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Vitamin D Status in Egyptian Children and Adolescents with Type 1 Diabetes Mellitus

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Abstract

Introduction: Vitamin D is an important factor for bone health especially in type 1 DM (T1DM). Thus, optimal supply of vitamin D may be of particular importance for bone health in children and adolescents with T1DM.

Objective: To assess the vitamin D status in children and adolescents with T1DM and to study related factors that may influence serum vitamin D level.

Methods: Sixty (30 prepubertal, 30 pubertal) Egyptian children and adolescents with T1DM were enrolled in this cross-sectional study, the mean age for the prepubertal group was 6.85 ± 1.64 years and for the pubertal group was 14.43 ± 1.524 years. Detailed history and complete physical examination laying stress on the sun exposure, skin color, exercise and detailed dietetic history. Dietary content of calcium (mg/day) and vitamin D (IU/day) were calculated. Laboratory assessment included serum calcium, phosphorus, 25-hydroxy-vitamin D (25OHD) and parathormone (PTH).

Results: Most of the study group (91.67 %) was vitamin D deficient. There was no significant correlation between serum vitamin D and serum calcium, phosphorus, parathormone, anthropometric measures, duration of diabetes, mean HbA1c, insulin dose, and sun exposure. Despite the high prevalence of vitamin D deficiency, there was a low prevalence of secondary hyperparathyroidism (11.67%) in the study group. Conclusion: Prevalence of vitamin D deficiency in diabetic children and adolescents is very high but underestimated. Therefore, screening and supplementation of vitamin D should be considered.

Keywords: Type 1 diabetes mellitus; 25-OH-cholecalciferol; Vitamin D; Calcium; Serum parathormone

Background

Diabetes is one of the fastest-growing chronic diseases worldwide. Vitamin D deficiency is common, and repletion might improve glycemic control in type 1 diabetes [1]. Also, evidence suggests that lack of vitamin D may be associated with hyperglycemia, increased hemoglobin A_{1c} (HbA1c), insulin resistance, progression of diabetes, as well as hypertension, and cardiovascular disease [2]. There is also a significantly higher insulin requirement in T1DM children with decreased serum25-hydroxy-vitamin D (25OHD) levels and decreased insulin sensitivity [3].

Vitamin D can be affected not only by diet but also by other factors as the skin color, clothing and physical activity. Proper nutrition is one of the most challenging issues for persons with diabetes not only for the control of the disease but also for the prevention of its complications [2].

Vitamin D status is determined by assessment of the levels of 25OHD, the inactive circulating form of vitamin D and an established marker of vitamin D availability, which has a half-life of 2 weeks [4].

Objectives

The aim of the current work was to assess vitamin D status in a children and adolescents with type 1 diabetes (T1DM) and to study related factors such as duration of diabetes, insulin dose, anthropometric measure, skin color, puberty, HbA1c, dietary vitamin D and calcium intake which may possibly influence serum vitamin D levels. In addition to assessment of the secondary hyperparathyroidism in vitamin D deficient patients.

Material and Methods

Study population

The current cross-sectional study included sixty children and adolescents with type 1 diabetes (T1DM) regularly followed at the Diabetes Endocrine and Metabolism Pediatric Unit (DEMPU), Children's Hospital, Cairo University during the period from January to April, 2012. Subjects were included if they have type 1 diabetes mellitus (T1DM) for one year or more and they were between 4 and 18 years old. Exclusion criteria were associated diseases that might interfere with calcium and phosphorus metabolism such as gastrointestinal (e.g. celiac disease), other endocrinal (e.g. hypoparathyroidism), hepatic disease, renal disease and overt bone disease, also, patients who received any type of calcium or vitamin D supplements. The patients were divided into two groups according to the pubertal status the prepubertal group and the pubertal group. Each group is further subdivided into 3 groups according to the serum vitamin D; vitamin D sufficiency, insufficiency, and deficiency. Informed consent was taken from their parents.

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Procedures

Detailed medical history including; duration of diabetes, age at onset, type and dose of insulin, detailed dietetic history in addition to family history of diabetes, hypertension, or history suggestive of diabetic microvascular and macrovascular complications. Moreover, residence, sun exposure duration and type of clothes, life style and exercise in addition to the presence of bony aches or fractures. Type of diet was recorded especially low-fat diet, and vitamin D rich diet. A nutritionist had analyzed the dietary components of each patient's diet and measured the mean values of vitamin D, and calcium in diet.

Recommended Dietary Allowance (RDA) for Vitamin D was calculated as 400 IU/day, and for calcium 1000 mg/day [5].

All patients were subjected to thorough clinical examination laying stress on height, weight, body mass index (BMI), early signs of puberty, in addition to skin color or signs of associated disorders.

Laboratory assessment for serum 25-hydroxy-vitamin D (25OHD), intact parathormone, total calcium, phosphate, and alkaline phosphatase. In addition to, the glycosylated hemoglobin (HbA1c) to assess the glycemic control. The criteria used to define vitamin D sufficiency, insufficiency, and deficiency were 25OHD levels of (≥ 30 ng/ml), (21 –29 ng/ml), and (<20 ng/ml), respectively [6].

Biochemical analysis

25- OH Vitamin D (25OHD) was assayed by a competitive protein binding assay kit (25- OH Vitamin D EIA Kit* Immunodiagnostik AG, Stubenwald-Allee, D64625 Bensheim). Based on the competition of 25OHD present in the sample with 25OHD tracer, for the binding pocket of Vitamin D binding protein. Since all circulating 25-OHD is bound to Vitamin D binding protein in vivo, samples have to be precipitated with precipitation reagent to extract the analyte. The supernatant was used without further treatment [7]. Alkaline phosphatase, calcium and phosphorus were assayed on automated chemical analyser. Parathormone was assayed by enzymatic chemiluminescence immunoassay on Immulite 2000 (Diagnostic Products Corp, Los Angeles).

Statistical analysis

Data was analyzed using the Statistical Package for Social Science (SPSS) version 15. The following methods were employed: percentage distributions, median, range, mean and standard deviation. Student t-test and Mann-Witney test will be used to compare quantitative variables, and Chi-square test or Fischer's exact test for comparison of categorical variables. Pearson's correlations were used to explore associations between numerical variables. P values less than 0.05 were considered statistically significant.

Results

The prepubertal group included thirty patients (15 males, 15 females) and the pubertal group included thirty patients (14 males, 16 females). The mean values of the age, diabetes duration and insulin dose were presented in Table 1.

The most frequent skin color in the study group was the dark intermediate type in 41 patients (68.33%) of the study group; 22 prepubertal and 19 pubertal patients (Figure 1). Regarding the sun exposure and exercise, the mean sun exposure period was 2.85 ± 1.05 hours/day (ranged from 1-5 hours/day) in the prepubertal group, and was 4.97 ± 1.85 hours/day (ranged from 1-10 hours/day) in the pubertal group. All of the prepubertal group practicing walking and/ or jumping as a part of their daily activities ranging from 2-10 hours daily and the mean duration was 5.13 ± 2 hours/day. Moreover, all of the pubertal group practicing walking as a part of their daily activities ranging from 2-8 hours daily and the mean was 3.83 ± 1.6 hours/day.

Regarding anthropometric measures (Growth Vision 2.0); the mean values for weight SDS, height SDS were normal in both groups (-0.17, -0.35 respectively in the prepubertal group) and (0.33, 1.36 respectively in the pubertal group). The mean BMI was 16.79 in the prepubertal group and 22.84 in the pubertal group. Short stature was found in three prepubertal and nine pubertal patients.

According to the dietetic history, the analysis of the dietary content of vitamin D, calcium revealed that all patients in the study had decreased mean dietary intake of vitamin D and calcium (Table 2). However, there were four prepubertal and four pubertal patients had adequate calcium intake.

The mean values of serum 25OHD in both groups were low. However, the mean value of calcium, phosphorus, parathormone and alkaline phosphatase in the study group were normal (Table 3).

Vitamin D status in the study group in relation to different variables is summarized in Table 4. Fifty-five patients (91.67%) were vitamin D deficient. Three prepubertal females (5%) were vitamin D sufficient and two pubertal females (3.33) who was vitamin D insufficient. Serum parathormone was high in 7 patients (11.67%) of the study group. All patients had deficient vitamin D intake, most of them (86.67%) had deficient calcium intake. All patients having short stature were vitamin D deficient.

There was no significant correlation between the serum 25OHD and insulin dose, diabetes duration, weight, height, serum phosphorus, calcium, sun exposure, mean HbA1c and parathormone (PTH) concentration (Figure 2).

	Prepubertal group (n=30)		Pubertal group (n=30)	
Variables	Mean ± SD*	Range	Mean± SD*	Range
Age (yrs)	6.85 ± 1.64	9-Apr	14.43 ± 1.52	17-Dec
Diabetes duration (yrs)	2.75 ± 1.39	6-Jan	5.08 ± 3.14	11-Jan
Insulin dose (IU/kg/day)	0.95 ± 0.29	0.5-1.5	1.42 ± 0.29	0.8-2.4

*SD: Standard deviation

Table 1: Age, duration of diabetes and insulin dose of the study group.

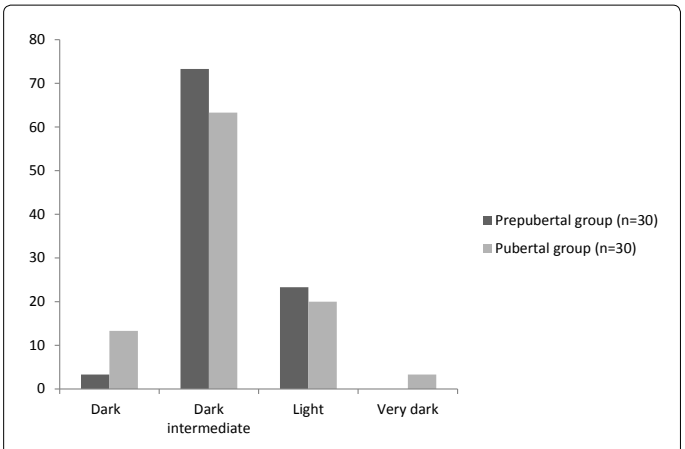

Figure 1: Distribution of the skin color in the study group. The most frequent skin color was the dark intermediate type; twenty-two patients (73.3%) in the prepubertal group and nineteen patients (63.3%) in the pubertal group.

Variables	Prepubertal group (n=30)		Pubertal group (n=30)	
	Mean ± SD*	Range	Mean ± SD*	Range
Vitamin D in diet (IU/day)	59.75 ± 51.29	0-178	38.59 ± 27.78	6- 128
Calcium in diet (mg/day)	684.42 ± 321.92	148- 1.447	691.88 ± 340.75	242- 1785

*SD: Standard deviation

Table 2: Dietetic analysis of the study group. Recommended Dietary Allowance (RDA) for vitamin D: 600 IU/day, for calcium: 1000 mg/day for patients 4- 8yrs, 1300 mg/day for patients 9-18yrs.

Variables	Prepubertal group (n=30)		Pubertal group (n=30)	
	Mean ± SD*	Range	Mean ± SD*	Range
Serum 25OHD (ng/ml)	11.88 ± 10.88	Apr-47	9.18 ± 7.09	3-27.5
Serum Ca (mg/dl)	9.14 ± 0.47	10-Aug	9.41 ± 0.7	12-Aug
Serum PO4 (mg/dl)	4.89 ± 0.89	3.4- 7.1	4.48 ± 0.93	3.2- 6.9
Serum ALP (IU/l)	222 ± 73.76	111- 423	197.07 ± 84.66	64- 345
Serum PTH (ng/dl)	4.16 ± 4.88	1.4- 26	5.07 ± 3.37	1.2- 14
Serum HbA1c (%)	7.65 ± 1.24	6- 11.4	8.44 ± 2.05	5.2- 15.7

*SD: Standard deviation

Table 3: Laboratory data of the study group. The reference range of serum calcium is 8.6-10.2 mg/dl, serum phosphorus is 3.2-5.5mg/dl, ALP is 35-300 IU/l, PTH is 1.2-7.2 ng/dl, 25OHD is 30-74 ng/ml, and HbA1c is 7.5-8%

Particulars	**Vitamin D deficient**		**Vitamin D insufficient**	**Vitamin D sufficient**
Study group	**Prepubertal group (n= 27)**	**Pubertal group (n=28)**	**Pubertal group only (n=2)**	**Prepubertal group only (n=3)**
Diet:				
- Vitamin D				
· Adequate	0	0	0	0
· Deficient	27	28	2	3
- Calcium				
· Adequate	4	4	0	0
· Deficient	23	24	2	3
Sex:				
· Male	15	16	0	0
· Female	12	12	2	3
Skin color:				
· Dark	1	4	0	0
· Dark intermediate	20	17	2	2
· Fair	6	6	0	1
· Very dark	0	1	0	0
Short stature				
· Male	1	5	0	0
· Female	2	4	0	0

Deficient (<20 ng/ml) - Insufficient (21 –29 ng/ml) - Sufficient (≥ 30 ng/ml)

Table 4: Summary of vitamin D status in the studied group.

Discussion

Many studies have suggested the relation between vitamin D deficiency and the risk of TIDM and suggested that vitamin D supplementation can reduce the incidence of T1DM [8,9]. The prevalence of vitamin D deficiency in children and adolescents with T1DM is very variable among the studies [3,10-12]. In the current study, 91.67% of the children and adolescents with T1DM were vitamin D deficient. This agrees with Bin Abbas et al., and Bener et al., who found that vitamin D deficiency was considerably higher in children with T1DM (84%, 90.67% respectively) [10,11]. Although, the prevalence in this study was higher than that reported by Janner et al, 2010 and Thnc et al, 2011 (60.5%, 28% respectively) [12]. This different prevalence in vitamin D deficiency given from different countries could be related to the variability of vitamin D deficiency definition, as well as geographical environment and latitude, skin color, nutritional, social habits and may be genetic influence.

In this study, despite the high prevalence of vitamin D deficiency, we found a low prevalence of secondary hyperparathyroidism (11.67%) in the study group. This could be explained by the normal average calcium level in the study group; however, ionized calcium wasn't assessed. These results are in agreement with Mutlu et al. who found only 11% of patients had secondary hyperparathyroidism in the study group whose mean 25OHD level was <20 ng/mL and also in line with Hatun et al. who found very low frequency (3%) of secondary hyperparathyroidism among healthy adolescent girls with vitamin D insufficiency or deficiency [13,14]. These findings indicate that not all vitamin D deficient T1DM patients have secondary hyperparathyroidism.

In the current work, there was no significant association between 25OHD level and glycemic control (HbA_{1C}), insulin requirements or duration of diabetes. This finding is in agreement with Janner et al who didn't find any relationship between HbA1c levels and vitamin D status in children and adolescents with T1DM. Similarly, Mutlu et al. had reported that there wasn't any significant relationship between serum 25OHD levels and HbA1c or duration of diabetes [12,13].

Dietary analysis of our patients revealed deficient vitamin D intake in the whole study group. This is in agreement with Liu, 2012 who explained this by that only a few natural foods contain significant quantities of vitamin D and supplementation is essential to achieve the recommended levels [15].

Conclusion

Vitamin D deficiency in children and adolescents with T1DM is very high (91.67%) but underestimated. No significant correlation was found between serum 25OHD and serum calcium, phosphorus, parathormone, anthropometric measures, duration of diabetes, mean HbA1c, insulin dose, and sun exposure. Despite the high prevalence of vitamin D deficiency, there was a low prevalence of secondary hyperparathyroidism (11.67%) in the study group.

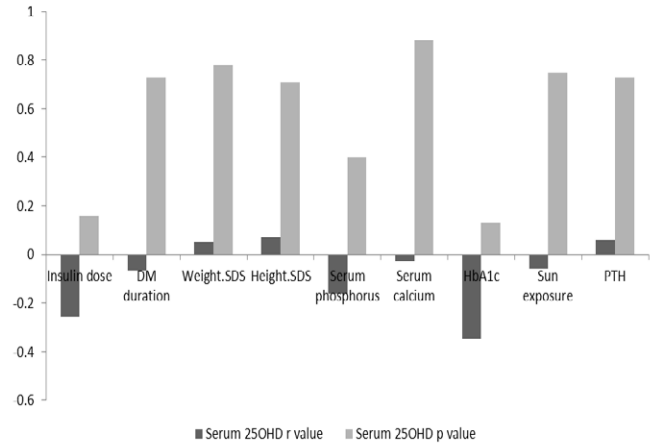

Figure 2: The correlation between serum 25OHD and the different variables in the study group. No significant correlations were found between serum 25OHD and different variables in the study.

Limitations

The limitations of this study derive from its cross-sectional design. Thus, we should recall the possible variations over time in the parameters studied. The sample size was the result of applying strict criteria for the selection of patients and excluding patients who received specific diet or any supplements for calcium or vitamin D or other medical problems or medications that may affect vitamin D level or if the patient was non-compliant to follow up as this can affect the full assessment of the glycemic control.

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