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The Effect of Vitamin D Status of Type 1 Diabetic Children on their Glycemic Control

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ABSTRACT

The aim of this study was to assess the relationship of vitamin D level and supplement with glycated hemoglobin level in children with T1DM attending a tertiary institution in Oman. In addition, we described the trend of vit D deficiency among included patients. For this, a prospective cohort study was conducted. Data was collected for total of 131 pediatric patients with T1DM. Vitamin D level was measured at the baseline (2014) and after one year. Their glycated hemoglobin was collected at the baseline of the study and at three subsequent time points from the baseline within the 1-year period. Subjects were categorized according to their vitamin D status at baseline to; sufficient, insufficient and deficient. Patients received vitamin D supplementation according to their vitamin D status for one year. At the end, the mean glycated hemoglobin for a 9 months period was compared. 59 patients (45%) were vitamin D sufficient, 46 (35%) were vitamin D insufficient and 26 (20%) were vitamin D deficient. Their baseline HbA1c was 9.6%, 9.6% and 8.7% for the three groups respectively. There was no significant difference in the subsequent mean HbA1c in the three groups. HbA1c of insufficient group changed insignificantly from 9.5% to 9.6%, while HbA1c of deficient group changed insignificantly from 8.7% to 9.3%. Vit D inadequacy dominates the trend of this vitamin in Omani children with type T1DM. It seems that neither the level, nor the supplementation of vitamin D supplementation has an effect on glycemic control.

1. INTRODUCTION

The knowledge of the important role of vitamin D in bone health is well-established. It has a direct effect on calcium and phosphate metabolism. Vitamin D deficiency is generally accepted as a serum level of 25-hydroxyvitamin D of less than 30 nmol/L [1], [2]. One of the extra skeletal effects is its role in glucose homeostasis such as pancreatic dysfunction and insulin resistance. It has a protective role to the beta cells from immune destruction and it improves insulin sensitivity of the target organs [3], [4]. metanalysis found

a higher incidence of diabetes in vitamin D deficient subjects compared to those with normal vitamin D level [5], [6]. Poor vitamin D status has been linked to high BMI and metabolic syndrome in adults, adolescents and children [7- 11]. Three large metanalysis evaluated the effect of vitamin D supplementation and the glycemic control in patients with type 2 DM. There was overall significant improvement in the glycated hemoglobin in the supplemented group as well as fasting blood glucose in the majority [12- 14]. However, the studies on the effect of vitamin D supplementation in pediatric patients with type 1 DM are limited. [15] studied vitamin D status among 271 children and evaluated the effect of treating vitamin D deficiency on their glycemic control. He found that the lower baseline vitamin D level and the higher glycated hemoglobin pre-treatment, the greater reduction in glycated hemoglobin post-post-treatment (p value 0.004 and <0.001 respectively) [15]. Savastio looked at vitamin D deficiency and glycemic control status in children and adolescents with type 1 DM and found a significant relation between vitamin D levels and glycemic control (p value <0.001) [16]. In contrast, [21] did not find any significant difference in glycated hemoglobin and insulin requirement in both supplemented and placebo group [21]. Therefore, we conducted this study to study the relationship between vitamin D level/supplement and glycemic control (HBA1c) among children with type 1 DM. In addition, we sought to describe the trend of vit D deficiency and assess the effect of vitamin D supplement on serum vitamin D level as among this group of diabetic patients.

2. Patients and Methods

This is a prospective study that was conducted in December 2014 in the National Diabetes and Endocrine Center (NDEC) in Royal Hospital which is a tertiary care center in Oman. The study included 131 children with type 1 DM who are being followed in the NDEC1 and their electronic records were reviewed. 25-hydroxy Vitamin D (25OHD) levels, bone profile, parathyroid hormone was obtained in the beginning of the study and after 1 year of vitamin D supplementation. Data related to vit D supplements was also collected. Their glycated hemoglobin was collected at the baseline of the study and at three subsequent time points from the baseline (at three, 6 & 9 months from baseline). The mean HBA1c for the 9-months period was considered the main compared outcome. Furthermore, the mean HBA1c was categorized as follow: good control (HbA1C < 7.5 %), mild-moderate poor control (HbA1c 7.5-8.5%) and poor control (HbA1c > 8.5%). Both vitamin D and HbA1c assays were performed by Architect Immunology Analyzer-i2000 (Abbott, USA) in clinical biochemistry laboratory at Royal Hospital. Measurement of Vitamin D was based on a one step chemiluminescent immunoassay reaction, whereas HbA1c was based on enzymatic method that specifically measure N-terminal fructosyl dipeptides of the B-chain of HbA1c. Both assays had excellent performance as judged by internal and external quality control data. The subjects were divided into 3 groups based on their initial vitamin D status and were defined according to Global Consensus Recommendations on Prevention and Management of Nutritional Rickets (1): vitamin D sufficiency (25OHD >50 nmol/L), vitamin D insufficiency (25OHD 30-50 nmol/ L), and vitamin D deficiency (25OHD <30 nmol/L). Patients with vitamin D deficiency and vitamin D insufficiency were treated with vitamin D supplement as per the protocol: 10,000 IU initially once every week for 6 weeks, then 10000 iu monthly for 6 months according to their age and their 25OHD levels. In addition, education about the importance of sun exposure, compliance with medication, and dietary advice was provided according to their vitamin D status.

All statistical workup was conducted using SPSS 22 software. Categorized variables were described in percentages, and continuous variables were presented in means ± standard deviation (SD). The paired T-test and Mann-Whitney test were used to compare patients' HbA1c mean values in various vit D groups and at baseline and after vitamin D supplementation. P-value of less than 0.05 was considered significant.

This study was ethically approved by the local Research Ethical Committee of the Royal Hospital.

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3. Results

Out of the 131 patients included in the study, 59 patients (45%) were vitamin D sufficient, 46 (35%) were vitamin D insufficient and 26 (20%) were vitamin D deficient. The baseline HbA1c was similar in the three aforementioned groups, being 9.6%, 9.6% and 8.7% respectively. The mean HbA1c among vitamin D sufficient group changed insignificantly within 9 months (from 9.6% to 9.2%, p value 0.22). Patients with insufficient vitamin D level had almost similar mean HbA1c at baseline and within 9 months, 9.6% and 9.5% respectively (p value 0.81). Although vitamin D deficient group had the best baseline mean HbA1c of 8.4%, it increased insignificantly to 9.3% within 9 months despite vit D supplement (p value 0.37). Table 1 and Figure 1 compares the mean HbA1c at baseline and within 9 months of vitamin D supplementation of the three study groups based on their vitamin D status.

Table 1: HbA1c levels at baseline and after vitamin D supplementation in the 3 studied groups according to vitamin D status. Data are presented as mean ± SD and median.

Vitamin D status	HbA1c (%) Baseline	Mean HbA1c (%) Within 9 months	P value
Sufficient (n= 59)	9.6 ± 1.8	9.2 ± 1.7	0.2171
	9.4 (5.5-14.3)	9.1 (5.1-14.0)	
Insufficient (n= 46)	9.6 ± 2.1	9.5 ± 1.9	0.8133
	9.0 (6.0-14.0)	9.2 (6.4-14.0)	
Deficient (n= 26)	8.7 ± 2	9.3 ± 2.6	0.3650
	8.4 (6.2-14.0)	9.2 (5.1-14.0)	
Total (n= 131)	9.4 ± 2.0	9.3 ± 1.9	0.6786
	9.0 (5.5-14.3)	9.2 (5.1-14.0)	

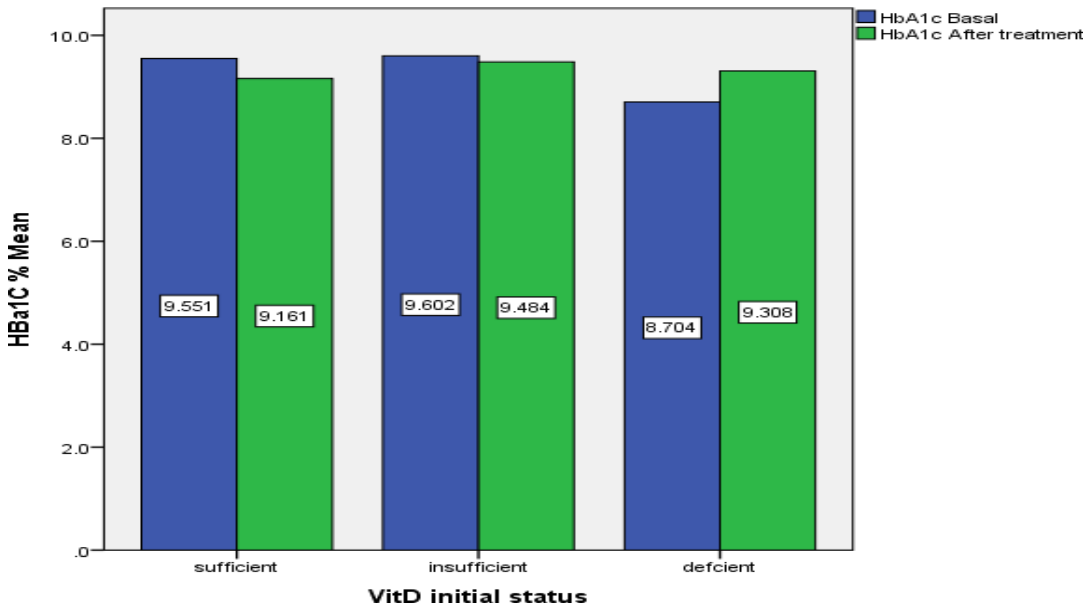

Figure 1: Bar graph showing mean HbA1c% values at baseline and after one year in the 3 groups according to vitamin D status.

Mean HbA1C values were compared in each group at baseline and within 9 months according to their glycemic control (good control with HbA1C <7.5 %, mild-moderate poor control with HbA1c 7.5-8.5%, and poor control with HbA1c >8.5%). However, the data showed no significant difference in mean HbA1C value in each group (p values 0.6786). Figure 2 gives more details on this issue. The patients with insufficient vitamin D level who had good or mild poor glycemic control had slight increase in their HbA1c after receiving vitamin D supplementation for 1 year. However, there was a mild improvement in the glycemic control in the vitamin D insufficient group and very poor glycemic control (mean HbA1c decreased from 10.55% to 10.08%, p value 0.8133). In vitamin D deficient group, those with moderate poor and very poor glycemic control had almost no change in their mean HbA1c at baseline and after vitamin D treatment (7.8 to 7.7% and 9.73 to 9.68% respectively).

Results demonstrated increase in mean HbA1c of vitamin D deficient patients who had good glycemic control in the beginning of the study (6.78 to 8.76%, p value 0.635).

In patients with sufficient vitamin D level there were minimal variable changes in the mean HbA1c which were statistically insignificant (p value <0.215). Figure 2 compares the change in mean HbA1c at baseline and within 9 months in the three groups (vitamin D sufficient, insufficient and deficient) according to their glycemic control (as defined above).

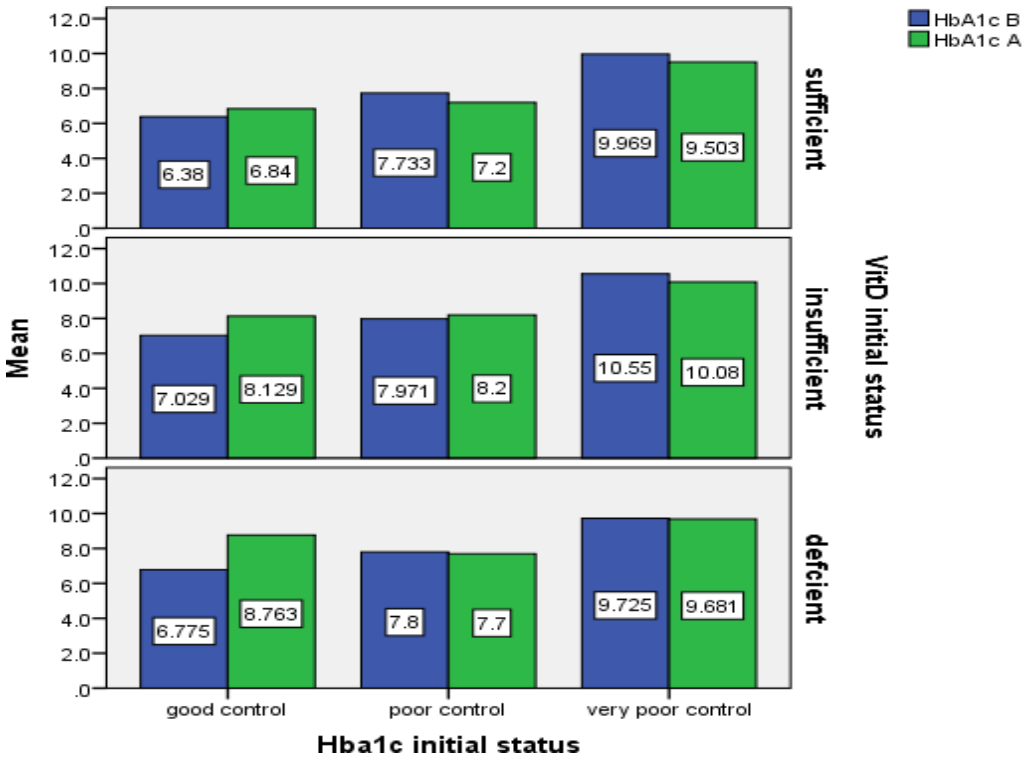

Figure 2: Bar graph showing mean HbA1c% at baseline (blue bar) and within 9 months in further subgroups according to their glycemic control.

As for the response to vitamin D treatment, both vitamin D deficient and insufficient groups had adequate mean of vitamin D levels after one year of supplementation. Figure 3 demonstrates the mean baseline vitamin D level of each group and after one year.

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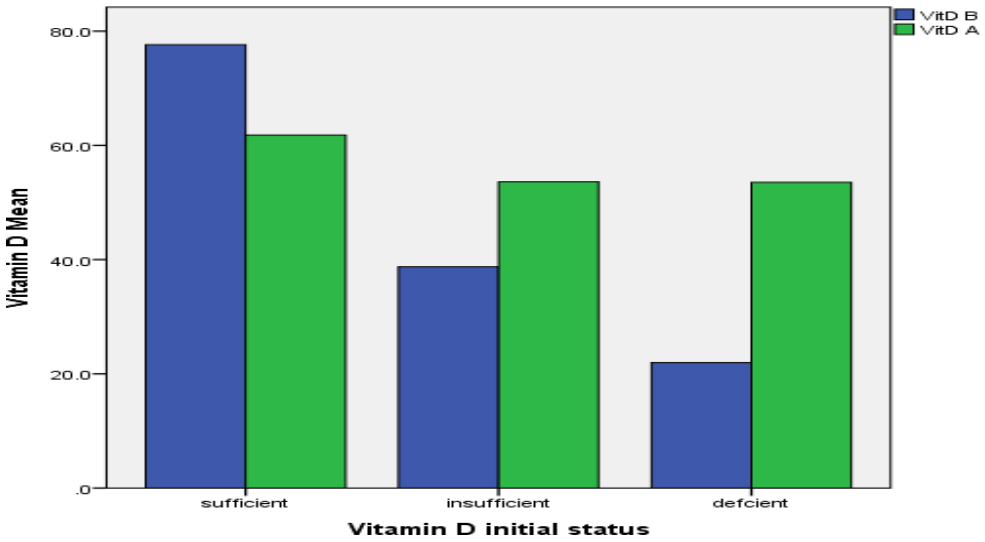

Figure 3: Mean value of 25OH vitamin D level (nmol/L) at baseline (vit.D B) and after (vitD.A) one year in the three groups based on their initial vitamin D status.

4. Discussion

There is increasing interest in the extra skeletal effects on vitamin D including diabetes. Hence, this is the first study to assess the trend of vit D level and its association among our local population in Oman. This study demonstrated the dominance of vit D inadequacy among Omani T1DM patients. It also revealed no association between vit D level/supplements and glycemic control among this group of patients. Majority of the patients (55%) in this study had inadequate vitamin D level; 20% had vitamin D deficiency and 35% had vitamin D insufficiency. These results are comparable to some extent with a study by [15], who investigated vitamin D status in children with type 1 DM14.8% of the subjects included in their study were vitamin D deficient, 31% were insufficient and 54% were sufficient [15]. However, vitamin D deficiency was more prevalent in other populations. A recent study found only 9.4% of Italian children had sufficient vitamin D at onset of type 1 DM [16]. These variable rates of vitamin D deficiency among type 1 diabetic children highlights the difference in contributing factors including environmental and genetic factors in different population. One of the important extra skeletal effects of vitamin D is its role in glucose homeostasis. Evidence suggests that vitamin D protects pancreatic beta cell function and improves insulin sensitivity of the target organs [4]. However, several studies demonstrated the impact of vitamin D status on glycemic control in adult population, few were conducted in pediatric population.

In this regard, our data demonstrated no association between vit D level/supplement and glycemic control. In contrast to our result, it was reported in other studies that the lower baseline vitamin D level, the greater the improvement in their glycemic control after treatment [15], [17], [16], [18]. In addition, several studies investigated the impact of vitamin D supplementation on glycemic control in type 1 diabetic patients with conflicting results. Some studies showed that in type 1 diabetic children who had vitamin D deficiency or insufficiency, a significant improvement was observed in their glycated hemoglobin after they received vitamin D supplementation. However, there are several studies which failed to demonstrate this positive impact on the glycemic control [19], which are consistent with our finding. Although [20] succeeded to demonstrate a significant improvement in the metabolic control of children and adolescents with type 2 DM after vitamin D supplementation, their study did not find similar improvement in type 1 diabetic subjects [20]. A randomized control trail on the effect of vitamin D supplementation to newly diagnosed type 1 DM adolescents and young adults also did not find any significant difference in glycated hemoglobin and insulin requirement in both supplemented and placebo group [21].

The main limitation of this study is that it did not consider important confounding factors that may contribute to glycemic control and therefore to the outcome of the study, including duration of diabetes, BMI, and insulin doses

5. Conclusion

Vit D inadequacy is the dominated trend among Omani T1DM patients. This study did not show any significant impact of vitamin D level or supplementation on the glycemic control. We recommend a larger long-term prospective randomized control trial to ensure better confidence of the study results. Other important contributing factors need to be investigated in more depth including duration of diabetes, insulin doses, treatment compliance and BMI.

6. Declarations

The authors declare that they have no competing interests, and that this work did not receive any funding support. Ethical approval for this study was obtained from the research ethical committee of the Royal Hospital prior to data collection.

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