**Vitamin B12 and folate deficiencies are not associated with nutritional or weight status in older adults**

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**ABSTRACT (233/250)**

It is not known whether undernutrition causes vitamin B12 and folate deficiencies. The present study aimed to determine whether nutritional status, measured using the Mini Nutritional Assessment (MNA) scale, and body mass index (BMI) are indicators of lower level serum vitamin B12 and folate in older adults. 1007 outpatients aged 65 years or over were included the study. MNA scores >23.5, 17-23.5, <17, were categorized as normal nutritional status, risk of malnutrition, and malnutrition, respectively. Weight status was assessed using BMI and categorized as under or normal weight (< 25 kg/m2), overweight (25-30 kg/m2), class I obese (30.0-35 kg/m2), class II obese (35-40 kg/m2), and class III obese (≥40 kg/m2). Vitamin B12 and folate deficiencies were defined as <200 pg/ml and <3 ng/ml, respectively. Among 1007 patients with an average age of 74.3±8.2 years, 6.9% were categorized as having malnutrition and 31.2% were categorised as at risk of malnutrition. While 45.7% of patients were categorized as having vitamin B12 deficiency and 0.9% folate deficiency. There were no differences between patients with malnutrition, at risk of malnutrition, and good nutrition in serum vitamin B12 or folate levels, or the presence of vitamin B12 or folate deficiency after adjustment for age, gender, and education (p>0.05). The results were the same across BMI classifications (p>0.05). Vitamin B12 and folate levels are not associated with nutritional or weight status and these should be evaluated independently of BMI and MNA values.

**Keywords:** vitamin B12; folate; nutrient; nutritional status; body mass index

**1.INTRODUCTION**

As the world population grows, the number of people with disabilities, who have longer hospitalization, and higher mortality, which leads to higher health care expenditures and caregiver burden, increases (1). One of the most common causes of disability is malnutrition in older people. The prevalence of malnutrition in older people varies according to the health care setting and dependency level of individuals: 3.1% for those living in the community, 17.5% of those in care homes, and 28.7% in long-term care (2). Although aging is a natural process, older people may experience some restrictions on the selection, preparation and intake of food, usually due to a decrease in their cognitive and physical functionality, which may result in malnutrition or malnutrition risk (2, 3). Malnutrition increases the risk of infection, sarcopenia, frailty, pressure injury, falls, fracture and mortality, causing delayed immune response and wound healing (2, 4). Despite all of these negative effects, malnutrition, a disorder that is often overlooked, remains an important and common public health problem (5). Regular nutritional status should be screened and nutritional therapy should be administered as soon as possible in older adults (6).

Terminological confusion has previously existed in statements used for definitions of nutritional conditions. The concepts of malnutrition, micronutrient abnormalities, and overnutrition have now been differentiated and defined in the guideline and all were collected under the title of nutritional disorders (7). Micronutrient abnormalities are as important as malnutrition in geriatrics clinical practice, since older adults have an increased risk of micronutrient deficiencies, particularly vitamin B12 and folate deficiencies, which cause a variety of negative consequences, similar to malnutrition (8, 9). There are many identified risk factors for both deficiencies such as inadequate daily intake of vitamins, bacterial overgrowth, and medications (8). However, it is not known whether nutritional status affects serum vitamin B12 and folate levels in older adults or whether people with normal nutrition may be deficient in vitamin B12 or folate in the blood. Also, it has not yet been demonstrated that Mini Nutritional Assessment (MNA), which is a recommended tool for the screening of nutritional status, and contains several items, such as depression, food intake, mobility, medication, living independently, can predict lower serum levels of vitamin B12 and folate (6). On the other hand, one of the most commonly used anthropometric measures is body mass index (BMI). BMI is a widely accepted gold-standard indicator of both malnutrition and overnutrition (7, 10). Because a few studies have reported the relationship between low vitamin B12 and folate levels and obesity, insulin resistance, and adiposity, BMI may aid in identifying vitamin deficiencies (11). However, to the best of our knowledge, no study exists regarding this topic in older adults.

For this reason, the present study aims to determine whether nutritional status, items of MNA, and classifications of BMI can estimate vitamin B12 and folate deficiencies in older adults.

**2.METHODS**

**2.1. Participants:**

A total of 1269 outpatients applied for any health issue to the geriatric center, which is part of an Education and Research Hospital in Kayseri, Turkey, between April 2017-July 2018. As a result of comprehensive geriatric assessment by a geriatrician, 1007 patients who did not have exclusion criteria, were included in this study. The investigation conformed to the Declaration of Helsinki and approved by the local ethics committee. Informed consent was provided by each participant or a legal guardian before participating in the study.

**2.2. Exclusion Criteria as follows:**

-Patients who have a history of severe illness that may lead to acute impairment of general health status, such as acute cerebrovascular event, gastrointestinal bleeding, sepsis, acute renal failure, acute coronary syndrome, acute liver failure, acute respiratory failure

-Patients under 65 years of age

-Patients who refused to participate

-Patients with any diseases causing malabsorption of vitamin B12 and folate deficiency, such as celiac disease, crohn’s disease, ileal resection, exocrine pancreatic insufficiency, short bowel syndrome, alcohol abuse

-Patients who took vitamin B12 or folate supplements

|  |
| --- |
| **2.3.Comprehensive Geriatric Assessment (CGA)** (12) |
|  |

Patients’ age, gender, education level, comorbidities, and numbers of prescription drugs used were recorded. During the admission, patients were asked whether they had fallen in the previous year. History of hypertension (HT), coronary artery disease (CAD), congestive heart failure, diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), hypothyroidism, urinary incontinence, dysphagia, were determined by patients’ self-report. All the patients underwent CGA, including Mini Mental State Examination (MMSE), Geriatric Depression Scale-15 (GDS) (13) for neurocognitive evaluation, Basic and Instrumental Activities of Daily Living (BADL, IADL) for functional evaluation, Tinetti Performance-Oriented Assessment of Mobility (POMA) and timed up and go test (TUG) for mobility evaluation, and MNA for nutritional evaluation.

Handgrip test of the dominant hand (mean of 3 measurements) was measured by a Jamar handheld dynamometer.  Dynapenia was defined as handgrip strength <20 kg for women and <30 kg for men, and the diagnosis of sarcopenia was defined according to the criteria of the European Working Group on Sarcopenia in Older People (14).

Frailty status was defined based on five dimensions of frailty phenotype, including shrinking, exhaustion, low levels of physical activity, weakness and slowness. People with 0 criteria were considered robust,1–2 pre-frail, and >3 frail, as suggested by Fried et al (15). A weight loss >4.5 kg within the past year was taken as a sign of shrinking. Exhaustion was defined by the patients’ answering the question “much or most of the time, have you felt tired or fatigued without reason during the past 2 weeks?”. Weakness, assessed by grip strength of the dominant hand with dynamometer, was accepted to be less than or equal to the cut-off points according to sex and BMI which were determined by Fried et al. Low levels of physical activity were considered as positive in patients who had no physical activity, spent most of the time sitting, or rarely had short walks in the past year. Low gait speed was evaluated by 4-meter walking test, and if it was less than or equal to the cut-off points according to sex and height’, it was regarded as “slowness”(15).

**2.4. Nutritional and Weight Assessment**

The MNA test is composed of simple measurements and 18 brief questions that can be completed in less than 10 minutes: anthropometric measurements (4 questions related to BMI, weight loss, brachial circumference, and calf circumference); Global assessment (6 questions related to lifestyle, medication, and mobility); Dietary questionnaire and subjective assessment (8 questions related to number of meals, food and fluid intake, and autonomy of feeding, self-perception of health and nutrition). If the total score was > 23.5, 17-23.5, <17, it was accepted that there was no malnutrition, risk of malnutrition, and malnutrition, respectively (6). MNA was performed in all patients even if their MNA-Short Form scores were ≥12. To calculate body mass index (BMI), height was measured to the nearest centimeter (cm) and weight was measured to the nearest half-kilogram (kg) with the same stadiometer. Weight status was assessed using Body Mass Index (BMI) and participants were categorized as under or normal weight (< 25 kg/m2), overweight (25-30 kg/m2), class I obese (30.0-35 kg/m2), class II obese (35-40 kg/m2), class III obese (≥40 kg/m2) (16).

**2.5. Vitamin B12 and folate assessment**

To evaluate the biochemical evidence of insufficient intake and the metabolic condition, blood samples were collected in the morning after at least 8 h of fasting. Blood sampling was performed for every subject on admission and assayed on visit day. Venous blood samples were drawn into a standard biochemical tube for biochemical assay from all patients. Folate and vitamin B12 levels were determined in serum with a homogenous chemiluminescent immunoassay using Beckman-Coulter, Woerden, the Netherlands. These biochemical tests were carried out on Diagnostic Modular Systems [autoanalyzer](https://www.sciencedirect.com/topics/medicine-and-dentistry/autoanalyzer) (Beckman Coulter DXD 800). All the blood sample were measured fresh. The inter-assay variation was 5.4% for folate and 4.7% for vitamin B12. Serum vitamin B12 level was considered to be deficient and low serum vitamin B12 level when it was below 200 pg/ml and below 400 pg/ml, respectively (17-19). folate deficiency and low folate level were evaluated according to both < 3 ng/ml and 6 ng/ml, respectively(20).

**2.6. Statistical Analyses:**

Data analyses were carried out using the Statistical Package for the Social Sciences 17. Descriptive statistics are reported as mean ± standard deviation for variables with a normal distribution, and the number of cases and percentage (%) for nominal variables. Demographic characteristics of participants were analyzed using descriptive statistics. When groups were present, the significance of differences between the groups in terms of averages was investigated by t test and in terms of median values was investigated by Mann-Whitney U test. When the number of groups was more than two, the significance of differences between the groups in terms of averages was investigated by the ANOVA test, post-hoc ANOVA test and the significance of medians was determined by the Kruskal Wallis test. Nominal variables were assessed by Pearson Chi-Square. In all analyses, p < 0.05 was considered to indicate statistical significance. Bonferroni Correction was also performed to protect analysis from Type I error.

**3.RESULTS**

The descriptive characteristics of 1007 patients, of whom the mean age was 74.3 ± 8.2 years, are shown in Table 1. Six hundred and twenty two participants (61.9%) had normal nutritional status, whereas 69 patients were diagnosed with malnutrition (6.9%) and 314 were diagnosed with malnutrition risk (31.2%).

There was no difference in the patients with malnutrition, the risk of malnutrition, or normal nutrition in terms of the presence of Parkinson’s disease, CAD, CHF, HT, COPD and hypothyroidism (for each p > 0.05). There was a significant difference between the 3 groups in terms of age, female participants, educational level, BMI, Charlson Comorbidity Index, history of falls, the presence of DM, polypharmacy, dysphagia, dementia, depression, cerebrovascular disease, urinary incontinence, sarcopenia, dynapenia, and frailty (p < 0.05 for all comparisons). It was determined that all those escalated increasingly from the normal nutritional status group to the malnutrition group. While MMSE, POMA, BADL, IADL, MNA scores were lower in malnutrition group; GDS scores and TUG were higher in malnutrition group compared to normal nutritional status (p<0.05).

45.7% of older adults showed vitamin B12 deficiency (< 200 pg/ml), and 40.9% had low serum vitamin B12 levels (200–400 pg/ml). 0.9% had folate deficiency (< 3 ng/ml) and 14.9% had low folate levels (<6 ng/ml). There was no difference in the patients with malnutrition, the risk of malnutrition, or normal nutritional status in terms of the presence of vitamin B12 deficiency and serum vitamin B12 levels (p>0.05), whereas low folate levels and folate deficiency were more prevalent in malnutrition group than in normal nutritional status (p<0.05). However, after adjustment for age and gender, statistical significance did not persist (p>0.05) (Table 2).

There was a significant correlation between the following items of MNA and folate deficiency (p <0.05): “Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?”, “Weight loss during the last 3 months”, “Mode of feeding” and “Consumes two or more servings of fruit or vegetables per day?” were significantly associated with folate deficiency (p <0.05). While vitamin B12 deficiency was significantly related to one question on the MNA querying “Lives independently” (p<0.05).

**Table 1. Descriptive characteristics of the participants according to nutritional status (n=1007)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Normal Nutrition**  **(624)** | **Malnutrition Risk**  **(314)** | **Malnutrition**  **(69)** | **p** |
| **Age** | 72.7±7.5 | 76.2±8.3 | 82.0±8.8 | < 0.001 |
| **Gender (female%)** | 67.6 | 84.7 | 65.2 | < 0.001 |
| **Education** |  | | |  |
| * Illiterate (0 yıl) | 45.9 | 70.4 | 72.5 | < 0.001 |
| * 1-5 | 37.2 | 23.8 | 17.3 |
| * 6-8 | 6.1 | 2.6 | 7.3 |
| * >8 | 10.8 | 3.2 | 2.9 |
| **Body mass index (kg/m2)** | 34.8±20.9 | 30.6±6.5 | 25.3±6.5 | < 0.001 |
| **CCI** | 0.9±3.6 | 1.3±5.0 | 2.7±11.5 | 0.032 |
| **Comorbidities (%)** | | | |  |
| Hypertension | 65.4 | 68.8 | 72.5 | 0.796 |
| Diabetes mellitus | 38.1 | 33.4 | 7.2 | < 0.001 |
| Congestive heart failure | 4.8 | 7.3 | 2.9 | 0.267 |
| Coronary artery disease | 12.8 | 10.5 | 10.1 | 0.703 |
| COPD | 11.2 | 16.0 | 13.0 | 0.318 |
| Cerebrovascular Disease | 3.0 | 7.3 | 8.7 | 0.03 |
| Hypothyroidism | 9.1 | 6.7 | 2.9 | 0.178 |
| Parkinson Disease | 4.8 | 4.5 | 4.3 | 0.575 |
| Urinary incontinence | 48.4 | 53.8 | 37.6 | 0.020 |
| Dysphagia | 1.0 | 7.3 | 18.8 | < 0.001 |
| Falls | 20.8 | 35.9 | 56.5 | < 0.001 |
| Polypharmacy | 26.7 | 46.2 | 40.5 | 0.029 |
| Depression | 28.8 | 47.8 | 47.8 | < 0.001 |
| Dementia | 6.7 | 7.3 | 10.1 | < 0.001 |
| Dynapenia | 35.9 | 47.8 | 72.4 | < 0.001 |
| Sarcopenia | 28.0 | 37.5 | 44.9 | < 0.001 |
| Frailty | 5.8 | 59.9 | 94.2 | < 0.001 |
| **Geriatric Assessment** | | | |  |
| MMSE | 25.6±3.2 | 22.7±5.4 | 16.8±6.3 | < 0.001 |
| BADL | 92.3±9.9 | 88.1±57.7 | 63.2±31.6 | < 0.001 |
| IADL | 19.3±5.8 | 14.6±7.8 | 7.6±7.3 | < 0.001 |
| GDS | 3.2±3.4 | 7.5±4.1 | 9.1±3.7 | < 0.001 |
| MNA | 26.3±1.6 | 20.6±1.7 | 13.1±3.4 | < 0.001 |
| TUG | 11.5±4.9 | 17.1±10.9 | 26.0±16.4 | < 0.001 |
| POMA | 26.5±11.1 | 22.4±6.5 | 15.3±9.7 | < 0.001 |

BADL: Basic Activity of Daily Living (0 [worst]–100 [best]); CCI: Charlson Comorbidity Index; COPD: Chronic obstructive Pulmonary disease; GDS: Geriatric Depression Score (15 [worst]–0 [best]); IADL: Instrumental activity of daily living (0 [worst]–23 [best]); MMSE: Mini-Mental State Examination (0 [worst]–30 [best]); MNA-SF: Mini-Nutritional Assessment-Short Form (0 [worst]–14 [best]); Mini-Nutritional Assessment (0 [worst]–30 [best]); POMA: Performance Oriented Mobility Assessment (0 [worst]–28 [best]); TUG: Timed up and go test

**Table 2. The levels of Vitamin B12 and folate according to nutritional status**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Normal nutritional status**  **(n=624)** | **Risk of Malnutrition**  **(n=314)** | **Malnutrition**  **(n=69)** | **p** |
| **Vitamin B12 (pg/ml)** | 264.9±194.0 | 264.5±202.2 | 268.49±189.8 | 0.786 |
| **Vitamin B12 groups (%)** | | | | |
| **<200 pg/ml** | 48.0 | 45.7 | 45.3 | 0.589 |
| **200-400 pg/ml** | 41.7 | 44.1 | 37.7 |
| **>400 pg/ml** | 10.3 | 10.2 | 17.0 |
| **Folate** (**ng/ml)** | 9.44±3.6 | 8.94±3.67 | 8.22±3.25 | 0.231\* |
| **Folate groups (%)** | | | | |
| **<3** **ng/ml** | 1.0 | 0.8 | 1.8 | NA |
| **3-6** **ng/ml** | 14.9 | 20.8 | 21.8 | 0.459\* |
| **>6** **ng/ml** | 84.1 | 78.4 | 76.4 |

\*p value after adjusting for age and gender

\*After adjustment for Charlson Comorbidity Index, the presence of DM, polypharmacy, dysphagia, dementia, depression, cerebrovascular disease, sarcopenia, dynapenia, and frailty, p value was still not significant (p> 0.05).

The percentage of patients with normal weight, overweight, class I obese, class II obese, and class III obese (≥40 kg/m2) were 13.9%, 27.7%, 29.4%, 20.4% and 8.7%, respectively. In each BMI group, it was found that that there was no difference in the levels of vitamin B12 and folate, or vitamin B12 and folate deficiencies after adjustment for the same confounders (p >0.05) (Table 3). The post hoc tests were used, but any differences were not found between BMI 30-34.9 group and other groups in terms of folate values. Also, after the Bonferroni correction, the results were not changed.

**Table 3. The levels of Vitamin B12 and Folate according to weight status**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **< 25**  **(n=140)** | **25-29.9 (n=279)** | **30-34.9**  **(n=296)** | **35-39.9**  **(n=205)** | **≥40**  **(n=87)** | **p** |
| **Vitamin B12 (pg/ml)** | 262.4±229.9 | 288.4±225.6 | 248.0±150.3 | 277.9±198.3 | 256.2±177.1 | 0.407 |
| **Vitamin B12 groups (%)** |  | | | | | |
| **<200 pg/ml** | 50.0 | 46.8 | 45.6 | 40.4 | 52.5 | 0.208 |
| **200-400 pg/ml** | 42.1 | 38.5 | 46.4 | 48.8 | 39.3 |
| **>400 pg/ml** | 7.9 | 14.7 | 8.1 | 10.8 | 8.2 |
| **Folate (ng/ml)** | 9.0±4.1 | 9.3±3.5 | 12.9±5.4 | 9.2±3.4 | 8.4±3.4 | 0.245\* |
| **Folate groups (%)** |  | | | | | |
| **<3 ng/ml** | 2.6 | 1.4 | 0.8 | 0.6 | 0 | NA |
| **3-6 ng/ml** | 20.5 | 16.2 | 12.2 | 16.8 | 21.7 | 0.132\* |
| **>6 ng/ml** | 76.9 | 82.4 | 86.9 | 82.6 | 78.3 |

\*p value after adjusting for age and gender.

\*After adjustment for Charlson Comorbidity Index, the presence of DM, polypharmacy, dysphagia, dementia, depression, cerebrovascular disease, sarcopenia, dynapenia, and frailty, p value was still not significant (p> 0.05).

**4.DISCUSSION**

In the present study, it has been shown that there is no difference in older patients with malnutrition, the risk of malnutrition, or good nutrition in terms of serum vitamin B12 and folate levels, or the presence of vitamin B12 and folate deficiencies. BMI was also not shown to be an indicator for the two deficiencies. Additionally, vitamin B12 deficiency is quite common even in older adults with normal nutritional status or obesity.

Nutrients deficiencies, just like malnutrition, are related to a variety of clinical outcomes (2). One of the most common evaluated nutrients in older people is vitamin B12. Although there are many complications such as depression, cognitive impairment, sarcopenia, and functional disabilities related to vitamin B12 deficiency in older adults, it can be easily and effectively treated (9, 19, 21, 22). However, a significant proportion of the older population have low vitamin B12 status which is not detected (8). Nutritional factors including adequate daily intake of vitamins are important factors to maintain high serum micronutrient status or to prevent all untoward issues associated with the deficiency (23-25). For example, a study, by [Brouwer-Brolsma EM](https://www.ncbi.nlm.nih.gov/pubmed/?term=Brouwer-Brolsma%20EM%5BAuthor%5D&cauthor=true&cauthor_uid=26389945) et al, including 600 community-dwelling adults (≥65 years) showed that higher intakes of daily, meat, and fish and shellfish were significantly associated with higher serum vitamin B12 concentrations (26). In another study, it has been found that higher intakes of vitamin B12 from food can decrease depression risk among older adults (27). It has also been demonstrated that dietary intakes of vitamin B12 was significantly lower in subjects with low serum vitamin B12 than those with normal serum vitamin B12 in female older adults aged 85 and over (26). Considering these and similar findings, it has been suggested that the level of serum vitamin B12 may be affected by nutritional status and that vitamin B12 deficiency may be less common in patients with normal nutritional status, but until now there is no clear evidence in the literature.

In the present study, the results showed that deficiency were common even in older adults who were obese and had normal nutritional status. Several reasons could explain these results. Older adults are at an increased risk of vitamin B12 deficiency due to aging-related impaired absorption; chronic use of some medication appears to increase this risk, including the use of acid-lowering therapy and metformin. First, Proton pump inhibitors (PPIs) decrease gastric acid secretion, which is required to release protein-bound cobalamin and its absorption (28). Decreased acid secretion also increases the pH in the small intestine which lead to bacterial overgrowth and competition for uptake of vitamin B12, further reducing cobalamin availability (28). A recent study showing that the most common inappropriate drug use is PPI in elderly people in Turkey, which contributes this result (12). Second, metformin is first line therapy for type 2 diabetes and is more prone to vitamin B12 deficiency. In our study, DM frequency (34.2%) may be the cause of the deficiency (29). Third, increased helicobacter pylori and atrophic gastritis with age may induce food-cobalamin malabsorption, which cause vitamin B12 deficiency in spite of the normal nutritional status (30). Finally, some nutritional habits of Turkish people can explain that there is no relationship between malnutrition and vitamin deficiency: Higher carbohydrate intake (bread, rice, and vegetables), lower meat consumption, generally eating two meals a day, and preparing hot meals may lead to the deficiency of vitamin B12 (31). The results of a study of 97 older patients living in care homes also showed that malnutrition or the risk of malnutrition was not associated with vitamin B12 and folate deficiencies (16). For this reason, it can be said that metabolism of vitamin B12 and its serum level are influenced by many factors different from dietary intakes.

On the other hand, folate deficiency appears to be an important factor for neuropsychiatric diseases such as dementia, depression in the geriatric population, in spite of the fact that it is very rare (17, 32). Similar to vitamin B12, serum folate level is associated with several factors, including poor cooking techniques, drug–nutrient interactions, alcohol abuse, atrophic gastritis, intestinal diseases (Crohn’s disease, celiac disease) (17). Reduced dietary intake of folate plays a role in folate deficiency in older people due to the age-related alterations in sensory function, appetite, dysphagia and mastication impairments (17). Another explanation for this may be related to intestinal bacterial flora that is a significant source of vitamins such as biotin, cobalamin, folates, and nicotinic acid for human. The gut microbiota of older adults is characterized by a reduced bacterial diversity and beneficial microorganisms, and increased facultative anaerobic bacteria, which may lead to deterioration in synthesis of micronutrients (33). Some questions of MNA evaluating decreased food intake due to loss of appetite, digestive problems, chewing or swallowing difficulties, weight loss, and consumption of fruit or vegetables were shown to be able to be indicators of the deficiency. However, it has been demonstrated that nutritional status assessed by MNA or BMI does not depend on this. The result suggests that maintaining the folate status, like vitamin B12, in older adults is not only dependent on nutritional and weight status. Additionally, the prevalence of folate deficiency (< 3 ng/ml) was found in 0.9% of participants in our study, which is lower than the previous studies found (5–20%) (17). There is no clear data on folate intakes in different locations, but it may be speculated that since Turkey is one of the Mediterranean countries, the consumption of folate increases with greater Mediterranean Diet (34) or that some genetic polymorphisms may be responsible for this.

This study has many strengths. First, malnutrition and malnutrition-risk groups were assessed separately. Second, the sample size was large. Third, both nutritional status by MNA-long form and weight status by BMI were used to evaluate the patients. The research has some limitations. The most important one is that it was a cross-sectional study. Another limitation is that the number of patients with folate deficiency was so low that it was not able to be analyzed. Still another limitation is that vitamin B12 and folate levels were not assessed by homocysteine and methylmalonic acid, because elevated levels of methylmalonic acid and homocysteine are a much more sensitive diagnostic clue than a low serum B12 level in the diagnosis of vitamin B12 deficiency and homocysteine also is a determinant of folate status. Finally, 6.9% of patients were categorized as undernourished which may have influenced the present findings.

**Conclusion**

Vitamin B12 and folate levels are not associated with nutritional or weight status; thus the two should be evaluated independently of BMI and MNA values in older adults. It should be kept in mind that vitamin B12 deficiency is very common in older adults with normal nutritional status or obesity, like in patients with malnutrition.

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**References**

1. Wu C, Kim DH, Xue QL, Lee DSH, Varadhan R, Odden MC. Association of Frailty with Recovery from Disability among Community-Dwelling Older Adults: Results from Two Large U.S. Cohorts. J Gerontol A Biol Sci Med Sci. 2018.

2. Granic A, Mendonca N, Hill TR, Jagger C, Stevenson EJ, Mathers JC, et al. Nutrition in the Very Old. Nutrients. 2018;10(3).

3. Soysal P, Isik AT, Stubbs B, Solmi M, Volpe M, Luchini C, et al. Acetylcholinesterase inhibitors are associated with weight loss in older people with dementia: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2016;87(12):1368-74.

4. Soderstrom L, Rosenblad A, Thors Adolfsson E, Bergkvist L. Malnutrition is associated with increased mortality in older adults regardless of the cause of death. The British journal of nutrition. 2017;117(4):532-40.

5. Visvanathan R, Newbury JW, Chapman I. Malnutrition in older people--screening and management strategies. Australian family physician. 2004;33(10):799-805.

6. Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition (Burbank, Los Angeles County, Calif). 1999;15(2):116-22.

7. Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition - An ESPEN Consensus Statement. Clinical nutrition (Edinburgh, Scotland). 2015;34(3):335-40.

8. Porter K, Hoey L, Hughes CF, Ward M, McNulty H. Causes, Consequences and Public Health Implications of Low B-Vitamin Status in Ageing. Nutrients. 2016;8(11).

9. Ng TP, Feng L, Niti M, Kua EH, Yap KB. Folate, vitamin B12, homocysteine, and depressive symptoms in a population sample of older Chinese adults. J Am Geriatr Soc. 2009;57(5):871-6.

10. Cook Z, Kirk S, Lawrenson S, Sandford S. Use of BMI in the assessment of undernutrition in older subjects: reflecting on practice. The Proceedings of the Nutrition Society. 2005;64(3):313-7.

11. Bird JK, Ronnenberg AG, Choi SW, Du F, Mason JB, Liu Z. Obesity is associated with increased red blood cell folate despite lower dietary intakes and serum concentrations. The Journal of nutrition. 2015;145(1):79-86.

12. Unutmaz GD, Soysal P, Tuven B, Isik AT. Costs of medication in older patients: before and after comprehensive geriatric assessment. Clinical interventions in aging. 2018;13:607-13.

13. Dokuzlar O, Soysal P, Usarel C, Isik AT. The evaluation and design of a short depression screening tool in Turkish older adults. Int Psychogeriatr. 2018;30(10):1541-8.

14. Ates Bulut E, Soysal P, Aydin AE, Dokuzlar O, Kocyigit SE, Isik AT. Vitamin B12 deficiency might be related to sarcopenia in older adults. Experimental gerontology. 2017;95:136-40.

15. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-56.

16. Nuttall FQ. Body Mass Index: Obesity, BMI, and Health: A Critical Review. Nutr Today. 2015;50(3):117-28.

17. Araujo JR, Martel F, Borges N, Araujo JM, Keating E. Folates and aging: Role in mild cognitive impairment, dementia and depression. Ageing Res Rev. 2015;22:9-19.

18. Bozoglu E, Isik AT, Doruk H, Kilic S. The Effects of Early Vitamin B12 Replacement Therapy on The Cognitive and Functional Status of Elderly Subjects. Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology. 2010;20(2):120-4.

19. Langan RC, Zawistoski KJ. Update on vitamin B12 deficiency. Am Fam Physician. 2011;83(12):1425-30.

20. Araujo DA, Noronha MB, Cunha NA, Abrunhosa SF, Rocha AN, Amaral TF. Low serum levels of vitamin B12 in older adults with normal nutritional status by mini nutritional assessment. Eur J Clin Nutr. 2016;70(7):859-62.

21. Vidal-Alaball J, Butler CC, Cannings-John R, Goringe A, Hood K, McCaddon A, et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Database Syst Rev. 2005(3):CD004655.

22. Soysal P, Turan Isik A. Vitamin B12 deficiency can be a cause of acute reversible parkinsonism and cognitive impairment in older adults. Geriatrics & gerontology international. 2018;18(4):650-1.

23. Laird E, Casey MC, Ward M, Hoey L, Hughes CF, McCarroll K, et al. Dairy Intakes in Older Irish Adults and Effects on Vitamin Micronutrient Status: Data from the TUDA Study. J Nutr Health Aging. 2017;21(9):954-61.

24. van Dijk M, Dijk FJ, Hartog A, van Norren K, Verlaan S, van Helvoort A, et al. Reduced dietary intake of micronutrients with antioxidant properties negatively impacts muscle health in aged mice. J Cachexia Sarcopenia Muscle. 2018;9(1):146-59.

25. Struijk EA, Lana A, Guallar-Castillon P, Rodriguez-Artalejo F, Lopez-Garcia E. Intake of B vitamins and impairment in physical function in older adults. Clinical nutrition (Edinburgh, Scotland). 2018;37(4):1271-8.

26. Brouwer-Brolsma EM, Dhonukshe-Rutten RA, van Wijngaarden JP, Zwaluw NL, Velde N, de Groot LC. Dietary Sources of Vitamin B-12 and Their Association with Vitamin B-12 Status Markers in Healthy Older Adults in the B-PROOF Study. Nutrients. 2015;7(9):7781-97.

27. Gougeon L, Payette H, Morais JA, Gaudreau P, Shatenstein B, Gray-Donald K. Intakes of folate, vitamin B6 and B12 and risk of depression in community-dwelling older adults: the Quebec Longitudinal Study on Nutrition and Aging. Eur J Clin Nutr. 2016;70(3):380-5.

28. Maes ML, Fixen DR, Linnebur SA. Adverse effects of proton-pump inhibitor use in older adults: a review of the evidence. Therapeutic advances in drug safety. 2017;8(9):273-97.

29. Kancherla V, Elliott JL, Jr., Patel BB, Holland NW, Johnson TM, 2nd, Khakharia A, et al. Long-term Metformin Therapy and Monitoring for Vitamin B12 Deficiency Among Older Veterans. J Am Geriatr Soc. 2017;65(5):1061-6.

30. Kalkan C, Karakaya F, Tuzun A, Gencturk ZB, Soykan I. Factors related to low serum vitamin B12 levels in elderly patients with non-atrophic gastritis in contrast to patients with normal vitamin B12 levels. Geriatrics & gerontology international. 2016;16(6):686-92.

31. Paker-Eichelkraut HS, Bai-Habelski JC, Overzier S, Strathmann S, Heseker H, Stehle P, et al. Nutritional status and related factors in elderly nursing home residents: comparative cross-sectional study in migrants and native Germans. J Nutr Gerontol Geriatr. 2013;32(4):330-42.

32. Soysal P, Isik AT, Ugur A, Kazancioglu R, Ergun F, Babacan Yildiz G. Vitamin B12 and folic acid levels are not related to length of stay in elderly inpatients. Nutrition (Burbank, Los Angeles County, Calif). 2013;29(5):757-9.

33. Morowitz MJ, Carlisle EM, Alverdy JC. Contributions of intestinal bacteria to nutrition and metabolism in the critically ill. The Surgical clinics of North America. 2011;91(4):771-viii.

34. Feart C, Alles B, Merle B, Samieri C, Barberger-Gateau P. Adherence to a Mediterranean diet and energy, macro-, and micronutrient intakes in older persons. Journal of physiology and biochemistry. 2012;68(4):691-700.