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ORIGINAL ARTICLE

The Relationship between Serum Vitamin B12 and Glycemic Indices, BMI, and Dietary Components in Elderly

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ABSTRACT

Background: Vitamin B12 plays an important role in many metabolic pathways, obesity, and insulin resistance and the elderly as a high-risk group are prone to its deficiency. In this regard, this study investigated the relationship between serum vitamin B12 and glycemic indices, dietary components and body mass index (BMI) in elderly population.

Methods: In a cross-sectional study, ninety elderly aged 65 years and older from an senior center were enrolled. After completing the demographic questionnaire and assessing BMI, 5 mL blood sample was provided to measure serum vitamin B12, insulin and blood glucose levels. On the other hand, the vitamin B12 content of the diet was extracted from the food frequency questionnaire (FFQ).

Results: About 58% of the elderly had serum vitamin B12 levels below normal. There was a significant correlation between low vitamin B12 levels, body weight and BMI. Furthermore, the relationship between low serum vitamin B12 level and fasting blood glucose level was also significant ($p<0.05$). FFQ results indicated a significant relationship between serum vitamin B12 level and the amount of different types of meat and eggs.

Conclusion: The favorable level of vitamin B12 was shown to play a role in hyperglycemia control and to reach a normal weight.

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Introduction

Similar to other communities around the world, the Iranian population experience aging too. Currently, the over 60-year old people in Iran constitute 8% of the population with approximately 5.5 million people. By continuation of this trend in late 2031, aging will reach its peak in Iran, and between 25 and 30 percent of the population would be 50 years or older (1). So today, there is a greater need for health care of the elderly population (2). Inappropriate nutritional status of the elderly, as the fundamental risk factor for many of the diseases, such as osteoarthritis, diabetes, insulin resistance, heart and vascular diseases, metabolic syndrome, hypertension, depression, Alzheimer's, and neurodegenerative disorders would imposes huge financial burden on governments, causing many problems in the economy, health and social spheres (3-5).

As we age, low food intake and malabsorption disorders lead to a decrease in nutrient levels. On the other hand, as the age increases, the sensitivity to taste and odor decreases; hence, food intake is impaired. Most studies have shown that a large proportion of people over the age of 60 have an asymptomatic gastritis with atrophy. Stomach hypochlorites and excessive colonization of intestinal bacteria also plays an important role in reducing nutrient storage (6). Nutrient deficiency including vitamin B12 amongst the elderly population in poor communities is more than 20 percent, especially in people older than 65 years; but in most cases, the symptoms of clinical diagnosis is not obvious (7, 8). These statistics in Iran are reported higher than other areas, where the elderly over 65 years old were at risk of vitamin B12 deficiency is 56-93 percent (9).

Vitamin B12 deficiency, as a nutrient that affects human health, leads to a wide range of disorders (10). This vitamin, which plays a role in DNA methylation, lipid metabolism, neuronal function, blood cell production, enzymatic activity, and the conversion of homocysteine to methionine, is obtained only from animal sources and enriched foods (11-14). On the other hand, the role of this vitamin in single-carbon cycles can control the risk of diabetes and obesity and it is worth noting that vitamin B12 deficiency is more prevalent among people with type 2 diabetes who have high BMI (15). Furthermore, as previous studies showed, obese children and adults had lower levels of vitamin B12 and vitamin B12 deficiency was inversely associated with insulin resistance in polycystic ovary syndrome (PCOS) (16-18).

The elderly is a high-risk group prone to deficiency of vitamin B12, and as far as we know, no study on the association of serum vitamin B12, glycemic components and BMI in elderly has been conducted. Hence, this study aimed to investigate the relationship between serum vitamin B12 with glycemic indices, BMI and dietary components amongst the elderly population, so that in future we can improve metabolic complications by correcting vitamin B12 deficiency.

Materials and Methods

In this cross-sectional study, 90 elderlies (15 males, 75 females) over 60 years old from the retirement center of Jahandidegan, Shiraz, Iran were recruited. The sampling was conducted since November, 2016 for three months, by simple sampling method after obtaining informed consent from the individuals. This study was approved by the Local Ethics Committee (10646-21-01-94). All the study steps were performed in accordance with the Helsinki Declaration. Entry criteria included not taking metformin and proton pump inhibitors, the absence of acute renal (CKD 3-5) and the liver (Final stage) diseases, no history of gastrointestinal surgery, no long-term intake of vegetarian diet and vitamin supplementation. The sample size was determined using the following formula (z_α=1/96, z_β=0.8, r=0.25), which according to the limitations, 90 people entered the study.

$$N=\left(\frac{z_\alpha+z_\beta}{C(r)}\right)^2+3$$

The qualified individuals completed 2 demographic and food frequency questionnaires (FFQ). The demographic information and patient's health status was assessed. The FFQ was valid and reliable and contained 168 food items and food intake was recorded based on daily, weekly and monthly consumption (19), and then based on the dietary sources of vitamin B12, the amount of food items with high vitamin B12 content (egg, fish, tuna, poultry, red meat and dairy) and poor sources of vitamin B12 (soy bean and legumes) were extracted from the questionnaire and converted to grams by using the NUT IV software (First Databank, San Bruno, CA, USA), in order to assess the relationship between serum vitamin B12 and dietary content of this vitamin. Data collection was carried out by an expert in the field. Anthropometric measurements including weight and height were recorded using a Seca scale (Germany) with a precision of 0.1 kg and a soft type meter with a precision of 0.1 cm (20). Body mass index (BMI) was calculated by (weight (kg)/height^2 (meter)) formula (21).

Five mL blood sample was taken by a nurse after 8 hours of fasting. Serum levels of vitamin B12 were measured by ELISA method (LifeSpan BioSciences, USA). Based on a previous study (22), vitamin B12 concentration was categorized in elderly and serum level of B12 less than 220 pmol/L was considered as deficient, the borderline level as 221-258 pmol/L and normal level as greater than 258 pmol/L (22). Fasting blood sugar was measured by enzymatic kits (Pars Test, Tehran, Iran). After measuring the fasting insulin with ELISA kit (Monobind Inc, USA), insulin resistance was determined using the following formula (23): HOMA-ir={[Fasting insulin (μU/ml)]×[Fasting blood glucose (mmol/l)]}/22.5.

Data analysis was performed by SPSS software (version 22, Chicago, IL, USA). Pearson correlation coefficient was used to determine the relationship between B12 level and insulin resistance, anthropometric indices and items obtained from NUT4 software. P<0.05 was considered to be statistically significant. At the end of the study, the recommendations to reach normal body weight and sufficient serum level of vitamin B12 (including food sources of vitamin B12) were given to participants by a nutritionist.

Results

Ninety elderly aged ≥60 (mean age 68.75±5.98 years) with an average weight of 65.08±9.48 kg and average BMI of 25.60±2.95 kg/m^2 were enrolled. Eighty-three percent of participants were female, while 44 percent were single (Table 1). The mean serum level of vitamin B12 between participants was 215 pmol/L, and according to vitamin B12 categorization, 58 percent of the elderly showed vitamin B12 serum levels below normal (≤220 pmol/L) and 33 percent had sufficient serum level of vitamin B12. There was a significant correlation between vitamin B12 level, weight and BMI (P<0.05) with a correlation coefficient -0.289 and -0.336 (Table 2).

Furthermore, correlation between serum vitamin B12 level and fasting blood glucose were also significant (P<0.05) with correlation coefficient of -0.332 (Table 3). FFQ showed that there was a significant correlation between serum vitamin B12 level and the amounts of egg, fish and tuna, poultry, red meat intakes (P<0.05). There was no significant correlation between vitamin B12 serum level, dairy, soybeans and legume intakes extracted from FFQ (Table 4).

Discussion

The present study showed that high percent of elderly population had low serum B12 and there was a significant correlation between serum vitamin B12 level, weight, BMI and fasting blood sugar. In addition, the results showed that there was a significant relationship between serum vitamin B12 and the consumption of red meat, poultry, fish and egg. It has been widely shown that inadequate nutritional intake of dietary foods during ageing not only develops chronic diseases such as cardiovascular diseases, osteoporosis or psychiatric disorders, but can also lead to acute illnesses such as infections. Given this background, in the past two decades, numerous studies have been conducted to assess the adequacy of nutrients amongst the elderly (24).

In the elderly, cobalamin deficiency is caused by inadequate consumption of foods containing cobalamin or pernicious anemia and it was shown that malabsorption of cobalamin causes 60-70% of cases of vitamin B12 deficiency in the elderly (8). Although various evidences consider normal serum cobalamin about 150 pmol/L, the preferred threshold in the elderly is raised to 220-258 pmol/L (22). As

Table 1: Characteristics of participants (n=90).

Variable	Mean±SD OR percent
Sex (% female)	83.33
Marital status (% single)	44.44
Age (years)	68.75±5.98
Weight (kg)	65.08±9.48
BMI (kg/m^2)	25.60±2.95

BMI: body mass index. Data are expressed as mean±standard deviation or percent

Table 2: Vitamin B12 serum level in the elderly population.

Serum vitamin B12 level (pmol/L)	Percent % (n)
Less than 220	57.78 (52)
221-258	8.89 (8)
Higher than 258	33.33 (30)

Table 3: The relation between serum vitamin B12, B12 content of diet, BMI, fasting blood glucose, insulin and HOMA-IR index.

Variable	Vitamin B12 content of diet (mcg)		BMI (kg/m^2)		Weight (kg)		FBS (mg/dl)		Insulin (mU/ml)		HOMA-IR	
Serum B12 level (pmol/L)	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
	0.038	0.776	-0.336	0.001	-0.289	0.006	-0.332	0.001	-0.151	0.158	0.042	0.671

BMI: Body mass index, FBS: Fasting blood sugar, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance. P<0.05 was considered to be statistically significant

Table 4: The Relation between serum vitamin B12 level and the intake of egg, fish, poultry, red meat, dairy, and legumes.

Variable	Egg (g)		Fish and tuna (gr)		Poultry (g)		Red meat (g)		Dairy (g)		Soy bean and legumes (g)	
Serum vitamin B12 level (pmol/L)	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*	r	*P*
	0.241	0.015	0.293	0.002	0.442	0.005	0.586	0.001	0.154	0.137	0.162	0.136

P<0.05 was considered to be statistically significant the results of the present study showed, the average serum levels of vitamin B12 were 215 pmol/L and 58% of the participants had insufficient vitamin B12 levels. A study undertaken by Joosten et al. showed that 5% of the elderly population had low serum levels of vitamin B12, while 39 and 60 percent of the population had increased levels of methyl malonic acid and homocysteine, respectively (25). In addition, the study done by Fakhrzadeh et al. in Iran, about 24% of the population aged 25-64 years suffered from vitamin B12 deficiency. Moreover, 66% of men, and 33% of women had hyperhomocysteinemia (26).

Based on the results of this study, the serum level of vitamin B12 did not significantly correlate with vitamin B12 content of diet in total. As the age increases, the risk of developing gastric atrophy and *Helicobacter pylori* might disrupt the absorption of vitamin B12, which is likely to justify the results of this study (27). *H. pylori* as an organism to be responsible in induction of gastritis and ulcers, that causes destruction of parietal cells and impairs production of intrinsic factor and vitamin B12 absorption. As Sarari and colleagues showed in their study, 67.4 percent of patients with B12 level lower than 200 pg/ml had positive *H. pylori* test (28).

Our results showed that vitamin B12 had an inverse relationship with fasting blood sugar, but no significant correlation with insulin level and HOMA-IR was noted. In line with our results, Pappa et al. indicated that vitamin B12 deficiency had no significant correlation with BMI and glycemic indices in women with gestational diabetes mellitus (GDM) (29). Although previous studies showed that vitamin B12 deficiency is correlated with dyslipedimia in diabetes mellitus (30), we cannot mention a specific mechanism for its effect on glycemic indices. The activation of methylene tetrahydrofolate reductase (MTHFR) enzyme is important for the metabolism balance by converting 5, 10-methylenetetrahydrofolate to 5-methyltetrahydrofolate. The mutation in MTHFR gene and conversion of number 677 nucleotide from C to T results in reduction of enzyme activity, homocysteine accumulation that further increases the risk of metabolic syndrome, type 2 diabetes and cardiovascular diseases (31, 32).

On the other hand, lower level of vitamin B12 is more prevalent among those with TT genotype and is associated with higher homocysteine level. Hence, low levels of vitamin B12 may increase the risk of metabolic syndrome and cardiovascular diseases. In this regard, in a study conducted by Chen et al. illustrated that the TT genotype of methylene tetrahydrofolate reductase gene was associated with insulin resistance by increasing CRP and UA levels and reducing serum B12 levels (32). Another animal study by Sianipar et al. showed that rats with vitamin B12 deficiency had significantly higher levels of glucose and homocysteine when compared to the control group (33). Moreover, Jayashri et al. demonstrated that vitamin B12 deficiency was associated with severity of glucose tolerance (34).

According to the results, vitamin B12 serum level had an inverse relationship with BMI. As shown in Hamiel et al.'s study, vitamin B12 concentration was lower in obese patients. Vitamin B12 deficiency can be due to abnormal absorption, gastric acid secreting drugs, mucosal disorders such as Crohn's and celiac disease, pernicious anemia and *Giardia lamblia* infection. Another factor can be the increased need for this vitamin with weight gain (18). Also a study by Baltaci et al. indicated the association of low vitamin B12 level with BMI in obese and overweight participants, but not with insulin resistance (35).

Other proposed mechanisms associated with vitamin B12 deficiency in obese people mentioned in study of krishnaveni et al. was reduction in absorption or intake of food, increased catabolism, and secretion of vitamin B12 in adipose tissue. Eating low-quality food that is high in energy, but low in nutrients might increase fat and decrease vitamin B12 levels, which can be amplified by ageing (36). Inadequate intake of high quality foods leads to lack of vitamins, which is associated with obesity. Most vitamins in the obese group have lower levels, including fat-soluble vitamins, B9, B12 and C. Adipose tissue is considered to be a metabolic and endocrine organ affecting homeostasis, and vitamin deficiency can worsen the pathological conditions of obese people (37).

On the other hand, vitamin B12 deficiency may affect body composition by trapping 5-methyltetrahydrofolate, which results in inhibition of methionine generation from homocysteine, following protein synthesis decrement and deposition of lean tissue (16). Furthermore, cellular inflammation by low concentration of vitamin B12 could affect adipocyte dysfunction. Moreover, gut microbiota conversion due to obesity might worsen vitamin B12 metabolism (17). In this regard, Allin et al. showed that lower vitamin B12 level was associated with increased BMI (38). Also, Gunanti et al. reported an inverse association between vitamin B12 status and body adiposity in children (39).

The results of our study indicated that serum vitamin B12 level had a significant positive correlation with the level of red meat, poultry, fish and eggs in the diet, but without any relationship to the legumes. Based on a previous study, animal sources (meat, milk, eggs, fish and shellfish) were the main sources of cobalamine, but plant foods were not considered as available sources of vitamin B12. However, some herbs such as algae or blue algae (synobacteria) contained a lot of vitamin B12 (40) which was not common in our dietary pattern .

The limitations of this study included the lack of blood markers measurement, including methyl malonic acid and homocysteine, which are more sensitive to lack of vitamin B12, but need expensive kits to measure. On the other hand, lack of cooperation amongst the elderly population was another limitation. Additionally, due to the nature of our study, it was impossible to determine the causal relationship. Considering the results of this study and the role of vitamin B12 in metabolic pathways, it is suggested that in future studies, the relationship between serum vitamin B12 level and body fat mass to be investigated.

Conclusion

The results of this study showed that optimal level of vitamin B12 might play a role in glycemic control, and normal weight results. Therefore, it is advised to consume food sources that contain vitamin B12, including meat and dairy groups, which might affect the serum level of vitamin B12 and its related metabolic pathways.

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Conflict of Interest

None declared.

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