Low serum 25(OH)D levels are associated to higher BMI and metabolic syndrome parameters in adult subjects in Turkey

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Abstract

Background: The aim of this study was to investigate the association of 25(OH)D levels with biochemical, anthropometric, and metabolic data obtained from normal and obese people.

Methods: This study was carried out on 90 individuals between the ages of 18 to 63 that had various body mass indexes. Blood samples and anthropometric measurements were taken.

Results: Waist circumferences, fat mass, LDL cholesterol levels, HDL cholesterol levels, 25(OH)D levels, and triglyceride levels were significantly different according to the body mass index groups of the participants ($p<0.05$). When compared to the normal body mass index group, both other groups (overweight and obese) had higher waist circumferences, triglyceride levels, LDL cholesterol levels, fasting insulin levels, HOMA-IR ratios, parathyroid hormone levels, and fat mass, and had lower 25(OH)D levels ($p<0.05$). The overweight group participants had higher 25(OH)D levels than the obese group, and had lower waist circumferences, fat mass, fasting insulin level, HOMA-IR ratios, and HbA1C and PTH levels than those in the obese group ($p<0.05$).

Conclusion: In conclusion, the mean level of 25(OH)D is very low in overweight and obese individuals and low serum 25(OH)D levels appear to be associated with obesity, visceral obesity, hypertriglyceridemia, insulin resistance, and metabolic syndrome in obese patients.

Keywords: Obesity, vitamin D, metabolic syndrome

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Introduction

25(OH)D deficiency is an important public health problem in both developed and developing countries, with a reported worldwide prevalence of 30–80% in children and adults[1-3]. The role of 25(OH)D in bone mineralisation is well-documented. However, numerous recent studies have reported a link between 25(OH) D deficiency and several chronic disorders, such as type 1 diabetes mellitus, systemic lupus erythematosus, multiple sclerosis, cardiovascular disease, and several malignancies[4-6].

Positive associations between 25(OH)D deficiency and the prevalence of obesity have been shown. Recent studies in the adult population suggested that adequate serum 25(OH)D levels could be connected with increased adipocyte activity and oxidation of fat, as well as the potential for improving insulin sensitivity, which can lead to weight loss[7,8]. The synthesis and processing of 25(OH)D confirmed that obese patients have lower basal 25(OH)D and higher serum parathyroid hormone concentrations than do nonobese people[9-11]. Several studies have shown that obese individuals tend to have lower serum concentrations of vitamin D_3 and 25(OH) D_3 than those with normal weights[9-12]. For example, in one study, whole-body irradiation produced an increase in serum vitamin D_3 levels in obese individuals [body

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mass index (BMI) 30 kg/m^2] that was 57% lower than that in age-matched, normal weight controls (BMI 25)[13].

Since there is an inverse relationship between 25(OH) D levels, the degree of obesity[14], and central adiposity[15], it has been difficult to distinguish the independent effects of obesity and 25(OH)D on metabolic syndrome. Furthermore, it is not known whether the association between 25(OH)D deficiency and the metabolic syndrome is still present at very high degrees of obesity, in which the possible effect of 25(OH)D status on the metabolic syndrome could be ameliorated or even completely overcome by the predominant effect of obesity[16].

Several mechanisms have been proposed to explain the low 25(OH)D levels in obese people and include the sequestration of 25(OH)D by fat tissues[17], as well as body size[18]. On the other hand, abnormal fasting serum or plasma lipid levels are the most prominent symptoms resulting from obesity[19], and the effect of 25(OH) D supplementation on lipid profiles remains controversial[20].

Studies showed that in Turkey, 25(OH)D deficiency is an important problem. There have been few studies about obesity and 25(OH)D levels in the Turkish population[21,22]. The aim of this study was to investigate the association of 25(OH)D levels and certain biochemical, antropometric, and metabolic data in normal and obese people.

Methods

Study population

This study was performed with the participation of 90 individuals between the ages of 18 and 63 with various BMIs that were admitted to the Endocrinology department of the Başkent University Ankara hospital's Ümitköy polyclinic from June to November 2013. They were healthy and thus did not have any health problems at the time of admission. People who were using any kind of medicines, vitamins, or minerals were not included in this study. Pregnant or lactating women, as well as people with a pre-diagnosed diseases or those diagnosed with a disease during the study period, were not excluded.

Clinical and anthropometric characteristics

Height, weight, waist and hip circumferences were measured from 08:00 to 10:00 hours after a 12 h fast. Height was measured using a stadiometer accurate to ±0.5 cm, and weight was obtained with participants wearing light clothing and no shoes using a calibrated scale, accurate to ±0.1 kg (Filizola S.A., São Paulo, SP, Brazil). The BMI was calculated using the standard equation (kilograms per meters squared). The waist circumference was measured with participants in the standing position, midway between the lower margin of the last rib and the iliac crest, at mid exhalation. The hip circumference was measured at the widest point of the hip/buttocks area with the measuring tape parallel to the floor. The waist-to-hip ratio was determined by dividing waist circumference by hip circumference. Anthropometric measurements were taken twice, and the mean values were used in all analyses. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice in the sitting position, with 15 min between the measurements, using standard sphygmomanometers of appropriate width, after a rest period for 30 min.

Biochemical analysis

The percentage of body fat was estimated by electrical bioimpedance using a Jawon IOI 353 body fat analyser (Biodynamics Corp., Seattle, WA, USA). We stratified adiposity as global adiposity (excessive adipose tissue, independent of site) and abdominal adiposity. BMI and percentage of body fat were used as global adiposity parameters. The waist circumference and waist-to-hip ratio were used to evaluate abdominal adiposity. Blood samples were collected after a 12 h fasting period. Biochemical evaluation included glucose, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triacylglycerols, calcium, phosfor, HbA1C, parathyroid hormone (PTH), and 25(OH)D.

Fasting plasma glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, TG, HbA1C, and calcium levels were measured using original kits and an Abbott-Aeroset autoanalyser (Architect C-8000, Chicago, Illinois, USA). Parathyroid hormone and fasting plasma insulin levels were measured using original kits using an Perfect Plus 400 autoanalyser (Mindray, UK). Insulin resistance was estimated from fasting serum measurements using the homeostasis model assessment-insulin resistance (HOMA-IR) [insulin (μU/mL) X glucose (mg/dL) ÷ 425]. Metabolic syndrome was diagnosed according to NCEPATP III[23]. Thus, a participant had MS if he or she had three or more of the following: (i) abdominal obesity: waist circumference >102 cm in men and >88

cm in women; (ii) plasma triglycerides: ≥150 mg/dL; (iii) plasma HDL cholesterol: <40 mg/dL in men and <50 mg/dL in women; (iv) SBP: ≥130 mmHg, DBP: ≥85 mmHg, or the use of antihypertensive medicine; (v) plasma glucose: ≥110 mg/dL or the use of antidiabetic medicine/insulin.

Statistical analysis

Data are reported as mean ±SD for continuous variables and as numbers or a percentage for categorical variables. Clinical and biochemical characteristics were compared using the Student's t test or the chi-square test when the variables were continuous or categorical, respectively. The Pearson correlation test was used to evaluate associations between serum 25(OH)D and components of anthropometric and metabolic syndrome. Statistical analyses were performed using SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Waist circumferences, fat mass, and LDL cholesterol, HDL cholesterol, 25(OH)D, and triglyceride levels were significantly different according to the BMI groups of the participants ($p<0.05$; Table 1). When compared to the normal BMI group, both other groups (overweight and obese) had lower waist circumference, triglyceride levels, LDL cholesterol levels, fasting insulin levels, HOMA-IR ratios, parathyroid hormone levels, and fat mass, and had higher 25(OH)D levels ($p<0.05$). The overweight group had higher 25(OH)D levels than obese group, and had lower waist circumferences, fat masses, fasting insulin levels, HOMA-IR ratios, and HbA1C and PTH levels than the obese group ($p<0.05$).

Table 1. Changes in biochemical and anthropometric indices between BMI classifications

Variables	Normal (n=30)		Overweight (n=30)		Obese (n=30)		*p*
	Mean	SD	Mean	SD	Mean	SD	
Age (year)	31.8	6.9	36.5	10.0	36.1	8.7	[a, b, c] p<0.05
BMI (kg/m^2)	22.1	2.1	26.4	1.3	33.1	3.2	[a, b, c] p<0.05
WC (cm)	78.6	7.5	88.9	6.7	103.6	10.7	[a, b, c] p<0.05
DBP	72.3	7.3	72.0	9.0	82.5	7.4	[b, c] p<0.05
SBP	109.3	8.3	108.3	11.8	124.8	12.1	[b, c] p<0.05
Fat mass (kg)	15.1	3.8	21.4	5.8	34.9	6.6	[a, b, c] p<0.05
Fat mass (%)	22.8	5.8	28.8	5.6	33.8	5.4	[a, b, c] p<0.05
Fasting glucose (mg/dL)	90.2	8.1	93.6	8.0	96.4	9.9	[b] p<0.05
TC (mg/dL)	172.7	29.4	183.5	37.6	196.4	40.3	[b] p<0.05
LDL-C (mg/dL)	106.3	24.0	125.8	33.0	133.5	35.6	[a, b] p<0.05
HDL-C (mg/dL)	52.9	12.3	44.6	13.3	44.2	8.8	[a, b] p<0.05
TG (mg/dL)	90.2	44.0	142.5	61.9	127.0	65.9	[a, b] p<0.05
Fasting insulin (μU/ mL)	7.0	2.9	8.1	3.0	12.8	3.9	[b, c] p<0.05
HOMA-IR ratio	1.6	0.7	1.9	0.7	3.1	1.1	[b, c] p<0.05
HbA1C (%)	5.2	0.5	5.3	0.5	5.7	0.7	[b, c] p<0.05
25(OH)D (μg/L)	27.5	8.3	21.3	5.8	16.2	4.4	[a, c] p<0.05
Blood Ca (mg/dL)	9.5	0.4	9.3	0.3	9.3	0.3	[b] p<0.05
PTH (pg/mL)	40.1	16.8	42.5	15.0	52.8	23.0	[b, c] p<0.05

BMI, body mass index;WC, waist circumference; BP, blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride; Ca, calcium; and PTH, parathyroid hormone.

[a] significant diffrences between normal weight and overweight ($p<0.05$).

[b] significant diffrences between normal weight and obese ($p<0.05$).

[c] significant diffrences between overweight and obese ($p<0.05$).

Table 2 lists the clinical and biochemical characteristics of the participants separated according to 25(OH) D levels: <20 ng/mL (deficiency) and ≥20 ng/mL (sufficiency). The mean TG and HDL-C level was significantly different in the sufficiency group than in the deficiency group ($p<0.05$). The deficiency group had slightly higher mean blood PTH, TC, LDL-C, TG, and fasting glucose levels when compared to those in the sufficiency group, although this trend was not statistically significant ($p>0.05$). The mean BMI, WC, fat mass, fasting insulin levels, HOMA-IR ratios, and HbA1C, DPB, and SBP levels were significantly lower in the sufficiency group than in the deficiency group ($p<0.05$).

Table 2. Characteristics of participants based on serum 25(OH)D concentrations

	Suficient (n=44) ≥20µg/L		Deficiency (n=46) <20µg/L		*p*
Metabolic syndrome	4 (9.0%)		12 (26.1%)		0.032 *
	Mean	S.D.	Mean	S.D.	
BMI (kg/m^2)	25.7	4.5	28.7	5.2	0.005 *
WC (cm)	86.6	11.1	94.0	14.3	0.008 *
Fat Mass (kg)	20.3	6.7	27.2	10.8	0.000 *
TC (mg/dL)	178.1	34.7	190.2	38.6	0.131
LDL-C (mg/dL)	117.0	31.2	126.5	34.3	0.174
HDL-C (mg/dL)	48.6	11.2	43.1	10.6	0.017
TG (mg/dL)	107.1	60.4	141.9	66.9	0.012 *
Fasting glucose (mg/dL)	92.9	9.2	93.9	8.8	0.615
Fasting insulin (µU/ mL	8.0	3.3	10.6	4.5	0.003 *
HOMA-IR ratio	1.9	0.8	2.5	1.2	0.006 *
HbA1C (%)	5.3	0.5	5.6	0.7	0.011 *
Diatolic BP (mmHg)	73.3	8.8	77.8	9.2	0.019 *
Sistolic BP (mmHg)	110.5	10.8	117.7	14.3	0.008 *
25(OH)D (µg/L)	27.7	6.4	15.9	3.6	0.000 *
Blood Ca (mg/dL)	9.4	0.4	9.3	0.3	0.449
PTH (pg/mL)	43.6	18.0	46.6	20.4	0.457

BMI, body mass index; WC, waist circumference; BP, blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride; Ca, calcium; and PTH, parathyroid hormone.

* significantly different between the two groups ($p<0.05$).

The Pearson's correlation coefficients (r) for selected baseline variables are shown in Table 3. At baseline, 25(OH)D levels correlated inversely with BMIs ($r = -0.469$; $p = 0.000$), waist circumferences ($r = -0.432$; $P = 0.000$), fat masses ($r = -0.419$; $p = 0.004$), fasting insulin levels ($r = -0.432$; $p = 0.000$), and HOMA-IR ($r = -0.341$; $p = 0.001$).

Table 3. Relationship between serum 25(OH)D levles and anthropometric and metabolic risk factors

	Total (n=90)			Female (n=45)			Male (n=45)		
	VIT D	Ca	PTH	VIT D	Ca	PTH	VIT D	Ca	PTH
BMI (kg/m^2)	-0.469**	-0.234*	0.320**	-0.519**	-0.244	0.266	-0.417**	-0.242	0.373*
WC (cm)	-0.432**	-0.105	0.195	-0.532**	-0.172	0.173	-0.407**	-0.192	0.232
DBP (mmHg)	-0.293**	-0.138	0.108	-0.342*	-0.278	0.070	-0.215	0.026	0.156
SBP (mmHg)	-0.311**	-0.280**	0.162	-0.359*	-0.397**	0.107	-0.235	-0.152	0.234
TC (mg/dL)	-0.172	0.008	-0.079	-0.089	0.098	-0.056	-0.274	-0.079	-0.102
LDL-C (mg/dL)	-0.183	-0.092	0.002	-0.096	0.009	0.086	-0.298*	-0.244	-0.103
HDL-C (mg/dL)	0.144	0.248*	-0.150	0.208	0.373*	-0.191	0.105	0.298*	-0.110
TG (mg/dL)	-0.129	0.023	0.025	-0.193	0.042	-0.040	-0.062	-0.066	0.066
Fat mass (kg)	-0.419**	-0.258	0.333*	-0.523**	-0.242	0.225	-0.419**	-0.258	0.333*
Fasting glucose (mg/dL)	-0.173	-0.067	0.143	-0.163	-0.169	0.092	-0.176	-0.029	0.187
Fasting insulin (µU/ mL)	-0.346**	-0.090	0.303**	-0.466**	-0.345*	0.342*	-0.282	0.007	0.298*
HOMA-IR ratio	-0.341**	-0.087	0.288**	-0.486**	-0.369*	0.348*	-0.287*	-0.007	0.284*
HbA1C (%)	-0.261*	-0.148	-0.115	-0.346*	-0.213	-0.066	-0.130	-0.160	-0.205

BMI, body mass index; WC, waist circumference; BP, blood pressure; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglyceride; Ca, calcium; and PTH, parathyroid hormone.
* $p<0.05$
** $p<0.01$

Discussion

25(OH)D deficiency is increasingly being recognised worldwide[2,24]. There have been prevalence studies on 25(OH)D deficiency and/or insufficiency in the Turkish population[25], and most have been performed on women, people in nursing homes, and the elderly[26-28]. Also, obesity leads to many health problems worldwide. It is a major public health problem and the most common nutritional disorder[29]. It is related to a host of health problems. In particular, abdominal obesity is associated with some serious problems, such as type 2 diabetes, cardiovascular and cerebrovascular diseases, hypertension, digestive disorders, and cancer[30]. The highest mean prevalence of obesity is 32.05% and was reported in the TEKHARF (men, 21.1%; women, 43.0%). The highest obesity frequency in women was also reported in this study (43.0%). The mean obesity in the TURDEP was 22.3% (men, 12.9%; women, 29.9%)[31]. Obesity is usually correlated with a higher prevalence of hypovitaminosis or a lower circulating

25(OH)D level[32,33]. However, in the present study, the prevalence of 25(OH)D deficiency was higher in the overweight and obese groups than in the normal weight group. Over the past few decades, research has shown positive and negative associations between weight loss and maintenance with increased 25(OH)D and calcium intake (particularly with dairy products) in adults[34-36]. Additionally, studies have demonstrated links between a high BMI and decreased sun exposure, as well as decreased 25(OH)D levels[37].

Previous studies have shown this association between 25(OH)D deficiency and metabolic syndrome in women[14] and in the general population[15], and our present findings confirm these results also in overweight and obese people. Pittas et al. reported that the risk for developing type 2 diabetes was lower for those whose 25(OH)D levels were higher[38]. On the other hand, in a study carried out in postmenopausal women, it has been reported that low 25(OH)D levels were not associated with a risk of developing diabetes[39]. In our study, the serum 25(OH)D deficieny was associated with high fasting insulin levels and hyperparathyroidism. In cross-sectional and epidemiological studies, the relationship of 25(OH)D deficiency with DM type I, metabolic syndrome, obesity, cardiovascular diseases, hypertension, and mortality, possibly due to the role of this vitamin in insulin resistance, secretion, and inflammatory processes, were reported[40-43.] It has also been shown that deficiencies in serum 25(OH)D levels decreases insulin secretion by reducing calcium absorption and, therefore, causing secondary hyperparathyroidism and increased peripheral insulin resistance[44].

The most promising study to date suggesting that 25(OH)D alters diabetes risk is a post hoc analysis from an osteoporosis intervention study in which 314 nondiabetic white adults were randomised to groups recieving either 700 IU of the vitamins D3 and 500 mg calcium citrate or placebos daily for 3 years. Treatment with 25(OH)D and calcium citrate demonstrated attenuated increases in fasting glucose in participants with baseline impaired fasting glucose (IFG), but not in those with normal fasting glucose. Participants with IFG who received 25(OH)D and calcium also had reduced progression of insulin resistance, as assessed by HOMA-IR[45]. Conversely, a Women's Health Initiative (WHI) study reported that daily supplementation with 400 IU of vitamin D3 and 1000 mg of calcium did not reduce risk of developing diabetes over 7 years, when compared to placebo[46]. In the present study, we found a significant difference between 25(OH)D deficient individuals and those with normal 25(OH)D level regarding HOMA-IR and HbA1c levels. This is in agreement with Chiu et al., who observed a positive relationship between 25(OH)D status and insulin sensitivity index in adults. In addition, they showed that 25(OH)D levels were negatively correlated with both first and second phase insulin responses during a hyperglycemic clamp and glucose levels during the oral glucose tolerance test. Therefore, they suggested that subjects with hypovitaminosis D not only displayed impaired β-cell function, causing impaired glucose homeostasis, but were also at increased risk of developing insulin resistance and metabolic syndrome when compared with vitamin D sufficient subjects[47]. Also, previous studies showed that serum 25(OH) D levels were inversely correlated with HbA1c, independent of body fat, implying higher ambient glucose concentrations in children with lower 25(OH)D concentrations[48,49].

Previous studies showed an inverse relationship between 25(OH)D levels and BMI[14], as well as central adiposity[15], making it difficult to distinguish the separate contributions of obesity and of 25(OH)D to the development of metabolic syndrome. Similarly, our findings indicated that a low 25(OH)D level is associated with a high BMI and central obesity. In contrast, Botella-Carratero et al.[16] reported that patients with and without 25(OH)D deficiency had similar BMIs and waist circumferences, so the differences in metabolic syndrome prevalence and lipid levels may indeed reflect a true association between 25(OH)D status and the metabolic syndrome, irrespective of adiposity.

Low serum 25(OH)D was associated with components of the metabolic syndrome, including abdominal obesity, hypertension, hypertriglyceridemia, and higher HbA1C and lower high-density cholesterol[50]. In the present study, we found that low serum vitamin D levels related to high abdominal obesity, high body fat, hypertriglyceridemia, and lower high-density cholesterol. Two cross-sectional studies (NHANES III and NHANES 2003–2004) showed a significant inverse association between serum 25(OH)D concentrations and metabolic syndrome[15,51].

In the current study, PTH levels correlated positively with BMI, fat mass, HOMA-IR ratio and fasting insulin levels. The association of PTH with impaired glucose tolerance is part of a newly proposed mechanism underlying the development of the metabolic syndrome[51]. Other studies have also suggested that individuals with hyperparathyroidism have an increased risk of developing type 2 diabetes[52]. Serum parathyroid concentrations have an important role in the mechanism of insulin resistance. Lee et al. shown that vitamin D levels are negatively correlated with metabolic syndrome frequency independent of serum parathyroid levels[53]. Hyperparathyriodism secondary to decrease in serum 25(OH)D levels was thought to be the main mechanism causing insulin resistance[54]. In a study conducted with 1017 morbid obese, Caucasian, male and female subjects, parathormone levels were found to be the only predictor of metabolic syndrome rather than vitamin D levels[55].

Limitations

This study had some limitations. The main one being the cross-sectional nature of this study, with no causality effect to report. The sunlight exposure and effect of 25(OH)D supplementation on weight gain also need to be considered.

Conclusion

The mean level of 25(OH)D is very low in overweight and obese indiviuals, and low serum 25(OH)D levels appear to be associated with obesity, visceral obesity, hypertriglyceridemia, insulin resistance, and metabolic syndrome in obese individuals. A broad-based effort to prevent 25(OH)D deficiency in Turkey should be undertaken.

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