

Relationship between 1,25-dihydroxy Vitamin D levels and homeostatic model assessment insulin resistance values in obese subjects

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Abstract

Aim: In this study, our aim is to evaluate the insulin resistance and quality of life in obese subjects and nonobese subjects and to find out the Vitamin D (VD) status and correlations between obesity and control groups and also according to their quality of life scores.

Materials and Method: The study was carried out between May and October 2013 which is the period of VD synthesis in Turkey. The participants of this study were volunteering individuals – obese and nonobese individuals defined according to the body mass index (BMI) – that did not receive any VD support in the last 1-year and did not have any known chronic diseases. 1,25-OH VD status and homeostatic model assessment insulin resistance (HOMA-IR) values were evaluated.

Results: The study population consisted of 39 individuals with normal weight (23 women, 16 men) and 66 individuals categorized as obese (51 women, 15 men). The difference in HOMA-IR and VD values between the group of obese individuals and the group of nonobese individuals was significant ($P < 0.001$ vs. $P < 0.001$). The median value of HOMA-IR was higher in the obese group than in the nonobese group ($P < 0.001$) while the median value of VD was higher in the nonobese group than in the obese group ($P < 0.001$). The results regarding the relationship of BMI with HOMA-IR and VD show that there was a positive correlation between HOMA-IR and BMI ($r_s = 0.507$; $P < 0.001$) and there was a negative correlation between HOMA-IR and VD ($r_s = -0.316$; $P = 0.0001$).

Conclusion: Given serious diseases associated with low serum VD levels such as diabetes and cardiovascular disorders as well as low side effect incidence and low cost of VD treatment, it would be a reasonable approach to identify routine serum 25(OH) D and/or 1,25-OH VD levels of obese patients and administer a treatment to patients with low levels of VD.

Key words: 1,25-OH Vitamin D, insulin resistance, obesity

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Introduction

Obesity is an important health issue which has a growing importance. According to the studies about the prevention of obesity, new strategies and new nutritional measures should be developed. Obesity is a multifactorial disease which was accepted as pandemic worldwide.^[1]

The main role of Vitamin D (VD) is to maintain calcium and phosphorus homeostasis and promote bone mineralization. 25-OH VD is accepted as the main indicator of VD status, and 1,25-OH VD is the active form of VD.^[2] In relevant studies, VD deficiency was found to be associated with the

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development of insulin resistance, obesity and also type 2 diabetes mellitus (DM). Insulin secretion is affected by VD, and it was found that VD deficiency induces impaired secretion of insulin that causes glucose intolerance.^[3-6]

Insulin resistance plays a key role in the development of type 2 DM.^[7,8] Obesity is accepted as one of the major risk factors of such chronic diseases.^[7,8] As the association between insulin resistance and VD deficiency is controversial, according to some studies; VD deficiency was seen more common in obese subjects and the patients with type 2 DM.^[7-9]

There is also evidence suggesting that low serum concentrations of VD are associated with impaired glucose tolerance and DM.^[1,10] In this study, our aim is to evaluate the insulin resistance in obese subjects and nonobese subjects and to find out the VD status and correlations between obesity and control groups.

In this study, our aim is to evaluate the insulin resistance and quality of life in obese subjects and nonobese subjects and to find out the VD status and correlations between obesity and control groups and also according to their quality of life scores.

Materials and Methods

The study was carried out between May and October, which is the period of VD synthesis in Turkey. The participants of this study were volunteering individuals – obese and nonobese individuals defined according to the body mass index (BMI) – that did not receive any VD support in the last 1-year and did not have any known chronic diseases. The participants were administered short form-36 (SF-36) quality of life instrument, and then their height, weight, waist and hip sizes were measured to calculate BMI values (kg/m²) and waist-to-hip ratio. For each participant, the following fasting tests were performed: Thyroid function tests, parathormone, fasting blood glucose, insulin, 1,25-OH VD, cortisol, creatinine, calcium, sodium, potassium, phosphorus and albumin. The individuals whose BMI value was 30 and over were defined as obese. Homeostatic model assessment insulin resistance (HOMA-IR) value was calculated by $HOMA-IR = \text{Fasting Glucose (mg/dL)} \times \text{Fasting Insulin (uIU/mL)} / 405$, and the insulin resistance was accepted as positive for patients with HOMA score ≥ 2.5 .^[9] 1,25-OH VD values were analyzed by high-performance liquid chromatography technique in the department of pharmacology and toxicology laboratory of the Faculty of Medicine, Eskişehir Osmangazi University, and the values between 18 and 72 pg/ml were accepted as the reference range.

Continuous data were defined in the form of mean \pm standard deviation. Categorical data were defined as percentages. The

Shapiro–Wilk test was used to check whether the data were normally distributed. The Mann–Whitney U-test was used to compare pair groups for continuous data that were not distributed normally. Chi-square test was performed to analyze the cross tables. IBM SPSS Statistics 21.0 (SPSS Inc., Chicago, IL) was used for the analysis. $P < 0.05$ was taken as a criterion for statistical significance. Ethical approval was taken from Eskişehir Osmangazi University Faculty of Medicine Ethical Committee.

Results

The study population consisted of 39 individuals with normal weight (23 women, 16 men; average age: 32.87 ± 12.17 years) and 66 individuals categorized as obese (51 women, 15 men; average age: 41.47 ± 11.67 years). The participants did not have any other endocrinal or physical chronic disease. Parathormone and thyroid function tests were performed for the individuals included in both groups, and all participants' test results were within the reference range. The average BMI value was 35.45 ± 5.07 in the group of obese participants and 23.9 ± 2.48 kg/m² in the group of participants with normal weight.

Normality test was performed on 1,25-OH VD and HOMA-IR values, and it was found that they were not distributed normally. Thus, the Mann–Whitney U-test was used to evaluate the difference between the groups. The difference in HOMA-IR between the group of obese individuals and the group of nonobese individuals was significant ($P < 0.001$) and 1,25-OH VD values between the group of obese individuals and the group of nonobese individuals was significant ($P < 0.001$).

The median value of HOMA-IR was higher in the obese group than in the nonobese group ($P < 0.001$) while the median value of 1,25-OH VD was higher in the nonobese group than in the obese group ($P < 0.001$) [Table 1]. The results regarding the relationship of BMI with HOMA-IR and 1,25-OH VD show that there was a positive correlation between HOMA-IR and BMI ($r_s = 0.507$; $P < 0.001$) and a negative correlation between 1,25-OH VD and BMI ($r_s = -0.316$; $P = 0.0001$). Insulin resistance rates according to their HOMA-IR values were found as 62.1% in the obese group and 20.1% in the control group, and such difference was found statistically significant ($P < 0.001$). The risk of insulin resistance in obese individuals was calculated, and it was found that the risk of insulin resistance was found more common in obese individuals than in nonobese individuals with an odd's ratio of 6.36. In patients that were detected to have insulin resistance according to their HOMA-IR value, there was no significant difference with regard to the level of VD deficiency (values lower than 18 pg/ml). In the group of obese patients, the rate (19.7% vs. 2.6%) of 1,25-OH

Table 1: The statistical data related to significant results of our study change this title

	Obese		Control		P
	Mean±SD	Median (Q1-Q3)	Mean±SD	Median (Q1-Q3)	
HOMA-IR values	3.7458±2.249022	2.78 (2.08-4.73)	1.8829±0.94101	1.79 (1.20-2.40)	<0.001
1,25-OH VD	28.3521±14.74365	25.96 (18.95-39.00)	40.5803±19.31109	36.00 (30.20-44.30)	<0.001
Physical function	24.0455±4.32677	25.00 (21.22-27.25)	27.4359±3.16057	28.00 (26.00-30.00)	<0.001
General health condition	15.2030±4.43906	15.00 (12.00-18.40)	18.9538±3.38183	19.40 (16.40-21.40)	<0.001
Energy scores	13.8788±5.93170	12.00 (10.00-17.25)	16.4103±4.17207	17.00 (14.00-20.00)	0.003

HOMA-IR=Homeostatic model assessment insulin resistance; SD=Standard deviation

VD deficiency was significantly higher ($P = 0.020$, $\chi^2 = 8.207$) in comparison with the normal subjects. The results regarding the relationship of waist-to-hip ratio with HOMA-IR and 1,25-OH VD show that there was a positive correlation between HOMA-IR and waist-to-hip ratio ($r_s = 0.277$; $P = 0.004$) and no correlation was found between 1,25-OH VD and waist-to-hip ratio.

Short form-36 instrument results reveal that there was a significant difference with regard to physical function, general health condition and energy scores in obese people compared to nonobese people (P values were respectively $P < 0.001$, $P < 0.001$, $P = 0.003$). There was no significant difference with regard to the other scores. The statistical data related to significant results of our study are provided in Table 1.

Discussion

Research has shown that obesity is a risk factor for VD deficiency.^[11,12] This is supported by our findings that the mean of 1,25-OH VD was significantly lower in the obese group. It is considered that this is because VD is subject to sequestration in the fatty tissue in obese individuals, as a result of which bioavailability is lower. VD deficiency causes muscle pains and reduces bone mineralization, causes muscle weakness and impairs neuromuscular coordination, which increases the tendency to fall and risk of fractures and hence impairs quality of life.^[1,10,11]

Researches have also revealed that VD deficiency is associated with diabetes and glucose intolerance.^[10,11,13] VD plays a significant role in insulin sensitivity and beta-cell function which are effective in the pathogenesis of insulin resistance and type 2 diabetes. 1,25-dihydroxy VD was accepted to have an important role in glucose homeostasis via different mechanisms. 1,25-dihydroxy VD improves insulin sensitivity of the target cells (liver, skeletal muscle, and adipose tissue) and enhances and improves β -cell function.

It is shown that the level of VD is low particularly in the early phase of type 1 diabetes.^[13] VD (400 – 1000 U/day) and calcium (600 – 1200 mg/day) support is considered to play an important role in the prevention of type 2 DM,

especially in groups at risk of developing type 2 DM and glucose intolerance.^[14]

It is also reported that low VD is associated with pancreatic cell dysfunction.^[3,4,6] Furthermore, VD deficiency is reported to be associated with increased cardiovascular diseases in both healthy population and patients of type 2 diabetes.^[15-17] Moreover, it is shown that, independent of all conventional risk factors; severe VD deficiency in type 2 diabetes patients is associated with increased mortality particularly due to cardiovascular causes.^[4,7,9,18]

As it is the case in many countries, obesity has been increasing in Turkey. The prevalence of obesity was reported between 22% and 32% in the studies conducted in Turkey.^[18,19] Large-scale epidemiological studies have revealed that obesity constitutes a major risk factor for chronic disorders such as coronary artery diseases, type 2 diabetes, hypertension, musculoskeletal diseases and cancer.^[1,10,20] Research has also shown that obesity remarkably deteriorates individuals' quality of life.^[20-22] In the present study, SF-36 instrument results provided significantly lower scores of physical function, general health condition and energy in obese individuals compared to those with normal weight. The life quality of obese people is impaired given that they suffer from decrease in physical capacity, pain, problems in interpersonal relations, decrease in self-esteem, depression, social labeling, difficulty of finding a job and refusal in school and work environments.^[20-24]

In this study, where we intended to reveal the association of obesity with 1,25-OH VD levels and insulin resistance according to our results; when the level of 1,25-OH VD declines, the level of HOMA-IR increases and there arises the tendency to insulin resistance. Furthermore, the average 1,25-OH VD value is lower in obese people than in nonobese people.

In our findings; physical function, general health condition and energy scores were found to be significantly lower in obese subjects. In obese subjects; a decline in quality of life was expected. There can be significant declines in functioning and distress levels (specifically in scores on the bodily pain, general health perception, vitality, physical functioning). In our subjects, as consistent with the

literature, obese subjects have significantly lower quality of life scores.^[20-22]

The data obtained in our study are consistent with research findings suggesting that increased BMI results in decrease in the level of 1,25-OH VD, and support the hypothesis that particularly obese individuals are under the risk of 1,25-OH VD deficiency. It is considered that low levels of 1,25-OH VD and 25-OH VD in obese individuals are associated with more than one factor, including less exposure to sunlight because of reduced movement resulting from increased weight and sequestration of 25-OH VD in adipose tissue.^[12,25-27] Research has shown that low level of 1,25-OH VD and deficiency of 25-OH VD in adults constitute a risk factor for diabetes, cardiovascular diseases and certain types of cancer along with osteoporosis.^[28] This is of particular importance for obese patients because the abovementioned disorders are associated with obesity independently of VD levels.^[28-32] Low levels of 25-OH VD and 1,25-OH VD increase the risk in this group of patients.

Conclusion

1,25-OH VD levels are negatively correlated with BMI and positively correlated with HOMA-IR, and VD deficiency is commonly seen in obese individuals. Given serious diseases associated with low serum 25-OH VD levels such as diabetes and cardiovascular disorders and low cost of VD treatment, it would be a reasonable approach to identify routine serum 25-OH VD and/or 1,25-OH VD levels of obese patients and administer a treatment to patients with low levels of VD.

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