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Original Article

Association of different vitamin D levels with metabolic syndrome components in type 2 diabetic patients in Gorgan

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Abstract

This study was designed to evaluate and compare different levels of serum VD in MetS and T2DM subjects, and without MetS subjects, and to determine its association with MetS components in Gorgan. The study included 270 type 2 diabetic patients in 3 groups: Patients with MetS and VD deficiency Group 1), patients with MetS and a normal level of VD (Group 2) and patients without MetS and a normal level of VD (Group 3). The MetS criteria were defined using the National Cholesterol Education Program's Adult Treatment Panel III guidelines. Waist circumference (WC), systolic and diastolic blood pressure (SBP, DBP), fasting blood sugar (FBS) and triglyceride (TG) were significantly higher, and High-density lipoprotein cholesterol (HDL-C) and VD levels were significantly lower in Groups 1 and 2 than in Group 3. FBS and TG levels were significantly higher, and VD levels were significantly lower in Group 1 than in Group 3. Negative correlations exist between VD, FBS, and TG in group 1. Vitamin D deficiency may increase the risk of Mets. The relationship between VD deficiency and an increase in FBS and TG levels suggests that subjects in this group should manage their FBS and TG levels.

Keywords: vitamin D, metabolic syndrome, components, type 2 diabetes

Introduction

Diabetes mellitus is a disease that predominantly affects the elderly [1]. The prevalence of diabetes has increased worldwide, and it is grouped as one of the main reasons for death and high morbidity rates [2–4]. Type 2 diabetes mellitus (T2DM) is believed to be a metabolic disorder associated with modern lifestyles comprising stress and insufficient physical activity [5]. Metabolic syndrome (MetS) is a set of parameters that increase the risk of T2DM, cardiovascular disease (CVD), and all-cause mortality [6]. The prevalence of MetS has increased, and it is considered a public health problem. The MetS exhibits different prevalence rates in other populations. Many studies have shown that MetS prevalence varies across different ethnic groups and genders [7–9]. Data from the National Health and Nutrition Examination Survey (NHANES) estimates that 35% of adults in the United States and 50% of the population over age 60 have a diagnosis of MetS. The prevalence of MetS in Europe is estimated to be 41% in men and 38% in women [10–12]. It is reported that the prevalence of MetS in the Middle East ranges from 20.7% to 37.2% in men and from 32.1% to 42.7% in women [13]. Data from China indicate a prevalence of 58.1% in individuals aged 60 years and older [14]. According to the Heshmat *et al.* study, a multi-center study conducted in various urban areas of Iran, the prevalence of vitamin D deficiency among participants over the age of 60 was reported to be approximately 44% [15]. The exact reason for MetS is unclear, but genetics and environmental factors may be major contributors to its onset and progression. Different pathophysiological mechanisms have been proposed for the effect of vitamin D on MetS [16]. Various studies have shown that healthy diets, herbs, and nutrients play a crucial role in the prevention and treatment

of chronic diseases, such as diabetes and metabolic syndrome [17–20]. Vitamin D (VD) may affect insulin secretion and sensitivity, which plays a key role in the development of MetS [21]. A study on non-diabetic young people showed an inverse relationship between VD levels and the presence of MetS [22]. Studies on Korean populations showed that there was a higher risk of MetS in Korean men and women over 65 years of age with low VD levels [23]. Other findings reported that VD levels were insufficient in 50% of the study population in Shanghai, China (aged 19–70 years), and a linear relationship was observed between VD levels and serum glucose and lipid concentrations. The prevalence of VD in different provinces in Iran differs with gender and age group, varying between 30–90% of adults with different degrees of VD in the Iranian population [24]. They demonstrated that a 1 ng/mL increase in VD levels was associated with a significant decrease in total and LDL cholesterol, as well as a 54% decrease in the risk of MetS [25]. Barbalo *et al*. indicated that 80% of patients in a cardiovascular unit were VD-deficient, and all patients with hypovitaminosis D had MetS. They also observed higher levels of glycemia, glycosylated hemoglobin, total cholesterol, LDL, triglycerides, and atherogenic indices, as well as a higher BMI, in patients with VD deficiency compared to those with sufficient VD levels [26]. At the same time, Vimaleswaran *et al*. reported that increasing plasma VD level may decrease the risk of developing hypertension [27]. Still, some other studies reported no significant effect on systolic blood pressure (SBP) or diastolic blood pressure (DBP) values [28]. According to controversial research findings from different studies, there is no exact evaluation of VD levels and their association with MetS components in type 2 diabetic patients in Gorgan. Therefore, this study aimed to assess and compare different serum VD levels in MetS subjects and Type 2 diabetes mellitus (T2DM), and without MetS subjects, and determine its association with MetS components, in Gorgan.

Material and methods

Samples were collected (age-related causal sampling) from patients who met the exclusion and inclusion criteria. Five mL blood samples were prepared after 12 hours of fasting from subjects referred to the non-governmental laboratory between September 2022 and February 2023. The study was conducted after obtaining ethical approval from the Ethics Committee of Golestan University of Medical Sciences (Ethical code: IR.GOUMS.REC.1401.350). Consent was obtained from all participants. We excluded those participants who met criteria such as diabetic ketosis, diabetic nephropathy or retinopathy complications, administration of insulin or VD, calcium, receiving medications and any other diseases which may affect vitamin D metabolism. We included those participants with type 2 diabetes, with and without Mets, VD deficiency and normal VD. This study included 270 type 2 diabetic patients, age-matched, who were divided into three groups. According to the Schmitt *et al*. study, the sample size, with a 95% confidence interval and 80% statistical power, in each group was calculated to be 90 subjects [29].

$$n = \left(\frac{1}{kpA(1-pA)} + \frac{1}{pB(1-pB)}\right)\left(\frac{z_{1-\alpha/2} + z_{1-\beta}}{\ln(OR)}\right)^2$$

Patients with MetS and VD deficiency (group 1, n=90), patients with MetS and normal level of VD (group 2, n=90) and patients without MetS and normal level of VD (group 3, n=90). The MetS criteria were defined by using the National Cholesterol Education Programme, Adult Treatment Panel III (NCEP, ATP III) [30]. Included subjects contained any three or more of the MetS criteria. The criteria according to ATP III were Waist circumference (WC): >102 cm (male), >88 cm (female); triglyceride (TG) levels: >150 mg/dl; high density lipoprotein cholesterol (HDL-C) levels: <40 mg/dl (male), <50 mg/dl (female); blood pressure: >110/85 mmHg; and fasting blood glucose (FBG) levels: >110 mg/dl. The FBS, TG, and HDL-C levels were measured using commercial kits (PARS AZMON, Iran) and a spectrophotometer method. The vitamin D levels (Cat. No ab213966 25 (OH)D, China) were assessed by the Enzyme-Linked Immunosorbent Assay (ELISA) kits (VD Deficiency: Serum levels of VD lower than 20 ng/ml and normal levels of VD: Serum levels of VD 30 ng/ml and higher). Waist circumference (WC) was measured by a tape in centimeters. A digital blood pressure monitor (Omron 70JCP; Omron Maussaka, Mie-Ken, Japan) was used to determine systolic and diastolic blood pressures. BMI (Body mass index) was calculated using the formula weight (in kilograms, kg) divided by square body height (in meters, m).

Statistical analysis

The results were analyzed using SPSS-17 software. The data were expressed as Mean±Standard Deviation (SD). The Mann-Whitney U test was used to compare differences between the study groups. The normality

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Table 1: Demographic and Biochemical parameters in subjects with and without MetS; and normal Vitamin D level.

Parameters	Subjects with MetS and normal VD (n=90)	Subjects without MetS and normal VD (n=90)	P-value
Age (years)	51.33±9.51	50.8±14.26	0.061
BMI (kg/m²)	25.71±2.47	24.78±3.40	0.089
WC (cm)	106.70±10.70	98.00±13.30	<0.001
SBP (mmHg)	133.60±20.3	118.70±17.95	<0.001
DBP(mmHg)	85.10±11.60	75.60±7.26	<0.001
FBS (mg/dl)	157.60±44.20	120.4±59.31	<0.001
TG (mg/dl)	170.01±65.81	118.70±49.91	<0.001
HDL-C (mg/dl)	43.10±9.72	49.50±11.92	<0.001
VD (ng/ml)	46.40±16.11	52.85±19.05	0.022

Note: P-values lower than 0.05 was significant. MetS – Metabolic syndrome; VD – Vitamin D; BMI: Body mass index; WC – Waist circumference; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; FBS – Fasting Blood Sugar; TG – Triglycerides; HDL-C – High-density lipoprotein-cholesterol.

of the data distribution was determined using the Shapiro-Wilk test. The correlation of VD with MetS components in different study groups was calculated using Spearman's rho and Pearson's correlation coefficient tests.

Results

Table 1 presents a comparison of biochemical parameters between groups with and without MetS, with a normal VD level. Based on the results, WC, SBP, DBP, FBS and TG levels (106.70±10.70 cm, 133.60±20.3 mmHg, 85.10±11.60 mmHg, 157.60±44.20 mg/dl and 170.01±65.81 mg/dl, P-value<0.001) were significantly higher and HDL-C (43.10±9.72 mg/dl, P-value<0.001) and VD levels (46.40±16.11 ng/ml, P-value=0.022) were significantly lower in subjects with MetS and normal VD compared to subjects without MetS and normal VD levels (WC, SBP, DBP, FBS and TG levels (98.00±13.30 cm, 118.70±17.95 mmHg, 75.60±7.26 mmHg, 120.4±59.31 mg/dl and 118.70±49.91 mg/dl); and HDL-C (49.50±11.92 mg/dl) and VD (52.85±19.05 ng/ml).

Table 2 presents a comparison of all parameters in groups with MetS and VD deficiency, as well as those without MetS and normal VD levels. WC, SBP, DBP,

Table 2: Demographic and Biochemical parameters in subjects with and without MetS; and deficient and normal Vitamin D level.

Parameters	Subjects with MetS and VD deficiency (n=90)	Subjects without MetS and normal VD (n=90)	P-value
Age (years)	49.78±10.84	50.8±14.26	0.442
BMI (kg/m²)	25.71±2.47	24.78±3.40	0.189
WC (cm)	106.22±9.61	98.00±13.30	<0.001
SBP (mmHg)	128.71±22.20	118.70±17.95	0.001
DBP(mmHg)	82.33±10.41	75.60±7.26	<0.001
FBS (mg/dl)	177.40±62.24	120.40±59.30	<0.001
TG (mg/dl)	209.91±92.43	118.70±49.90	<0.001
HDL-C (mg/dl)	41.61±8.72	49.50±11.90	<0.001
VD (ng/ml)	18.91±6.01	52.85±19.05	<0.001

Note: P-values lower than 0.05 was significant. MetS – Metabolic syndrome; VD – Vitamin D; BMI: Body mass index; WC – Waist circumference; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; FBS – Fasting Blood Sugar; TG – Triglycerides; HDL-C – High-density lipoprotein-cholesterol.

Table 3: Demographic and biochemical parameters in subjects with MetS; and deficient and normal Vitamin D level.

Parameters	Subjects with MetS and VD deficiency (n=90)	Subjects with MetS and normal VD (n=90)	P-value
Age (years)	49.78±10.84	51.30±9.51	0.061
BMI (kg/m²)	25.71±2.47	25.49±2.40	0.422
WC (cm)	106.22±9.61	106.72±10.71	0.635
sSBP (mmHg)	128.71±22.20	133.63±20.30	0.098
DBP(mmHg)	82.33±10.41	85.12±11.61	0.102
FBS (mg/dl)	177.40±62.24	157.62±44.23	0.020
TG (mg/dl)	209.91±92.43	170.01±65.81	0.006
HDL-C (mg/dl)	41.61±8.72	43.11±9.72	0.398
VD (ng/ml)	18.91±6.01	46.42±16.12	<0.001

Note: P-values lower than 0.05 was significant. MetS – Metabolic syndrome; VD – Vitamin D; BMI: Body mass index; WC – Waist circumference; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; FBS – Fasting Blood Sugar; TG – Triglycerides; HDL-C – High-density lipoprotein-cholesterol.

FBS and TG levels (106.22±9.61 cm, 128.71±22.20 mmHg, 82.33±10.41 mmHg, 177.40±62.24 mg/dl and 209.91±92.43 mg/dl, P-value<0.001) were significantly higher and were significantly higher and HDL-C (41.61±8.72 mg/dl, P-value<0.001) and VD levels (18.91±6.01 ng/ml, P-value<0.001) were significantly lower in subjects with MetS and VD deficiency compared to subjects without MetS and normal VD (WC, SBP, DBP, FBS and TG levels (98.00±13.30 cm, 118.70±17.95 mmHg, 75.60±7.26 mmHg, 120.4±59.31 mg/dl and 118.70±49.91 mg/dl); and HDL-C (49.50±11.92 mg/dl) and VD (52.85±19.05 ng/ml).

Table 3 presents a comparison of biochemical parameters in a group with MetS and VD deficiency, and in a group with MetS and normal VD. Based on the results, FBS and TG levels (177.40±62.24 mg/dl [p-value=0.020] and 209.91±92.43 mg/dl, [p-value=0.006]) were significantly higher, and VD levels (18.91±6.01 ng/ml, p-value<0.001) were significantly lower in subjects with MetS and VD deficiency compared to subjects with MetS and normal VD.

Table 4 presents the correlation between different levels of VD and MetS components across various groups. Based on the results, there are negative correlations between VD and FBS (r=-0.489, P-value=0.042) and TG (r=-0.456, P-value=0.035) in subjects with MteS and VD deficiency. There were no significant correlations

Table 4: Correlation of different VD levels with MteS components in different groups.

Parameters	Subjects with MteS and VD deficiency		Subjects with MteS and normal VD level		Subjects without MteS and normal VD level	
	r	P-value	r	P-value	r	P-value
Age (years)	0.201	0.057	0.189	0.061	0.187	0.078
BMI (kg/m²)	0.170	0.109	0.093	0.382	- 0.191	0.067
WC (cm)	0.268	0.090	0.150	0.159	- 0.046	0.663
SBP (mmHg)	0.034	0.748	0.107	0.316	0.059	0.575
DBP (mmHg)	- 0.086	0.423	0.076	0.478	0.064	0.543
FBS (mg/dl)	-0.489	0.042	0.118	0.269	0.046	0.662
TG (mg/dl)	-0.456	0.035	0.025	0.818	- 0.111	0.291
HDL-C (mg/dl)	0.015	0.887	0.050	0.639	- 0.056	0.595

Note: P-values lower than 0.05 was significant. MetS – Metabolic syndrome; VD – Vitamin D; BMI: Body mass index; WC – Waist circumference; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; FBS – Fasting Blood Sugar; TG – Triglycerides; HDL-C – High-density lipoprotein-cholesterol.

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between VD and other parameters in subjects with and without MetS and normal VD levels (P-value>0.05).

Discussion

The results of this study showed that WC, SBP, DBP, FBS and TG were significantly higher. HDL-C and VD levels were significantly lower in subjects with MetS and normal VD, and VD-deficient when compared to subjects without MetS and normal VD levels. FBS and TG were significantly higher, and the VD was significantly lower in those with MetS and VD deficiency than in those with MetS and normal VD. The correlation of VD with MetS components in a group with MetS and VD deficiencies revealed a negative correlation between VD, FBS and TG. According to controversial results from different studies, there is no exact evaluation of VD levels and their association with MetS components in type 2 diabetic patients. A study on the relationship between VD levels and the occurrence of T2DM in a Chinese population showed that low VD status is significantly associated with the risk of developing T2DM, and low levels of VD may contribute to the occurrence of T2DM in Chinese populations [31]. A study on the Qatari population found that serum VD was lower in those with MetS. They concluded that VD deficiency is common in Qatari individuals and MetS is associated with VD deficiency [32]. Another study on the relationship between serum level of VD and MetS in Qatari populations showed no relationship between serum VD and BP, FBS, HDL-C, and TG, which was not in agreement with our results except for FBS and TG parameters [33]. Hosseinzadeh *et al*. have revealed the relation between serum VD levels in elderly Iranians and the risk of MetS development. Their results showed that higher levels of VD are associated with a reduced prevalence of MetS and favorable conditions of HDL-C, WC and FBS [34]. Another research study on the association of VD levels with MetS in Chinese adolescents and adults has indicated that the prevalence of VD deficiency was significantly lower in participants with MetS [35].

Other studies have reported that people with MetS, compared to non-metabolic subjects, show significantly lower VD levels. They concluded that low VD levels are a risk factor for MetS [36]. A study by Kim *et al*. showed the association between VD deficiency and MetS among Korean adolescents. Their results revealed that among the MetS components, VD deficiency was associated with an increased risk of elevated FBS. They found that the association of VD deficiency with an increased risk of high levels of FBS suggests that adolescents in this population should manage their diabetes [37]. Barbalo *et al*. assessed the association between MetS risk factors and VD in patients referred to a cardiovascular center. VD was negatively correlated with FBS, TG, and BP. They concluded that there is a significant prevalence of low VD levels in patients with cardiovascular risk factors [26]. Their study in subjects with VD deficiency and MetS also showed that TG levels were significantly higher and HDL-C levels were significantly lower compared with subjects with VD deficiency and without MetS [26]. Several studies have shown an association between low serum VD levels and diabetes and MetS. A population-based study from Norway reported that the serum level of VD is inversely correlated with the average blood sugar levels and insulin resistance [38]. Mirhoseini *et al*. studied the relationship between VD deficiency and MetS in obese individuals. Their results showed that TG and FBS had a negative correlation with serum VD, which was in agreement with our results [39]. Verrusio *et al*. assessed the correlation between serum VD levels and MetS components. Their results show that VD had a significant negative correlation with FBS, which is consistent with our findings [40]. The results of our study were consistent with those of some previous studies, which found that the VD level was significantly lower among patients with MetS [26, 31, 32, 34–40].

Some studies have reported a link between VD levels and MetS in certain populations, which varies depending on age, sex, and country. Studies of MetS components showed that lower TG and high HDL-C levels correlate with high VD levels [41]. Studies on the association between VD levels and components of MetS in urban Chinese adolescents showed that Serum VD was significantly inversely associated with MetS, but not with elevated TG, elevated blood pressure, and impaired fasting blood glucose [42]. Another study on the relationship between VD and MetS reported that serum VD in women with and without MetS showed no significant difference. They concluded that VD status was not associated with MetS components [43]. Wang *et al*. reported an inverse relationship between MetS and VD levels in elderly subjects without VD deficiency. They concluded that a low VD level is an independent risk factor for MetS in older adults without VD deficiency [44]. Kasab *et al*. reported the relationship between VD deficiency and MetS markers in obesity and overweight adults. There was no significant relationship between VD deficiency and MetS components [45]. Our results

are inconsistent with those of researchers who have shown a relationship between MetS and VD levels in patients with MetS [34, 41–45]. Some other studies have shown an inverse association between VD level and FBS [46, 47], while other findings showed that the blood VD level is inversely associated with hypertension [48]. The inverse association between serum VD and FBS in this study is consistent with other reports [49, 50]; however, some studies have not confirmed such an association [51, 52]. It has been reported that plasma HDL-C levels have a direct relationship with the VD level [53–54], while other studies did not find any correlation between VD deficiency and serum triglyceride levels [55]. A correlation study found an association between VD levels and MS components (WC, BP, TG and HDL-C) [46, 56]. Our results revealed a negative correlation between VD deficiency and serum triglyceride levels, which is in accordance with some other findings [57]. The study by Chacko *et al*. does not support the hypothesis of a relationship between VD and LDL, HDL and glucose [58]. The mechanism of these relationships is not entirely clear, and it remains incompletely understood. Many researchers have reported VD deficiency as a risk factor in the pathogenesis of MetS and diabetes. There has been some suggestion that VD deficiency increases the risk of cardiovascular disease [59–61]. Some studies do not indicate that VD deficiency is a risk factor for the development of MetS [62] and suggest that a low VD level may be a consequence of insulin resistance, rather than its cause. Various mechanisms have been proposed to examine the impact of VD on MetS components. VD may affect the secretion and sensitivity of insulin, which can play a significant role in the development of MetS.

The most significant limitations of this study were the matching of three groups by age, BMI and VD levels among different groups with type 2 diabetes mellitus.

Conclusion

The main points of this study were that all study groups consisted of type 2 diabetic subjects. This means that our study indicated the effect of VD status on MetS components when compared to the three groups. Our study revealed significant adverse correlations between VD, FBS, and TG in Group 1. Thus, VD deficiency may increase the risk of Mets. The relationship between VD deficiency and an increase in FBS and TG levels suggests that subjects in this group should manage their FBS and TG levels.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Golestan University of Medical Sciences (approval ID: IR.GOUMS.REC.1401.350).

Consent to participate

Written informed consent was obtained from all the participants.

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