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Body weight and waist circumference as predictors of vitamin D deficiency in patients with type 2 diabetes and cardiovascular disease

Telesna masa i obim struka kao prediktori nedostatka vitamina D kod bolesnika sa dijabetesom tipa 2 i kardiovaskularnom bolešću

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Abstract

Background/Aim. Vitamin D deficiency is a well-established risk factor for bone disease, but emerging data suggest that altered vitamin D homeostasis may play a role in the development of type 2 diabetes mellitus (T2DM), dyslipidemia hypertension, and other cardiovascular diseases (CVD). The aim of this study was to investigate the prevalence of vitamin D deficiency in patients with T2DM with/without CVD, to correlate it with anthropometric and metabolic parameters and to determine the predictors of vitamin D deficiency. **Methods.** A total of 88 patients with T2DM (49 male/39 female, aged 61.0 ± 0.9 yrs, body mass index (BMI) 29.9 ± 0.4 kg/m^2) and 67 patients (44 male/23 female, aged 63.6 ± 1.0 yrs, BMI 29.2 ± 0.5 kg/m^2) with T2DM and CVD (myocardial infarction in 57 patients and angina pectoris in 10 patients) were included in this study. These patients were compared with 87 healthy subjects (35 male/52 female, aged 52.8 ± 1.4 yrs, BMI 27.2 ± 0.5 kg/m^2). Weight, height, waist circumference and BMI were recorded in all patients. Also, total cholesterol, triglycerides, hemoglobin A1c (HbA_{1c}) and 25-hydroxy-vitamin D [25(OH)D] levels were measured in all. According to 25(OH)D level, all subjects were divided into three categories: severe vitamin D deficiency (≤ 15 ng/mL), vitamin D insufficiency (15–20 ng/mL) and vitamin D sufficiency (20 ng/mL). We correlated vitamin D levels with anthropometric and metabolic status and determined the predictors of vitamin D deficiency. **Results.** Severe vitamin D deficiency was registered in 16.1% healthy subjects, in 21.6% patients with T2DM and in 26.9% patients with T2DM and CVD. Patients with T2DM who were vitamin D deficient had increased weight, waist circumference, cholesterol and triglyceride levels when compared with patients with T2DM who had sufficient vitamin D level. 25(OH)D levels correlated with BMI and waist circumference in all subjects, but did not correlate with metabolic parameters (lipids, HbA_{1c}). The best predictors of vitamin D level in all subjects were weight, waist circumference and BMI. **Conclusion.** The high prevalence of vitamin D deficiency in patients with T2DM and particularly in patients with T2DM and CVD suggests that supplementation with vitamin D may be beneficial although there is still not sufficient evidence for recommending prescribing vitamin D.

Key words:
diabetes mellitus, type 2; cardiovascular disease; vitamin d deficiency; body weight; body mass index; risk factors.

Apstrakt

Uvod/Cilj. Nedostatak vitamina D je poznat faktor rizika od oboljenja skeleta. Sve je više podataka o ulozi nedostatka vitamina D u razvoju dijabetesa melitusa tipa 2 (T2DM), dislipidemije, hipertenzije, i drugih kardiovaskularnih bolesti (KVB). Cilj studije bio je da se ustanovi učestalost nedostatka vitamina D kod bolesnika sa T2DM sa ili bez KVB, korelacija nedostatka vitamina D sa antropometrijskim i metaboličkim parametrima i odrede prediktori nedostatka vitamina D. **Metode.** U studiju je bilo uključeno 88 bolesnika sa T2DM [(49 muškaraca/39 žena, životno doba 61,0 ± 0,9 god, indeks telesne mase (ITM) 29,9 ± 0,4 kg/m^2)] i 67 bolesnika (44 muškaraca/23 žena, životno doba 63,6 ± 1,0 god, ITM 29,2 ± 0,5 kg/m^2) sa T2DM i KVB (infarkt miokarda kod 57 bolesnika i angina pektoris kod 10 bolesnika). Ovi bolesnici su upoređeni sa 87 zdrava ispitanika (35 muškarca/52 žena, životno doba 52,8 ± 1,4 god, ITM 27,2 ±

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0,5 kg/m²). Mereni su telesna masa, visina, obim struka i ITM, kao i nivo holesterola, triglicerida, hemoglobina A1c (HbA_{1c}) i 25-hidroksi vitamin D[25(OH)D]. Prema nivou 25(OH)D svi ispitanici bili su podeljeni u tri grupe: težak nedostatak vitamina D (≤ 15 ng/mL), nedostatak vitamina D (15–20 ng/mL) i zadovoljavajući nivo vitamina D (≥ 20 ng/mL). Ispitana je korelacija nivoa vitamina D sa antropometrijskim i metaboličkim parametrima i određeni su prediktori nedostatka vitamina D. **Rezultati.** Težak nedostatak vitamina D registrovan je kod 16,1% zdravih ispitanika, 21,6% bolesnika sa T2DM i 26,9% bolesnika sa T2DM i KVB. Bolesnici sa T2DM koji su imali težak nedostatak vitamina D imali su veću telesnu masu, obim struka, nivoe holesterola i triglicerida u poređenju sa bolesnicima sa T2DM koji su imali zadovoljavajući nivo vitamina D. Nivo 25(OH)D korelisao je sa ITM i obimom struka kod svih ispitanika, ali nije korelisao sa metaboličkim parametrima (lipidi, HbA_{1c}). Najbolji prediktori nivoa vitamina D kod svih ispitanika bili su telesna masa, obim struka i ITM. **Zaključak.** Visoka učestalost nedostatka vitamina D kod bolesnika sa T2DM, a posebno kod bolesnika sa T2DM i KVB ukazuje na potrebu supstitucije vitaminom D iako još uvek nema dovoljno podataka o tome.

Ključne reči:
dijabetes melitus, insulin-nezavisni; kardiovaskularne bolesti; vitamin d, nedostatak; telesna težina; telesna masa, indeks; faktori rizika.

Introduction

Vitamin D is crucial not only to maintain bone strength, but research also suggests it plays a role in immune system functioning, cancer prevention, glucose and lipid metabolism and cardiovascular health [1]. Just recently Task Force of the Endocrine Society released guidelines to clinicians for the evaluation, treatment and prevention of vitamin D deficiency with an emphasis on the care of patients who are at risk for deficiency [2]. Considering that vitamin D deficiency is very common in all age groups and that few foods contain vitamin D, Task Force recommended supplementation depending on age and clinical circumstances.

Vitamin D is formed mainly in the skin by photolysis of steroid precursors by ultraviolet B radiation and is also found in fish, eggs, fortified milk, cod liver oil, and supplements. Newly formed vitamin D is bound to vitamin D binding protein (DBP) and transported to the liver where is hydroxylated to 25-hydroxyvitamin D [(25(OH)D)]. 25(OH)D is further hydroxylated in the kidney to 1,25-dihydroxyvitamin D [$(25(OH)_2D)$], the most active metabolite of vitamin D [3]. However, serum 25(OH)D is regarded as the best indicator of vitamin D status in individuals without kidney disease, because it is the substrate for the renal and nonrenal production of $1,25(OH)_2D$, has a longer biological half-life than $1,25(OH)_2D$ and circulates in much higher concentrations. Serum 25(OH)D reflects the total production of vitamin D from both endogenous and exogenous sources, including exposure to ultraviolet-B radiation and intake of various dietary forms. People who are at high risk for vitamin D deficiency are the elderly, dark skinned, obese, those who cover all exposed skin or use sunscreen, patients with fat malabsorption syndromes or inflammatory bowel disease [4–7].

At present, there is no consensus on the optimal level of vitamin D; however, it has been suggested that serum 25(OH)D levels greater than 25 ng/mL (Endocrine Society Guidelines 30 ng/mL) are required for optimal health and that values less than 15 ng/mL (Endocrine Society Guidelines 20 ng/mL) have been associated with decreases in bone density and other negative effects of vitamin D deficiency [2, 8].

Recently, many studies have reported an inverse associations between serum 25(OH)D levels and the risk of a variety of diseases, including diabetes mellitus (DM), cardiovascular disease (CVD), cancer, autoimmune diseases, infections, or cognitive decline [9]. Clinically, vitamin D has been shown to be linked with glucose and insulin homeostasis. Observational studies show a relatively consistent association between low vitamin D status and DM, both type 1 DM and type 2 (T2DM) or metabolic syndrome [10–12]. It's already well-known that children living in areas of the world without much sunlight, such as Finland, have higher rates of type 1 diabetes than those in sunnier parts of the world. In fact, infants in Finland are 400 times more likely to develop DM than infants in Venezuela [13]. Some research indicates that infants and children given vitamin D supplements are less likely to develop type 1 DM. Many studies have shown that supplementing with vitamin D and calcium slows the progression to T2DM. Vitamin D deficiency is commonly found in people with poor DM control. As the deficiency worsened, so did DM control. A minority of DM patients took vitamin D supplements. The molecular mechanisms of association of vitamin D deficiency with DM, hypertension, obesity and CVD remain incompletely understood.

As low vitamin D status has been suggested to be a risk factor for T2DM and for CVD, the aim of this study was to determine vitamin D levels in patients with T2DM and in patients with T2DM and CVD and correlate the levels of vitamin D to their anthropometric and metabolic status.

Methods

A total of 88 patients with T2DM [49 male and 39 female, aged 61.0 ± 0.9 yrs, body mass index (BMI) 29.9 ± 0.4 kg/m²] and 67 patients (44 male and 23 female, aged 63.6 ± 1.0 yrs, BMI 29.2 ± 0.5 kg/m²) with history of both T2DM and CVD (myocardial infarction in 57 patients and angina pectoris in 10 patients were included in this study). These patients were compared with 87 healthy subjects (35 male and 52 female, aged 52.8 ± 1.4 yrs, BMI 27.2 ± 0.5 kg/m²) with no history of DM or CVD.

Informed consent for the study was obtained from all patients and from healthy subjects. The protocol was ap-

proved by the Ethical Committee of University Clinical Center Podgorica.

The patients' age, weight, height, waist circumference and calculated BMI were recorded. Serum samples were obtained in the morning after an overnight fast. In serum samples we measured total cholesterol, triglycerides, hemoglobin A_{1c} (HbA_{1c}) and 25(OH)D levels. HbA_{1c} was measured with immunoturbimetric analysis (COBAS INTEGRA), cholesterol was measured with enzymatic methodology, while triglycerides were measured with glycerol phosphate oxidase methodology. The HbA_{1c} provides an average measurement of blood sugar control over about a 12-week span. For people with DM, the goal is 7%, for healthy people, the normal range is 4%–6%. Serum levels of 25(OH)D were measured by commercial enzyme immunotest (EIA, Immunodiagnostic system, UK). The limit of detection for 25(OH)D was 5 ng/mL.

Parameters of descriptive statistics are presented as mean ± standard error (SE). For statistical analysis we used parametric *t*-test, nonparametric Mann-Whitney test and ANOVA. We analyzed the influence of sex, age, weight, waist circumference and BMI on vitamin D level. We analyzed the correlation between anthropometric and metabolic parameters and vitamin D level using Spearman's correlation. We used the multiple regression analysis for determination of predictors of vitamin D level. Statistical analysis was performed with SPSS for Windows (version 15.0). *P* value < 0.05 was considered as statistically significant.

Results

Clinical characteristics of three groups of participants in the study (patients with T2DM, patients with T2DM and CVD, and healthy subjects, are presented in Table 1.

HbA_{1c} and lipid levels in patients with T2DM and patients with T2DM and CVD are presented in Table 2. Patients with T2DM had higher levels of HbA_{1c} and cholesterol compared with patients with T2DM and CVD ($p < 0.01$).

Vitamin D levels in patients and healthy subjects are shown in Table 3.

There were no differences in 25(OH)D levels between male and female subjects in all investigated groups (data not shown). There was no difference in vitamin D levels between patients with hypertension (51.0 ± 1.8 ng/mL) and with normal blood pressure (54.1 ± 1.6 ng/mL; $p > 0.05$).

Table 2
Hemoglobin A_{1c} (HbA_{1c}), cholesterol and triglyceride levels in the patients with type 2 diabetes mellitus (T2DM) and the patients with T2DM and cardiovascular disease (CVD)

Parameters	T2DM	T2DM and CVD
HbA_{1c} (%)	7.6*	7.2
Cholesterol (mmol/L)	6.1*	5.5
Triglycerides (mmol/L)	2.8	2.3

*$p < 0.01$ *vs* T2DM and CVD

Table 3
25-hydroxyvitamin D [25(OH)D] level in the patients with type 2 diabetes (T2DM), the patients with T2DM and cardiovascular disease (CVD) and in the healthy subjects

Groups of patients	25(OH)D (ng/mL)
T2DM	21.7 ± 0.8 (6.8–44.8)
T2DM and CVD	19.4 ± 0.8* (7.6–33.2)
Healthy subjects	22.6 ± 0.8 (8.0–55.2)

*SE – standard error; $p < 0.01$ *vs* healthy subjects

In all subjects, 25(OH)D levels inversely correlated with BMI (r = -0.127, $p = 0.048$) and waist circumference (r = -0.165, $p = 0.010$), but did not correlate with metabolic parameters (lipids, HbA_{1c}). According to 25(OH)D level, we divided all subjects into three categories: severe vitamin D deficiency (less than 15 ng/mL), vitamin D insufficiency (15 to 20 ng/mL) and vitamin D sufficiency (above 20 ng/mL). Table 4 shows the vitamin D status in all studied patients. The percentages of patients with severe vitamin D deficiency and vitamin D insufficiency were the highest (26.9% both) in patients with T2DM and CVD.

Nineteen patients with T2DM (21.6%) were severe vitamin D deficient. Clinical characteristics of these patients are presented in Table 5. Patients with T2DM who were vitamin D deficient had increased body weight and waist circumference ($p < 0.05$) compared with patients with T2DM and vitamin D > 20 ng/mL. Cholesterol and triglyceride lev-

Table 1
Clinical characteristics of the patients with type 2 diabetes mellitus (T2DM), the patients with T2DM and cardiovascular disease (CVD) and in the healthy subjects

Characteristics	T2DM patients (n = 88)	T2DM and CVD patients (n = 67)	Healthy subjects (n = 87)
Sex (male/female), n	49/39	44/23	35/52
Age (years), $\bar{x} \pm SE$	61.0 ± 0.9	63.6 ± 1.0	52.8 ± 1.4
Duration of diabetes mellitus (years), $\bar{x} \pm SE$	7.6 ± 0.6	10.2 ± 0.8	–
Hypertension (yes/no), n	40/48	49/18	–
Weight (kg), $\bar{x} \pm SE$	88.2 ± 1.6*	85.5 ± 2.0	81.8 ± 1.5
Height (cm), $\bar{x} \pm SE$	172.6 ± 1.0	171.8 ± 1.2	173.6 ± 1.1
BMI (kg/m^2), $\bar{x} \pm SE$	29.9 ± 0.4*	29.2 ± 0.5*	27.2 ± 0.5
Waist (cm), $\bar{x} \pm SE$	99.5 ± 1.2*	99.7 ± 1.4*	91.5 ± 1.5
Therapy			
insulin	45	35	–
OAD	43	32	–

*$p < 0.01$ *vs* healthy subjects; SE – standard error; BMI – body mass index; OAD – oral antidiabetics

Table 4

Percentage of subjects with severe vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency in the patients with type 2 diabetes mellitus (T2DM), patients with T2DM and cardiovascular disease (CVD) and in healthy subjects

25(OH)D (ng/mL)	Vitamin D status	T2DM patients (%)	T2DM and CVD patients (%)	Healthy subjects (%)
< 15	severe deficiency	21.6	26.9	16.1
15–20	insufficiency	18.2	26.9	14.9
> 20	sufficiency	60.2	46.2	69

25(OH)D – 25-hydroxyvitamin D

Table 5

Clinical characteristics of 88 patients with type 2 diabetes mellitus (T2DM) divided in 3 categories according to vitamin D status (severe vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency)

Variables	25(OH)D in patients with T2DM		
	≤ 15	15–20	> 20
Number (%)	19 (21.6)	16 (18.2)	53 (60.2)
Age (years), ± SE	59.7 ± 1.9	62.4 ± 2.1	61.0 ± 1.3
Weight (kg), ± SE	88.8 ± 4.0*	85.9 ± 4.0	88.7 ± 1.9
Height (cm), ± SE	169.4 ± 2.5	169.3 ± 2.3	174.8 ± 1.3
BMI (kg/m^2), ± SE	31.0 ± 1.0	30.4 ± 1.1	29.4 ± 0.5
Waist (cm), ± SE	103.8 ± 2.6*	99.4 ± 3.2	97.9 ± 1.3

***p < 0.05 *vs* 20 ng/mL; BMI – body mass index; [25(OH)D] – 25-hydroxyvitamin D**

els were higher in patients with severe vitamin D deficiency compared to those with vitamin D 15–20 ng/mL and > 20 ng/mL ($p < 0.01$; Table 6).

Eighteen patients with T2DM and CVD (26.9%) had severe vitamin D deficiency and the same number of patients had vitamin D insufficiency. Clinical characteristics of these patients are presented in Table 7. There were no differences in various parameters (anthropometric, lipids, or HbA_{1c}) between three subgroups of patients divided according to vitamin D status (severe vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency, Table 8).

Table 6

Hemoglobin A_{1c} (HbA_{1c}), cholesterol and triglyceride levels in the patients with type 2 diabetes (T2DM) divided in 3 categories according to vitamin D status (severe vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency)

25(OH)D (ng/mL)	Vitamin D status	HbA1c (%)	Cholesterol (mmol/L)	Triglycerides (mmol/L)
< 15*	severe deficiency	7.7	6.8*	4.7*
15–20*	insufficiency	7.4	5.7	2.3
> 20*	sufficiency	7.6	5.9	2.3

***p < 0.05 *vs* group with 15–20 ng/mL and 20 ng/mL 25(OH)D**

Table 7

Clinical characteristics of 67 patients with type 2 diabetes (T2DM) and cardiovascular disease (CVD) divided in 3 categories according to vitamin D status (severe vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency)

Variables	Vitamin D status measured by 25-hydroxyvitamin D level in patients with T2DM and CVD		
	≤ 15 ng/mL	15–20 ng/mL	> 20 ng/mL
Number of patients (%)	18 (26.9)	18 (26.9)	31 (46.2)
Age (years), ± SE	63.7 ± 1.7	64.1 ± 2.4	63.2 ± 1.5
Weight (kg), ± SE	87.1 ± 5.1	85.0 ± 4.6	84.9 ± 1.9
Height (cm), ± SE	169.5 ± 2.1	173.7 ± 3.0	172.1 ± 1.6
BMI (kg/m^2), ± SE	30.2 ± 1.2	28.3 ± 0.9	29.3 ± 0.6
Waist (cm), ± SE	102.7 ± 3.2	98.6 ± 2.6	98.5 ± 1.7

Table 8

Hemoglobin A_{1c} (HbA_{1c}), cholesterol and triglyceride levels in the patients with type 2 diabetes (T2DM) and cardiovascular disease (CVD) divided in 3 categories according to vitamin D status (severe vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency)

25(OH)D (ng/mL)	Vitamin D status	HbA1c (%)	Cholesterol (mmol/L)	Triglycerides (mmol/L)
< 15*	severe deficiency	7.3	5.3	2.4
15–20*	insufficiency	7	5.4	2.3
> 20*	sufficiency	7.2	5.6	2.2

The best predictors of 25(OH)D levels in all subjects were weight (p = 0.0001), waist circumference (p = 0.006) and BMI (p = 0.001). In patients with T2DM predictors of 25(OH)D levels were weight (p = 0.0001) and waist circumference (p = 0.004). In patients with T2DM and CVD the best predictor of 25(OH)D level was BMI (p = 0.006).

Discussion

According to our results, a substantial percentage of patients with T2DM, patients with T2DM and CVD, as well as healthy subjects were vitamin D deficient. The worst situation was in the group of patients with T2DM and CVD in which 27% were vitamin D deficient. We found a negative correlation between serum vitamin D levels and BMI and waist circumference in our patients, which is in accordance with other studies [4, 7]. We did not find any gender differences in serum vitamin D levels, in contrast to other studies in which the authors reported higher levels in men than in women [5, 6]. We did not find any correlation between serum vitamin D levels and age or metabolic parameters ($HbA1_c$, lipids).

The strongest relationship (inverse) was found between 25(OH)D levels and BMI and waist circumference. The negative relationship between 25(OH)D and fat mass has been attributed to increased sequestration of fat-soluble vitamin D in adipocytes. It is hypothesized that vitamin D generated in the skin or orally ingested is sequestered into adipocytes before it is transported to the liver and converted to 25(OH)D [14]. It is not known whether the adipocytes simply store vitamin D or actively catabolize it. Other study showed that changes in 25(OH)D levels with age, gender, or fat mass are not due to genetic variability of vitamin D binding protein [15]. Consistently observed negative relationships of 25(OH)D with body composition have a biological origin other than adaptation to plasma transport. Thus obese people are at risk for vitamin D deficiency and may need 2–3 times more vitamin D for their age group to satisfy their bodies vitamin D requirement [2].

Vitamin D deficiency is highly prevalent worldwide and essentially everyone is at risk [2]. Low levels of 25(OH)D are present in as many as one third to one half of otherwise healthy middle-aged to elderly adults [1, 16, 17]. Limited cutaneous synthesis due to inadequate sun exposure or pigmented skin and inadequate dietary intake are the principal causes of low 25(OH)D levels. Although the best characterized consequences of vitamin D deficiency involve the musculoskeletal system, a growing body of evidence suggests that low levels of vitamin D may negatively affect the glucose and insulin homeostasis and the cardiovascular system as well, leading to hyperglycemia, insulin resistance, hypertension, heart disease and cognitive decline in the elderly population [18, 19]. Observational studies showed the association between vitamin D levels deficiency and impaired glucose tolerance or T2DM [10, 11, 20–22]. Glycemic control in T2DM depends on the season, with the lowest HbA_{1c} levels during summer [23]. Data from the Nurses' Health Study found that women who took a combination of 1,200 mg of calcium and more than 800 IU of vitamin D daily had a 33% lower chance of getting T2DM than women taking smaller amounts of these nutrients [10]. It seems that subjects with vitamin D deficiency are at higher risk of insulin resistance and the metabolic syndrome. The unredlying mechanism could be an effect of vitamin D on insulin sensitivity, on β-cell function, or on both [11]. The pancreatic β-cells express vitamin D receptor [24]. Vitamin D deficiency inhibits insulin secretion and modulates lipolysis [25]. Vitamin D supplementation improves insulin secretion, insulin sensitivity and glucose tolerance in vitamin D-deficient animals and in humans [26–28]. Treatment with vitamin D_3 in patients with T2DM increased plasma 25(OH)D and the first phase of the insulin secretion evaluated by an intravenous glucose tolerance test [28].

Cardiovascular system is also affected by vitamin D deficiency. Vitamin D deficiency has been observed in patients with acute myocardial infarction, stroke and heart failure and CVD [29–32]. Data from the Framingham Heart Study indicate that patients with the lowest levels of vitamin D were 62% more likely to have either a heart attack or a stroke than those with higher vitamin D levels. The results were so impressive that authors believe that people should take between 1,000 and 2,000 IU of vitamin D every day. Patients with heart failure have lower plasma levels of 25(OH)D and $1,25(OH)_2D$ than controls [31, 33]. Another large prospective study of Wang et al. [34] in more than 1,700 subjects showed that vitamin D deficiency is associated with increased cardiovascular risk [34]. The authors showed that the higher risk (2-fold risk) was evident among subjects with hypertension, in whom 25(OH)D levels were bellow 15 ng/mL. With this cut point, the prevalence of vitamin D deficiency in the study of Wang et al. [34] was 28%, similar to our results and results reported in other large epidemiological studies [35].

In the UK an increased cardiovascular morbidity was associated with low plasma 25(OH)D concentrations in winter. Similarly, blood pressure was higher in winter than in summer, varies with skin pigmentation and is higher in subjects with vitamin D deficiency [36, 37]. Vitamin D receptors are identified in many tissues, including vascular smooth muscle, endothelium and cardiomyocytes [1, 38]. *In vitro*, $1,25(OH)_2D$ suppresses renin gene expression, regulates the growth and proliferation of vascular smooth muscle cells and cardiomyocytes [39, 40]. In knockout mice model, the absence of vitamin D receptor activation results with the upregulation of the renin-angiotensin system, hypertension and left ventricular hypertrophy [27, 41]. Vascular smooth muscle cells and endothelial cells have the ability to convert circulating 25(OH)D to $1,25(OH)_2D$ [42]. Furthermore, atherosclerosis may be viewed as a chronic inflammatory disease that involves several cytokines (TNF-α, IL-6). Active vitamin D can suppress these cytokines *in vivo* and TNF-α is inversely related to plasma 25(OH)D *in vivo* [43].

Management of vitamin D deficiency may be a simple and cost-effective method to improve blood sugar control, arterial hypertension, dyslipidemia, atherosclerosis and prevent the serious complications associated with these pathological conditions. Diet alone may not be sufficient to manage vitamin D levels. Based on our and other studies people at risk for DM, dyslipidemia and CVD should be screened

for low vitamin D levels which allow health care professionals to identify a nutrient deficiency early on. Getting 25(OH)D consistently above 30 ng/mL may requier 1000–2,000 IU/day of vitamin D as suggested by the recent Endocrine Society Guideline [2].

Conclusion

The results of the present study suggest that vitamin D deficiency is highly prevalent in patients with T2DM and particularly in patients with T2DM and CVD. The best predictors of vitamin D status seem to be weight, BMI and waist circumference all related to the metabolic status. There is no sufficient evidence yet to recommend prescribing vitamin D to attain the benefit for cardiovascular protection, however interventional studies are awaited.

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