Original Article

A Comparative Study of 25 (OH) Vitamin D Serum Levels in Patients with Metabolic Syndrome and Healthy Individuals

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Abstract

Background: The incidence of metabolic syndrome has been rising in the Iran population. In parallel, vitamin D deficiency has also been increasing in Iran. This study aims to explore the association of vitamin D serum concentrations with metabolic syndrome and its components in the Iranian population. **Materials and Methods:** A case-control study was managed. We enrolled 110 metabolic syndrome patients, according to the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria as a case group and 130 healthy individuals as a control group. The serum level of 25-hydroxy vitamin D (25 (OH)D), lipid profile, and fasting blood glucose(FBS) status were determined using a commercially available ELISA method. Enzymatic methods determined total cholesterol (Chol), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL), and triglyceride (TG) levels. **Results**: In case group, the prevalence rate of 25 (OH)D deficiency (<10 ng/mL) was 10%, 25 (OH)D insufficiency (10–29 ng/mL) was 71.0%, and 25 (OH)D sufficiency (>30 ng/mL) was 19.0%. A non-significant association between Chol level and age was noted (p=0.46, p=0.124). The levels of FBS and TG were significantly higher, and the levels of 25 (OH)D, LDL, and HDL were significantly lower in the case of the group compared to the control group. **Conclusion:** We found that the serum level of 25 (OH)D in patients with metabolic syndrome is lower than in the healthy group, and a low level of 25 (OH)D is related to increased risk of metabolic syndrome and its components.

Keywords*:* Metabolic syndrome, 25 (OH)D, Triglyceride, High-density lipoprotein, Low-density lipoprotein.

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Introduction

Metabolic syndrome, also known as syndrome X, is a complex metabolic disorder with known clinical findings, including hyperglycemia, central obesity, dyslipidemia, insulin resistance, and high blood

pressure, which are the potent predictors of diabetes and cardiovascular diseases (1). According to the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria, the existence of at least three items of following disorders considered as a metabolic syndrome: abdominal obesity ≥ 88 cm for female and ≥ 102 cm for male, high-density lipoprotein cholesterol (HDL-c) levels < 50 mg/dl for female and < 40 mg/dl for male, increased triglyceride level ≥ 150 mg/dl, fasting blood sugar (FBS) > 100 mg/dl, high blood pressure (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg) (2). The prevalence of metabolic syndrome is estimated at 27.46%–33.7% in Iranian adults. Besides, the rising prevalence of metabolic syndrome is due to physical inactivity, increasing age, unhealthy food habits, and obesity involved both developed and developing societies. (3).

Accumulating evidence suggests that low serum levels of 25 (OH) D are also related to metabolic syndrome pathogenesis and its components (4). Vitamin D deficiency has been increasing globally, with a high prevalence in the Iran population (5, 6). Vitamin D is a steroid-derived hormone that is associated with bone health and phosphate and calcium homeostasis (7). 1,25-dihydroxy vitamin D3 [1,25(OH)2D3] is the hormonal form of vitamin D, which is involved in the regulation of many genes in humans through its binding to vitamin D receptor (VDR) in the nucleus (8). The supplementation of Vitamin D has been exhibited to confer benefits against cardiovascular and type 2 diabetes disorders, especially in individuals with a positive history for vitamin D deficiency (9-11). The serum level of 25-hydroxyvitamin D (25(OH)D) is the best measurable marker for the determination of vitamin D status. Due to the increasing incidence of metabolic syndrome and vitamin D deficiency in Iran, the analysis of the relationships between vitamin D levels and the development of metabolic syndrome in different populations of Iran is a necessity. Our attempts to analyze these relationships will undoubtedly help to successful therapeutic interventions. The aim of this study is the comparative of 25 (OH) vitamin D serum levels in healthy individuals and patients with metabolic syndrome in Shahid Doran hospital of Shiraz.

Methods

Our research was a case-control study. We enrolled randomly 110 women from definitive metabolic syndrome patients based on clinical findings that were recorded in Shahid Doran hospital of Shiraz as a case group. Also, we enrolled 130 healthy women randomly from Shahid Doran hospital's staff as a control group. The ages of the healthy and patient participants were recorded. We included them if they had the following criteria: no usage of vitamin D supplement or calcium, and no recognized diseases associated with the deficiency of vitamin D such as rickets. The exclusion criteria were D vitamin supplementation and all recognized disorders associated with vitamin D. Under the National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria, metabolic syndrome was defined in the presence of three or more of the following components: waist circumference ≥102 cm in men and ≥ 88 in women, fasting glycemia ≥100 mg/dL, serum triglyceride level ≥150 mg/dL, HDL cholesterol level <50 mg/dL in women and < 40 mg/dl in men, and elevated blood pressure (systolic blood pressure ≥130 and/or diastolic blood pressure ≥85 mmHg) (12). We informed all participants about the purposes and details of this research before the start. None of the control and case participants were excluded from our study. This study was designed, compiled, and written based on the data recorded in the laboratory of Shahid Doran Hospital in Shiraz.

Clinical measurements. After 14-12 hours of fasting, 10 ml of the blood sample was taken, collected, and sent to the hospital laboratory for measurement of lipid profile, FBS parameter, and 25-hydroxy vitamin D level. Blood samples were centrifuged at room temperature for 10 min at 3000 rpm. Serum concentrations of total cholesterol, LDL-C, FBS, HDL-C, and serum triglyceride were determined by enzymatic and colorimetric methods (Pars Azmun, Karaj, Iran). The level of serum 25(OH)-vitamin D was determined by the ELISA method (Immunodiagnostic Systems, Paris, France). All experiments were done in Shahid Doran hospital laboratory.

Statistical Analysis. Data analysis was performed by IBM SPSS Statistics, version 15 (SPSS

Inc, Chicago, IL). Data were analyzed using Student – t-test and Mann-Whitney-U tests, and $p< 0.05$ and $p< 0.01$ were considered as statistically significant.

Results

This study examined 130 healthy individuals as a control group and 110 patients with metabolic syndrome as a case group. All healthy and patients individuals in the present study were women. After collection and analyses of data, all participants in the control and case groups were divided into three categories deficient, insufficient and sufficient on the base of their measured 25-(OH) vitamin D serum concentrations. The mean levels of 25-(OH) vitamin D in the case and control group for all categories are shown in Table 1. As shown in Table 1, the prevalence rate of 25 (OH)D of sufficient, insufficient and deficient categories in the control group were 52 (40%), 68 (52.3%), and 10 (7.7%), respectively.

Table1. The mean levels of 25(OH)D in two case and control groups.

	Case group		Control group		
25(OH)D serum levels (ng/ml)	mean±SD	N	mean±SD	N	p
25(OH)D < 10 (ng/ml)	7.85±1.86	11	8.06±1.64	10	0.66
29 <25(OH)D < 10(ng/ml)	20.50±4.21	78	24.74±3.09	68	0.00
25(OH)D > 30(ng/ml)	35.57±4.16	21	37.67±5.54	52	0.51

Data are represented as mean±SD. P<.05 was considered statistically significant

Table2. The mean values of metabolic syndrome components FBS, TG, LDL, HDL, Chol, and VitD3. Abbreviations: FBS, fasting blood sugar; HDL, high-density lipoproteins; LDL, low- density lipoproteins; TG, triglyceride; Chol, cholesterol. VitD3, Vitamin D3.

	Case group	Control group	
	mean±SD	mean±SD	p-value
Age (years)	44.30±12.08	47.09±12.60	0.124
FBS (mg/dl)	110.38±16.71	88.34±8.53	0.000
TG (mg/dl)	204.96±60.01	124.07±56.31	0.000
Chol (mg/dl)	219.82±31.88	168.65±26.16	0.000
HDL (mg/dl)	37.5616±4.63	43.20±6.50	0.000
LDL (mg/dl)	141.27±35.61	100.63±30.34	0.000
VitD3 (ng/ml	22.17±8.53	28.41±9.61	0.01

Data are represented as mean±SD. P<.01 and was considered statistically significant.

These numbers for patient group were 21 (19%), 78 (71%), 11 (10%), respectively. The mean age, lipid profile, FBS, and vitamin D levels in both control and case groups are shown in Table 2. The mean level of

Table3. Correlations of metabolic syndrome components with vitamin D in whole study populations.

		Age	FBS	TG	Chol	HDL	VitD	LDL
Age	R	1	-.040	-.040	-.063	-.005	.066	-.047
	Pvalue		.572	.572	.374	.948	.355	.509
FBS	R	-.040	1	.342**	.350**	-.214**	-.451**	.258**
	Pvalue	.572		.000	.000	.002	.000	.000
TG	R	-.040	.342**	1	.285**	-.226**	-.412**	-.046
	Pvalue	.572	.000		.000	.001	.000	.517
Chol	R	-.063	.350**	.285**	1	-.280**	-.433**	.932**
	Pvalue	.374	.000	.000		.000	.000	.000
HDL	R	-.005	-.214**	-.226**	-.280**	1	.244**	-.364**
	Pvalue	.948	.002	.001	.000		.001	.000
VitD	R	.066	-.451**	-.412**	-.433**	.244**	1	-.319**
	Pvalue	.355	.000	.000	.000	.001		.000
LDL	R	-.047	.258**	-.046	.932**	-.364**	-.319**	1
	Pvalue	.509	.000	.517	.000	.000	.000	

**. Correlation is significant at the 0.01 level (2-tailed).

Table4. Correlations between metabolic syndrome components and vitamin D in patients with metabolic syndrome.

		Age	FBS	TG	Chol	HDL	VitD	LDL
Age	R	1	-.060	.049	-.043	.064	-.014	-.063
	Pvalue		.615	.683	.719	.593	.907	.597
FBS	R	-.060	1	.065	-.096	.102	-.154	-.121
	Pvalue	.615		.586	.418	.390	.194	.307
TG	R	.049	.065	1	-.163	-.079	-.075	-.473**
	Pvalue	.683	.586		.168	.508	.530	.000
Chol	R	-.043	-.096	-.163	1	.102	.052	.937**
	Pvalue	.719	.418	.168		.393	.662	.000
HDL	R	.064	.102	-.079	.102	1	.066	-.013
	Pvalue	.593	.390	.508	.393		.578	.914
VitD	R	-.014	-.154	-.075	.052	.066	1	.063
	Pvalue	.907	.194	.530	.662	.578		.596
LDL	R	-.063	-.121	-.473**	.937**	-.013	.063	1
	Pvalue	.597	.307	.000	.000	.914	.596	

**. Correlation is significant at the 0.01 level (2-tailed).

25-hydroxy vitamin D in the control group was 28.41±9.61 ng/ml, and in the case group was 22.17±8.53 ng/ml, and there was a significant difference between serum levels of vitamin D in both groups (P=0.01). There was not any significant relationship between mean age (P=0.124) level in control and case groups. There was also a significant difference between FBS (P=0.000), TG (P=0.000), LDL (P=0.000), Chol (P=0.000), and HDL (P=0.000) levels in both control and case groups. FBS, LDL, Chol, and TG levels were significantly higher, and HDL was significantly lower in the case group compared to the control group. Also, the relationship between vitamin D level and other metabolic syndrome parameters was investigated. In Table 3, in the study population, there was significant positive correlation between vitamin D and HDL (P=0.001, r=0.244). There were significant negative correlations between vitamin D and LDL (P=0.000, r= -0. 319), Chol (P=0.000, r=-0.433), TG (P=0.000, r=-0.412) and FBS (P=000, r=-0.451). The results of Table 3 also shows the relationship between other lipid parameters and glucose in the entire control and patient populations. In the population of metabolic syndrome, no significant

relationship was observed between vitamin D and parameters (Table 4).

Discussion

We found that the serum level of vitamin D, LDL, and HDL in patients with metabolic syndrome are lower than in the normal group. FBS and TG were significantly higher in the metabolic syndrome group compared to the control group, but there is any significant association between Chol level and age in the control group and patients with metabolic syndrome.

Metabolic syndrome prevalence is growing globally because of increasing age and obesity in all communities around the world in the last decades (1). This syndrome is described by the clustering of clinical findings, including abdominal obesity, increased blood glucose levels, high TG and low HDL levels, and hypertension, which mostly occur together (13). The metabolic syndrome is related to increased risk of type 2 diabetes and atherosclerotic cardiovascular morbidity and mortality (14, 15). According to NCEP-ATP III criteria, metabolic syndrome prevalence was found to be 41.1% in different studies conducted in Iran (16). Considerable studies have focused on associations between vitamin D levels and the clinical finding of metabolic syndrome. Some reports demonstrate an inverse association between serum 25(OH)D and insulin resistance, diabetes, and metabolic syndrome (4, 17). Nuclear vitamin D receptors are expressed in pancreatic β-cells, which may be effective in insulin synthesis and secretion. Vitamin D deficiency enhances the risk of insulin resistance, increased blood glucose, lipotoxicity, obesity, and the risk of cardiovascular development (4, 18). Vitamin D deficiency can be due to inadequate exposure to sunlight, reduced nutritional intake of vitamin D or limited its absorption, increased catabolism of vitamin D. Also, renal and/or liver diseases can also prevent the conversion of vitamin D to its active form (4).

A meta-analysis of 28 kinds of research (including 99745 participants) reported that high levels of serum 25(OH)D were associated with a 55%, 51%, and 33% decreased risk of diabetes, metabolic syndrome, and cardiovascular disease, respectively (19). Gagnon et al. studied 4164 adults (mean age 50 years) and reported that serum 25(OH)D was inversely associated with waist circumference, TG, and FBS serum levels but not with HDL-C level and blood pressure (20, 21). Vitamin D deficiency has a high prevalence among the Iranian population, and inverse associations between serum vitamin D and numerous skeletal and non-skeletal diseases have been reported in the Iranian women population (22, 23). Women with vitamin D deficiency noticeably suffer skeletal and non-skeletal disorders such as osteoporosis, fractures, and diabetes, which may be improved by interventions such as vitamin D (5, 24). A significant improvement in serum FBS and insulin has been reported after treatment with vitamin D in 100 patients with type 2 diabetes in an Arak diabetes clinic (23). In the present study, we investigate serum levels of 25(OH)D, FBS, Chol, TG, LDL, and HDL in patients with metabolic syndrome compared to the control group. All subjects were divided into three categories on the base of their measured 25-(OH) vitamin D serum levels. 25(OH)D levels as sufficient (> 30), insufficiency (20-29 ng/mL) and deficiency (< 20 ng/mL). Insufficiency of 25-(OH) vitamin D has the highest rate among both patient and control groups. FBS, LDL, Chol, and TG were significantly higher, and HDL was significantly lower in the metabolic syndrome group compared to the control group. We also explored the correlations between metabolic parameters and vitamin D in the whole studied population and metabolic syndrome patients referred to Shiraz's Shahid Doran Hospital. In the whole population, there was a significant positive correlation between serum vitamin D and HDL, but there was a significant negative correlation between serum vitamin D and LDL, Chol, TG, and FBS, respectively. However, no significant relationship was observed between vitamin D and metabolic parameters in patients with metabolic syndrome.

Conclusion

In conclusion, the results of current research indicated that there is a significant association between metabolic syndrome and 25(OH)D levels. The highest rates for the patient with metabolic syndrome belong to insufficiency categories (20-29 ng/mL). The finding of this study also showed that 25(OH)D levels were significantly lower in the metabolic syndrome group compared to the control group.

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Conflict of interests

The authors declared no conflict of interest.

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