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ORIGINAL ARTICLE

Vitamin-D Deficiency among Patients with Diabetes Mellitus in Northern Borders Area of Saudi Arabia

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Running Head: *VITAMIN-D DEFICIENCY AND SHOCK*

ABSTRACT

Diabetes mellitus, a chronic illness, is characterized by pancreatic and insulin dysfunction. Under the influence of sunlight, vitamin D (V-D) is produced in the skin in a non-enzymatic manner. Furthermore, V-D can be obtained via fish or plant sources. Different studies conducted in Saudi Arabia have been shown high occurrence of V-D inadequacy. Obesity and type 2 diabetes are both linked to V-D insufficiency. Still, this relationship's causality is unknown. A growing body of research suggests that changes in V-D and calcium homeostasis may play a role in the development of type 2 diabetes. This study aimed to ascertain the occurrence of V-D deficiency in the Northern borders (NB) of Saudi Arabia and to verify the connection between V-D deficiency and other features of study subjects. During the period from July 2018 to February 2019, a cross-sectional study was carried out. A random sampling method was employed to choose the required numbers of subjects who have type 1 or type II diabetes and are registered in NB region health centers and hospitals. The sample size was calculated using the one-sample proportion formula and the results of similar studies. These results revealed the situation in the NB Region of Saudi Arabia among diabetic patients and highlight the importance of addressing the issue. The correlation between V-D and hypertension was also found in the study, requiring further investigation and explanation.

Keywords: Diabetes mellitus; vitamin D deficiency; hypertension; Saudi Arabia

INTRODUCTION

Diabetes mellitus (DM) is a chronic illness characterized by pancreatic and insulin dysfunction, which results in several complications, thus leading to increased morbidity. The estimated prevalence of both types of DM has risen from 4.6% to 9.3% among people aged 20-79 from 2000 to 2019 worldwide and has been projected to grow to 10.2% and 10.9% in 2030 and 2045, respectively [1]. In 2018, 34.2 million people, or 10.5% of the US population, had DM, and in 2017 it was the seventh leading cause of death in the United States [2]. The incidence of type 2 DM is increasing at an alarming rate both nationally and worldwide. Prevalence of DM is the highest in the Middle East and North African region (12.2%) compared to other International Diabetes Federation Regions, and Saudi Arabia (SA) has one of the highest age-adjusted prevalences of DM in adults aged 20-79 (15.8%) in the Middle East and North African region [1]. By the incidence rate of Type I DM among children aged 10-14, SA ranks in 5th place globally [1].

V-D (cholecalciferol) is generally synthesized in the skin and can also be supplemented from food like fish [3]. The hydroxylated form of V-D (25-hydroxy V-D or 25(OH)D) circulates in the blood. A concentration of < 30 ng/mL (50 nmol/L) of 25(OH)D in the blood is considered as V-D deficiency [4]. The deficiency of V-D is seen in people avoiding sun exposure, wearing whole body clothes all the time, and having celiac disease [5,6]. The studies conducted in SA have revealed a high prevalence of V-D deficiency, wherein about 87% healthy men and about 80% healthy women showed this deficiency [7,8]. The deficiency of V-D causes osteoporosis, metabolic disorders, obesity, multiple sclerosis, arthritis, and DM [9-13]. The V-D deficiency is also linked to DM [14-20]. Therefore, the titled study has been carried out in the Northern borders (NB) of SA.

MATERIALS AND METHODS

The NB is the least populated region of SA, where the healthcare services are mainly being provided in primary health care centers, private and public hospitals, and clinics [21]. A cross-sectional study has been conducted in this region between July 2018 and February 2019. A random sampling technique was used to choose the required numbers of subjects who have type 1 or type II DM and are registered in NB region health centers and hospitals. The sample size was calculated using the one-sample proportion formula and the results of similar studies [22,23]. To be eligible to participate in the study, inclusion criteria were having either Type I or Type II DM. Patients who took V-D supplements were excluded from participating in the study.

The level of V-D has been obtained from medical files of patients who visited the clinics during this period. When they did not get tested for V-D level in cooperation with physicians testing for V-D level had been requested. Also, patients' demographic data, HbA1clevel, duration of DM, also information about dyslipidemia, and statin use were collected using a pre-designed questionnaire. The data has been coded, entered to Stata 13.0, and cleaned.

Data Analysis: The descriptive analysis was conducted to report the demographic characteristics of the study subjects and their mean level of V-D, the mean level of HbA1C%, data on dyslipidemia, and statin use. V-D level was recoded into three categories. V-D deficiency was defined as <20ng/ml, insufficiency as 20-30 ng/ml, and normal as >30 ng/ml [24]. For the HbA1C%, more than 7.2 mmol/L was considered as uncontrolled DM, whereas less than or equal to 7.2 mmol/L as controlled [25]. All the continuous variables, including age, V-D levels, and HbA1C, are expressed in the mean and SD. Also, categorical variables such as V-D level (normal, insufficiency, deficiency), HbA1C (controlled and

uncontrolled), gender, dyslipidemia, statin use, type of DM, and other comorbidities are reported in numbers and percentages. Secondary data analysis was conducted for the association between the level of V-D and other variables. The student's t-test was used to determine the association of continuous variables, and Pearson's chi-square test was for finding the association between categorical variables at the level of significance 5%.

Ethical considerations: A written consent form was obtained from all the eligible participants before taking their V-D levels and administering the questionnaire.

RESULTS

Overall, 141 participants were recruited, and the generated data was analyzed. From the final dataset, two participants were excluded because of missing data. The mean level of V-D among study participants was 19.08±9.55, 58.87% had V-D deficiency, 31.21% had insufficiency, and only 9.93% had normal levels. Participants' mean age was 46.80 (16.02), 70.92% were female, and 29.08% were male. The main sociodemographic characteristics of study subjects are summarized in Table 1.

The student's test was used to compare the mean levels of V-D between the groups of patients of controlled and uncontrolled HbA1c, and there was no significant difference (p=0.75). The student's t-test was also used to compare the mean level of V-D between 2 types of DM and between the two groups of study subjects with and without dyslipidemia and hypertension. The mean levels of V-D among the groups as mentioned above and p values are reported in Table 2. Also, Pearson's chi-square test was used to determine an association between the three groups of V-D states (normal, insufficiency, deficiency) other categorical variables. There was no significant association between the categorical status of V-D and HbA1c groups (p = 0.832). There was also no significant association between V-D levels and dyslipidemia, statin use, and DM type (Table 3).

Table 1. Main sociodemographic characteristics of study subjects

Age (mean ± SD)	46.80 ±16.02
Gender, n (%)	
Female	100 (70.92)
Male	41 (29.08)
HbA1c (mean ± SD)	8.14 ± 1.82
HbA1c level	
Uncontrolled n (%)	92 (65.25)
Controlled n (%)	49 (34.75)
V-D (mean ± SD)	19.08 ± 9.55
V-D level	
Normal ≥ 30 n (%)	14 (9.93)
Insufficiency (20-29) n (%)	44 (31.21)
Deficiency (<20) n (%)	83 (58.87)
Dyslipidemia, n (%)	
Yes	10 (7.09)
No	131 (92.91)
Statin use, n (%)	
Yes	60 (42.55)
No	81 (57.45)
Comorbidities	
Thyroid problems, n (%)	21 (14.89)
Hypertension, n (%)	44 (31.21)
DM type, n (%)	
Type I	26 (18.44)
Type II	115 (81.56)

Table 2. Mean levels of V-D among the groups and p values

	V-D, mean (SD)	p-value
HbA1c%		
Controlled	18.73 (9.07)	0.753
Uncontrolled	19.27 (9.85)	
DM type		
Type I	19.56 (10.12)	0.781
Type II	18.98 (9.47)	
Dyslipidemia		
Yes	17.08 (7.18)	0.493
No	19.24 (9.72)	
Hypertension		
Yes	16.84 (5.73)	0.060
No	20.10 (10.73)	
Gender		
Female	18.78 (9.69)	0.561
Male	19.82 (9.30)	

Table 3. Association between V-D levels and dyslipidemia, statin use, and DM type

	V-D			Total	p-value
HbA1C	Normal	Insufficiency	Deficiency		
≤ 7.2 (controlled)	5	18	26	49	0.557
>7.2 (uncontrolled)	9	26	57	92	
Dyslipidemia					
Yes	0	3	7	10	0.522
No	14	41	76	131	
Statin use					
Yes	3	18	39	60	0.195
No	11	26	44	81	
DM type					
Type I	5	8	13	25	0.201
Type II	9	36	70	116	
Hypertension					
Yes	0	12	32	44	0.013
No	14	32	51	97	
Gender					
Female	8	34	58	100	0.334
Male	6	10	25	41	

DISCUSSION

V-D deficiency is a public health problem worldwide, and testing rates to identify this problem have increased in recent years [26]. The prevalence of V-D has been reported to be 40.4% in Europe [27] and 24% in the USA [28]. It has been shown that V-D deficiency is associated with multiple diseases such as rickets, osteomalacia, respiratory infections, asthma, and tuberculosis [29].

All the study participants conducted among female students of the NB Region of SA had V-D deficiency, and 89.1% of them had severe V-D deficiency [30]. Our study, conducted in the same area, has been shown similar results and confirms that V-D deficiency is a considerable concern public health concern in this area. The high prevalence of V-D deficiency among diabetic patients has been reported previously in different studies. The study conducted in Greece has shown that 63.3% of diabetic patients had less than 20ng/ml of V-D [31]. Another study found that 57% of American non-pregnant adult diabetic patients have V-D deficiency [32]. A high prevalence of V-D deficiency was also found in another study among diabetic patients; moreover, research has shown that V-D deficiency is associated with a higher risk of diabetic

complications such as neuropathy, nephropathy, and retinopathy [33].

Despite the normal intake of dairy products exposure to the sun, the mean level of V-D was very low among healthy adults in SA [34]. A high prevalence of V-D among diabetic patients has been detected in previous studies in SA. The normal level of V-D among diabetic patients in the Sothern Region of SA was reported only in 1.2% of diabetic patients [35]. The results of these studies are consistent with our study results, which have also shown that V-D deficiency is prevalent among diabetic patients, and it is even higher in SA. The mean level of V-D significantly differed between males and females in a study conducted in SA [36]. However, no statistically significant difference was observed in another study, where the mean level of V-D among males and females was reported to be 10.1 (4.65) and 10.04 (4.42), respectively [37] In our study also, the difference was not significant.

A recent study conducted in Kenya by Karau et al. did not find any association between V-D deficiency and hypertension [38]. Nevertheless, another study from India reported an association between hypertension and V-D deficiency [39]. Moreover, meta-analysis has shown that supplementation of V-D has a small but significant effect on peripheral blood pressure [40]; however, more research is required to demonstrate a causal relationship between blood pressure and V-D [41]. Our study results support that there is an association between the two variables as deficiency and insufficiency were significantly associated with hypertension ($p<0.05$).

Our study results are consistent with previous research on V-D among the general population and diabetic patients and corroborate that V-D deficiency and insufficiency are still a public health concern. Our study was limited by small sample size, and no significant association was possible to demonstrate between the V-D level and other characteristics of patients. Also, further data collection about hypertension could have allowed us to deeply understand the genetic and clinical association between V-D and blood pressure. Further cross-sectional or interventional studies could address the sample size issues and find out more risk factors that contribute to or explain V-D deficiency.

CONCLUSIONS

V-D deficiency is an evolving problem and a risk factor for a variety of diseases. It is a considerable problem in the Middle East and particularly in SA. This study reports the situation in the NB Region of SA among diabetic patients and highlights the importance of addressing the issue. The association between V-D and hypertension was also found in the study, requiring further investigation and explanation.

Conflicts of Interest: The authors declare no conflict of interest.

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