Serum Vitamin D Level in Children with and without Type 1 Diabetes Mellitus

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Abstract

For years, vitamin D has been associated to many immune disorders. Several studies have shown association between low serum 25 OH vitamin D and type 1 diabetes mellitus (T1DM).

Objective: To compare 25 hydroxy vitamin D (25 OHD) level in T1DM patients to non-diabetic children hospitalized or seen in emergency for other diseases at the same period.

Methods: It was a case-control study including 29 patients with T1DM and 28 non-diabetic control children. They were comparable in age, gender, weight, length, BMI and season of blood sampling. Epidemiological and clinical data were collected and 25OHD serum level was measured with a radioimmunoassay kit.

Results: 25OHD level was significantly lower in diabetic patients (mean: 19.62 ng/ml, range 15-26 ng/ml) than in control patients (24.64 ng/ml, 20-28 ng/ml), p=0.00. All participants (T1DM patients and controls) had inadequate levels of vitamin D.

Conclusion: Children with T1DM have lower vitamin D levels than control group.

Keywords: Vitamin D; Deficiency; Type 1 diabetes mellitus; Children

Introduction

Type 1 diabetes mellitus (T1DM) is an autoimmune disease with contribution of environmental factors in its causation. In susceptible persons, cytokine production and lymphocyte proliferation have been postulated to be decreased by immunomodulatory actions of vitamin D [1]. For years, interest in diabetes mellitus and vitamin D metabolism has grown. Many epidemiological studies have found high prevalence of vitamin D deficiency in children with type 1 diabetes mellitus, suggesting a strong relationship between the two [2,3]. It is hypothesized that vitamin D may have a therapeutic role in T1DM via its immune-modulatory properties [4].

To the best of our knowledge, there are no population-based studies that have examined the association between vitamin D and T1DM in Tunisian children.

The purpose of our study is to measure vitamin D levels in young children with T1DM and to compare them with levels in non-diabetic subjects at the same period.

Methodology

Subjects

We proceeded to a case control study performed in the department of pediatrics of Mongi Slim hospital in Marsa, Tunisia, from June 2014 to June 2015. The study included 29 children diagnosed as T1DM on the basis of the American diabetes society criteria (symptoms of diabetes and casual plasma glucose ≥ 7.0 mmol/L or a 2-h post load glucose concentration ≥ 11.1 mmol/L during an oral glucose tolerance test) [5] and without any medical comorbidities or any other chronic disease. This sample included youth with recently diagnosed T1DM and youth with established T1DM. Age of patients ranged from 7 months to 14 years. As control group, 28 children randomly recruited from emergency or admitted to hospital in the same period were studied. All did not report any chronic or auto immune disease. Participants and their families then completed a set of questionnaires and youth provided a blood sample for analysis. They were comparable in age, gender, weight, length, BMI and season of blood sampling. We categorized each participant’s blood sample according to the follow division of the calendar year: spring (1 March-31 May), summer (1 June-31 August), fall (1 September-30 November), winter (1 December-28 February)

Serum 25 (OH) D levels

The standard indicator of vitamin D status is serum 25-hydroxyvitamin D (25OHD) which is composed of cholecalciferol (vitamin D3) and ergocalciferol (vitamin D2). Serum concentrations of 25 (OH) D were measured with a radioimmunoassay kit that detects both forms [6]. In our study, concentrations of vitamin D were measured by a radioimmunoassay Kit (Dia-Sorin, Stillwater, MN, USA) and performed using ELISA technique. The collected serum was immediately shaded from direct light and stored at -20°C. All samples were analyzed simultaneously at the same laboratory, using the same technique conducted by one technician. Level values were reported in nanograms per millilitre. In descriptive analysis, vitamin D levels were categorized as sufficient (≥30 ng/ml), insufficient (≥20 ng/ml and <30 ng/ml) and deficient (<20 ng/ml) on the basis of previous recommendations [7].
Ethics

Informed parental consent was obtained to be eligible for enrollment into the study. It was done according to the rules of the local ethics committee of our hospital.

Statistical analysis

Values for all parameters, expect gender and season of blood sampling, were expressed as mean ± SD. Two-tailed unpaired Student’s t test was used for comparison of normally distributed variables (with the Mann–Whitney U test for skewed data), and the Chi2 test for categorical variables (with the Fisher exact test for skewed data). A P value<0.05 defined the level of statistical significance. Data analysis was performed using the SPSS 15.0 statistical software package.

Results

Mean disease duration in our study was 35.03 ± 42.4 months (range= 0-168) with 7 newly diagnosed cases. The control group and the diabetic one were comparable as regards age, gender, weight, length, BMI, or season of blood sampling respectively (Table 1).

In this study, we found that all participants had inadequate levels of vitamin D. Serum 25OHD in children with T1DM as a group (established and newly diagnosed T1DM combined) was significantly lower compared to control children (Figure 1).

15 diabetics (51.7%) were deficient (17.4 ± 1 ng/ml). 14 diabetics were insufficient (21.9 ± 2 ng/ml), meanwhile all controls were insufficient (p<0.001; OR=3 IC 95%:1.95-4.60) (Figure 2). No difference in vitamin D level between newly diagnosed diabetics and those with established T1DM.

In bivariate analysis, age, gender, BMI, duration of T1DM, season of blood sampling, insulin requirements and HbA1C level were similar among diabetic patients with vitamin D deficiency and insufficiency (Table 2).

Discussion

Our study showed that vitamin D level was considerably lower in T1DM patients compared with non-diabetic children. A significant difference in the mean value of vitamin D between the two groups was found (p=0.00). It confirms previous results of other studies in T1DM children that showed that serum 25 OHD was lower in T1DM patients than in control group [8-12]. However, in these studies, controls were healthy subjects, while in our study controls were children admitted to hospital or seen in emergency for other reasons and thus expected to have lower serum 25 OHD than healthy children supporting the role of vitamin D in defense mechanism [13]. In fact, low vitamin D level has been reported in both acute and chronic diseases [14,15]. It was implicated in cardiovascular diseases [16], kidney disease [17], asthma [18], multiple sclerosis [19], rheumatoid arthritis [20], several malignancies [21] and immune disorders [22].

Although our use of hospital controls, serum 25 OHD in diabetic subjects was significantly lower and this is strength of our study supporting the potential role of vitamin D in the development of auto immune diseases as it was reported by Bruna et al. [23].

Because vitamin D status is linked to exposure to sunlight, we examined 25 OHD levels as a function of season of blood sampling. In Switzerland, vitamin D deficiency rose to 84.1% in winter in T1DM children [3], which shows season as an important contributor to vitamin D status. However, in our study, we did not observe significant difference while comparing 25OHD levels among the study groups through the four seasons.

On the other hand, in the present study, all participants had inadequate level of vitamin D despite Tunisia is a solar rich country. These findings implicate that vitamin D deficiency may be seen even in children without any auto immune or chronic disease. This agreed with a study performed in Egypt who revealed that both T1DM and controls were vitamin D insufficient however serum vitamin D levels were not.
It has been shown that high doses of 1, 25 di-hydroxy vitamin D inhibit the expression of inflammatory cytokines in monocytes, such as IL 6, TNF alpha and IL12 in normal individuals. The influence of vitamin D on cytokine production by lymphocytes may be another important link between immune system and 25 OHD [32]. Also, it has been proved that vitamin D supplementation in mice prevents the onset of diabetes [33]. Furthermore, it has been suggested that supplementation with vitamin D during pregnancy and early childhood may reduce the risk of early onset T1DM by 80 % [34], and perhaps, even after the onset of diabetes, it may improve glycemic control [35].

In conclusion, vitamin D deficiency and insufficiency were found in Tunisian children with and without T1DM. It seems that vitamin D supplementation should be provided for both auto immune and other diseases.

**Conclusion**

This study revealed that vitamin D level in diabetic subjects is significantly lower than non-diabetic patients. However, even control patients were vitamin D insufficient despite the high sunlight exposure of our country. It will be of interest to future studies to investigate in vitamin D supplementation for auto immune diseases particularly T1DM.

**References**


**Table 2:** Characteristics of T1DM participants.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total sample N=29</th>
<th>Vit D insufficient n=14 (48.3%)</th>
<th>Vit D deficient n=15 (51.7%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, months</td>
<td></td>
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<tr>
<td>Mean ± SD Range</td>
<td>106.3 ± 47.7 [7-182]</td>
<td>107.5 ± 51.3 [20-182]</td>
<td>105.1 ± 45.9 [76180]</td>
<td>0.89</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
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<tr>
<td>F M</td>
<td>15 (51.7%) 14 (48.3%)</td>
<td>9 (60%) 5 (35.7%)</td>
<td>6 (40%) 9 (64.3%)</td>
<td>0.17</td>
</tr>
<tr>
<td>BMI, kg/m² mean ± SD Range</td>
<td>18.15 ± 3.80 [14.5-32.8]</td>
<td>18.68 ± 4.72 [14.96-32.87]</td>
<td>17.58 ± 2.54 [15.96-21.08]</td>
<td>0.44</td>
</tr>
<tr>
<td>Duration of T1DM mean ± SD Range</td>
<td>35 ± 42.3 [0-168]</td>
<td>38 ± 52.3 [0-168]</td>
<td>32 ± 32 [0-102]</td>
<td>0.69</td>
</tr>
<tr>
<td>Season of blood sampling</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Summer</td>
<td>1(3.4%) 7(24.1%)</td>
<td>3(21.4%) 5(35.7%)</td>
<td>4(26.6%) 4(26.6%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Winter</td>
<td>9(31.1%) 12(41.4%)</td>
<td>5(35.7%) 6(42.8%)</td>
<td>6(40%) 6(40%)</td>
<td>0.44</td>
</tr>
<tr>
<td>Spring</td>
<td>10.30 ± 1.9 [6.5-14]</td>
<td>10.02 ± 1.6 [7.1-14]</td>
<td>11.17 ± 2.2 [6.5-14]</td>
<td>0.13</td>
</tr>
<tr>
<td>Fall</td>
<td>0.93 ± 0.2 [0.55-1.7]</td>
<td>0.91 ± 0.1 [0.64-1.2]</td>
<td>0.97 ± 0.3 [0.55-1.7]</td>
<td>0.59</td>
</tr>
<tr>
<td>Hb A1C (%) mean ± SD Range</td>
<td>19.62 ± 2.7 [15-26]</td>
<td>21.9 ± 2 [20-26]</td>
<td>17.4 ± 1 [15-19]</td>
<td>0.00</td>
</tr>
</tbody>
</table>

D successfully reduce the incidence of diabetes by decreasing the number of effector T cells, inducing T reg cells and reducing chemokine production by islet cells [31]. In vivo, it has been reported that 1, 25 di-hydroxy vitamin D reduces the number of effector T cells, inducing T reg cells and reducing chemokine production by islet cells [31].


