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Effect of Vitamin D Levels on Egyptian Children with Type-1 Diabetes Mellitus

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ABSTRACT

Background: There are some explanations for the relationship between vitamin D (Vit. D) low levels and type 1 diabetes mellitus (T1DM). T1DM is an autoimmune disorder that affects pancreatic cells, Vit. D acts an immunomodulatory function via the Vit. D receptor abundant on immune and pancreatic cells. By lowering the number of effector "T" cells, it has been demonstrated that great concentrations of 1,25-dihydroxyvitamin D positively lower the diabetes' occurrence. Our study's aimed to assess the potential role of Vit. D concentration in early infancy as an indicator of possibly developing islet autoimmunity or clinical T1DM. **Method:** This was a case-control study involving 40 T1DM-diagnosed children aged 6 to 12 years and 20 healthy children as controls with comparable gender, height (cm), age, weight (Kg), and body mass index (BMI). For all subjects, serum hydroxyl Vit. D (25 OHD) was measured using chemiluminescence immunoassay. Serum total Ca, ph, ALP and PTH were measured. Also, Hb_{A1C}% was measured win both groups, and blood glucose was also measured. Mg, AST and ALT were also assessed. **Results:** The mean serum 25OHD in T1DM children was less than Healthy controls 9.3+1.4Vs 59.2+18.7ng/ml respectively with ($p < 0.0001$) and diabetic cases showed negatively significant relationship between vitamin D versus HbA1c% and glucose, ($r = -0.8, -0.9$) respectively ($p < 0.0001$). **Conclusion:** Vitamin D deficiency is frequent in children with T1DM, and it is important to pay attention to this issue. Future studies will be interested in investigating vitamin D supplementation for autoimmune diseases, particularly T1DM.

Key words:
Vitamin D, T1DM, PTH and Hb_{A1C}

1. INTRODUCTION

T1DM is an autoimmune disorder affecting the pancreatic islets. The disorder can impact people of every stage of life, but it typically manifests in children and young adults, resulting in 90% of diabetes cases in children and adolescents [1]. China had the estimated prevalence of 1.01 T1DM occurrences per 100,000 person-years for all ages [2].

Even before the islet autoantibodies can be detected, the disease process of T1DM may begin in infancy as a result of largely unidentified factors inducing immune system alterations [3].

As a result of vitamin D's active role in modulating the immune system, vitamin D deficiency during childhood, fetal development, and adolescence is one of the environmental variables involved in the etiology of T1DM. Prior studies analyzing the association between Vit. D and T1DM focused either on serum 25-hydroxyvitamin D (25 OHD) concentration (regarded as a marker of vitamin D reserves) caused by supplemental and dietary Vit. D consumption or on vit. D metabolism-associated genetic factors [4].

The link between risk of T1DM and serum 25OHD concentration at birth was dependent on the VDR genotype (rsl 1568820) [5]. VDR is recognized to regulate the hundreds of genes' expression, a number of which are involved in immune system function [6].

Vitamin D deficiency may influence the complications, prevalence, and advancement of T2DM [7]. The kidneys produce 1,25 (OH) 2D3 by hydroxylate 25 OHD. 25 OHD is therefore typically measured in serum to determine vitamin D status, and 25 OHD is more hydroxylated by the kidneys to generate 1,25 (OH) 2D3[8].

Our study's aim was to evaluate the potential role of serum 25-hydroxyvitamin D (25 OHD) concentration in early infancy as an indicator of the chance of developing islet clinical or autoimmunity T1DM later in life.

2. PATIENTS AND METHODS

Total of 60 children and adolescents aged between 6-12 years who visited Abo- Elrish Hospital Cairo University from June 2017 to August 2018.

Subjects encompassed 40 patients with T1DM and 20 healthy controls without a vit. D supplementation or drug utilization history that might impact serum vit. D levels, including systemic glucocorticoids or anticonvulsants, as well as chronic hepatic and kidney disorders' cases.

Samples Collection and Analysis:

Blood specimens were obtained from June to August from individuals with T1DM who had a history of bone fracture or deformity. Abo Elrish hospital went through and approved this research, and scripted informed consent was gathered from the participants and their parents. The subjects' age, height, gender, weight, BMI kg/m2, and laboratory profiles were recorded. Fasting blood glucose (mg/dl), Serum calcium (mg/dl); magnesium (mg/dl), phosphorus (mg/dl), and alkaline phosphatase ALP (U/l) levels were measured by colorimetric method, while parathyroid hormone (PTH) (Pg/ml),
ALT and AST (U/l) were validated by Elisa kit.

Serum vitamin D (vit. D) ng/ml quantities and glycosylated hemoglobin (Hb_{A1c} %) were assessed utilizing chemilum-inescence immunoassay through Siemens Dimension X pand plus apparatus.

Statistical Analysis:

All questionnaires gathered were reviewed for completeness. The data gathered were encoded and input into the computer via the 2007 "Microsoft Office Excel Software" spreadsheet program Version 21 of the statistical application for social science (SPSS) was employed to analyze the data.

The data was presented by percentage and number for qualitative parameters, standard deviation and mean for normally distributed quantitative parameters, and interquartile range (IQR) and median for non-normally distributed quantitative parameters.

Chi-square or Fischer's Exact test was employed to compare groups for qualitative variables; analysis of variance (ANOVA) test and independent sample t-test for normally distributed quantitative factors; and

non-parametric test for non-normally distributed quantitative factors. For non-normally distributed quantitative variables, the Kruskal-Wallis and Mann-Whitney tests are employed also.

To assess for linear relationships between parameters, correlations were performed. p-values less than or equivalent to 0.05 were deemed statistically significant [9].

3. RESULTS

In this study, there were 40 T1DM Children, and 20 control, Baseline characteristics among control and diabetic groups were described in **(Table 1).** Age and height (cm) did not vary significantly between control and diabetic groups (p=0.2 and 0.5, respectively). While there was significant differences between two studied groups, as regards sex, weight (kg) and BMI (p 0.01, <0.0001 and 0.02) respectively pie chart showing sex distribution among control and diabetic groups in **(Fig. 1).**

As shown in Table 2 & Fig. 2 the studied biochemical parameters, among diabetic and control group mean ± SD of all parameter were: Vit. D 25(OH)D ng/ml 9.3±1.4vs 59.2±18.7, Ca (Total) mg/dL 5.7±1.2vs 9.1±1.0 $Hb_{A1c\ \%}$ 10.5±1.3vs 4.5±1.4, ph mg/dL 7.5±2.4vs 4.4±1.3, Alp U/L 503.9±11.5vs 373.7±65.4, Mg mg/dL 1.8±0.3vs 1.9±0.4, PTH pg/mL 72.2±5.5vs 34.7±11.6, AST U/L 23.9±7.7vs 25.5±7.5, ALT U/L 25.2±9.8vs 29.9±9.1, glucose mg/dl 231.8c11.0 vs 88.1±10.1. Vit. D25, Ca (Total), HbA1c, ph, Alp, PTH and glucose were a highly significant differences between two groups (p= < 0.0001). On the other hand, Mg, AST and ALT were nonsignificant differences. (P > 0.05)

(Table 3) revealed significant links with weight, Height and BMI (r=0.6, p<0.0001, r = 0.3, p0.02 and r=0.3, p<0.02) consecutively. Ca and Mg (mg/dl) showed also positive significant correlations r = 0.8,0.3 with p<0.0001 and 0.01 consecutively. In contrast, vitamin D serum levels demonstrated significant negative links with fasting blood glucose (mg/dL) and HbA1C %. (r =- 0.9,-0.8) p<0.0001. Ph (mg/dl), ALP (U/L), and PTH (pg/ml) had also, negative correlations significantly with vitamin D (r = - 0.5,- 0.7 and - 0.8 consecutively, p < 0.0001) **(Table 3).**

4. DISCUSSION

Various tissues, involving beta-cells and T lymphocytes, contain receptors for vit. D that act an essential function in immune system maintenance [10].

As vitamin D deficiency is believed to act a direct function in inducing immune-mediated B-cell destruction and calcium-mediated dysfunction that results in the development of clinical Diabetes, vitamin D levels must be minimal at the moment of diagnosis [11].

The current study indicated that the vit. D levels of children with T1DM were significantly less than those of children without diabetes. A greatly significant difference was noticed between the mean vitamin D levels of the two groups (p-value less than 0.0001).

It verifies the findings of prior research that serum vit. D was less in those with T1DM than in the control group [12].

Considering age and height, our research revealed no significant differences between vit. D-deficient diabetic children and control children (P= 0.5 and 0.2, respectively). Another research [13] revealed that vit. D deficiency was more prevalent in girls than in boys, particularly among adolescents. This may be due to the clothing choices of Turkish females, while vit. D deficiency was more prevalent among obese people [14].

Our present study showed significant differences between vit. D lacking diabetic children and those of control regarding weight (kg) and BMI, p estimates less than (<0.0001 and 0.02 consecutively), and significant positive link was found between the two groups in weight, and BMI p= 0.02 respectively[15] were agreement with the present study in the obese children were further probable to be vit. D deficient than non-obese children (71% vs 29%) and, they noted also significant link between BMI and vit. D deficiency (p=0.035), and no significant links of vitamin D deficiency with gender. In previous studies, a significant negative link existed between 25(OH) vit. D and BMI (p<0.01). They found that a higher BMI

in children and adolescents is associated with rapid bone growth, as these individuals are taller than average and have slightly advanced bone age [16].

Azab et al.,[17] additionally found highly significant differences in serum phosphorus, calcium, PTH, and ALP levels between vit. D deficient diabetic children and healthy children (all p less than 0.01), Serum vitamin D levels were not linked with fasting blood glucose or HbA1c ($p>0.05$).

Our consequences were in line with azeb et al., [17] and others in significant differences between the two study's groups but with highly significant (p-value less than 0.0001). While serum levels of vitamin D demonstrated positive links with calcium and magnesium ($r = 0.8$ and 0.3 with p values 0.000l and 0.01 respectively

While negative correlations were obtained between the two groups in our present study with phosphorus, ALP, PTH and also fasting blood glucose and HbA1c ($r = -0.5, -0.7, -0.8, -0.9$ and -0.8 consecutively, with ($p<0.000l$). Bae et al., [18] were in agreement with our results.

The parathyroid hormone's elevated levels in vitamin D deficiency represent a feedback process in response to reduced vit. D concentrations [19]. Alp and PTH are the two most important biochemical parameters with regard to the vitamin D deficiency's adverse impacts on the skeleton. 20 or 30ng/ml is the concentration of serum 25OHD that the average serum PTH quantity starts elevate [20].

Prior research [21] demonstrated that serum 25(OH)D concentrations had an inverse link with HbA1c regardless of body fat, indicating that children with less vit. D levels had higher ambient glucose concentrations. Our findings were consistent with these findings.

Conversely, Sonia et al. [22] found no differences in Hb_{A1c} concentrations and need for insulin among vit. D-deficient individuals. Furthermore, AL Zahrani and AL shaikh., [23] found no link between vit. D deficiency and HbA1c. They found that pubertal development and growth, in addition to adherence and behavioral concerns, may act a significant function in suboptimal glycemic control. AL Zahrani and AL shaikh., [24] concluded that glycemic control was lower among Saudi children with T1DM compared to other children. And they implemented a program to combat weak suboptimal glycemic control and adherence, both of which are urgently required.

5. CONCLUSION

The aim of the present study to assess vitamin D deficiency in children with type 1 diabetes with laboratory assessments and studying the correlation with risk of T1DM and vitamin D levels.

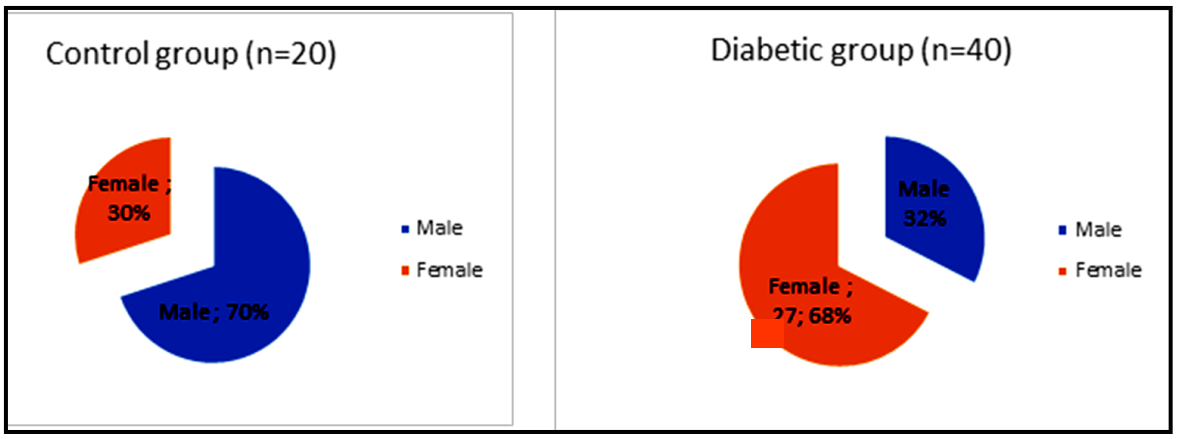

Fig. (1): Distribution among diabetic and control groups

Table 1: Baseline characteristics among Control and diabetic groups

Variables		**Control** (n=20)	**Diabetic group** (n=40)	p value
Sex	Male female	14(70%) 6(30%)	13(32.5%) 27(67.5%)	0.01
Age		8.4±3.0	7.9±2.7	0.5
Weight (kg)		44.2± 11.5	35.9±4.1	<0.0001
Height (cm)		127.4±13.2	122.4±13.5	0.2
BMI (Kg/m^2)		26.9±3.2	24.4±4.0	0.02

Table 2: Studied Biochemical parameters among control groups and diabetic groups

Variables	**control groups (n=20)**	**diabetic groups (n=40)**	**P value**
ViT D25(OHD) ng/ml	59.2±18.7	9.3±1.4	<0.0001
Ca (Total) mg/dL	9.1±1.0	5.7±1.2	<0.0001
Hb_{A1c}%	4.5±1.4	10.5±1.3	<0.0001
ph mg/dL	4.4±1.3	7.5±2.4	<0.0001
Alp U/L	373.7±65.4	503.9±11.5	<0.0001
Mg mg/dL	1.9±0.4	1.8±0.3	0.1
PTH pg/mL	34.7±11.6	72.2±5.5	<0.0001
AST U/L	25.5±7.5	23.9±7.7	0.4
ALT U/L	29.9±9.1	25.2±9.8	0. 1
Glucose mg/dl	88.1±10.1	231.8±11.0	<0.0001

Table 3: Relationship between Vit D and other tests

Variable	r	P value
Vit D25(OHD)		
Weight (kg)	0.6	<0.0001
Hight (cm)	0.3	0.02
BMI (Kg/m^2)	0.3	0.02
Ca (Total) mg/Dl	0.8	<0.0001
HbA1c%	-0.8	<0.0001
ph mg/dL	-0.5	<0.0001
Alkaline phosphatase U/L	-0.7	<0.0001
Mg mg/dL	0.3	0.01
PTH pg/mL	-0.8	<0.0001
AST U/L	0.2	0.2
ALT U/L	0.2	0.05
Glucose mg/dl	-0.9	<0.0001

6. Recommendations

We suggest a baseline measurement of vit. D levels at the moment of T1DM diagnosis and the vit. D supplement's initiation if serum vit. D level is 30ngml, in order to preserve serum vit. D levels between 30-60ngml.

7. Conflict of interest

There are no competing interests.

8. Fund

No specific grant was awarded to this research by public, private, or nonprofit funding organizations.

9. Data availability

At Abu Al-Rish children's Hospital, affiliated to the Faculty of medicine, Cairo University, all data on infected children were collected on children with T1DM and vitamin D deficiency were collected, as was completed by Dr. Heba Ahmed helped us to collect all the required data on children and give a Medical History of all .

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