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High Prevalence of Vitamin D Deficiency Among Saudi Children And Adolescents With Type 1 Diabetes In Albaha Region, Saudi Arabia

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Abstract:
Background: *Vitamin D inadequacy constitutes an increasingly recognized comorbidity among Saudi populations. There were limited data about its prevalence in Saudi children with type 1 diabetes mellitus (T1DM).*
Aim: *To evaluate the prevalence of vitamin D deficiency among Saudi children and adolescents with T1DM in Albaha region, southwestern of Saudi Arabia.*
Methods*:*
A cross-sectional study was conducted on 117 Saudi children and adolescents with T1DM. These patients were recruited from Albaha diabetic center, Saudi Arabia. The range of age of the participants was 1–18 years.. All participants were subjected to history taking including, age, gender, duration of diabetes, clinical presentation at the onset of diabetes. Measurement of serum 25 hydroxy vitamin D was done in all participants.
Results: *There were 117 Saudi children and adolescent with T1DM, 52 (44.4%) were boys, and 65 (55.6%) were girls with a mean age 8.8 ± 3.4 and 9.2 ± 3.9 for boys and girls respectively (p=0.52). The mean serum 25-hydroxy vitamin D levels among them was 17.1± 10.1 ng/ml and the prevalence of vitamin D inadequacy was 88.9% (59.9% of subjects had vitamin D deficiency and 29 % had vitamin D insufficiency) and 11.1% had sufficient levels of 25-hydroxy vitamin D. There was a significant difference in vitamin D level among different groups of vitamin D level (p< 0.001). The prevalence of Vitamin D deficiency was greater in the girls with 34.2%, as compared to 25.6% among boys. Vitamin D deficiency was more common among children in the range of age 1-10 years (52.1% vs 36.8%). In vitamin D deficient group, the mean levels of vitamin D were significantly lower in patients presented with DKA as compared to those presented with hyperglycemic symptoms (p= 0.016).*
Conclusion: *Vitamin D deficiency is common in Saudi children and adolescent with T1DM in Albaha region. This is more common in girls and in the younger age groups. Therefore, screening for vitamin D deficiency, creating awareness to increase sunlight exposure, increase the fortification of food products with vitamin D and vitamin D supplementation for these patients should be warranted to prevent future morbidity.*
Keywords: *25 hydroxy vitamin D, Saudi, Type 1 diabetes, vitamin D deficiency*

I. Introduction

Type 1 diabetes (T1DM) is an autoimmune disease occurring in the pancreatic islets (1). It accounts for 90% of diabetes in children and adolescents (2). The annual incidence has been increasing worldwide, possibly related to genetic, dietary, and environmental factors that might interfere with its pathogenesis (3). There has been appealing evidence on the role of vitamin D in many autoimmune diseases including rheumatoid arthritis, scleroderma, psoriasis, multiple sclerosis, and also T1DM (4,5).

Vitamin D is a steroid hormone that contributes to calcium and phosphorus metabolism for healthy bone mineralization. Vitamin D includes vitamin D_2 (derived from plants) and vitamin D_3 (derived from animals) as well as vitamin D metabolites. Vitamin D_3 (also known as cholecalciferol) appears to be more effective than vitamin D_2 (also known as ergocalciferol (6). In humans, ~90% of vitamin D arises from endogenous synthesis by conversion of 7-dehydroxycholesterol into previtamin D by ultraviolet B radiations and then to vitamin D by a nonenzymatic transformation. Considering that vitamin D is biologically inactive, it is activated in a two-stage hydroxylation process: first, hepatic hydroxylation that results in 25-hydroxyvitamin

D (25[OH]D) and, second, hydroxylation of 25(OH)D in the kidneys, resulting in 1,25-$(OH)_2D$ which is the active form of vitamin D (7).

With respect to the relatively short half-life of 1,25(OH)2D (~4 hours), vitamin D status is best monitored by 25(OH)D which is the major circulating form of vitamin D with a long half-life (2-3 weeks). In clinical practice, definitions commonly used are those provided by both the Institute of Medicine (IOM) and the Endocrine Society. According to both groups, vitamin D deficiency is defined as 25(OH)D below 20 ng/ml, insufficiency as 25(OH)D of 21–29 ng/ml, and sufficiency as 25(OH)D of 30–100 ng/ml (8,9).

Few studies were done on vitamin D status in Saudi children with T1DM. However, there were limited data from different regions of Saudi Arabia about the prevalence of vitamin D deficiency among Saudi children with T1DM. This study was conducted to evaluate the prevalence of vitamin D deficiency among Saudi children and adolescent with T1DM in albaha region, southwestern of Saudi Arabia.

II. Methods

This was designed as a cross sectioned study, which enrolled 117 Saudi children and adolescent with T1DM from those received medical care at an Abaha diabetic center, Kingdom of Saudi Arabia (KSA). Albaḥah region is located in the southwestern of Saudi Arabia, having an area of 9,921 km², with population aged from 0-19 years old are 132,712 (35.3%) (10). Albaḥah region is located 2500 meters above the sea level and includes Abaḥah city, Almikhwah, Baljorashi, Rahwat Albar, and Sabt Alalaya.. All participants were subjected to history taking (age, sex, clinical presentation, and duration of diabetes). The serum levels of 25 hydroxy vitamin D were done in all participants.

The diagnosis of T1DM was made according to the World Health Organization (WHO) criteria (11). Any patient above 18 years, T2DM and those with diabetes secondary to cystic fibrosis, or steroid therapy were excluded from the study. Our patients were divided into four age groups as: infancy and toddlerhood group (0-2 years), preschool group (3-5 years), middle childhood group (6-10 years) and adolescence group (11-18 years) (12). The patients also subdivided according to the clinical presentation at the onset into, these presented with hyperglycemic symptoms (defined as polyuria, polydypsia, nocturia and weight loss) and those presented by diabetic ketoacidosis (DKA) (defined by glucose >250 mg/dL, arterial pH<7.30, blood bicarbonate <15 mmol/L and ketonaemia of over 5 mmol/l. (13). Also, the patients were grouped according to their vitamin D levels into: vitamin D deficiency (<20 ng/ml), vitamin D insufficiency (20-29.9 ng/ml); and sufficient vitamin D level (≥30ng/ml) (8, 14). The study was approved by the ethics committee of Albaha college of medicine, Albaha region, KSA.

25-hydroxy vitamin D levels was assayed in the serum by electrochemiluminescence immunoassay (ECLIA) by Cobas e411 machine. (Roche Diagnostics, GmbH, Mannheim, Germany) and commercially available IDS kits (IDS Ltd, Boldon Colliery, Tyne & Wear, UK). The inter- and intra-assay coefficients of variation (CV) for 25 (OH) D were 5.3% and 4.6%, respectively, with 100% cross-reactivity to 25 (OH) D3 and 75% cross reactivity to 25 (OH) D2.

Statistical analysis

Statistical analyses carried out using the Statistical Package for Social Sciences (SPSS; Student version 21). Data were expressed as frequencies [n (%)], whereas means and standard deviation were used for continuous variables. Chi-square statistics was used to compare between categorical variables. The Independent T-test was applied to compare two quantitative variance and analysis of variance (ANOVA) to compare more than two quantitative variables. A Pearson correlation was used to correlate vitamin D level with the age and duration of diabetes. A p-value smaller than 0.05 was accepted as statistically significant.

III. Results

This study included 117 Saudi children and adolescent with type 1 diabetes, 52 participants (44.4%) were boys, and 65 (55.6%) were girls with a mean age 8.8 ± 3.4 and 9.2 ± 3.9 years for boys and girls respectively (p=0.52). The range of age of participants was 1–18 years. The mean duration of diabetes was 2.2±1.8 years.

The mean levels of 25-hydroxy vitamin D among Saudi children and adolescent with T1DM was 17.1± 10.1 ng/ml (18.3±10.9 in boys vs 16.1±9.4 in girls, p=0.24). The prevalence of vitamin D inadequacy among T1DM patients in Albaha region was 88.9% (59.9% of subjects had vitamin D deficiency and 29 % had vitamin D insufficiency) and 11.1% had sufficient levels of 25-hydroxy vitamin D. There was a significant difference in vitamin D level among different groups of vitamin D level (p< 0.001) Table 1.

The prevalence of Vitamin D deficiency was greater in the girls with 34.2%, as compared to only 25.6% among boys but this not reach the significant level. T1DM patients with Vitamin D insufficiency is also common among female patients (Table 1).

Vitamin D deficiency was more common among children in the range of age 1-10 years (52.1% vs 36.8%). (Figure 1). There was no significant correlation between vitamin D levels, duration of diabetes and age of the studied patients (p>0.05).

In vitamin D deficient group, the mean levels of vitamin D were significantly lower in patients presented with DKA when compared with those presented with hyperglycemic symptoms (p= 0.016) (Table 2).

IV. Figures And Tables

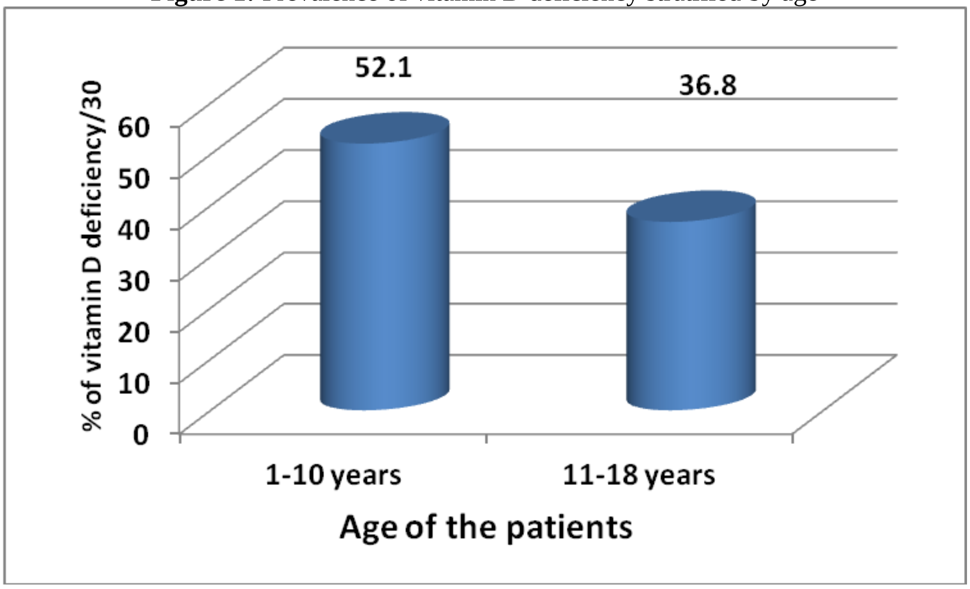
Table 1: Comparing the clinical data and 25 hydroxy vitamin D levels in the study population in different Groups of vitamin D.

Vitamin D state	Vitamin D deficiency	Vitamin D insufficiency	Sufficient vitamin D	P
Number (%)	70 (59.9%)	34 (29%)	13 (11.1)	
Age years	9.2±3.7	9.1±3.7	8.2±3.7	0.66
Gender				
Boys Mean± SD*	11.4±5.8	23.3±2.9	37.5±9.6	
Number (%)**	30 (25.6%)	15 (12.8%)	7 (6.1%)	**0.76
Girls Vitamin D* Mean± SD	10.2±5.4	22.7±2.7	34.6±4.9	
Number (%)**	40 (34.2%)	19 (16.2%)	6 (5.1)	
P*	0.4	0.5	0.65	**0.76
Age group				
0-2 years	2	3	1	0.85
3-5 years	11	3	2	
6-10 years	28	14	5	
11-18 years	29	14	5	
Duration of DM	2.1±1.6	2.4±1.3	2.1±1.9	0.73
Vitamin D levels Mean± SD	10.7±5.6	22.9±2.8	36.2±7.6	**P □ 0.001**

Table 2: Comparison of vitamin D levels between diabetic participants presented at the onset with DKA and hyperglycemic symptoms.

	Hyperglycemia 72 cases	**DKA 45 cases**	**p**
Vitamin D level	16.5±8.3	18±12.5	0.44
Vitamin D state			
Vitamin D deficiency number (mean± SD)	47 (11.8±5)	23 (8.4±4.1)	**0.016**
Vitamin D insufficiency number (mean± SD)	20 (23.1±2.9)	14 (22.7±2.5)	0.66
Sufficient vitamin D number (mean± SD)	5 (34.1±5.7)	8 (37.4±8.7)	0.48

Figure 1: Prevalence of vitamin D deficiency stratified by age



V. Discussion

The incidence of diabetes and other metabolic disorders is increasing at an alarming rate in countries of the Arabian Gulf, possibly due to dramatic changes in lifestyle and food intake patterns since the discovery of oil in the 1950s (15,16). A growing literature suggests that vitamin D homeostasis may play a role in the etiology of type 1 and type 2 diabetes (17–19). Few studies from the Middle East have examined the association between vitamin D status and diabetes (19-21. Few studies were done on vitamin D status in Saudi children with T1DM, therefore this study aimed to evaluate the prevalence of vitamin D deficiency among Saudi children and adolescents with T1DM in Albaha region, southwestern of Saudi Arabia.

Although a low vitamin D status has been reported in populations of Saudi Arabia, our study is the first one designed to evaluate vitamin D status in T1DM in Albaha region.

In our study, Saudi children and adolescent with T1DM in Albaha region have an alarmingly low vitamin D status. Nearly 60 % of the Saudi children had vitamin D deficiency and 29 % had vitamin D insufficiency, these together suggest that, 88.9 % of the Saudi children with T1DM are at risk for inadequate vitamin D. Our results are in accordance with the findings from countries of the Arabian Gulf, in Saudi children, vitamin D deficiency was considerably higher in T1DM Saudi children (84%) compared to healthy Saudi children (59%) (27). Also, in Qatari youth, with T1DM demonstrated a significant increase in the prevalence of vitamin D deficiency (25OHD/30 ng/ ml) in the T1DM subjects (90.6%), in a country in which vitamin D deficiency in non-diabetic children were also high (85.3%), (28).

However, our results were contradictory to previous Western studies analyzing subjects with T1DM. The prevalence of vitamin D deficiency was 60.5% in a Swiss study (22), 43% in an Australian study(23), approximately 25% in an Italian study (24), and 15% in a North American study (25).

Bierschenk and coworkers (26), demonstrated that median 25 hydroxy vitamin D levels were comparable between established T1DM subjects, new-onset T1DM subjects and control subjects, when studied in individuals residing in a solar rich environment in the United States. Interestingly, however, in this study, vitamin D levels in all groups were suboptimal, with 76.1% of new-onset T1DM, 68.5% of established T1DM and 70.1% of control subjects having 25 hydroxy vitamin D levels below 30 ng/ml (26).

To explain the higher prevalence of vitamin D deficiency in our study, although Saudi Arabia is a country with ample sunshine, the high prevalence of vitamin D deficiency in Saudi children and adolescent with T1DM may result from limited exposure to sunshine, lack of awareness about vitamin D deficiency, low dietary intake of fortified products and dietary supplements. Another explanation for the high prevalence of vitamin d deficiency in Saudi children and adolescent with T1DM is a racial difference in vitamin D concentration or a genetic predisposition to vitamin D deficiency among Saudi Arabians. Moreover Albaha's climate is moderate in summer and cold in winter due to its location at 2,500 meters (8,200 ft) above sea level and Saudi Arabia is a country that has been experiencing a marked increase in the prevalence of obesity in the past decade, which can additionally contribute to a low vitamin D status (31). These findings point to the need of continuous monitoring vitamin D status in T1DM and identifying contributing factors.

In this study, we observed that, the mean value of 25 hydroxy vitamin D was lower in girls compared to boys and the prevalence of vitamin D deficiency was also greater in the girls than in boys, but this not reach the significant level. A possible explanation for that result, due to girls covering of their bodies with dark veils for cultural and religious reasons and sunscreen usage before sun exposure, which prevents the penetration of the UVB light needed for the synthesis of vitamin D. In the human body, sun exposure represents,the most important source of vitamin D production (29). Certainly Hobbs et al, reported severe vitamin D deficiency in Arab–American women who wear the veil (30). However, this does not explain why Saudi Arabian boys had similarly low levels of vitamin D. Even if we hypothesize that Saudi Arabians have a mildly dark skin, which could limit the penetration of UVB light.

Low vitamin D status has been associated with an increased risk of diabetes in populations of North America and Europe (31, 32). Our results suggest that low vitamin D status in Saudi children and adolescent with T1DM is also strongly associated. The possible mechanisms for this association may include the presence of vitamin D receptors in pancreatic beta cells to which circulating vitamin D binds (33). Vitamin D has been well recognized for its role in regulating extracellular calcium flux, and insulin secretion is known as a calcium dependent process (34). Several studies reported an impaired insulin release in association with vitamin D deficiency (35,36), and vitamin D supplementation has been shown to improve insulin release in randomized controlled trials (37). In addition, vitamin D may improve insulin sensitivity by reducing systematic inflammation (38) and this may explain the important finding in our study, in vitamin D deficiency group, the mean levels of vitamin D were significantly lower in patients presented with DKA when compared with those presented with hyperglycemic symptoms ($p = 0.016$). 25-OH D deficiency has been prevalent upon the initial presentation of T1DM patients who presented with DKA, making it a contributing factor. However, that low levels improved spontaneously after correction of acidosis, the direct contribution of 25-OH D deficiency in the acute presentation of DKA remains controversial (39). Our result was similar to the results of Savastio et al.

who reported that, children with T1DM show a generalized 25OHD deficiency that impact on metabolic status and glycemic homeostasis and 25OHD levels were inversely related to diabetic ketoacidosis severity ($p<0.05$) (40).

VI. Conclusion

Vitamin D deficiency is common in Saudi children and adolescent with T1DM in Albaha region. This is more common in girls and in the younger age groups. The lower levels of vitamin D may be attributed to wearing of traditional clothes, deliberate avoidance of the sun, genetic factors and inadequate dietary intake. Therefore, screening for vitamin D deficiency, fortification of food with vitamin D and vitamin D supplementation for these patients should be warranted to avoid more morbidity. Additionally, we suggest the need for more studies to assess the role of vitamin D deficiency in pathogenesis of T1DM aiming for proper control and prevention of T1DM.

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