

## The Relationship between HbA1c and 25-hydroxy Vitamin D Levels in Adult Diabetic Patients

*Yetişkin Diyabetik Hastalarda HbA1c ve 25-hidroksi D Vitamini Düzeyleri Arasındaki İlişki*

Mehmet Özdin\*<sup>1</sup>, Durhasan Mundan<sup>2</sup>

<sup>1</sup>Sakarya University, Training and Research Hospital, Biochemistry, Sakarya, Türkiye

<sup>2</sup>Harran University Faculty of Veterinary Medicine, Department of Animal Science, Şanlıurfa, Türkiye

**Cited:** Özdin M, Güler DM. (2023). The relationship between HbA1c and 25-hydroxy Vitamin D levels in adult diabetic patients. *Van Sağlık Bilimleri Dergisi*, 16(1), 25-29.

### ABSTRACT

**Objective:** The aim of this study was to determine vitamin D levels in patients with type II Diabetes Mellitus who applied to the internal medicine diabetes and endocrinology polyclinic of a training and research hospital, and to determine the relationship between HbA1c and 25-hydroxy vitamin D levels.

**Material and Method:** Type II Diabetes Mellitus patients constituted the material of the study. The study was conducted between 2018-2019. The data were obtained from the hospital information management system. Those with bone-derived malignancies and pregnant women were excluded from the study. A total of 65 patients, 40 (61%) female and 25 (39%) males were included in the study. Statistical analyzes were made with the help of IBM SPSS for Windows 26.0 package program. The normal distribution was tested for the categories of factors affecting vitamin D levels. Accordingly, the hypothesis test was chosen and the descriptive statistics values suitable for the used hypothesis test were calculated. Variables indicated by measurement mean  $\pm$  SD, smallest and largest; Variables that are represented by numbers are indicated by %. Pearson correlation coefficients were used to evaluate the correlations.

**Results:** HbA1c and 25-hydroxy vitamin D levels were determined in the patients included in the study. HbA1C levels were found to be  $9,023 \pm 1.72$  (%) higher than the normal values. 25-hydroxy vitamin D levels were  $13.94 \pm 4.12$  ng/ml and were lower than normal values. HbA1c levels and 25-hydroxy vitamin D levels were found to be statistically significant in type II Diabetes Mellitus patients ( $p < 0.05$ ). A negative correlation was calculated between 25-hydroxy vitamin D levels and HbA1c levels ( $r = -0.51$ ).

**Conclusion:** As a result, HbA1c values were found to be high as expected in patients with Type II Diabetes Mellitus. On the other hand, 25-hydroxy vitamin D levels were found to be low. In these patients, low 25-hydroxy vitamin D makes vitamin supplementation important. However, the permanent inclusion of 25-hydroxy vitamin D in treatment protocols necessitates further research.

**Keywords:** Correlation, HbA1c, Type II Diabetes Mellitus, Vitamin D

### ÖZET

**Amaç:** Bu çalışmanın amacı, bir eğitim ve araştırma hastanesinin dahiliye diyabet ve endokrinoloji polikliniğine başvuran tip II Diabetes Mellituslu hastalarda D vitamini düzeylerini belirlemek ve HbA1c ile 25-hidroksi D vitamini düzeyleri arasındaki ilişkiyi belirlemektir.

**Materyal ve Metod:** Çalışmanın materyalini, tip II Diabetes Mellitus hastaları oluşturdu. Çalışma, 2018-2019 yılları arasında yapıldı. Veriler, hastane bilgi yönetim sisteminden elde edildi. Kemik kaynaklı malignitesi olanlar ve gebeler çalışma dışı bırakıldı. Çalışmaya 40 (%61) kadın ve 25 (%39) erkek olmak üzere toplam 65 hasta dahil edildi. İstatistiksel analizler, IBM SPSS for Windows 26.0 paket programı yardımı ile yapılmıştır. D vitamini düzeylerini etkileyen faktörlerin kategorileri için normal dağılım test edildi. Buna göre hipotez testi seçilmiş ve kullanılan hipotez testine uygun betimsel istatistik değerleri hesaplanmıştır. Ölçümle gösterilen değişkenler ortalama  $\pm$  SD, en küçük ve en büyük; Sayı ile gösterilen değişkenler % ile gösterilir. Korelasyonları değerlendirmek için Pearson korelasyon katsayıları kullanıldı.

**Bulgular:** Çalışmaya alınan hastalarda HbA1c ve 25-hidroksi D vitamini düzeyleri belirlendi. HbA1C düzeyleri belirlenen normal değerlerden  $9,023 \pm 1.72$  (%) yüksek bulundu. 25-hidroksi D vitamini düzeyleri  $13.94 \pm 4.12$  ng/ml idi ve normal değerlerden düşüktü. Tip II DM hastalarında HbA1c düzeyleri ve 25-hidroksi vitamin D düzeyleri istatistiksel olarak anlamlı bulundu ( $p < 0.05$ ). 25-hidroksi D vitamini düzeyleri ile HbA1c düzeyleri arasında negatif korelasyon hesaplandı ( $r = -0,51$ ).

**Sonuç:** Sonuç olarak, Tip II Diabetes Mellitus'lu hastalarda HbA1c değerleri beklendiği gibi yüksek bulundu. Öte yandan, 25-hidroksi D vitamini seviyeleri ise düşük bulundu. Bu hastalarda 25-hidroksi D vitamin düşüklüğü vitamin takviyesini önemli kılmaktadır. Ancak, 25-hidroksi D vitaminin tedavi protokollerinde kalıcı olarak yer alması daha geniş araştırmaları gerekli kılmaktadır.

**Anahtar kelimeler:** D vitamini, HbA1c, Korelasyon, Tip II diabetes mellitus

\*Corresponding author: Mehmet Özdin. E-mail address: [drmozdin33@gmail.com](mailto:drmozdin33@gmail.com).

ORCIDS: Mehmet Özdin: [0000-0003-3077-7171](https://orcid.org/0000-0003-3077-7171), Durhasan Mundan Güler: [0000-0002-9503-9850](https://orcid.org/0000-0002-9503-9850)

Received: 23.05.2022, Accepted: 01.03.2023 and Published 30.04.2023



## INTRODUCTION

Vitamin D is a vitamin synthesized in the body. Vitamin D deficiency is mainly due to bone mineralization. For many years osteoporosis etc. been shown to be related to diseases (Holick, 2004; Holick, 2005). Vitamin D has been extensively studied in both human and animal studies as a modifiable risk factor (Pittas and Dawson-Hughes, 2010).

Diabetes Mellitus (DM) is a metabolic disorder characterized by high blood sugar due to a malfunction in insulin secretion, insulin action, or both. DM is a group of carbohydrate metabolism disorders that affects approximately 5-10% of the world population and manifests itself with hyperglycemia due to the underuse of glucose. 25-hydroxy vitamin D is a steroid hormone and is known to be effective in insulin secretion in the pancreas. 25-hydroxy vitamin D is a fat-soluble vitamin. 25-hydroxy vitamin D can also be synthesized in an endogenously suitable biological medium. It has important effects on phosphorus and calcium metabolism and bone mineralization (Bringhurst et al., 2005; Champe et al., 2007).

Type II DM is a complex disease associated with many other clinical conditions (Yarbag et al., 2015). Type II DM is a chronic metabolic disease characterized by insufficient use of carbohydrates, fats and proteins as a result of a deficiency of the hormone insulin. All over the world, and the incidence of type II DM in Turkey is over 10%. While 90-95% of these cases are type II DM, the remaining 5-10% are type I DM and 2-3% are other forms of diabetes (Satman, 2007).

The HbA1c test is easy to use and is widely used. Metabolic control monitoring is performed with glycosylated HbA1C to prevent diabetes-related complications. The use of this test has increased since HbA1c was accepted as a type II DM diagnostic criteria by the WHO and the American Diabetes Association (WHO, 2011). However, in order for HbA1c to be used in DM diagnosis, standardization of the measurement method is required as there are different measurement methods as suggested by American Diabetes Association. The HbA1c test is a test used to monitor type II DM. In recent years, the use of HbA1c in the diagnosis of DM has become widespread due to its practicality and inclusion in the diagnostic criteria of DM by the World Health Organization. However, for HbA1c to be used as a diagnostic test in DM, the measurement method must comply with standardization. In this study, we aimed to put the relationship between HbA1c levels in type II DM patients and 25-hydroxy vitamin D levels (Özdin et al., 2019).

## MATERIAL and METHOD

Our study will consist of type II DM patients who apply to the Internal Medicine Diabetes Polyclinic and Endocrinology Polyclinic of our hospital. HbA1c and 25-hydroxy vitamin D levels will be determined by examining the file data of 65 patients with type II DM. A total of 65 patients, 40 (61%) female and 25 (39%) males, were included in the study.

HbA1c and 25 hydroxy vitamin D tests were studied in the biochemical laboratory of Sakarya. They were divided into two groups according to their HbA1c levels as  $\leq 7\%$  and  $>7\%$ . Again, the same parameters were compared in terms of vitamin D levels. The HbA1c test was performed on the ADAMS A1c HA-8180V and the 25 hydroxy vitamin D test on the ADVIA Centaur XPT Immunoassay System.

In the study, a serum D level of  $<20$  ng/mL was considered severe insufficiency, 20-30 ng/mL insufficiency, 30-100 ng/mL adequacy, and  $>100$  ng/mL toxicity. These biochemical parameters were compared in terms of diabetes.

The study was performed after the approval [By the Ethics Committee, Sakarya University Medicine Faculty, Number: 71522473/050.01.04/72].

### Statistical Analysis

The data were analyzed using the IBM SPSS 26.0 package program. Normal distribution was tested for the categories of factors affecting vitamin D levels. Accordingly, the hypothesis test was chosen and the descriptive statistics values suitable for the used hypothesis test were calculated. Variables indicated by measurement are mean  $\pm$  SD, smallest and largest; Variables indicated by count are indicated by %. To evaluate the correlations, Pearson correlation coefficients were used.

## RESULTS

The ages of the patients included in the study ranged from 40 to 83 years. The mean age of the patients was  $59.55 \pm 9.6$  years. The study included 65 type II DM patients admitted to the internal medicine diabetes and endocrinology polyclinic in our hospital. A total of 65 patients with type II DM were evaluated. HbA1C levels were  $9.023 \pm 1.72\%$ , higher than normal values. HbA1c values were found to be similar in male and female patients. No significant difference was found between them. 25-hydroxy vitamin D levels were  $13.94 \pm 4.12$  ng / ml and lower than normal values were determined. 25-hydroxy vitamin D levels were lower in female patients than in male patients. HbA1c levels and 25-hydroxy vitamin D levels were found to be statistically significant in type II DM patients ( $p < 0.05$ ). A negative correlation between HbA1c and 25-hydroxy vitamin D levels is given in Table 1 ( $r = -0.51$ ).

**Table 1.** Descriptive statistics and correlation of HbA1c and 25-hidroksi vitamin D

Variable	Mean	SD	R
HbA1c	9.023	1.72	-
25-hidroksi vitamin D	13.94	4.12	0.51*

## DISCUSSION

In one study, the prevalence of vitamin D deficiency was found to be 34% in patients with type II DM (Bringhurst et al., 2005). Vitamin D deficiency was detected in 37.9% of patients with type II DM. In the study of Kull et al. (2009), vitamin D deficiency was found to be lower in women than in men. In a study conducted in Japan (Suzuki et al., 2006), vitamin D deficiency was reported as 70.6%, in the United States (Di Cesar et al., 2006) 63.5%, and in a study among the South Asians in England (Tahrani et al., 2010) 83%. In another study of female type II DM patients, the prevalence of vitamin D deficiency was reported to be 39% (Isaia et al., 2001). Although different results have been obtained in each study conducted by the researchers, the prevalence of vitamin D deficiency is increasing in patients with type II DM. The necessity of examining vitamin D levels in these patients gains importance. Studies have shown that vitamin D deficiency is associated with the development of type II DM (Pittas et al., 2007). Gilani et al. (2019) found low 25-hydroxy vitamin D levels in obese and diabetic patients in a study. Similar results were reported by Bani-Issa et al. (2017). In a study of United Arab Emirates, they found low levels of 25-hydroxy vitamin D in 74% of patients. Pittas et al. (2007), reported in their study that vitamin D intake would be beneficial in reducing the risk of type II DM. Rafiq et al. (2018), as a result of the meta-analysis of their observational studies in patients with type II DM, they found vitamin D levels to be statistically significant. In our study, we found low levels of 25-hydroxy vitamin D as  $13.94 \pm 4.12$  ng / ml. When we compared 25-hydroxy vitamin D levels in female patients compared to male patients, we found that their levels were low in female patients. In a study followed by Forouhi et al. (2008) for 10 years, they found a significant correlation between 25-OH vitamin D levels and insulin and HOMA-IR. This finding supports that insulin resistance increases as vitamin D levels decrease in patients with type II DM.

Studies in Europe and China have shown that HbA1c measurement increases the number of defined prediabetic individuals (Kim et al., 2008; Sato et al., 2009). Kim et al. (2012) evaluated the patients according to HbA1c and observed a significant increase in the number of prediabetic individuals. Gerdhem et al. 2005, studies in non-Latin American black people were found to be higher than the average HbA1c. This may be due to

the variability of erythrocyte half-life and glycation according to race / ethnic groups (Mosekilde, 2005). According to a study published in the Johns Hopkins School of Medicine, 91% of patients with type II DM had a deficiency of 25-hydroxy vitamin D. In our study, we found high levels of HbA1c in type II DM patients. In our patient group, we found statistically significant results between HbA1c levels and 25-OH vitamin D levels.

Cetin et al. (2020) reported that 37% of the patients were male, 63% were female, and the mean age was  $49.3 \pm 10.4$  years. In addition, they found that HbA1c was lower than 5.7% in 15% of the cases, between 5.7-6.4% in 60%, and higher than 6.5% in 25%. Öner et al. (2016), in their study, 274 patients (85.6%) with vitamin D levels below 20 ng/mL, 37 patients between 20-30 ng/mL (11.6%), and 9 patients with a vitamin D level above 30 ng/mL. (2.8%) used the patient as material. In addition, they found a statistically significant difference in the vitamin D values of the patients between the HbA1c groups ( $p < 0.05$ ). They reported that vitamin D value was lower in the HbA1c  $> 7\%$  group compared to the HbA1c  $\leq 7\%$  group. A negative correlation was found between vitamin D and HbA1c levels. But the p-value was 0.083 and it was not statistically significant.

In a 17-year cohort study, an inverse relationship was found between type 2 DM and vitamin D, and it was found that vitamin D protects against DM (Knekt et al., 2008). In a study by Liu et al. (2010), it was determined that high vitamin D levels reduce the risk of developing type 2 DM. Pittas et al. (2006) They found that 4843 of 83,779 adult women followed for 20 years developed DM. In addition, it was found that women who took higher levels of vitamin D and Ca had a 13% lower risk of developing type 2 DM compared to those who took lower levels of vitamin D and Ca.

It has been reported that there may be low levels of HbA1c, which is characterized by seasonal variation, in relation to vitamin D levels, and that it reaches its lowest levels in summer (Beaulieu et al., 1993). As a result of another study in which 171 patients with type 2 DM were followed for about 10 years, it was determined that 125 (73%) patients had vitamin D deficiency, 14 patients had vitamin D insufficiency and the other 32 patients had optimal vitamin D levels. However, it has been reported that patients with vitamin D deficiency have higher HbA1c levels (Khaleeli et al., 2007). It was found similar to the studies in our study. Vitamin D level was found to be higher in male patients. Öner et al. (2016) found no relationship between vitamin D and HbA1c levels in their study. In the study conducted by Suzuki et al. (2006), no significant correlation was found between the vitamin D levels of the patients and the treatment modalities ( $p = 0.205$ ). They also found a negative correlation between vitamin D and HbA1c. However, this relationship was not

statistically significant ( $p=0.083$ ). Kör (2018), reported that 25(OH) D levels were deficient or insufficient in 31.8% of the patients in his study. There was no statistically significant difference between 25(OH)D values according to the HbA1c levels of the patients. According to Baykan et al. (2022) reported that there was no significant relationship between HbA1c and vitamin D, according to their study. In their study, Hyppönen et al. (2001) reported that Vitamin D deficiency in diabetic patients caused high HbA1c value, that is, poorly controlled diabetes.

### Conclusion

HbA1c values were found to be higher in patients with type II DM, as expected. 25-hydroxy vitamin D levels were found to be low. The low 25-hydroxy vitamin D level in these patients reports that they need vitamin supplements. However, the permanent inclusion of 25-hydroxy vitamin D in treatment protocols necessitates further research.

### Conflict of Interest

The author has no conflicts of interest to declare.

### Financial Disclosure

The author declares that this study has received no financial support.

### Ethical Approval

The study was performed after the approval [By the Ethics Committee, Sakarya University Medicine Faculty, Number: 71522473/050.01.04/72].

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