

# Evaluation of Vitamin D Deficiency in Patients with Metabolic Syndrome and its Effect on Anxiety-Depression

## Metabolik Sendromlu Hastalarda Vitamin D Eksikliğinin Değerlendirilmesi ve Anksiyete-Depresyon Üzerine Etkisinin İncelenmesi

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**ABSTRACT Objective:** To evaluate vitamin D deficiency in patients with metabolic syndrome and to examine its effect on anxiety-depression. **Material and Methods:** Seventy one participants diagnosed with and without metabolic syndrome according to the International Diabetes Federation 2005 criteria were included into the study (35 participants in metabolic syndrome group, 36 participants in control group). Participants with rheumatological disease, fibromyalgia, anxiety-depression, history of orthopedic surgery and/or medication for any psychiatric illness were excluded from the study. The study was planned retrospectively. Demographic characteristics, waist and hip circumference measurement were examined. Blood triglyceride, HDL cholesterol, fasting plasma glucose, vitamin D levels, systolic and diastolic blood pressures and hospital anxiety-depression (HAD) scale were recorded retrospectively at the date when the HAD scale were applied. **Results:** Gender, age, height, weight, body mass index and hip circumference measurement were similar in both groups. Waist circumference measurement was significantly higher in the metabolic syndrome group compared to the control group ( $p=0.031$ ). Triglyceride, fasting plasma glucose level, systolic and diastolic blood pressure were found to be significantly higher in the metabolic syndrome group compared to the control group. There was no significant difference in vitamin D level between two groups. While the anxiety score was found to be similar between two groups, the depression score was significantly higher in the metabolic syndrome group compared to the control group (respectively;  $p=0.917$ ,  $p=0.008$ ). There was no correlation between blood vitamin D level and waist circumference, hip circumference measurements, blood triglyceride, HDL cholesterol, fasting plasma glucose levels, anxiety and depression scores in the metabolic syndrome group. **Conclusion:** Independent of vitamin D deficiency, an increase in the level of depression was detected in participants with metabolic syndrome. It was thought that there was no relationship between depression, anxiety and vitamin D levels in patients with metabolic syndrome.

**Keywords:** Vitamin D deficiency; metabolic syndrome; anxiety-depression

**ÖZET Amaç:** Bu çalışmada, metabolik sendromlu hastalarda vitamin D eksikliğinin değerlendirilmesi ve anksiyete-depresyon üzerine etkisinin incelenmesi amaçlandı. **Gereç ve Yöntemler:** Uluslararası Diyabet Federasyonu 2005 kriterlerine göre metabolik sendromu olan 35 katılımcı, metabolik sendromu grubunda ve metabolik sendromu olmayan 36 katılımcı, kontrol grubunda olmak üzere toplam 71 katılımcı çalışmaya dâhil edildi. Romatolojik hastalığı, ortopedik cerrahi öyküsü, fibromiyaljisi olan, anksiyete-depresyon ve/veya herhangi bir psikiyatrik hastalık nedeniyle ilaç tedavisi altındaki katılımcılar çalışmadan dışlandı. Çalışma, retrospektif olarak planlandı. Katılımcıların demografik özellikleri, bel çevresi ve kalça çevresi ölçümü kayıtları incelendi. Tüm katılımcıların Hastane Anksiyete-Depresyon (HAD) ölçeği ve HAD ölçeği uygulandığı tarihteki kan trigliserid, HDL kolesterol, açlık glukozu, vitamin D düzeyleri, sistolik ve diyastolik kan basınçları retrospektif olarak kaydedildi. **Bulgular:** İki grup arasında cinsiyet, yaş, boy, kilo, beden kitle indeksi ve kalça çevresi ölçümü açısından anlamlı fark yoktu. Bel çevresi ölçümü metabolik sendrom grubunda, kontrol grubuna göre anlamlı olarak fazla idi ( $p=0.031$ ). Trigliserid, açlık kan glukozu düzeyi, sistolik ve diyastolik kan basıncı metabolik sendrom grubunda kontrol grubuna göre anlamlı derecede yüksek saptandı. İki grup arasında vitamin D düzeyi açısından anlamlı fark saptanmadı. Anksiyete skoru 2 grup arasında benzer saptanırken, depresyon skoru metabolik sendrom grubunda kontrol grubuna göre anlamlı derecede yüksek saptandı (sırasıyla;  $p=0.917$ ,  $p=0.008$ ). Metabolik sendromu olan grupta vitamin D düzeyi ile bel çevresi, kalça çevresi, trigliserid düzeyi, HDL kolesterol düzeyi, açlık kan şekeri, anksiyete ve depresyon skorları arasında korelasyon saptanmadı. **Sonuç:** Metabolik sendromu olanlarda, vitamin D eksikliğinden bağımsız olarak depresyon düzeyinde artış olduğu saptandı. Metabolik sendromu olanlarda, depresyon ve anksiyete ile vitamin D düzeyleri arasında ilişki olmadığı düşünüldü.

**Anahtar Kelimeler:** Vitamin D; metabolik sendrom; anksiyete-depresyon

Vitamin D deficiency is a common vitamin deficiency leading to common musculoskeletal pain, daytime sleepiness and fatigue. Low physical activity

and decreased daily living activities can lead to increased anxiety and depression. Although the evidence in the literature supports the relationship

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Peer review under responsibility of Journal of Physical Medicine and Rehabilitation Science.

**Received:** 28 Jun 2020

**Received in revised form:** 11 Sep 2020

**Accepted:** 14 Sep 2020

**Available online:** 18 Jan 2021

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between vitamin D and depression, there is no study in which exact relationship is determined.<sup>1,2</sup> According to the literature, when 25 (OH) vitamin D level is below 20 ng/mL, it is defined as vitamin D deficiency and when 25 (OH) vitamin D level is between 21-29 ng/mL, it is defined as vitamin D insufficiency.<sup>3</sup>

Metabolic syndrome is a public health problem characterized by central obesity, increased blood pressure, hypertriglyceridemia, decreased HDL cholesterol level, glucose dysregulation and insulin resistance. The prevalence of metabolic syndrome is increasing rapidly all over the world. Cardiovascular diseases and type 2 diabetes mellitus are two main components of metabolic syndrome. The International Diabetes Federation (IDF), the American Heart Association and the National Heart, Lung, and Blood Institute define metabolic syndrome as 2 or more determination of risk factor (fasting plasma glucose >100 mg/dL, blood pressure  $\geq$ 130/85 mm-Hg, triglyceride level >150 mg/dL, HDL cholesterol level <40 mg/dL in men and <50 mg/dL in women), in addition to central obesity (waist circumference >94 cm in men and >80 cm in women).<sup>4-6</sup>

Vitamin D deficiency was found in obese patients with and without metabolic syndrome. Additionally, an inverse relationship was found between vitamin D level and blood triglyceride, fasting plasma glucose levels and blood pressure.<sup>7</sup> Recent evidence shows that vitamin D is also associated with diabetes mellitus, obesity, cancer and depression.<sup>8</sup>

We aimed to evaluate vitamin D deficiency in patients with metabolic syndrome and to examine the effect of vitamin D deficiency on anxiety-depression.

## MATERIAL AND METHODS

Seventy-one participants diagnosed with and without metabolic syndrome according to the IDF 2005 criteria were included in the study between the dates 01/01/2019 and 01/02/2020 (35 participants in metabolic syndrome group, 36 participants in control group). Participants with rheumatological disease, the history of orthopedic surgery, fibromyalgia, anxiety-depression and/or any psychiatric disease were excluded from the study. The study was planned retrospectively. Demographic

characteristics, waist and hip circumference measurements were examined retrospectively. Blood triglyceride, HDL cholesterol, fasting plasma glucose, vitamin D levels and hospital anxiety-depression (HAD) scale were recorded retrospectively at the date when HAD scale was applied. This study was designed in accordance with the Helsinki Declaration principles. Ethics committee approval was obtained from Gazi University Faculty of Medicine, Clinical Research Ethics Committee for this study.

## STATISTICAL ANALYSIS

All data were analyzed using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) 15.0 program for Windows. The variables were investigated using visual and analytical methods to determine whether or not they are normally distributed. Parametric variables are expressed as mean $\pm$ SD, non-parametric variables are expressed as median (25-75%) and categorical variables as numbers and percentages.  $\chi^2$  test was used for categorical variables and Student t-test was used for parametric variables. Mann-Whitney U test was used for nonparametric variables. A value of  $p < 0.05$  was considered statistically significant.

## RESULTS

Age, height, weight, gender distribution, body mass index and hip circumference measurement were similar in both groups (Table 1). Waist circumference was significantly higher in the metabolic syndrome group compared to the control group ( $p=0.031$ ).

Blood triglyceride, fasting plasma glucose levels, systolic and diastolic blood pressures were significantly higher in the metabolic syndrome group compared to the control group (Table 2). There was no significant difference in vitamin D level between the two groups (Table 2). While the anxiety score was similar between the two groups, the depression score was significantly higher in the metabolic syndrome group compared to the control group (Table 2). There was no correlation between vitamin D level and waist circumference, hip circumference, blood triglyceride, HDL cholesterol, fasting plasma glucose levels, anxiety and depression scores in the metabolic syndrome group.

**TABLE 1:** Demographic features of participants with metabolic syndrome and healthy controls.

	Metabolic syndrome group n=35	Control group n=36	p value
Gender	8 (male) 27 (female)	7 (male) 29 (female)	0.725
Age (year)	56.34±8.52	54.11±8.62	0.277
Height (cm)	160 (155-165)	160 (156-165)	0.401
Weight (kg)	80 (71-86)	76 (69.25-85)	0.147
BMI (kg/m <sup>2</sup> )	30.78 (29.13-34.13)	29.51 (26.50-32.98)	0.075
Waist circumference (cm)	108.28±10.12	102.75±11	0.031
Hip circumference (cm)	106 (100-115)	109 (103.25-119.25)	0.214

BMI: Body mass index, p<0.05

**TABLE 2:** Clinical and laboratory variables of participants with metabolic syndrome and healthy controls.

	Metabolic syndrome group n=35	Control group n=36	p value
Vitamin D level (ng/mL)	13 (9.4-21)	15.50 (11.66-20.50)	0.451
Triglyceride level (mg/dL)	180 (160-215)	125 (87-176.75)	<0.000
HDL cholesterol level (mg/dL)	48.25±11.95	55.38±12	0.014
Blood fasting glucose lever (mg/dL)	110 (92-136)	87.50 (82.25-95.25)	<0.000
Systolic blood pressure (mm-Hg)	110 (110-120)	100 (100-110)	<0.000
Dyastolic blood pressure (mm-Hg)	70 (70-80)	70 (60-70)	0.003
Anxiety score	8 (5-12)	8.5 (4-11)	0.917
Depression score	9.206.80±3.373.94	6.80±3.37	0.008

p<0.05

## DISCUSSION

We examined the presence of vitamin D deficiency and the effect of vitamin D levels on anxiety-depression in patients with metabolic syndrome in this study. There was no difference in vitamin D levels between two groups. In this study, it was not known whether the participants took vitamin D supplements or not. As a matter of fact, some participants from both groups might or might not have taken vitamin D supplements.

Hyperparathyroidism, which is due to low vitamin D levels, is known to cause an increased intracellular calcium in adipose tissue.<sup>9</sup> Increased intracellular calcium increases lipogenesis and causes weight gain.<sup>10</sup> Recent evidences suggest that vitamin D deficiency is associated with metabolic syndrome components such as obesity and diabetes mellitus.<sup>8</sup> However, it is not known exactly whether vitamin D deficiency causes metabolic syndrome. Since vitamin

D is sequestered in adipose tissue, low vitamin D levels can be detected in obese people.<sup>11</sup>

There are at least three lines of evidence supporting the relationship between vitamin D and depression: 1. Increased vitamin D receptors in brain regions which play an important role in mood regulation, such as prefrontal and cingulate cortex, 2. immune modulating role of vitamin D in depression, 3. neuro-protective role of vitamin D.<sup>12-16</sup> Although the evidences in the literature support the relationship between vitamin D and depression, the exact relationship has not been revealed yet.<sup>17</sup> Because most of the studies are cross-sectional. According to randomized controlled trials, vitamin D supplementation is thought to have superior therapeutic benefits in clinical depression.<sup>17</sup> Depression scores were found higher in participants with metabolic syndrome in this study. Since vitamin D levels were similar in both groups, increased depression scores in metabolic syndrome group seem to be independent of vitamin D

level. It has been shown that there is a relationship between low blood vitamin D level and anxiety in adolescents and children undergoing hemodialysis.<sup>18</sup> There was no significant difference in anxiety levels between two groups in this study. This result may have been found due to the similar vitamin D levels in two groups. In a study, a relationship between low blood vitamin D level and glucose metabolism was found in healthy individuals. However no relationship was found between blood vitamin D level, anxiety and depression.<sup>19</sup> In our study there was no relationship between blood vitamin D, triglyceride, HDL cholesterol, fasting plasma glucose levels and anxiety-depression scores in metabolic syndrome group.

Our study is one of the few studies in the literature evaluating the presence of vitamin D deficiency and the relationship between vitamin D deficiency and anxiety-depression in patients with metabolic

syndrome. However, the low number of participants and being a retrospective study are the limitations of our study. Also the laboratory data of the participants belong to the autumn and winter seasons, it may have affected the results as the vitamin D level varies seasonally. Additionally not knowing whether the participants took vitamin D supplements was one of the limitations of our study. Prospective randomized controlled studies are needed to clearly determine vitamin D deficiency and the relationship between vitamin D deficiency and presence of anxiety-depression in patients with metabolic syndrome.

## CONCLUSION

Independent of vitamin D deficiency, increased depression level was detected in participants with metabolic syndrome. It was thought that there was no relationship between depression, anxiety and vitamin D levels in patients with metabolic syndrome.

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