

The evaluation of relation between vitamin B12 and body mass index

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ABSTRACT

Objectives: Obesity has become a pandemic all around the world, etiology of obesity consists multiple factors and it causes serious health problems. It is known that the low level of vitamin B12 has adverse effects on many systems, mainly cell DNA. In our study, it was planned to evaluate whether there is a relation between body mass index and serum vitamin B12 level.

Methods: We included 168 patients aged 18-67 years, who did not have a chronic disease and who applied to the outpatient clinic in our center. We divided the patients into 3 groups according to the body mass index (BMI): Group I: normal weight (BMI: 18.50-24.99 kg/m²); Group II: overweight (BMI: 25-29.9 kg/m²) and Group III: obese (BMI: ≥ 30 kg/m²). Vitamin B12 levels were evaluated between these groups.

Results: There was a statistically significant difference between the groups in terms of glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride. Vitamin D levels were not statistically significant between the groups. The mean serum vitamin B12 levels of the individuals were 299 ± 125 pmol/L, 298 ± 148 pmol/L and 313 ± 143 pmol/L in Group I, Group II and Group III, respectively. There was no statistically significant difference and correlation between BMI and serum vitamin B12 levels in the groups.

Conclusions: The etiology of obesity, a serious health problem in today's society, has proven to be multifactorial. No significant association was found between BMI and vitamin B12 levels at the end of the study. It was concluded that similar studies should be performed with a large case series.

Keywords: vitamin B12, cobalamin, obesity, body mass index

Obesity, which is one of the most important health problems of the developed and developing countries in the world today, is a chronic energy metabolism disorder which is caused by excess fat accumulation in the body and can cause physical and mental problems [1]. Obesity is a complex disease involving appetite regulation and energy metabolism, not a simple eating problem due to lack of autocontrol [2]. Psychological, hormonal, metabolic disorders and

pharmacological factors play a role in the formation of obesity, as well as various environmental factors that trigger genetic predisposition and impaired energy balance [3].

The endocrine, cardiovascular, respiratory, gastrointestinal, genitourinary and musculoskeletal system and skin, as well as psychosocial state are affected by obesity at varying rates. In addition, studies have shown that obesity leads to various diseases such as

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malignancy (breast, over and endometrium in women, colon and prostate in men), gout, stroke and depression [4]. Many methods of measurement are used in the evaluation of obesity. Among these, the body mass index (BMI), which is practical in clinical practice, was first described by Quetelet in 1835 and is now the most commonly used method [5].

Vitamin B12 acts as an important coenzyme and cofactor in the synthesis of deoxyribonucleic acid (DNA) and is necessary for the maintenance of normal hematopoiesis and for the continuity of the nervous system [6]. Clinical findings are rare in vitamin B12 deficiency; however, hematologic, neuropsychiatric and gastrointestinal signs and symptoms are most frequently seen [7]. The prevalence of vitamin B12 deficiency in the whole population is not fully understood but it is known that the incidence of vitamin B12 deficiency increases with age. It is frequently seen in about 10-15% over the age of 60 [8, 9].

Many studies have shown that the etiology of obesity, a public health problem on a global scale, is multifactorial. It is known that the low level of vitamin B12 has adverse effects on many systems, mainly cell DNA. In our study, it was planned to evaluate whether there is a relation between body mass index and serum vitamin B12 level.

METHODS

We included 168 patients aged 18-67 years, who did not have a chronic disease and who applied to the outpatient clinic in our center from January 2015 to December 2016. Exclusion criterias were rheumatoid arthritis, ankylosing spondylitis, collagen tissue disease, celiac, hypo-hyperthyroidism, hematologic disease, malignancy, leukemia, lymphoma, malnutrition, malabsorption, and active infection. We also excluded patients previously treated with vitamin B12 and immunosuppressive drug. Written consent of the study participants, and ethics committee approval from our center were obtained. We divided the patients into 3 groups according to the BMI: Group I: normal weight (BMI: 18,50-24,99 kg/m²); Group II: overweight (BMI: 25-29.9 kg/m²) and Group III: obese (BMI: \geq 30 kg/m²).

Complete blood counts were obtained with tubes containing ethylenediaminetetraacetic acid (EDTA)

and examined with the Bt pro 2401 instrument. Biochemical measurements were determined by using a biochemical analyzer for serum glucose and lipid panel Cobas 6000 C501 (Roche Diagnostics GmbH, Mannheim, Germany) in blood samples taken after at least 12-14 hours of fasting. Serum vitamin D and vitamin B12 levels were determined by the Cobas e 411 (Roche Diagnostics GmbH, Mannheim, Germany) analyzer. The normal range of serum vitamin B12 was accepted as 200-800 pg/mL.

The height and weight of the subjects were measured to calculate BMI. Weight of the subjects was measured in the upright position after 12-14 hours of fasting. Height measurement of the subjects was made by measuring the distance from the head to the base, ensuring that the subjects were standing upright, with their feet naked and adjacent. BMI was calculated based as weight in kilograms divided by the square of the height in metres (kg/m²).

Statistical Analysis

Statistical analyzes were performed using the SPSS 24.0 program (SPSS Inc. Chicago, IL). The normal distribution of the variables was tested by Kolmogorov smirnov and the variance equation by the Levene test. All analyzes were performed by parametric tests, since the data were normally distributed. Continuous variables were expressed as mean \pm standard deviation, and categorical variables as percent. Independent-Samples T-Test for numerical variables and Chi square test for categorical variables were used to compare group averages. The relationship between BMI and biochemical parameters was assessed by Pearson correlation analysis. Parameters that were statistically significant in binary comparisons were included in the multivariate model. The results were evaluated in a confidence interval of 95% and a significance level of $p < 0.05$.

RESULTS

Of the 168 individuals included in the study, 125 (66.1%) were females and 43 (33.9%) were males. The average age is 37.6 ± 8.8 years. In all the subjects studied, the mean height was 166.0 ± 8 cm and the mean BMI was 27 ± 6.5 kg/m². The patients were divided into 3 groups according to the BMI and 77

Table 1. Comparison of age, height, weight and BMI of groups

Variables	Group I (n = 77)	Group II (n = 35)	Group III (n = 56)	p value
Age (year)	27 ± 10	40 ± 12	46 ± 11	< 0,001
Height (cm)	164 ± 7	168 ± 8	164 ± 8	0.034
Weight (kg)	57 ± 8	78 ± 8	94 ± 17	< 0.001
BMI (kg/m ²)	21 ± 2	28 ± 2	35 ± 5	< 0.001

patients, 35 patients and 56 patients were included in to the Group I (normal weight), Group II (overweight) and Group III (obese), respectively. When the cases grouped according to BMI were examined according to age; the mean age of the individuals in Group I was 27 ± 10 years, the mean age of individuals in Group II was 40 ± 12 years and the mean age of individuals in Group III was 46 ± 11 years. There was a statistically significant difference in age between groups ($p < 0.001$) (Table 1).

When the groups were examined according to the serum glucose levels, the mean serum glucose level of the individuals was 90 ± 8 mg/dL, 96 ± 10 mg/dL, and 103 ± 14 mg/dL in Group I, Group II and Group III, respectively. There was a statistically significant difference between the groups in terms of serum glucose level ($p < 0.001$) (Table 2).

When the groups were examined according to the mean serum total cholesterol level, mean total

cholesterol levels were 162 ± 32 mg/dL in Group I, 193 ± 45 mg/dL in Group II and 195 ± 43 mg/dL in Group III. Mean serum LDL-cholesterol levels; 93 ± 24 mg/dL in Group I, 120 ± 36 mg/dL in Group II and 122 ± 37 mg/dL in Group III. When the groups were examined according to the mean HDL-Cholesterol level, mean HDL cholesterol levels were detected 54 ± 12 mg/dL in group I, 48 ± 13 mg/dL in group II and 46 ± 12 mg/dL in group III. Mean serum triglyceride levels were 81 ± 30 mg/dL in Group I, 135 ± 97 mg/dL in Group II and 138 ± 68 mg/dL in Group III. There was a statistically significant difference between the groups in terms of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglyceride ($p < 0.001$) (Table 2).

When the serum vitamin D levels of the groups were examined, the mean serum vitamin D level of the individuals was 12 ± 11 ng/mL, 13 ± 5 ng/mL and 13 ± 7 ng/mL in Group I, Group II and Group III,

Table 2. Comparison of glucose and lipid levels of groups

Parameters	GROUP I (n = 77)	GROUP II (n = 35)	GROUP III (n = 56)	p value
Glucose (mg/dL)	90 ± 8	96 ± 10	103 ± 14	< 0.001
Total Cholesterol (mg/dL)	162 ± 32	193 ± 45	195 ± 43	< 0.001
LDL-Cholesterol (mg/dL)	93 ± 24	120 ± 36	122 ± 37	< 0.001
HDL-Cholesterol (mg/dL)	54 ± 12	48 ± 13	46 ± 12	< 0.001
Triglyceride (mg/dL)	81 ± 30	135 ± 97	138 ± 68	< 0.001

Table 3. Comparison of serum vitamin D levels in groups

Variables	Group I (n = 77)	Group II (n = 35)	Group III (n = 56)	p value
BMI (kg/m ²)	21 ± 2	28 ± 2	35 ± 5	0.750
Vitamin D (ng/mL)	12 ± 11	13 ± 5	13 ± 7	

Table 4. Comparison of serum vitamin B12 levels in groups

Variables	Group I (n = 77)	Group II (n = 35)	Group III (n = 56)	p values	r values
BMI (kg/m ²)	21 ± 2	28 ± 2	35 ± 5	0.430	0.014
Vitamin B12 (pmol/L)	299 ± 125	298 ± 148	313 ± 143		

respectively. There was no statistically significant difference in serum vitamin D levels between the groups ($p = 0.750$) (Table 3).

The mean serum vitamin B12 levels of the individuals in Group I were 299 ± 125 pmol/L, the mean serum vitamin B12 levels of the individuals in Group II were 298 ± 148 pmol/L and the mean serum vitamin B12 levels of the individuals in Group III were 313 ± 143 pmol/L. There was no statistically significant difference and correlation between BMI and serum vitamin B12 levels in the groups ($p = 0.430$, $R = 0.014$) (Table 4) (Fig. 1).

DISCUSSION

Obesity is a multifactorial and complex disease that is the result of interaction of genetic and environmental factors [10]. The main risk factors for obesity development are; decreased physical activity, wrong eating habits, increasing age, being female, number of births, marriage, smoking and alcohol intake. Reasons for the progressive increase in obesity, a decrease in activity due to sedanter's lifestyle and an increase in fast food-style eating habits and excessive calorie intake [3].

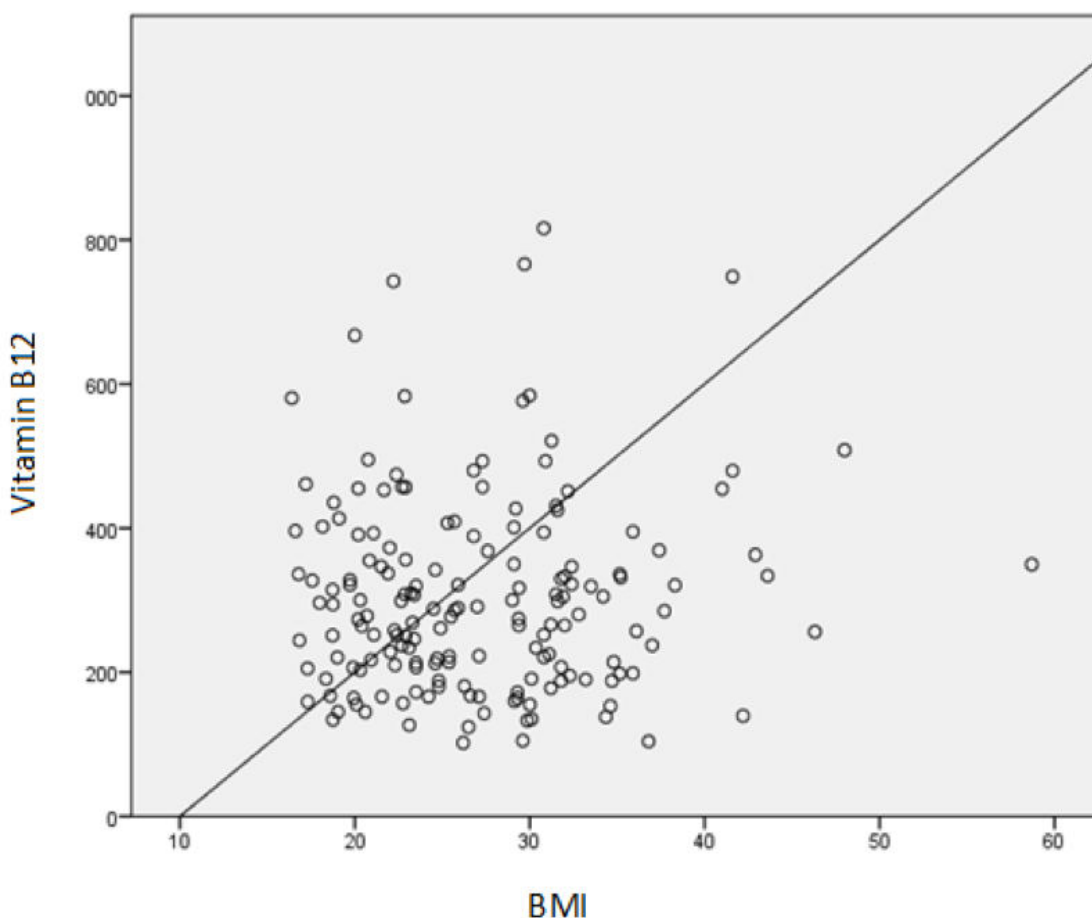


Fig. 1. Correlation of BMI and serum vitamin B12 levels.

In some studies evaluating the relation of obesity with age, an increase in obesity was observed with increasing age [11]. In a study conducted by Lagunova *et al.* [12], in which 2126 subjects were included, a significant relationship was found between BMI and age. In another study conducted by Akman *et al.* [13], it was observed that the prevalence of obesity increased in parallel with the increase in age up to the age of 60. Similar to these studies, there was a statistically significant difference between the groups in terms of the age groups grouped according to BMI ($p < 0.001$).

Many studies have shown that abdominal fat tissue accumulation, an indicator of obesity, is associated with atherogenic and diabetic disorders such as insulin resistance, hyperinsulinemia, glucose intolerance, dyslipoproteinemia, and hypertension. The relative risk of diabetes mellitus increases up to 60.9% when BMI exceeds 35 kg/m² [14]. It is thought that the duration of obesity and its type, that is, central type fat accumulation, is more effective in the development of diabetes mellitus and glucose intolerance than the degree of obesity [15, 16]. A study conducted by Kutlutürk *et al.* [17] investigated the relationship between obesity and metabolic risk factors and found a significant relationship between obesity and fasting serum glucose levels. Innocent *et al.* [18] found a positive but weak correlation between BMI and serum glucose level in their studies. Similar to these studies, in our study, there was a statistically significant difference in serum glucose levels between the subjects grouped according to BMI ($p < 0.001$).

Obesity causes adverse changes in lipid metabolism. These include high total cholesterol, LDL-cholesterol, VLDL-cholesterol, triglyceride levels and low HDL-cholesterol. HDL-cholesterol levels were 5% lower in obese subjects [19]. In general, in obese subjects, fasting plasma triglyceride values tend to increase and plasma HDL-cholesterol levels tend to decrease [20]. In a study conducted by Faheem *et al.* [21], a total of 2,270 patients were included in the study, and a positive correlation was found between the BMI and cholesterol parameters. In our study, when the cases were grouped according to BMI, there was a negative correlation between BMI and total cholesterol, LDL-cholesterol and triglyceride, and a negative correlation between BMI and HDL-cholesterol.

Low vitamin D levels have been demonstrated in many studies involving obesity, diabetes mellitus, and the metabolic syndrome. This relationship is explained by the demonstration of vitamin D receptor (VDR) expression in fat tissue, the solubility of vitamin D in fat and its storage in fat tissue. However, vitamin D has been shown to play a role in the modulation of insulin production and secretion in animal studies, with a negative correlation between BMI and vitamin D levels. Active vitamin D has been shown to stimulate calcium exchange in pancreatic β cells and mouse models *in vitro*. There is strong evidence that vitamin D affects the release of insulin from β -cells of the pancreas, and that active vitamin D inhibits lipolysis and enhances lipogenesis by inhibiting uncoupling protein-2 protein in fat cells. In mice without VDR, it was reported that all fat mass decreased, serum leptin level decreased and energy consumption increased [22, 23].

There are, however, studies suggesting that there is no significant relationship between vitamin D levels and obesity. In Gronborg *et al.*'s study [24], it was observed that there was basically no relation between vitamin D level and body fat ratio, and body fat ratio did not respond to vitamin D supplementation. In our study, there was no statistically significant difference in serum vitamin D levels between the cases grouped according to BMI ($p = 0.750$). All of the groups in our study had vitamin D deficiency. It is thought that vitamin D deficiency in all groups is due to the fact that the geographical region where we are studying is high altitude, heavy winter climate, low sun light due to climate conditions and low exposure sunlight due to clothing style.

Vitamin B12, which plays a vital role in the functioning of many important molecules and hormones, especially in the production of DNA, which is essential for cell division and proliferation, is an important essential vitamin. It can not be synthesized in the human body and is abundant in proteins, especially those derived from animal origin. Approximately 6 micrograms per day should be taken [7]. It can be stored in small quantities in the body, 80% of which occurs in the liver. In the case of deficiency, it takes 3-4 years for clinical signs to appear in case of deficiency [25].

The prevalence of vitamin B12 deficiency in the world is not known precisely. However, it is generally

known that the incidence increases with age. In one study, vitamin B12 deficiency was detected in about 15% of people over 65 years of age. In general, the incidence of vitamin B12 deficiency in adults is 5-20% on average [8, 26, 27]. In a surveillance study in the United States; when the basal level of vitamin B12 was taken as 148 pmol/L, vitamin B12 deficiency was found in 3% between 20-39 years, 4% between 40-59 years and 6% over 60 years. In another study, vitamin B12 deficiency was found to be 14-16% between 20-59 years and 20% over 60 years when taking 221 pmol/L [28, 29].

Vitamin B12 is a cofactor in methionine synthesis from homocysteine [30]. Deficiency of vitamin B12 causes hyperhomocystinemia. Cohort studies have shown that even mild hyperhomocystinemia increases cardiovascular morbidity and mortality [31, 32]. Martos *et al.* [33] found that hyperhomocystinemia correlates with insulin resistance in obese prepubertal children [33]. Güven *et al.* [34] found low levels of vitamin B12 in patients with adult metabolic syndrome compared to normal healthy individuals. In another study, it was shown that homocysteine levels returned to normal range with folate and vitamin B12 treatment in patients with metabolic syndrome with low serum folate and serum vitamin B12 levels. It has been found that it has a positive effect on the recovery of insulin resistance and contributes to the regression of endothelial dysfunction [35].

In the study performed by Baltaci *et al.* [36], 680 female subjects aged 18-68 years were divided into two groups as obese and normal weight according to BMI and serum vitamin B12 level was found to be low in the group with high BMI. In this study, it was suggested that in obese individuals, vitamin B12 deficiency is independent of nutritional status. In the same study, there was no correlation between serum vitamin B12 levels and insulin resistance and visceral obesity [36]. In a study conducted by Ho *et al.* [37], a significant portion of obese adolescents bearing the risk of type 2 diabetes mellitus were found to have low or borderline serum vitamin B12. In addition, negative correlations were found between serum vitamin B12 levels and BMI in this study [37]. In a study conducted by Goyal *et al.* [38], authors reported that serum vitamin B12 deficiency was more common in the morbidly obese population. In another study, 995 women who were on the 28th week of their gestation

were included to the study and a 0.6% decrease in serum vitamin B12 was detected for every 1% increase in BMI. However, the differences in socioeconomic status, the presence of vitamin supplements or vegetarian diet-style nutrition, the number of parities and the lack of full exclusion of hemodilution due to pregnancy were the the limitation of the study [39].

In a study, 228 normal weight and 164 obese participants included to the study and serum vitamin B12 levels were found to be low in 10.4% of the obese participants and only 2.2% of the participants with normal weight [40]. The authors explained that the reason for this that the nutritional content of obese individuals is low in terms of vitamin B12 despite being rich in terms of carbohydrate and fat [40]. In another study, serum vitamin B12 levels were examined in adolescents between 10 and 17 years of age with clinical features of pre-diabetes and/or insulin resistance [41]. In adolescents with serum vitamin B12 level ≤ 221 pmol/L, BMI was higher and gender difference was not observed. It was emphasized that this low level was caused by low vitamin B12 in the nutritional content [41]. Vitamin B12 plays an important role in DNA methylation. Recent genomic analysis has suggested that increased DNA methylation is associated with increased BMI in adults [42].

On the other hand, in a study involving Brazilian overweight adolescents, serum vitamin B12 concentrations were compared with BMI and no significant difference was found [43]. In the study conducted by Reitman *et al.* [44], there was no statistically significant difference in the levels of serum vitamin B12 in patients overweight and obese compared to those in normal weight. Abu-Samak *et al.* [45] found that the mean serum vitamin B12 level was low in overweight (BMI = 25-29.9 kg/m²), but there was no decrease in vitamin B12 levels in obese (BMI ≥ 30 kg/m²). El-Quadah *et al.* [46] observed that serum vitamin B12 levels increased as the BMI increased for the subjects included in the study.

In our study, when the serum vitamin B12 levels of the cases grouped according to BMI were examined, serum vitamin B12 levels of the individuals in Group I were 299 ± 125 pmol/L, serum vitamin B12 levels of the individuals in Group II were 298 ± 148 pmol/L serum vitamin B12 levels of the individuals

were 313 ± 143 pmol/L. There was no statistically significant difference in serum vitamin B12 levels between the groups. Statistical analysis of serum vitamin B12 and BMI did not reveal significant association ($p = 0.430$, $R = 0.014$).

CONCLUSION

As a result, the etiology of obesity, a serious health problem in today's society, has proven to be multifactorial. In this study, we also investigated whether there is a relationship between vitamin B12 and obesity. However, the retrospective nature of our study and the inclusion of only a small cross-sectional group were among the limitations of this study. No significant association was found between VKI and vitamin B12 levels at the end of the study. It was concluded that similar studies should be performed with a large case series.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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