal BMI (18.50-24.99 g/m^2).

Compared to the reference (25(OH) D 75 nmol/L), the mean values of 25 (OH) D in serum were decreased (Table 2). According to Wolters et al (2004), the mean values of vitamin B12 indicate a deficiency, as a concentration of 300 to 350 pmol/L is considered desirable for the elderly (Table 2).

Low status of vitamin B12 was found in 57% of outpatients, folic acid in 24% and 25 (OH) D in 75% of outpatients.

Eating habits and eating behaviors of the outpatients were assessed using a modified non-quantitative food frequency questionnaire. The results in Figure 1 show a change and rigidity in eating behavior among the outpatients. 15% of patients ate the same food every day, with rigidity in the way they ate (e.g., some patients always ate potatoes first, then vegetables, and finally meat for lunch). The results showed that 22.5% of outpatients always ate food in the same order and 50% of patients always ate food at the same time. In another study, it was found that approximately the same number of outpatients (42.5%) ate for a longer time and 55% of outpatients did not change the duration of food intake. It has been found that 10% of outpatients were found to be in the habit of eating food by hand.

When examining the changes in the intake of carbohydrates (bread, pasta and cakes), the results show that 53% of the outpatients changed the amount of intake (Figure 2), while 25% changed the preference of food. The results of frequency of food intake over 12 months are shown in Table 3. Most families of outpatients reported increased consumption (compared to before) of foods such as: Fast food, biscuits and sweets, cakes, higher consumption of sugar and honey and juices. The results show that most patients frequently consumed sweets, puff pastry and sweet pastries.

Reduced consumption of vegetables and fruits is noticeable in a large number of outpatients, with only 25% meeting the recommended daily intake of vegetables (Smolin & Grosvenor 2008). Contrary to expectations, a large number of patients did not consume berries at all during 12 months. Consumption of red meat and poultry meat is equally present in the daily intake of patients (Marcason 2015).

Table 1. Demographic characteristics of patients

Characteristic	Outpatient n=40
Age (years)	77±6 (63;88)*
Body weight (kg)	75.1±15.8 (51; 118)*
Body mass index (kg/m^2)	27.3±5.4 (20.9; 40.8)*
Underweight (<18.5 kg/m^2) (%)	0
Normal body weight (18.50-24.99 kg/m^2 (%)	43
Overweight (25-29.99) (%)	33
Obesity Class I (30-34.9 kg/m^2) (%)	10
Obesity Class II (35-39.9 kg/m^2) (%)	10
Extreme Obesity Class III (>40 kg/m^2) (%)	4
Age of the outpatients with first symptoms of the disease No (%)	75±6 (87) (63; 87)*
Gender No (%)	
Males	15 (37)
Females	25 (63)
Tipe of the disease No (%)	
Alzheimer's	21 (52.5)
Mild cognitive impairment (MCI) or initial form of dementia	8 (20)
Fronttemporal dementia	2 (5)
Vascular dementia	1 (2.5)
Dementia in general	8 (20)
First symptoms of the disease No (%)	
Memory	40 (100)
Memory and reasoning	24 (60)
Opinion. memory and reasoning	2 (5)
Opinion and memory	1 (2.5)
Who noticed the first symptoms No (%)	
Patient	19 (47.5)
Family	20 (50.0)
Family history with dementia No (%)	7 (17.5)
Education No (%)	
Primary school	15 (36.5)
High school	16 (40)
College	8 (20)
Post graduate study	1 (2.5)
Working status No (%)	
Pensioner	40 (100)
Marriage status No (%)	
Single	18 (45)
In marriage	22 (55)
Comorbities No (%)	
Arterial hypertension	18 (45)
Hyperlipidemia	10 (25)
Hypothyroidism	6 (15)
Diabetes mellitus	5 (12.5)
Diagnosed depression or symptoms of depression	14 (35)
Other psychological disorders (anxiety)	2 (5)

Results expressed as mean value ± SD; *(min;max); No: number of patients; %: percentage of patients

Table 2. Biochemical parameters

Characteristic	Patient n=40
Vitamin B_{12} (pmol/L)	242±133 (89; 391)*
Folic acid (nmol/L)	10.8±4.5 (3.1; 15.7)*
25 (OH) D (nmol/L)	59±40 (15; 109)*

Results expressed as mean value ± SD; *(min; max)

According to the recommendations, 32.5% of outpatients consume fish 1-2 times per week, while 35% of respondents do not eat fish. Sunflower oil was the most commonly used for food preparation while olive oil was only used by 5% of the outpatients. The results on the frequency of consumption of nuts show a reduced consumption of these foods, only 17.5% of patients meet the recommended daily intake (Marcason 2015) (Table 3).

Table 3. Frequency on intake of certain foods and eating behavior over 12 months

	*Frequency %				
	1 p.d.	2-3 p.d.	1-2 p.w.	1 p.m.	Never
How often did you consume purchased fruit juices?	10.0	20.0	12.5	17.5	37.5
How often have you consumed syrups?	7.5	22.5	7.5	7.5	52.5
How often did you consume soft drinks?	0.0	2.5	10.0	7.5	77.5
How often have you consumed beer. alcoholic or non-alcoholic?	2.5	0.0	7.5	17.5	70.0
How often have you consumed wine?	2.5	2.5	7.5	15.0	70.0
How often have you consumed strong alcoholic drinks?	5.0	0.0	2.5	5.0	85.0
How often have you consumed coffee. with or without caffeine?	52.5	22.5	2.5	2.5	17.5
How often did you consume bread. buns and pastries (NOT in a sandwich)?	30.0	50.0	12.5	2.5	2.5
How often have you consumed pizza?	2.5	5.0	10.0	37.5	42.5
How often did you consume cakes (biscuits, bakery products, puff pastry, muffins, sweet pastries etc.)?	10.0	7.5	45.0	22.5	12.5
How often have you consumed cakes (baked cakes, pies etc.)?	2.5	10.0	40.0	30.0	15.0
How often have you consumed salty dry crackers, chopsticks etc.?	0.0	2.5	10.0	22.5	62.5
How often did you consume chips, figs, popcorn etc.?	2.5	2.5	2.5	20.0	2.5
How often did you consume whole grains (brown rice, barley, oats, millet, etc.)?	15.0	2.5	32.5	25.0	17.5
How often have you consumed cooked green vegetables (such as spinach, beets, kale, chard and kale)?	25.0	7.5	47.5	10.0	5.0
How often have you consumed raw green vegetables (like arugula, chicory, lettuce)?	35.0	17.5	22.5	7.5	10.0
How often have you consumed legumes. beans or peas (fresh. canned or frozen)?	10.0	2.5	65.0	7.5	7.5
How often did you consume forest fruits (like strawberries, raspberries, blueberries etc.?)	32.5	2.5	17.5	12.5	30.0
How often have you consumed turkey and chicken cold cuts (like ham)?	22.5	0	35.0	20.0	17.5
How often did you consume other cold cuts (like sausages, straw etc.)?	15.0	2.5	35.0	17.5	25.0
How often did you consume hot dogs?	5.0	0.0	22.5	35.0	32.5
How often have you consumed pate?	2.5	2.5	27.5	25.0	37.5
How often did you consume sausages?	2.5	2.5	20.0	37.5	32.5
How often did you consume bacon?	5.0	5.0	37.5	30.0	17.5
How often did you consume red meat?	12.5	2.5	70.0	7.5	2.5
How often did you consume poultry?	5.0	12.5	70.0	2.5	5.0
How often did you consume cevapi, burgers, kebabs etc.?	7.5	0.0	20.0	25.0	42.5
How often have you consumed fish and seafood?	2.5	2.5	32.5	22.5	35.0
How often did you eat cottage cheese?	17.5	5.0	52.5	7.5	12.5
How often have you consumed hard cheese?	2.5	0.0	50.0	22.5	20.0
How often have you consumed eggs, egg whites and egg substitutes (NOT including eggs as part of meals and desserts but YES eggs in salads)?	2.5	5.0	52.5	25.0	10.0
How often have you used margarine?	7.5	2.5	35.0	15.0	35.0
How often have you used butter?	7.5	37.5	17.5	32.5	95.0
How often have you used mayonnaise as a spread or as part of a meal?	0.0	0.0	2.5	20.0	72.5
How often did you consume meals to which animal fat was added?	17.5	7.5	10.0	25.0	2.5
How often have you consumed peanuts. hazelnuts. seeds and other nuts?	17.5	2.5	12.5	20.0	42.5
How often did you add sugar to coffee or tea?	52.5	15.0	2.5	2.5	22.5
How often did you add honey to your tea?	30.0	7.5	22.5	15.0	20.0
How often have you added sweetener to coffee or tea?	7.5	2.5	0.0	2.5	82.5
How often have you added ketchup to dishes or dressings to salads?	0.0	0.0	5.0	12.5	75.0

*Legend: p.d. - per day; p.w. - per week; p.m. - per month

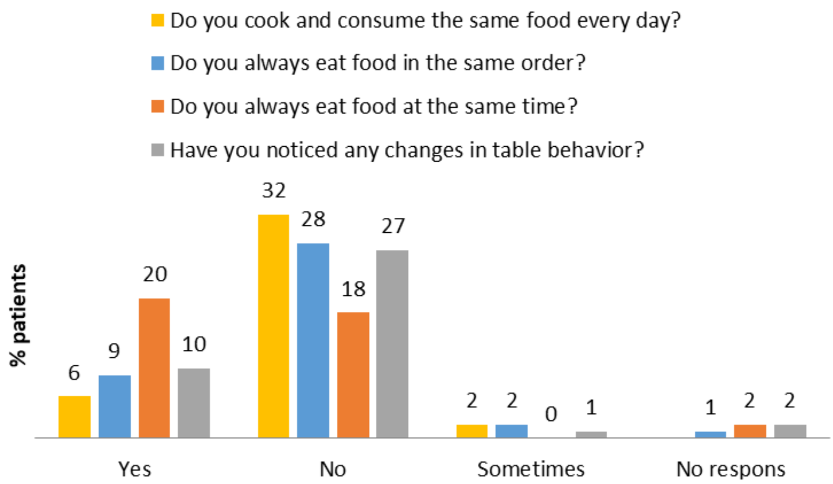

Figure 1. Demonstration of the frequency of behavioral changes during food consumption in outpatients with dementia (n=40)

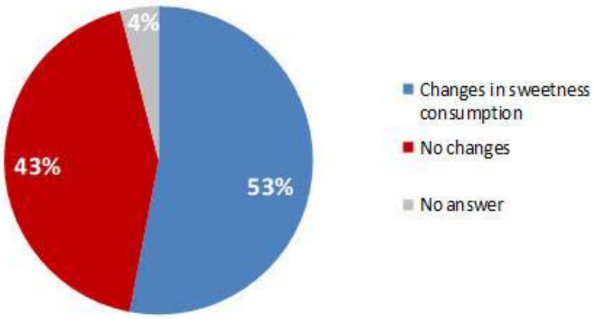

Figure 2. Display of change in sweetness in outpatients with dementia (n=40)

DISCUSSION

Symptoms of different forms of dementia (e.g., Alzheimer's disease and vascular dementia) may influence nutritional status (Mole et al. 2017). The findings presented in our study suggest that poor nutritional status is associated with unhealthy eating habits that may lead to micronutrient malnutrition.

This research provided a comprehensive insight into the nutrition of outpatients with dementia and the importance of early (after a dementia diagnosis is given) detection of changes in nutritional status, behavior, and eating habits of individuals with primary progressive dementia.

Previous research has demonstrated the association between poorer nutritional status and poorer clinical features of dementia, such as cognitive and functional impairment and neuropsychiatric symptoms (Volkert et al. 2015, Cipriani et al. 2016, Mole et al. 2017). Screening nutritional status is useful for predicting the clinical course of dementia (Sanders et al. 2018). Nutritional status can serve as an important target for interventions per se and as an indirect pathway for maintaining cognitive health. Due to the fact that there is still no effective cure and that available treatments have only benefited the symptoms of the disease, scientists are increasingly interested in how to delay the possibility of developing dementia through healthy diet and eating habits.

Although many studies have highlighted the increased risk of malnutrition (Mole et al. 2017), our results of anthropometric assessments showed that the majority of outpatients are overweight. The average BMI of outpatients was significantly higher than that observed in the study by Hsiao et al. (2019), in which the average BMI was 23.61±3.6 kg/m^2 observed in the early stage of dementia, and in the Swedish study by Faxen-Irving et al. (2014), in which the BMI was also lower at 24.6±4.3 kg/m^2 in patients at the time of diagnosis.

Previous studies have observed changes in body mass during disease progression in different forms of dementia, particularly weight loss in patients with AD and weight gain in patients with FTD (due to hyperphagia) (Cipriani and al. 2016). Although increased body mass is characteristic of patients with FTD, it can also be observed in patients with AD, which is also evident in our results.

Most patients had normal body mass, but due to possible changes in eating behavior (loss of appetite) characteristic of AD, normal body mass could become a risk factor later on. A study by Ciszewska-Czarnecka and Kłoszewska (2016) showed that weight loss in AD was associated with slower eating rate and consumption of smaller portions.

A higher BMI shows a potential protective effect by reducing the risk of death (Cipriani 2016). Low BMI in individuals with dementia is a predictive factor for mortality and they may benefit from higher BMI values (Cipriani 2016). García-Ptacek et al. (2014) showed in their study of 11,398 patients that a higher BMI was associated with a lower risk of mortality. Nalder et al. (2021) reported that older men and women with high BMI were potentially at risk in the cognitive domains of attention/executive function and visuospatial construction. In addition, there are conflicting reports that high BMI in old age is protective against AD and cognitive impairment, while a high waist-to-hip ratio is associated with increased cognitive impairment (Nadler et al. 2021, Coin et al. 2012, Zhang et al. 2018).

Increased body mass is also a consequence of altered eating behavior, which was demonstrated in a study by Ciszewska-Czarnecka and Kłoszewska, (2016) on 217 patients with AD. Namely, in 13% of patients, increased body mass was associated with increased appetite and faster consumption of larger portions, while in 34%, loss of body mass was associated with slower consumption of smaller portions and decreased appetite.

In addition, changes in eating behavior such as hyperphagia and increased tendency to eat sweets are the result of increased body mass.

The FFQ results in our study showed that 25% of outpatients changed their food preferences and families reported a tendency towards increased cravings for fast food, meat, sweets and sugar. Cipriani et al. (2016) reported that the tendency to eat sugary foods ranged from 5% to 39% in individuals with AD.

The study by Kai et al. (2015) showed a higher frequency of changes in food preferences and most of these changes (47.6%) were observed in individuals with moderate AD. The addition of strong spices in food, such as soy sauce, was also of interest. One possible reason for this behavior is impaired taste function in patients with AD, but researchers are not yet certain.

Based on the research to date, it can be concluded that a specific change in increased propensity for sweets was seen in our outpatients and a pattern of food stockpiling was confirmed in 20% of respondents.

Our findings are also confirmed by the research of Ciszewska-Czarnecka and Kłoszewska (2016). The authors showed that every fourth patient with AD (25.9%) consumed significantly more sugary foods than before. Also, the study by Mungas et al. (1990) compared patients with AD and vascular dementia with a control group and the results showed that dementia patients had a significantly greater tendency to eat sweets than the control group. An interesting trend was also observed between genders, namely that male patients showed a greater tendency to eat sweets compared to females. Therefore, the researchers suggest that a tendency to eat sugary foods may be a significant part of the clinical dementia syndrome.

Previous research has shown that omega-3 polyunsaturated fatty acids (eicosapentaenoic acid- EPA and docosahexaenoic acid- DHA) in combination with B-complex vitamins (folic acid, vitamins B6 and B12), vitamin D3, flavonoids (resveratrol), and polyphenols and alkaloids (caffeine) can prevent the progression of AD and MCI through enhanced elimination of β-amyloid and anti-inflammatory properties (Abate et al. 2017).

The status of B vitamins, with emphasis on folic acid and vitamin B12, is often inadequate in the elderly and may subsequently lead to a decline in cognitive function. Low levels of the vitamin B complex are often observed in patients with dementia. Due to the deficiency of B vitamins, high homocysteine levels (hyperhomocysteinemia) leads to impairment of the "cognitive system" and causes dementia and Alzheimer's disease. Studies conducted in the hippocampus (brain region involved in learning and memory processes) found that homocysteine increases excitotoxicity and neurodegeneration (Robinson et al. 2018), therefore high homocysteine levels are considered a strong risk factor for cognitive impairment and Alzheimer's disease (Mikkelsen et al. 2016). Researchers suggest that undiagnosed B12 deficiency may be an important omission in preventing dementia and stroke, so it is important to identify the deficiency as early as possible and consider B12 supplementation (in the form of methylcobalamin or hydroxycobalamin) (Spence, 2016).

According to Mikkelsen (2016), the prevalence of folic acid and vitamin B12 deficiency in the elderly is more than 20%, which is very close to our findings. The results of Moore et al (2012) showed that clinically low vitamin B12 levels (250 pmol/L) were associated with Alzheimer's disease, vascular dementia and Parkinson's disease, while vitamin B12 deficiency (150 pmol/L) was associated with cognitive impairment. According to a study by Wang et al. (2001), serum vitamin B12 levels of 250 pmol/L were associated with twice the risk of AD within three years in individuals aged 75 years (Wang et al. 2001). Vitamin B12 deficiency is associated with the development and progression of depression, especially when vitamin B12 deficiency is accompanied by folic acid deficiency.

We found an inverse association between serum vitamin B12 levels and obesity status. Our findings are consistent with some previous studies in which serum vitamin B12 levels were inversely associated with overweight and obesity (Sun et al. 2018). The negative correlation between B12 and BMI and the effects of both factors on attention and memory in B12-deficient elderly have not been reported in previous literature. Nalder et al. (2021) found that increased BMI and low circulating vitamin B12 were independent risk factors for impaired attention/executive, visuospatial abilities, and memory processes.

Prolonged vitamin D deficiency has been shown to play a role in neurodegenerative changes by increasing the harmful accumulation of Aβ (amyloid beta), which contributes to the development of AD. Our patients have low vitamin 25 (OH) D levels on average, suggesting that vitamin D deficiency could potentially lead to more rapid disease progression (Keeney & Butterfiled 2015).

The low status of vitamin B12, folate and 25 (OH) D in the serum of the outpatients could be the result of inadequate dietary intake. Reduced frequency of intake of dark green leafy vegetables, which are a natural source of folate, and lower intake of poultry meat, fish and eggs, which are sources of vitamin B12, were observed in the outpatients.

There is growing evidence that increased intake of saturated fatty acids may have negative effects on MCI, while in populations with increased fish consumption and high intake of monounsaturated fatty acids and polyunsaturated fatty acids, particularly omega-3 fatty acids, a reduction in the risk of cognitive impairment has been found (Solfrizzi et al. 2018). Evidence for this comes from observational studies that have shown that intake of oily fish, EPA and DHA is associated with a lower risk of AD (Szczechowiak et al. 2019).

Therefore, it is of concern that patients showed a low frequency of consumption of fish, olive oil, nuts, and berries. Although fruit shows no direct effect on reducing dementia, a large prospective cohort study has shown that berries may show a protective effect against cognitive loss (Morris et al. 2015a).

In recent years, the influence of different dietary patterns on cognitive impairment and dementia has been observed. As a result of the research, the MIND diet (Mediterranean - DASH intervention for Neurodegenerative Delay) was created as a combination of the Mediterranean and DASH (Dietary Approach to Systolic Hypertension) diets to lower blood pressure. For example, research by Morris et al. (2015a) concluded that adherence to the MIND diet improved cognitive function, reduced risk, and slowed the progression of AD. The MIND diet reduced the risk of AD in 53% of participants who strictly followed the diet and about 35% in those who moderately adhered. The MIND diet combines these two diets and emphasizes the consumption of natural and plant-based foods, especially berries and green leafy vegetables, and limited intake of animal and saturated fat- rich foods (Marcason 2015).

Over the years, researchers have studied a large number of risk factors that may impact the development of dementia. One of the most commonly studied risk factors is age, which is considered the strongest risk factor for dementia. In recent decades, research studies have also suggested a wide range of potentially "modifiable" factors that could be the target for prevention strategies. The most consistent evidence relates to vascular risk factors (hypertension, diabetes, obesity), psychosocial factors (depression), and lifestyle (low mental and physical activity, smoking). Higher education, engaging in mentally stimulating activities and regular physical activity have shown protective properties against dementia (Canevelli et al. 2018). Although some potentially reversible conditions, such as hypothyroidism or vitamin B12 deficiency, are thought to cause dementia, unfortunately only 1.5% of cases of mild to moderate dementia are fully reversible. Although these clinical and demographic variables may be useful for prognosis, they are not modifiable. In contrast, indicators of nutritional status are considered a "variable" factor in the progression of dementia, defined by a number of interrelated factors. Given the rapid progression of the disease, nutritional monitoring and intervention should be initiated immediately after the diagnosis of dementia, with the aim of reducing nutritional deficits and preventing further and more severe impairment of cognitive function. An individualized and personalized nutritional approach shows positive effects and leads to an improvement in nutritional status, but also to its maintenance (Mole et al. 2017).

Individuals with dementia who have an increased tendency to sweets and other pathological behaviors should be monitored and limit the intake of high-sugar foods and replace the intake of such foods with berries or nuts to balance the diet (MIND) and consequently prevent weight gain and other comorbidities.

Limitations of the study

Several limitations must be considered when interpreting the results of this study. A small number of patients were included in the study and the results cannot be presented by type of dementia. In addition, the study of the medical history showed that some of the patients live alone and therefore the family could not be informed about the actual state of the patients' behavior and food intake. It is important to note that the data were based on a subjective assessment of family members, so they should not reflect the objective reality. Due to impaired cognitive function, other validated methods of assessing food intake should be used that do not rely on individuals' memory.

CONCLUSION

Poor nutritional status of individuals with primary progressive dementia is associated with unhealthy dietary habits leading to micronutrient malnutrition. Although all patients were in the "normal body weight" or "overweight" category, they are at nutritional risk due to possible changes in eating patterns.

Dietary monitoring and intervention should be initiated immediately after the diagnosis of primary progressive dementia with the aim of reducing nutritional deficiencies and preventing further and more severe impairment of cognitive function.

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Contribution of individual authors:

Irena Martinis & Martina Bituh: design of the study, literature searches and analyses, statistical analyses, interpretation of data, manuscript writing.

Anđelko Vrca: design of the study, interpretation of data, manuscript writing.

Milenko Bevanda, Sanja Botić-Štefanec, Jasna Bađak, Dinka Kušter & Tatjana Suttil: interpretation of data.

Kim Bolarić, literature searches and analyses, interpretation of dana, statistical analyses.

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