ORIGINAL ARTICLE

DOI: 10.4274/hamidiyemedj.galenos.2022.52724

Hamidiye Med J 2023;4(1):9-14

The Relationship Between Insulin Resistance Markers and Vitamin B12 Level in Obese People

Obez Kişilerde B12 Vitamini Düzeyi ile İnsülin Direnci Belirteçleri Arasındaki İlişki

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ABSTRACT

Background: Obesity is a global health problem whose prevalence has been increasing in recent years.In this study, we investigated whether there is a relationship between triglyceride/high-density lipoprotein-cholesterol ratio (TG/HDL-C), triglyceride/glucose index (TGI), which is a marker of insulin resistance, and vitamin B12 levels in people with obesity.

Materials and Methods: One hundred seventy-one patients with a body mass index (BMI) above 25 kg/m^2 who applied to the internal medicine outpatient clinic of our hospital between January and December 2017 with the complaints of obesity were retrospectively included in the study. They were divided into two groups as those with Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) >2.5 (group 1) (n=92) and those with HOMA-IR <2.5 (group 2) (n=79). These two groups were compared in terms of age, gender, BMI, HOMA-IR, TG/HDL-K, TGI, vitamin B12, fasting blood glucose, triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol, HDL-cholesterol (HDL-C), aspartate aminotransferase, alanine aminotransferase, thyroid-stimulating hormone, FT4.

Results: Vitamin B12 levels were significantly lower in group 1 (p<0.001). TG/HDL-C and TGI were also significantly higher in group 1 (p<0.001). There was a weak and significant negative correlation between vitamin B12 and TG/HDL-C and TGI in all patients (p<0.001) (r=-0.302, r=-0.287). There was a moderately significant negative correlation between vitamin B12 levels and HOMA-IR in all patients (p<0.001) (r=-0.414).

Conclusion: In this study, we found that vitamin B12 was significantly lower in obese people with insulin resistance, and there was a negative correlation between vitamin B12 levels and new insulin resistance markers, TG/HDL-K, TGI, in people with obesity.

Keywords: Vitamin B12, obesity, insulin resistance, triglyceride/glucose index (TGI), triglyceride/HDL-cholesterol ratio (TG/HDL-C)

ÖZ

Amaç: Obezite, son yıllarda yaygınlığı giderek artan küresel bir sağlık sorunudur. Bu çalışmada, obezitesi olan kişilerde insülin direncinin bir belirteci olan trigliserit/yüksek yoğunluklu lipoprotein-kolesterol oranı (TG/HDL-C), trigliserid/glikoz indeksi (TGI) ile vitamin B12 düzeyleri arasında bir ilişki olup olmadığını araştırdık.

Gereç ve Yöntemler: Hastanemiz dahiliye polikliniğine Ocak-Aralık 2017 ayları arasında obezite şikayeti ile müracaat edip vücut kitle indeksi (VKİ) 25 kg/m^2 üzerinde olan 171 hasta retrospektif olarak çalışmaya dahil edildi. Bunlar daha sonra İnsülin Direncinin Homeostatik Modeli Değerlendirmesi (HOMA-IR) >2,5 olanlar (grup 1) (n=92) ve HOMA-IR <2,5 olanlar (grup 2) (n=79) olarak iki gruba ayrıldılar. Bu iki grup yaş, cinsiyet, VKİ, HOMA-IR, TG/HDL-K, TGI, B12 vitamini, açlık kan şekeri, trigliserit, total kolesterol, düşük yoğunluklu lipoprotein-kolesterol, HDL-kolesterol, aspartat aminotransferaz, alanin aminotransferaz, tiroid uyarıcı hormon, FT4. yönünden karşılaştırıldı.

Bulgular: Vitamin B12 düzeyleri grup 1'de anlamlı olarak düşüktü (p<0,001). TG/HDL-C ve TGI da grup 1'de anlamlı olarak yüksekti (p<0,001). Tüm hastalarda B12 vitamini ile TG/HDL-C ve TGI arasında zayıf ve anlamlı negatif korelasyon vardı (p<0,001) (r=-0,302, r=-0,287). Tüm hastalarda vitamin B12 düzeyleri ile HOMA-IR arasında orta derecede anlamlı negatif korelasyon vardı (p<0,001) (r=-0,414).

Sonuç: Bu çalışmada, insülin direnci olan obez kişilerde B12 vitamininin anlamlı olarak daha düşük olduğunu ve obezitesi olan kişilerde B12 vitamini seviyeleri ile yeni insülin direnci belirteçleri olan TG/HDL-K, TGI arasında negatif korelasyon olduğunu bulduk.

Anahtar Kelimeler: B12 vitamini, obezite, insülin direnci, trigliserid/lukoz indeksi (TGI), trigliseirid/HDL kolesterol oranı (TG/HDL-K)

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Received: 28.07.2022 **Accepted:** 04.11.2022

Introduction

Obesity is a problem for world health whose prevalence has been rising consistently in the recent past. The fact that obesity is connected with a variety of diseases, including insulin resistance (IR), type 2 diabetes mellitus (DM), hypertension (HT), hyperlipidemia, non-alcoholic fatty liver disease (NAFLD), and cardiovascular disease, emphasizes the disease's significance (1).

Vitamin B12 (vit-B12) which is a water-soluble vitamin, is mostly found in beef, and salmon and less in eggs and cow milk. This vitamin has important effects on the neurological, hematopoietic system and DNA synthesis in the body. Vit-B12 also has an effect on muscle, bone and epithelial tissue regeneration, and participates in protein, fat and carbohydrate metabolism. Additionally, it is necessary for the transformation of fatty acids into energy (2,3,4,5). Several studies in the literature suggest that vit-B12 insufficiency is widespread in people with IR, DM, overweight, and that vit-B12 supplementation has a favorable effect on IR and obesity (6).

The triglyceride/glucose index (TGI) is a simple, reliable, easily accessible and cost-effective screening method used in the screening of IR. TGI is thought to be a more accurate diagnostic tool than Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) in the diagnosis of IR in some cases (7,8,9). The triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio was first put forth as an atherogenic index in coronary artery disease by Gaziano et al. (10). Developed by Dobiasova and Frolich (11), it has been stated that this can be used in the evaluation of diabetic dyslipidemia and DM risk. According to recent research, TGI and TG/HDL-C calculations are novel easy and low-cost indicators of IR. It has also been reported to have a higher predictability for IR than conventionally used methods (12,13).

In this study, we investigated whether there is a relationship between TGI and TG/HDL-K ratio, which is a marker of IR, and vit-B12 levels in people with obesity.

Material and Methods

One hundred seventy-one people with a body mass index (BMI) over 25 kg/m^2 who applied to our hospital due to obesity between January and December 2017 were retrospectively included in the study. The exclusion criteria for the people to be included in the study were those with DM, pregnancy, malabsorption syndromes, vegetarians, gastrectomy, ileal resection, taking vit-B12 supplements, taking drugs that cause vit-B12 deficiency (phenytoin, metformin, DHF reductase inhibitor).

The individuals included in the study were divided into two groups as those with a HOMA-IR ≥2.5 (group 1) (n=92), and those with a HOMA-IR <2.5 (group 2) (n=79). These groups were compared age, gender, BMI, HOMA-IR, TG/HDL-K, TGI, vit-B12, fasting blood glucose (FBG), triglyceride (TG), total cholesterol, low-density lipoprotein-cholesterol, HDL-cholesterol, aspartate aminotransferase (AST), alanine aminotransferase (ALT), TSH, FT4.

The correlation between vit-B12 level and HOMA-IR, TG/HDL-C, TGI was also examined in all individuals included in the study.

HOMA-IR was calculated using fasting glucose (mg/dL) x fasting insulin (μU/mL)/22.5 formula. HOMA-IR ⩾2.5 was accepted as the presence of IR in patients (14).

The correlation between HOMA-IR and TG/HDL-C and TGI, which are indicators of IR, were also examined (15).

We defined the TG/HDL-C ratio using the following calculation: TG (mg/dL)/HDL-C (mg/dL).

We calculated the TGI using the formula below: In [TG (mg/dL) x fasting glucose (mg/dL)/2]

FBG, ALT, AST, TG, HDL levels were measured using the Abbott i8000 device and Abbott kits in our central laboratory. FBG levels were measured by hexokinase method and ALT, AST were measured by enzymatic method. TG and HDL were measured by photometric method.

The insulin levels were studied using the Abbott i16000 device and the chemiluminescent microparticle immunoassay (CMIA) method.

Vit-B12 was measured with the Abbott i16000 device and chemiluminescence immunoassay method.

Approval was obtained from the University of Health Sciences Türkiye, Ümraniye Training and Research Hospital Ethics Committee for the study (no: 113, date: 08/04/2021).

Statistical Analysis

Descriptive statistics were used to describe continuous variables (mean, standard deviation, minimum, median, maximum). Comparison of two independent and normally distributed continuous variables with Student's t-test, comparison of two independent and normally distributed variables with Mann-Whitney U test has been made. The comparison of more than two independent and non-normally distributed variables was made with the Kruskal-Wallis test. Spearman's rho correlation analysis was used to analyze the relationship between two continuous variables that did not fit normally.

Statistical significance level was determined as 0.05. Analyzes MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013) carried out using the program.

Results

The median age of the 171 study participants was 33+11, 84.8% being female (n=145) and 15.2% being male (n=26) and the mean BMI was 32.9±4.81.

In terms of gender and mean year, there was no difference between the two groups. The BMI was significantly different and it was higher in group 1 (p<0.001).

In group 1, vit-B12 levels were considerably lower. TG/HDL-C and TGI were also significantly higher in group 1 (p<0.001) (p<0.001) (Table 1).

There was a weak and significant negative correlation between vit-B12 and TG/HDL-C and TGI in all patients (r=-0.302, r=-0.287) (p<0.001) (p<0.001) (Figures 1, 2) (Table 2).

There was a moderately significant negative correlation between vit-B12 levels and HOMA-IR in all patients (r=-0.414) (p<0.001) (Figure 3).

There was a moderate positive correlation between HOMA-IR and TG/HDL-C and TGI in all patients (r=0.502, r=0.533) (p<0.001) (p<0.001) (Figure 4).

Discussion

The presented study reported that vit-B12 was significantly lower in obese people with IR and there was a negative correlation between vit-B12 level and TG/HDL-C, TGI, which are novel IR markers, in people with obesity.

Table 1. Comparison of parameters according to groups

		Grup 1 (n=92)	Grup 2 (n=79)	p
Gender		n (%)	n (%)	
	Male	18 (19.6)	8 (10.1)	0.093*
	Woman	74 (80.4)	71 (89.9)	
		Mean + SD Med. (min-max)	Mean + SD Med. (min-max)	p
Age		32±11 31 (16-64)	33±10 35 (17-54)	0.455
BMI		34.67±4.74 33.88 (24.98-47.45)	30.86±4.03 29.76 (25.56-44.81)	**<0.001**
FBG		98±11 98 (76-125)	91±9 90 (71-110)	**<0.001****
T.KOL		193±34 189 (127-263)	185±36 186 (82-335)	0.148
LDL-K		119±30 121 (46-197)	117±29 114 (58-232)	0.572
HDL-K		41±9 39 (27-75)	45±11 44 (17-71)	**0.007**
TG		173±80 158 (63-422)	118±51 115 (35-290)	**<0.001**
TGI		8572±4196.8 7649 (3200-23210)	5391±2465.8 4945 (1577-15660)	**<0.001**
TG/HDL-K		4.58±2.63 4.11 (0.84-13.61)	2.82±1.48 2.43 (0.92-8.06)	**<0.001**
Vit-B12		220±74 200 (108-514)	276±113 256 (118-903)	**<0.001**
ALT		26±24 20 (6-207)	18±13 14 (7-85)	**<0.001**
AST		20±9 18 (12-79)	19±16 16 (9-150)	**0.008**
TSH		1.85±0.98 1.68 (0.06-7.65)	1.88±0.9 1.76 (0.36-4.47)	0.744
FT4		0.97±0.11 0.97 (0.71-1.31)	0.96±0.11 0.96 (0.71-1.22)	0.500

*Fisher's Exact test, **Student's t-test, BMI: Body mass index, FBG: Fasting plasma glucose, TGI: Triglyceride/glucose index, TG/HDL-C: Triglyceride to high-density lipoprotein cholesterol ratio, TG: Trigliseride, SD: Standard deviation

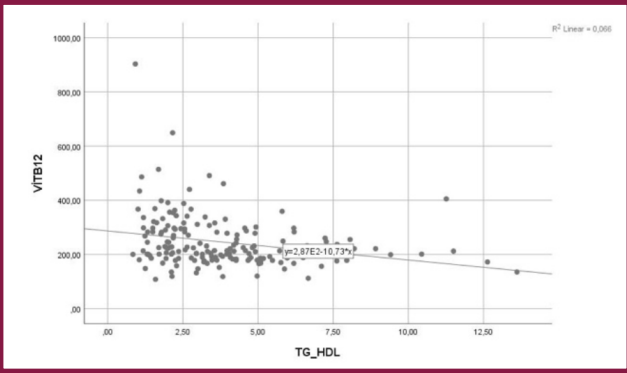

Figure 1. Correlation graph between vitamin B12 level and TG/HDL-C
TG/HDL-C: Triglyceride to high-density lipoprotein cholesterol ratio

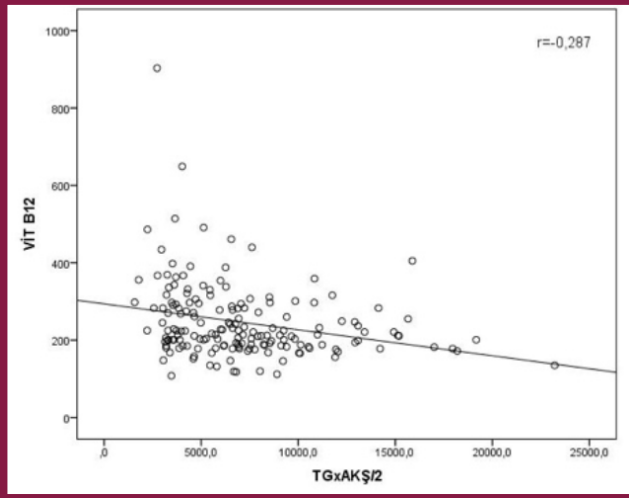

Figure 2. Correlation graph between vitamin B12 level and TGI
TGI: Triglyceride/glucose index

Table 2. Correlation analysis

		HOMA-IR	Vit-B12	TG/HDL-K	TG index
Vit-B12	**R**	**-0.414**	1.000	**-0.302**	**-0.287**
	p	**<0.001**	-	**<0.001**	**<0.001**
TG/HDL-K	**R**	**0.502**	**-0.302**	1.000	**0.913**
	p	**<0.001**	**<0.001**	-	**<0.001**
TGI	**R**	**0.533**	**-0.287**	**0.913**	1.000
	p	**<0.001**	**<0.001**	**<0.001**	-
HOMA-IR	**R**	1.000	**-0.414**	**0.502**	**0.533**
	p	-	**<0.001**	**<0.001**	**<0.001**

Spearman's rho correlation, TG/HDL-C: Triglyceride to high-density lipoprotein cholesterol ratio, TGI: Triglyceride/glucose index, Vit-B12: Vitamin B12, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance

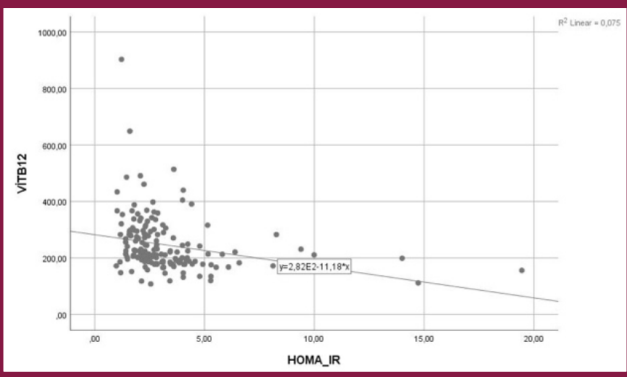

Figure 3. Correlation between vitamin B12 level and HOMA-IR
HOMA-IR: Homeostatic Model Assessment for Insulin Resistance

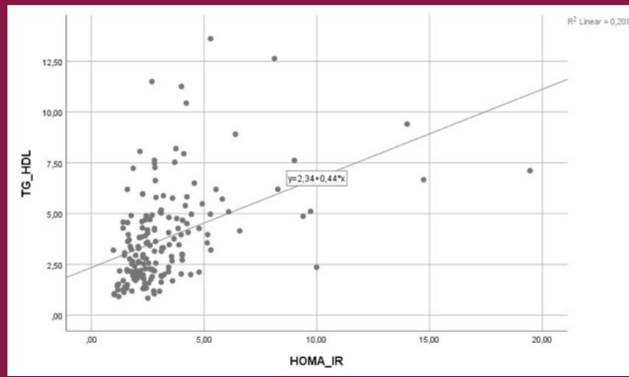

Figure 4. Correlation between HOMA-IR and TG/HDL-C ratio
TG/HDL-C: Triglyceride to high-density lipoprotein cholesterol ratio, HOMA-IR: Homeostatic Model Assessment for Insulin Resistance

Obesity is an important disease accompanied by many comorbidities such as IR, DM, HT, hyperlipidemia, NAFLD, cardiovascular diseases (1). Increased TNF-alpha in adipocytes of obese individuals, decreased number and function of insulin receptors and increased free fatty acids are among the reasons for the relationship between obesity and IR (16). It is known that IR is frequently seen in people with obesity,and there are many publications in the literature on this subject (1). In our study, similar to the information in the literature, BMI was found to be statistically significantly higher in the group with IR (group 1) ($p<0.001$).

Vit-B12 has very important effects on the neurological and hematopoietic systems in the body. It is also necessary for muscle, bone, epithelial tissue regeneration, protein, fat, carbohydrate metabolism and conversion of fatty acids into energy (2,3,4,5).

In recent studies, it has been reported that obesity is frequently seen in patients with vit-B12 deficiency (17,18,19). In a study conducted on 75 people in India, it was shown that the homocysteine levels of people with metabolic syndrome were higher than the control group, and the levels of vit-B12 were lower (20). In another study conducted on 140 people in Saudi Arabia, it was stated that there was a negative correlation between vit-B12 level and fasting blood sugar and HOMA-IR (21). In the study conducted by Baltacı et al. (22), it was observed that vit-B12 levels were low in obese patients with metabolic syndrome and IR. The effect of vit-B12 on HOMA-IR and metabolic syndrome was examined in a study involving 278 severely fatness individuals, and it was discovered that those with low vit-B12 levels had greater HOMA-IR (23). In the research by Setola et al. (24), it was found that folate and vit-B12 supplementation improved IR and endothelial dysfunction and decreased homocysteine levels in people with metabolic syndrome. In our study, we found that vit-b12 levels were significantly lower in people with IR, as in other studies in the literature. In addition, we found a weak and considerably negative correlation between vit-B12 level and TG/HDL-C and TGI in obese individuals (Figures 1, 2) (Table 2). We also found a moderate negative correlation between vit-B12 level and HOMA-IR in these individuals (Figure 3). In contrast to these studies, Gammon et al. (25) determined no association between vit-B12 levels and HOMA-IR in a study on obese people in India.

Vit-B12 acts as a cofactor in two main enzyme system pathways in the body. The first is the remethylation pathway, which converts homocysteine to methionine, and the second is the deoxidation pathway that enables the conversion of methyl malonyl coenzyme A to succinyl coenzyme A (26).

The remethylation pathway takes place in the cytoplasm, while the deoxidation pathway takes place in the mitochondria. The deoxidation pathway is also known as the fatty acid β-oxidation pathway. Through this pathway, methyl malonyl coenzyme A is converted to succinyl coenzyme A. In the absence of this conversion, the level of methyl malonyl coenzyme A increases and the activity of carnitine palmitoyl transferase, which controls the ratio of long-chain fatty acids to mitochondria, is inhibited. This results in the accumulation of fatty acids in the cytosol. Inhibition of the β-oxidation pathway in vit-B12 deficiency results in fatty acid accumulation in the cytosol (27).

In other words, vit-B12 deficiency accumulates methylmalonic acid, which leads to inhibition of fatty acid B-oxidation, lipogenesis, and IR. We think that the combination of obesity, IR, and vit-B12 deficiency resulted from this mechanism in our study. Li et al. (23) emphasized in their study that vit-B12 deficiency leads to obesity and IR with the same mechanism.

TGI was first described in 2008 as a marker of IR. However, in some studies, TGI is thought to be a more accurate diagnostic tool in the diagnosis of IR than HOMA-I in some cases (28,29). TGI was linked to IR and hyperinsulinemia in a study conducted in Peru by 9. Toro-Huamanchumo et al. (9). Vasques stated in his study that TGI outperformed HOMA-IR (8).

Gaziano et al. (10) first suggested using TG/HDL-C as an atherogenic measure for coronary artery disease. Pantoja-Torres et al. (28) found a positive correlation between TG/HDL-C and HOMA-IR and hyperinsulinemia in their research. In our study, we found that TGI and TG/HDL-C were significantly higher in people with IR (Table 1). Additionally, we observed a favorable connection between HOMA-IR, TGI and TG/HDL-C in all research participants (Figure 4). Thus, we confirmed that TGI and TG/HDL-C can also be used as IR parameters.

The fact that this study was conducted retrospectively is one of its shortcomings. Another is the tiny sample size of the study's participants. Future studies examining the connection between IR and vit-B12 ought to be prospectively planned with bigger sample numbers.

Conclusion

In this study, there was a correlation between IR markers and vit-B12 levels. We would like to emphasize that vit-B12 deficiency should be investigated in obese patients with IR.

Ethics

Ethics Committee Approval: Approval was obtained from the University of Health Sciences Türkiye, Ümraniye Training and Research Hospital Ethics Committee for the study (no: 113, date: 08/04/2021).

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: H.Ş.A., Design: H.Ş.A., Data Collection or Processing: H.Ş.A., Analysis or Interpretation: H.Ş.A., Literature Search: H.H.P., Writing: H.Ş.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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