



The Frequency of Vitamin D Deficiency in Obese Patients on Bariatric Surgery Wait List: Is there any Association with Co-existence of Prediabetes or Diabetes?

Bariyatrik Cerrahi Bekleme Listesindeki Obez Hastalarda Vitamin D Eksikliğinin Sıklığı: Eşlik Eden Prediyabet veya Diyabet ile İlişkili mi?

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Abstract

Objective: The impact of co-existence of prediabetes on 25(OH)D3 deficiency is less known. We investigated the prevalence and predictors of 25(OH)D3 deficiency in obese adults on the bariatric surgery waitlist.

Material and Methods: One hundred ninety-nine patients without known chronic diseases including diabetes mellitus (DM) and hypertension were included. Anthropometric, biochemical, and hormonal [fasting insulin, C-peptide, 25(OH)D3] parameters were analyzed. Insulin resistance (IR) was calculated using the homeostasis model assessment of IR (HOMA-IR). Patients having HOMA-IR of ≥ 2.5 were considered insulin resistant. Patients were divided into subgroups according to body mass index (BMI), fasting blood glucose, HOMA-IR, glycated hemoglobin A1c (HbA1c), and 25(OH)D3 levels.

Results: According to HbA1c levels, prediabetes and DM were diagnosed in 39.6% (n=79) and 27.1% (n=54) of patients. The 25(OH)D3 levels were severely deficient, deficient, and insufficient in 47.2%, 36.7%, and 10.6% of patients; however, the levels were sufficient (≥ 30 ng/mL) only in 5.5%. The mean 25(OH)D3 level was 9.59, 9.76, and 12.08 ng/mL in nondiabetic, prediabetic, and diabetic patients ($p > 0.05$). BMI and 25(OH)D3 levels were negatively correlated ($p = 0.045$, $r = -0.142$). HOMA-IR was not correlated with 25(OH)D3 levels ($p = 0.98$); it was similar in patients with different 25(OH)D3 levels. Age ≥ 40 years and male gender were significant predictors for severe 25(OH)D3 deficiency, but IR, prediabetes, and DM were not significant predictors.

Conclusion: Increased BMI was associated with decreased 25(OH)D3 levels. The co-existence of prediabetes does not seem to affect 25(OH)D3 levels. Age ≥ 40 years and male gender were significant predictors for severe 25(OH)D3 deficiency. Severe 25(OH)D3 deficiency was frequent in obese patients on the bariatric surgery waitlist. Vitamin D deficiency was also shown in other studies on obesity. 25(OH)D3 levels should be measured in all patients undergoing bariatric surgery and managed accordingly. The effect of preoperative vitamin D replacement on postoperative weight loss will clarify the association between vitamin D levels and obesity.

Keywords: Vitamin D deficiency; prediabetes; diabetes mellitus; insulin resistance; obesity

Özet

Amaç: Eşlik eden prediyabetin 25(OH)D3 eksikliği üzerindeki etkisi az bilinmektedir. Bariyatrik cerrahi bekleme listesindeki obez hastalarda, 25(OH)D3 eksikliğinin prevalansı ve prediktörlerini araştırmayı amaçladık.

Gereç ve Yöntemler: Diabetes mellitus (DM) ve hipertansiyon gibi bilinen kronik hastalıkları olmayan 199 hasta dâhil edildi. Antropometrik, biyokimyasal ve hormonal [açlık insülin, C-peptid, 25(OH)D3] parametreler analiz edildi. İnsülin direnci, "homeostasis model assessment of IR (HOMA-IR)" ile hesaplandı. HOMA-IR $\geq 2,5$ olan hastalarda insülin direnci [insulin resistance (IR)] varlığı kabul edildi. Hastalar beden kitle indeksi (BKİ), açlık kan şekeri, HOMA-IR, hemogloblin A1c (HbA1c) ve 25(OH)D3 düzeyine göre gruplandırıldı.

Bulgular: HbA1c düzeyine göre, hastaların %39,6 (n=79)'sında prediyabet, %27,1 (n=54)'inde DM saptandı. 25(OH)D3 düzeyi hastaların %47,2'sinde ciddi eksik, %36,7'sinde eksik, %10,6'sında yetersiz, yalnızca %5,5'inde yeterliydi (≥ 30 ng/mL). Diyabetik olmayan, prediyabetik ve diyabetik gruplarda ortalama 25(OH)D3 düzeyi 9,59, 9,76 ve 12,08 ng/mL saptandı ($p > 0,05$). BKİ ile 25(OH)D3 arasında negatif korelasyon saptandı ($p = 0,045$, $r = -0,142$). HOMA-IR ile 25(OH)D3 korele değildi ($p = 0,98$). Farklı 25(OH)D3 kategorilerinde HOMA-IR değerleri benzerdi. İleri yaş (≥ 40) ve erkek cinsiyet ciddi 25(OH)D3 eksikliği için önemli birer prediktör olarak bulundu. İR, prediyabet veya DM ciddi 25(OH)D3 eksikliği için önemli bir prediktör değildi.

Sonuç: Artmış BKİ, düşük 25(OH)D3 düzeyiyle ilişkiliydi. Eşlik eden prediyabetin 25(OH)D3 düzeyi üzerinde önemli bir etkisi yoktu. İleri yaş ve erkek cinsiyet ciddi 25(OH)D3 eksikliği için önemli prediktörlerdi. Bariyatrik cerrahi bekleme listesindeki obez hastalarda, ciddi 25(OH)D3 eksikliğinin sık görüldüğü akıld tutulmalıdır. Obezitede vitamin D eksikliği başka çalışmalarda da gösterilmiştir. 25(OH)D3 düzeyi, bariyatrik cerrahi yapılacak tüm hastalarda ölçülmelidir ve gerektiğinde uygun bir şekilde replase edilmelidir. Preoperatif vitamin D replasmanının postoperatif kilo kaybına etkisinin araştırılması, obezite ve vitamin D arasındaki ilişkiyi daha net ortaya koyacaktır.

Anahtar kelimeler: Vitamin D eksikliği; prediyabet; diabetes mellitus; insülin direnci; obezite

We presented our study in the 19th European Congress of Endocrinology 2017 (20–23 May 2017, Lisbon, Portugal) as an electronic poster (EP703). However, we expanded the statistical analysis before the preparation of article.

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Introduction

Vitamin D also acts as a hormone because individuals having sufficient exposure to sunlight can produce adequate amounts of vitamin D in the skin. Vitamin D has several extraskeletal effects on target tissues. Higher 25(OH)D₃ levels (>30-40 ng/mL) are related to a lower risk of autoimmune diseases, cancer, and cardiovascular disorders (1-3). The deficiency of 25(OH)D₃ has increased worldwide. Several studies have investigated the status of vitamin D deficiency in Turkey (4-6). The studies have shown that the deficiency was more prevalent in women, especially veiled women and older women (4-6).

Vitamin D deficiency was also suggested to be related to obesity, insulin resistance (IR), and type 2 diabetes mellitus (DM) (7-9). The deficiency was defined as an important contributor to IR by either affecting insulin sensitivity or beta-cell function (10-12). A study in Turkey showed that the frequency of vitamin D deficiency was increased in diabetic patients with obesity (13).

Obesity is a disorder of increased adiposity and commonly measured by body mass index (BMI). Similar to the other regions of the world, obesity has been increasingly detected in Turkey. The prevalence of obesity is as high as 22-32% in Turkey (14). Obesity is a risk factor in the development of type 2 DM and is the most common cause of IR (15), and is also associated with vitamin D deficiency (16). IR may be defined as a lesser degree of biological activity with a certain amount of insulin. IR bridges between obesity and the development of type 2 DM (17,18).

In our study, we examined the prevalence, contributors, and predictors of 25(OH)D₃ deficiency in obese adults on the bariatric surgery waitlist. We specifically chose such adults because we expected that we could detect low vitamin D levels and subclinical deficiency of other hormones, such as thyroid, in these adults. We particularly wanted to reveal the effect of co-existence of prediabetes on vitamin D deficiency, if present. We also aimed to reveal the association between IR, BMI, and 25(OH)D₃ levels.

Material and Methods

Obese adult patients (age between 18 and 65 years) who were referred to our clinics for bariatric surgery between January 2016 and December 2017 were included. Patients with chronic diseases (such as DM, hypertension, prediabetes, and chronic liver or renal failure) or using any medication continuously were excluded; finally, 199 patients were included. Patients with known DM or using antidiabetics were excluded because antidiabetics could affect insulin, IR, and fasting blood glucose (FBG) measurements. Patients younger than 18 years or older than 65 years were excluded.

Our study was approved by the Ethics Committee of our university and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All participants gave informed consent prior to their inclusion in the study.

The electronic files of the patients were evaluated retrospectively. Anthropometric measurements of the patients (height, body weight, and BMI) were noted and analyzed. Biochemical (FBG, glycated hemoglobin [HbA_{1c}]) and hormonal (fasting insulin, C-peptide, 25[OH]D₃) results of the patients were also analyzed. We calculated IR by using the homeostasis model assessment of IR (HOMA-IR) as follows: $\text{FBG (mg/dL)} \times \text{fasting insulin (mU/L)} / 405$. Patients having an HOMA-IR value of ≥ 2.5 were considered insulin resistant.

FBG was measured after an overnight fast by using the glucose oxidase method. In our routine clinical practice, HbA_{1c} was measured as the National Glycohemoglobin Standardization Program units by using high-performance liquid chromatography. Fasting insulin (mU/L) and C-peptide (ng/mL) levels were measured after an overnight fast by using radioimmunoassay and immunometric assay, respectively. The levels of 25(OH)D₃ (ng/mL) were measured using an immunoassay.

Patients were grouped according to their BMI as 35-39.9 kg/m² (n=16), 40-49.9 kg/m² (n=145), and ≥ 50 kg/m² (n=38).

Patients were also classified according to their vitamin D status as sufficient [25(OH)D₃ ≥30, n=11], insufficient (25(OH)D₃=20-29.9, n=21), deficient (25(OH)D₃=10-19.9, n=73), and severely deficient (25(OH)D₃ <10, n=94). Furthermore, patients were also grouped according to HOMA-IR values: insulin resistant (n=178) and noninsulin resistant (n=21). Patients were also grouped according to their HbA1c (<5.7, 5.7-6.4, and ≥6.5) and FBG values (<100, 100-125, and ≥126 mg/dL) as nondiabetic, with prediabetes, or having new-onset DM. Prediabetes was defined as having an FBG value of 100-125 mg/dL and/or HbA1c of 5.7-6.4%.

Statistical Analysis

Study data were analyzed by using SPSS version 22.0 (IBM Corporation, Armonk, New York, USA). The conformity of univariate data to normal distribution was evaluated with the Shapiro-Wilk test and the Kolmogorov-Smirnov test and the homogeneity of variance were evaluated with the Levene test. Categorical variables were compared with each other by Pearson's Chi-square test. Independent-Samples t-test was used to compare independent groups with each other according to quantitative data. Furthermore, one-way ANOVA for parametric analysis and the Kruskal-Wallis H test for nonparametric analysis were used to compare more than two independent groups according to quantitative data. The Conover test was used for post hoc analyses. Pearson's correlation test was used to analyze the correlations of variables with each other. Multivariate logistic regression (LR) analysis was used to determine the risk groups for parameters causing severe vitamin D deficiency. Odds ratio (OR) was calculated with 95% confidence intervals (CIs) to show that risk groups had a higher risk compared with other subjects. Quantitative variables are shown as mean±standard deviation (SD) and median (minimum, maximum) and categorical variables as n (%) in tables. A p-value <0.05 was accepted as statistically significant.

Results

Of the patients, 64.9% patients were women. The mean age and BMI were similar in both genders (p=0.055 and p=0.49). The mean FBG, insulin, and HOMA-IR values were significantly higher in male patients (p=0.002, p=0.001, and p=0.001) than in female patients. The mean basal fasting C-peptide level was also significantly higher in male patients (p<0.0001) than in female patients. The mean 25(OH)D₃ and HbA1c levels were similar in both groups (Table 1). According to the FBG values, prediabetes and new-onset DM were diagnosed in 28.1% (n=56) and 22.1% (n=44) of patients. According to the HbA1c levels, prediabetes and new-onset DM were diagnosed in 39.6% (n=79) and 27.1% (n=54) of patients.

The male/female ratio, mean age, FBG, insulin, HOMA-IR, and HbA1c levels were higher in diabetic and prediabetic groups than in the nondiabetic group. The mean 25(OH)D₃ level was 9.59, 9.76, and 12.08 ng/mL in nondiabetic, prediabetic, and diabetic groups. The level of 25(OH)D₃ and BMI were not significantly different in the three groups. HOMA-IR was significantly higher in the diabetic group than in the prediabetic group or the nondiabetic group. Insulin levels were significantly higher in the diabetic group than in the nondiabetic group (Table 2). Overall, 91.9% of patients were morbidly obese; the remaining patients were also obese but their BMI was 35-39.9 kg/m². The mean 25(OH)D₃, FBG, insulin, HOMA-IR scores, HbA1c, and C-peptide levels were similar in the different BMI subgroups (Table 3). The levels of 25(OH)D₃ were significantly lower in the groups having BMI ≥50 kg/m² and 40-49.9 kg/m² in comparison with the group having BMI 35-39.9 kg/m² (p=0.042 and p=0.025).

The 25(OH)D₃ levels were severely deficient, deficient, and insufficient in 47.2%, 36.7%, and 10.6% of patients, respectively. However, it was sufficient (≥30 ng/mL) only in 5.5% of patients. There were no differences regarding the distribution of BMI in 25(OH)D₃ subgroups; BMI was similar in different 25(OH)D₃ subgroups (Table 4).

Table 1. Clinical and laboratory parameters of the patients.

	Male (n=61)	Female (n=138)	p
	mean ±SD		
Age	40.26±11.027	36.93±11.33	0.055
BMI (kg/m ²)	45.82±5.47	45.24±5.38	0.490
FBG (mg/dL)	135.08±72.15	110.29±37.52	0.002
Insulin (mIU/L)	49.67±47.09	25.71±32.13	0.001
HOMA-IR	18.03±24.65	6.48±4.81	0.001
C-peptide (ng/mL)	5.85±3.69	3.61±1.48	<0.0001
HbA1c (%)	6.73±1.62	6.49±4.80	0.710
25(OH)D3 (ng/mL)	13.22±6.40	12.17±8.99	0.410

Table 2. Clinical and laboratory features of the patient groups according to HbA1c groups.

Variables	Nondiabetic (n=53)	Prediabetic (n=79)	Diabetic (n=54)	Total (n=186)	p value
Gender (m/fm)	11/42	24/55	24/30	59/127	0.030
Median (min.-max.)					
Age	32 (20-56)	36 (20-60)	47 (23-62)	38 (20-62)	0.001
BMI	43.5 (38.4-76.3)	44.6 (38.7-58)	44.4 (36-58.3)	44.3 (36-76.3)	0.415
25(OH)D3	9.59 (3-40.7)	9.76 (3-36.2)	12.08 (3-52.1)	10.49 (3-52.1)	0.103
FBG	92 (72-113)	98 (78-125)	145.5 (94-436)	101 (72-436)	0.001
Insulin	20.8 (2-100)	21.2 (5-361)	27.25 (6-300)	22.35 (2-361)	0.048
HOMA-IR	4.56 (0.46-24.93)	5.49 (1.40-36.74)	11.07 (1.96-166)	5.88 (0.46-166)	0.001
HbA1c	5.3 (4.5-5.6)	5.9 (5.0-6.4)	7.1 (6.4-12.2)	5.9 (4.5-12.2)	0.001
C-peptide	3.54 (0.7-9.9)	3.65 (1.2-15)	4.09 (1.5-20)	3.62 (0.7-20)	0.052

Table 3. Comparison of laboratory parameters between the BMI subgroups.

	BMI subgroups (kg/m ²)			Total (n=199)	p value
	35-39.9 (n=16)	40-49.9 (n=145)	≥50 (n=38)		
mean±SD					
25(OH)D3	17.03±9.85	12.13±8.08	12.01±8.0	12.50±8.28	0.073
FBG	129.13±57.32	115.43±50.94	122.53±53.20	117.89±51.80	0.503
HOMA-IR	11.81±16.11	9.54±16.21	11.12±9.66	10.02±15.13	0.752
Insulin	36.14±41.65	29.39±29.99	45.71±60.44	33.05±38.85	0.066
HbA1c	6.62±1.94	6.24±1.19	7.88±9.12	6.57±4.07	0.108
C-peptide	4.07±2.11	4.04±2.35	5.25±3.26	4.28±2.57	0.035

Table 4. Distribution of BMI subgroups between 25(OH)D3 subgroups.

	25(OH)D3 (ng/mL)				Total	p value
	<10	10-19.9	20-29.9	≥30		
n (%)						
BMI (kg/m ²)						
35-39.9	6 (37.5)	4 (25.0)	3 (18.8)	3 (18.8)	16 (100)	0.249
40-49.9	71 (49.0)	54 (37.2)	14 (9.7)	6 (4.1)	145 (100)	
≥50	17 (44.7)	15 (39.5)	4 (10.5)	2 (5.3)	38 (100)	
Total	94 (47.2)	73 (36.7)	21 (10.6)	11 (5.5)	199 (100)	
BMI (kg/m ²) (Mean±SD)	45.59±5.05	45.65±5.94	45.51±4.75	42.27±5.47	45.42±5.40	0.267

Table 5. Distribution of 25(OH)D3 subgroups between insulin resistant and nonresistant patients.

		HOMA-IR subgroups			p-value	HOMA-IR mean ±SD	p-value
		Resistant	Non-resistant	Total			
25(OH)D3	Severely deficient	80 (85.1)	14 (14.9)	94 (100)	0.140	10.43 ±18.42	0.980
	Deficient	69 (94.5)	4 (5.5)	73 (100)			
	Insufficient	18 (85.7)	3 (14.3)	21 (100)			
	Sufficient	11 (100)	0 (0)	11 (100)			
	Total	178 (89.4)	21 (10.6)	199 (100)			

However, BMI was lower in the group having 25(OH)D3 level ≥30 ng/mL in comparison with the group having 25(OH)D3 level <10 ng/mL (p=0.05). No difference was found regarding the distribution of 25(OH)D3 in insulin-resistant and nonresistant groups. The mean HOMA-IR scores were similar between the different 25(OH)D3 subgroups (p=0.980) (Table 5). 25(OH)D3 levels were higher in insulin-resistant patients (Table 6). BMI correlated positively with C-peptide

Table 6. Comparison of 25(OH)D3 levels between insulin resistant and nonresistant patients.

HOMA-IR subgroups	25(OH)D3		
	n	mean±SD	p-value
Resistant	178	12.86±8.39	0.032
Non-resistant	21	9.41±6.72	

levels and negatively with 25(OH)D3 levels (Table 7 and Figure 1). Glucose levels pos-

Table 7. Correlation between the variables.

		BMI	FBG	Insulin	HOMA-IR	C-peptide	HbA1c	25(OH)D3
BMI	r	1	-0.024	0.128	0.033	0.149*	0.061	-0.142*
	p		0.732	0.072	0.647	0.039	0.411	0.045
	n	199	199	199	199	192	186	199
FBG	r		1	0.166*	0.486**	0.148*	0.231**	0.086
	p			0.019	0.000	0.040	0.002	0.228
	n		199	199	199	192	186	199
Insulin	r			1	0.721**	0.639**	0.005	-0.027
	p				0.0001	0.0001	0.943	0.702
	n			199	199	192	186	199
HOMA-IR	r				1	0.677**	0.074	0.001
	p					0.0001	0.316	0.988
	n				199	192	186	199
C-peptide	r					1	-0.015	0.008
	p						0.845	0.910
	n					186	180	192
HbA1c	r						1	0.058
	p							0.434
	n						186	186
25(OH)D3	r							1
	p							
	n							199

*Correlation is significant at the 0.05 level. **Correlation is significant at the 0.01 level.

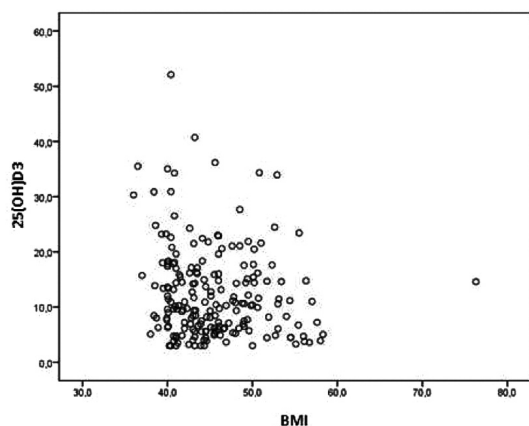


Figure 1: Correlation between 25(OH)D3 levels and BMI.

*Correlation coefficient: -0.142 and p-value: 0.045.

Table 8. Multivariate forward logistic regression showing predictors for severe vitamin D deficiency in obese patients.

Variables	OR (95% CI)	p value
Age (≥ 40 or < 40)	2.017 (1.109-3.668)	0.021
Gender (male or female)	1.957 (1.023-3.744)	0.043
BMI (≥ 40 or < 40)	1.544 (0.539-4.424)	0.416
FBG (≥ 126 or < 100)	0.496 (0.239-1.029)	0.058
FBG (100-125 or < 100)	0.700 (0.362-1.352)	0.287
HbA1c (≥ 6.5 or < 5.7)	0.523 (0.241-1.136)	0.100
HbA1c (5.7-6.4 or < 5.7)	1.039 (0.518-2.084)	0.914
C-peptide (≥ 5 or < 5)	0.870 (0.440-1.721)	0.688
HOMA-IR (≥ 2.5 or < 2.5)	0.408 (0.157-1.060)	0.059

itively correlated with insulin, HOMA-IR, HbA1c, and C-peptide levels. Insulin levels also positively correlated with HOMA-IR and C-peptide levels. Glucose, insulin, HOMA-IR, C-peptide, and HbA1c levels did not correlate with 25(OH)D3 levels (Table 7).

Multivariate forward LR was performed to show the predictors for severe vitamin D deficiency (25[OH]D3 < 10 vs. ≥ 10 ng/mL) (Table 8). Age ≥ 40 years and male gender were predictors for severe vitamin D deficiency. The other parameters could not be entered into the model. Thus, IR (according to HOMA-IR), pre-DM, and DM were not predictors of severe vitamin D deficiency.

Discussion

The 25(OH)D3 levels were lower in patients with morbid obesity compared with other patients. The mean vitamin D level was similar in nondiabetic, prediabetic, and diabetic patients. Age ≥ 40 years and male gender were significant predictors for severe vitamin D deficiency. However, IR, prediabetes, DM, and morbid obesity were not predictors. In contrast to previous studies, we found no correlation between 25(OH)D3 levels and HOMA-IR (19-21). The Third National Health and Nutrition Examination Survey showed a negative association between 25(OH)D3 levels and IR in non-Hispanic white people and Mexican Americans (21). One study including subjects in Korea also showed a negative relation between 25(OH)D3 levels and IR (22). These findings were confirmed by other reports (23). Chiui et al. showed decreased first and second phase insulin secretion response in vitamin D-deficient subjects (10). Similarly, in a study including young adult women with obesity, an inverse relation was detected between vitamin D3 levels and IR (24). Many studies have revealed the role of vitamin D deficiency in insulin secretion or resistance and inflammatory processes (25-29). Vitamin D deficiency decreases insulin secretion; glucose uptake to the liver, striated muscles, and adipose tissue; and decreases GLUT-4 (glucose transporter-4) expression in skeletal muscles (30). However, conflicting results exist regarding the benefits of vitamin D replacement on insulin sensitivity (10,31,32).

Bilge et al. investigated the relationship between BMI and IR or 25(OH)D3 levels (33). The authors demonstrated a negative correlation between vitamin D3 levels and BMI (33). Other studies have also shown this negative correlation (23,24,34), and this correlation was seen both in summer and winter (31). An analysis showed that each 1 kg/m² increase in BMI was associated with 1.15% decrease in vitamin D3 levels (35). In our study, 25(OH)D3 levels were negatively correlated with BMI. However, some reports have shown that BMI was not different in different vitamin D subgroups (36). Central adiposity is also an

important contributor to this association (15,23). We found a higher mean vitamin D level in the insulin-resistant group. Although obesity was found as a risk factor in vitamin D deficiency (23,24,34,37,38), our findings might suggest that the possible effects of the factors other than IR. However, in our study, neither IR nor BMI were found as predictors for severe vitamin D deficiency.

IR plays an important role in the pathogenesis of type 2 DM from the beginning of the process. The higher rate of vitamin D deficiency in type 2 DM was thought to occur through IR (19-21). Pittas et al. showed that the risk for type 2 DM was lower in patients with higher levels of vitamin D₃ (39). Song et al. showed that the risk of diabetes decreased by 38% in the group with the highest vitamin D₃ level comparing with the group with the lowest level (40). A meta-analysis found that diabetes risk increased by 50% in the low vitamin D group than in the high vitamin D group (41). However, in another report, lower 25(OH)D₃ levels were not associated with the risk of diabetes (42). The deficiency of 25(OH)D₃ was observed to be associated with glucose intolerance in several studies (37,43,44). 25(OH)D₃ has an important place in insulin sensitivity, as it increases insulin sensitivity of the liver and skeletal muscles and increases beta-cell function. Decreased vitamin D levels were found in patients with beta-cell dysfunction (45-47). In one study, 25(OH)D₃ deficiency was associated with increased fasting insulin levels (23). However, we found that 25(OH)D₃ levels were higher in insulin-resistant patients, negatively correlated with BMI, and were similar in diabetic, prediabetic, and nondiabetic groups. These findings showed that vitamin D had complex interactions with diabetes other than obesity and IR. Studies analyzing the effect of co-existence of prediabetes or DM on vitamin D levels are limited. In our study, the co-existence of DM or prediabetes seems to have no important effect on vitamin D levels. However, in one study, the prediabetic state was found to be associated with vitamin D₃ levels in the first quartile compared with the

fourth quartile with an odds ratio of 1.47 (48).

The prevalence of vitamin D deficiency is the highest in elderly or hospitalized patients. One study showed that nearly 60% of nursing or hospitalized patients had vitamin D deficiency (49,50). However, two-thirds of young adults also had vitamin D deficiency in the United States (51). In older subjects, vitamin D production decreases and they require increased nutritional intake of vitamin D (52). Similarly, we found that age ≥ 40 was an important predictor of severe vitamin D deficiency. The rate of vitamin D deficiency was found higher in the Middle East than in the other parts of the world (53-57). About 70-80% of young adults in the Middle East have severe vitamin D deficiency, and it was more common in women. However, in our study, male gender was an important predictor for severe vitamin D deficiency. Vitamin D deficiency is common in Turkey; however, it is more common in obese patients on a bariatric surgery waitlist.

Limitations and Strengths

In several studies investigating vitamin D status in obese patients, overweight and/or normal weight adult subjects were also included. However, we could not include a subgroup having a normal BMI to compare with obese patients. Similarly, in contrast to the previous studies, we did not evaluate the waist-to-hip ratio of the patients, which might be an important factor in affecting vitamin D status. Lipid measurements also might be included to detect the possible link between lipids and vitamin D deficiency. Our study has several strengths such as including the adult subjects on a bariatric surgery waitlist. To the best of our knowledge, studies investigating vitamin D status in such adult subjects are limited. Additionally, our sample consisted mostly of morbidly obese patients. Another strength was the exclusion of patients using any medication continuously or having chronic illness.

Conclusion

Our findings suggest that BMI and vitamin D levels are negatively correlated. We found

that new-onset prediabetes and DM were diagnosed in a remarkable number of patients awaiting bariatric surgery. However, the co-existence of prediabetes seems to have no important effect on vitamin D levels. Being older and male gender were significant predictors for severe vitamin D deficiency. Severe vitamin D deficiency was frequent in obese patients on a bariatric surgery waitlist, especially in morbidly obese patients. Additionally, vitamin D deficiency is a common phenomenon after bariatric surgery. It may contribute to post-operative complications such as muscle loss or decreased bone density. If the deficiency is not corrected preoperatively and in the presence of other mineral and vitamin deficiencies developing in the immediate post-operative period, cardiac or neuromuscular complications would also occur. Therefore, vitamin D levels should be measured in all patients before bariatric surgery and managed accordingly.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Author Contributions

Idea/Concept: Ömercan Topaloğlu, İbrahim Şahin, Saim Yoloğlu; Design: Ömercan Topaloğlu, İbrahim Şahin, Saim Yoloğlu; Control/Supervision: Ömercan Topaloğlu, İbrahim Şahin, Bahri Evren, Şelale Şahin; Data Collection and/or Processing: Ömercan Topaloğlu, Bahri Evren; Analysis and/or Interpretation: Ömercan Topaloğlu, İbrahim Şahin, Şelale Şahin, Saim Yoloğlu;

Literature Review: Ömercan Topaloğlu, İbrahim Şahin; Writing the Article: Ömercan Topaloğlu, Bahri Evren, İbrahim Şahin, Şelale Şahin; Critical Review: Ömercan Topaloğlu, İbrahim Şahin; References and Fundings: Ömercan Topaloğlu, Bahri Evren; Materials: Ömercan Topaloğlu, İbrahim Şahin.

References

1. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007;357:266-281. [[Crossref](#)] [[PubMed](#)]
2. Bouillon R, Van Schoor NM, Gielen E, Boonen S, Mathieu C, Vanderschueren D, Lips P. Optimal vitamin D status: a critical analysis on the basis of evidence-based medicine. *J Clin Endocrinol Metab*. 2013;98:E1283-E1304. [[Crossref](#)] [[PubMed](#)]
3. Rosen CJ, Adams JS, Bikle DD, Black DM, Demay MB, Manson JE, Murad MH, Kovacs CS. The nonskeletal effects of vitamin D: an Endocrine Society scientific statement. *Endocr Rev*. 2012;33:456-492. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
4. Atli T, Gullu S, Uysal AR, Erdogan G. The prevalence of vitamin D deficiency and effects of ultraviolet light on vitamin D levels in elderly Turkish population. *Arch Gerontol Geriatr*. 2005;40:53-60. [[Crossref](#)] [[PubMed](#)]
5. Alagöl F, Shihadeh Y, Boztepe H, Tanakol R, Yarman S, Azizlerli H, Sandalci O. Sunlight exposure and vitamin D deficiency in Turkish women. *J Endocrinol Invest*. 2000;23:173-177. [[Crossref](#)] [[PubMed](#)]
6. Guzel R, Kozanoglu E, Guler-Uysal F, Soyupak S, Sarpel T. Vitamin D status and bone mineral density of veiled and unveiled Turkish women. *J Womens Health Gend Based Med*. 2001;10:765-770. [[Crossref](#)] [[PubMed](#)]
7. Scragg R, Holdaway I, Singh V, Metcalf P, Baker J, Dryson E. Serum 25-hydroxyvitamin D3 levels decreased in impaired glucose tolerance and diabetes mellitus. *Diabetes Res Clin Pract*. 1995;27:181-188. [[Crossref](#)] [[PubMed](#)]
8. Baynes KC, Boucher BJ, Feskens EJ, Kromhout D. Vitamin D, glucose intolerance and insulinaemia in elderly men. *Diabetologia*. 1997;40:344-347. [[Crossref](#)] [[PubMed](#)]
9. Gagnon C, Lu ZX, Magliano DJ, Dunstan DW, Shaw JE, Zimmet PZ, Sikaris K, Grantham N, Ebeling PR, Daly RM. Serum 25-hydroxyvitamin D, calcium intake, and risk of type 2 diabetes after 5 years: results from a national, population-based prospective study (the Australian Diabetes, Obesity and Lifestyle study). *Diabetes Care*. 2011;34:1133-1138. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
10. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. *Am J Clin Nutr*. 2004;79:820-825. [[Crossref](#)] [[PubMed](#)]

11. Deleskog A, Hilding A, Brismar K, Hamsten A, Efendic S, Östenson CG. Low serum 25-hydroxyvitamin D level predicts progression to type 2 diabetes in individuals with prediabetes but not with normal glucose tolerance. *Diabetologia*. 2012;55:1668-1678. [[Crossref](#)] [[PubMed](#)]
12. Frouhi NG, Ye Z, Rickard AP, Khaw R, Langenberg C, Wareham NJ. Circulating 25-hydroxyvitamin D concentration and the risk of type 2 diabetes: results from the European Prospective Investigation into Cancer (EPIC)-Norfolk cohort and updated metaanalysis of prospective studies. *Diabetologia*. 2012;55:2173-2182. [[Crossref](#)] [[PubMed](#)]
13. Altinova AE, Aktürk M, Törüner F, Kaya M, Bukan N, Yetkin İ, Çakır N, Arslan M. The prevalence of vitamin D deficiency and its relationship with CRP, fibrinogen, glycemic control and insulin resistance in patients with type 2 diabetes mellitus. *Gazi Med J*. 2010;21:117-120.
14. Satman I, Yilmaz T, Sengül A, Salman S, Salman F, Uygur S, Bastar I, Tütüncü Y, Sargin M, Dinççag N, Karsidag K, Kalaça S, Ozcan C, King H. Population-based study of diabetes and risk characteristics in Turkey: results of the Turkish diabetes epidemiology study (TURDEP). *Diabetes Care*. 2002;25:1551-1556. [[Crossref](#)] [[PubMed](#)]
15. Ford ES, Ajani UA, McGuire LC, Liu S. Concentrations of serum vitamin D and the metabolic syndrome among U.S. adults. *Diabetes Care*. 2005;28:1228-1230. [[Crossref](#)] [[PubMed](#)]
16. Harris MI, Hadden WC, Knowler WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20-74 yr. *Diabetes*. 1987;36:523-534. [[Crossref](#)] [[PubMed](#)]
17. Bogardus C, Lillioja S, Mott DM, Hollenbeck C, Reaven GM. Relationship between degree of obesity and in vivo insulin action in man. *Am J Physiol*. 1985;248:E286-291. [[Crossref](#)] [[PubMed](#)]
18. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E, Knowler WC, Bennett PH, Bogardus C. Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus. Prospective studies of Pima Indians. *N Engl J Med*. 1993;329:1988-1992. [[Crossref](#)] [[PubMed](#)]
19. Lu L, Yu Z, Pan A, Hu FB, Franco OH, Li H, Li X, Yang X, Chen Y, Lin X. Plasma 25-hydroxyvitamin D concentration and metabolic syndrome among middle-aged and elderly Chinese individuals. *Diabetes Care*. 2009;32:1278-1283. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
20. Pham NM, Akter S, Kurotani K, Nanri A, Sato M, Hayabuchi H, Yasuda K, Mizoue T. Serum 25-hydroxyvitamin D and markers of insulin resistance in a Japanese working population. *Eur J Clin Nutr*. 2012;66:1323-1328. [[Crossref](#)] [[PubMed](#)]
21. Scragg R, Sowers M, Bell C; Third National Health and Nutrition Examination Survey. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. *Diabetes Care*. 2004;27:2813-2818. [[Crossref](#)] [[PubMed](#)]
22. Ock SY, Ha KH, Kim BK, Kim HC, Shim JS, Lee MH, Yoon YM, Kim DJ. Serum 25-hydroxyvitamin D concentration is independently inversely associated with insulin resistance in the healthy, non-obese Korean population. *Diabetes Metab J*. 2016;40:367-375. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
23. Tosunbayraktar G, Bas M, Kut A, Buyukkaragoz AH. Low serum 25(OH)D levels are associated to higher BMI and metabolic syndrome parameters in adult subjects in Turkey. *Afr Health Sci*. 2015;15:1161-1169. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
24. Abdelkarem HM, El-Sherif MA, Gomaa SB. Vitamin D status and insulin resistance among young obese Saudi females. *Saudi Med J*. 2016;37:561-566. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
25. Ford ES, Zhao G, Tsai J, Li C. Associations between concentrations of vitamin D and concentrations of insulin, glucose, and HbA1c among adolescents in the United States. *Diabetes Care*. 2011;34:646-648. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
26. Holick MF. Vitamin D: evolutionary, physiological and health perspectives. *Curr Drug Targets*. 2011;12:4-18. [[Crossref](#)] [[PubMed](#)]
27. Zittermann A, Gummert JF, Bergermann J. Vitamin D and mortality. *Curr Opin Clin Nutr Metab Care*. 2009;12:634-639. [[Crossref](#)] [[PubMed](#)]
28. Gupta AK, Brashear MM, Johnson WD. Prediabetes and prehypertension in healthy adults are associated with low vitamin D levels. *Diabetes Care*. 2011;34:658-660. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
29. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2007;92:2017-2029. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
30. Peterson CA, Tosh AK, Belenchia AM. Vitamin D insufficiency and insulin resistance in obese adolescents. *Ther Adv Endocrinol Metab*. 2014;5:166-189. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
31. Jorde R, Sneve M, Emaus N, Figenschau Y, Grimnes G. Cross-sectional and longitudinal relation between serum 25-hydroxyvitamin D and body mass index: the Tromsø study. *Eur J Nutr*. 2010;49:401-407. [[Crossref](#)] [[PubMed](#)]
32. Lee P, Greenfield JR, Seibel MJ, Eisman JA, Center JR. Adequacy of vitamin D replacement in severe deficiency is dependent on body mass index. *Am J Med*. 2009;122:1056-1060. [[Crossref](#)] [[PubMed](#)]

33. Bilge U, Ünalacak M, Ünlüoğlu I, Ipek M, Çeler Ö, Akalin A. Relationship between 1,25-dihydroxy Vitamin D levels and homeostatic model assessment insulin resistance values in obese subjects. *Niger J Clin Pract.* 2015;18:377-380. [[Crossref](#)] [[PubMed](#)]
34. Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridker PM. Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older US women. *Diabetes Care.* 2005;28:2926-2932. [[Crossref](#)] [[PubMed](#)]
35. Vimalaswaran KS, Berry DJ, Lu C, Tikkanen E, Pilz S, Hiraki LT, Cooper JD, Dastani Z, Li R, Houston DK, Wood AR, Michaëlsson K, Vandenput L, Zgaga L, Yerges-Armstrong LM, McCarthy MI, Dupuis J, Kaakinen M, Kleber ME, Jameson K, Arden N, Raitakari O, Viikari J, Lohman KK, Ferrucci L, Melhus H, Ingelsson E, Byberg L, Lind L, Lorentzon M, Salomaa V, Campbell H, Dunlop M, Mitchell BD, Herzig KH, Pouta A, Hartikainen AL; Genetic Investigation of Anthropometric Traits-GIANT Consortium, Streeten EA, Theodoratou E, Jula A, Wareham NJ, Ohlsson C, Frayling TM, Kritchevsky SB, Spector TD, Richards JB, Lehtimäki T, Ouwehand WH, Kraft P, Cooper C, März W, Power C, Loos RJ, Wang TJ, Jarvelin MR, Whittaker JC, Hingorani AD, Hyppönen E. Causal relationship between obesity and vitamin D status: bi-directional Mendelian randomization analysis of multiple cohorts. *PLoS Med.* 2013;10:e1001383. [[PubMed](#)]
36. Botella-Carretero JI, Alvarez-Blasco F, Villafrauela JJ, Balsa JA, Vázquez C, Escobar-Morreale HF. Vitamin D deficiency is associated with the metabolic syndrome in morbid obesity. *Clin Nutr.* 2007;26:573-580. [[Crossref](#)] [[PubMed](#)]
37. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr.* 2008;87:1080S-1086S. [[Crossref](#)] [[PubMed](#)]
38. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr.* 2000;72:690-693. [[Crossref](#)] [[PubMed](#)]
39. Pittas AG, Sun Q, Manson JE, Dawson-Hughes B, Hu FB. Plasma 25-hydroxyvitamin D concentration and risk of incident type 2 diabetes in women. *Diabetes Care.* 2010;33:2021-2023. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
40. Song Y, Wang L, Pittas AG, Del Gobbo LC, Zhang C, Manson JE, Hu FB. Blood 25-hydroxy vitamin D levels and incident type 2 diabetes: a meta-analysis of prospective studies. *Diabetes Care.* 2013;36:1422-1428. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
41. Afzal S, Bojesen SE, Nordestgaard BG. Low 25-hydroxyvitamin D and risk of type 2 diabetes: a prospective cohort study and metaanalysis. *Clin Chem.* 2013;59:381-391. [[Crossref](#)] [[PubMed](#)]
42. Robinson JG, Manson JE, Larson J, Liu S, Song Y, Howard BV, Phillips L, Shikany JM, Allison M, Curb JD, Johnson KC, Watts N. Lack of association between 25(OH)D levels and incident type 2 diabetes in older women. *Diabetes Care.* 2011;34:628-634. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
43. Tamer G, Mesci B, Tamer I, Kilic D, Arik S. Is vitamin D deficiency an independent risk factor for obesity and abdominal obesity in women? *Endokrynol Pol.* 2012;63:196-201. [[PubMed](#)]
44. Sung CC, Liao MT, Lu KC, Wu CC. Role of vitamin D in insulin resistance. *J Biomed Biotechnol.* 2012;2012:634195. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
45. Mathieu C, Gysemans C, Giulietti A, Bouillon R. Vitamin D and diabetes. *Diabetologia.* 2005;48:1247-1257. [[Crossref](#)] [[PubMed](#)]
46. Norman AW, Frankel JB, Heldt AM, Grodsky GM. Vitamin D deficiency inhibits pancreatic secretion of insulin. *Science.* 1980;209:823-825 [[Crossref](#)] [[PubMed](#)]
47. Cade C, Norman AW. Vitamin D3 improves impaired glucose tolerance and insulin secretion in the vitamin D-deficient rat in vivo. *Endocrinology.* 1986;119:84-90. [[Crossref](#)] [[PubMed](#)]
48. Devaraj S, Jialal G, Cook T, Siegel D, Jialal I. Low vitamin D levels in Northern American adults with the metabolic syndrome. *Horm Metab Res.* 2011;43:72-74. [[Crossref](#)] [[PubMed](#)]
49. Elliott ME, Binkley NC, Carnes M, Zimmerman DR, Petersen K, Knapp K, Behlke JM, Ahmann N, Kieser MA. Fracture risks for women in long-term care: high prevalence of calcaneal osteoporosis and hypovitaminosis D. *Pharmacotherapy.* 2003;23:702-710. [[Crossref](#)] [[PubMed](#)]
50. Thomas MK, Lloyd-Jones DM, Thadhani RI, Shaw AC, Deraska DJ, Kitch BT, Vamvakas EC, Dick IM, Prince RL, Finkelstein JS. Hypovitaminosis D in medical inpatients. *N Engl J Med.* 1998;338:777-783. [[Crossref](#)] [[PubMed](#)]
51. Tangpricha V, Pearce EN, Chen TC, Holick MF. Vitamin D insufficiency among free-living healthy young adults. *Am J Med.* 2002;112:659-662. [[Crossref](#)] [[PubMed](#)]
52. Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. *Am J Clin Nutr.* 2004;79:362-371. [[Crossref](#)] [[PubMed](#)]
53. van der Wielen RP, Löwik MR, van den Berg H, de Groot LC, Haller J, Moreiras O, van Staveren WA. Serum vitamin D concentrations among elderly people in Europe. *Lancet.* 1995;346:207-210. [[Crossref](#)] [[PubMed](#)]

54. Gannagé-Yared MH, Chemali R, Yaacoub N, Halaby G. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. *J Bone Miner Res.* 2000;15:1856-1862. [[Crossref](#)] [[PubMed](#)]
55. Looker AC, Gunter EW. Hypovitaminosis D in medical inpatients. *N Engl J Med.* 1998;339:344-346. [[Crossref](#)] [[PubMed](#)]
56. Fuleihan GE, Deeb M. Hypovitaminosis D in a sunny country. *N Engl J Med.* 1999;340:1840-1841. [[Crossref](#)] [[PubMed](#)]
57. Mishal AA. Effects of different dress styles on vitamin D levels in healthy young Jordanian women. *Osteoporos Int.* 2001;12:931-935. [[Crossref](#)] [[PubMed](#)]