Original Paper

Vitamin-D Status in Type 1 Diabetic Children and Teenagers in Karbala, Iraq

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Abstract

Background: Vitamin-D deficiency is a very important subject in clinical endocrinology. Low vitamin-D levels detected in many metabolic and immune disorders like Diabetes-Mellitus type 1 (T1DM).
Aim: Evaluate vitamin-D status of children & teenagers with T1DM in Karbala, Iraq.
Patients and Methods: (171) subjects were enrolled in a case-control study, consisted of two groups; diabetic patients (121) cases (48 male and 73 female), aged 5-16 years and the control non-diabetic (50) (26 female and 24 male) children with matched age and sex. 25 (OH) D3 measured for all subjects, glycosylated hemoglobin was measured for diabetic cases.
Results: The level of vitamin-D was significantly lower for diabetic cases (p=.003). Further analysis of vitamin-D using 10ng/ml as cutoff level to assess vitamin-D severe deficiency between diabetic patients and controls shows that percent of severity of vitamin-D deficiency within diabetic cases (42%) was more than control (12%) which was highly significant (p=0.0001).
Conclusion: diabetic children are more susceptible to deficiency of vitamin-D than non-diabetics are, with more prevalence of severe deficiency among them. We recommend Measuring of vitamin-D for all T1DM children.
Keywords: Vitamin-D status, T1DM, children and teenagers, Karbala, Iraq

Introduction

T1DM is a metabolic disease results from defective insulin production characterized by hyperglycemia due to autoimmune destruction of B-cells of the pancreas islets, which leads to insulin deficiency [(1)]. T1DM represent 10% of diabetes [(2)]. The incidence of T1DM vary worldwide, which is more in Finland which could be due to dietary, genetic and environmental factors that might interfere with its pathogenesis. Its frequency is increasing around the world, maybe due to better socioeconomic state and level of urbanization [(3)]. Environmental and genetic risk factors are main agents participating in this autoimmune process [(4)]. Many studies reported an association between deficiency of vitamin-D and T1DM [(5)]. Deficiency of Vitamin-D is very important subject in clinical endocrinology and it is prevalent among geographical regions, all ages, races and socioeconomic states. Vitamin-D is necessary for calcium and phosphorous metabolism. It possesses immune modulatory properties and its deficiency identified in many autoimmune disorders [(6)]. Vitamin-D (calciferol) is one of fat steroids. The main forms are D2 and D3 (ergocalciferol and cholecalciferol). Both types undergo similar metabolism. Vitamin-D obtained by intake via limited dietary sources and synthesized by skin through ultraviolet sun light exposure, Then it is metabolized to 25(OH)-D3 by liver, which has prolong half-life. It is an essential metabolite of vitamin-D. In kidneys 25(OH)-D3 is metabolized by 25(OH)-D-1(alpha)-hydroxylase (CYP27B1) to active form, 1, 25(OH) 2 D3, which exerts its effects by steroid nuclear receptors. The actions of vitamin-D3 are

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those of hormones. Eventually vitamin-D3 regarded as a pro-hormone, rather than a vitamin [6]. Recently, the extra skeletal actions of vitamin-D have increased interest as particular receptors has been detected in many cells, including pancreatic B-cells and immune system cells. The major extra-skeletal effect of vitamin-D action in nucleus of cell where it can manage translation of (3%) of genome [7]. Many studies found a reliable correlation between T1DM complications and deficiency of vitamin-D. Increasing evidence that T1DM patients are more susceptible to develop low 25(OH) D3 level. Low vitamin-D correlated with high HbA1c. T1DM patients commonly have low vitamin-D level. Therefore, many studies recommended to measure vitamin-D levels for T1DM patients regularly[8].

Patients and Methods

Study performed in Diabetes and Endocrinology Clinic at Karbala Teaching Hospital for Children between second of September 2016 to the 30th 0f October 2017. 171 subjects enrolled in this case-control study aged 5 to 16 years consisted of two groups; 121 cases (48 male and 73 female) with T1DM for more than one year without any chronic illness rather than T1DM and 50 controls (26 female and 24 male) non diabetic attending the pediatrics clinic. Subjects were out of the study if they consumed vitamin-D and or calcium therapy within last one year.

Serum total 25(OH) D3 level measured using "Enzyme-Linked Fluorescent Assay" in Minividas immuno-assay analyzer. We classified Vitamin-D according to "American academy of pediatrics" recommendations. Severe deficiency of vitamin-D defined as 25(OH) D3 less than (5 ng/ml) (12.5nmol/l), mild-moderate deficiency as 25(OH) D3 between (5-15 ng/ml) (12.5-37.5nmol/l), insufficiency between (16-20ng/ml) (40-50nmol/l) and sufficiency (safety margin to minimize hypercalcemia) as 25(OH) D3 between (21-100 ng/ml) (52.5-250nmol/l). Glycosylated Hemoglobin measured using High-performance gel chromatography technique "HPLC BIO-RAD D10".

Results

Sample characteristics: we compared between cases and controls regarding sex and age of subjects to ensure similarity. There was no difference in age between cases (M=11.28, SD=3.26) and controls (M=10.62, SD=3.80) groups; t (169) =1.14, p=0.252 (table 1).

There was no case-control gender difference $\chi 2$ (1, N = 171) =1.007, p = 0.31 (Table 2)

Inspection of vitamin-D level "frequency histograms" and "Q-Q plots" for cases and controls showed that vitamin-D level was not "normally distributed" for both. Skewness =1.123 (SE 0.219) for cases and 1.192 SE (0.336) for controls figures (1, 2)

Statistics: Mann-Whitney-U test indicated that level of vitamin-D was significantly lower for diabetic cases (Mdn = 11.4) than for controls (Mdn = 13.8), U = 2161.5, Z=-2.93, p = .003 table (3 and 4).

Deficiency of vitamin-D further evaluated for severity within subjects. vitamin-D level (10ng/ml) used as cutoff level to assess the severity of vitamin-D deficiency between diabetic cases and controls shows that percent of severe vitamin-D deficiency within diabetic cases (42%) is more than control (12%). (Table 5)

There was highly significant case-control difference in severe vitamin-D deficiency $\chi 2$ (1, N = 171) = 14.4, p = 0.0001

"Pearson product correlation coefficient" computed to assess the relationship between the level of hemoglobin-A1C and vitamin-D in diabetic cases. There was a strong negative correlation between the two variables, (R) = - 0.490, n = 170, p <0.0001 figure (3).

Table1. Case-control age comparison

	Case	Control
N	121	50
Mean(yr)	11.28	10.62
SD.	3.26	3.80
SEM	0.29	0.53

Table2. Case-control gender comparison

		case	control
Male	N	48	24
	%	40%	48%
Female	N	73	26
	%	60%	52%

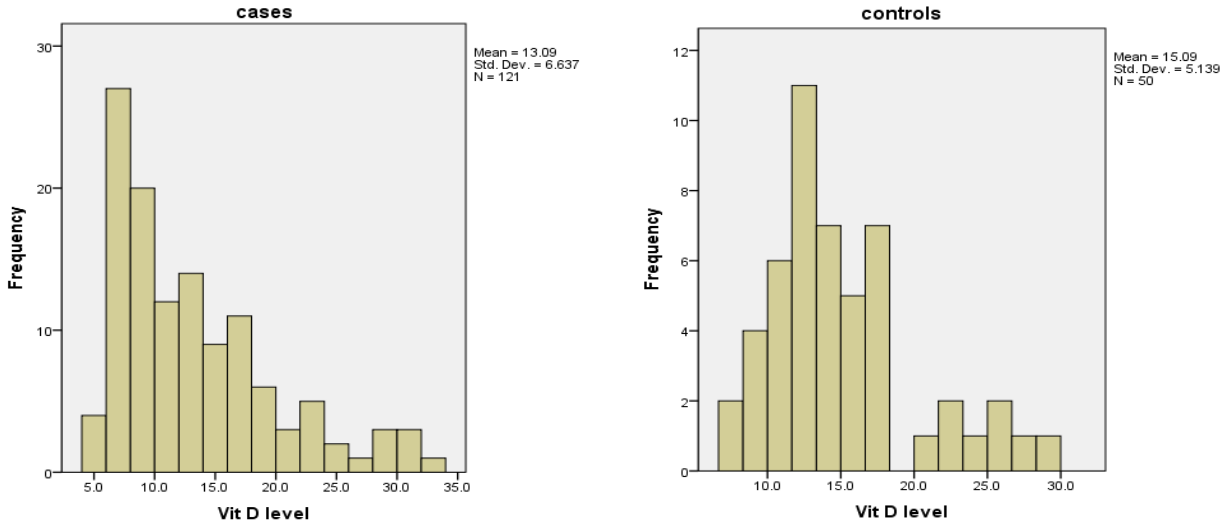

Figure1. Case-control histogram of vitamin-D level frequency

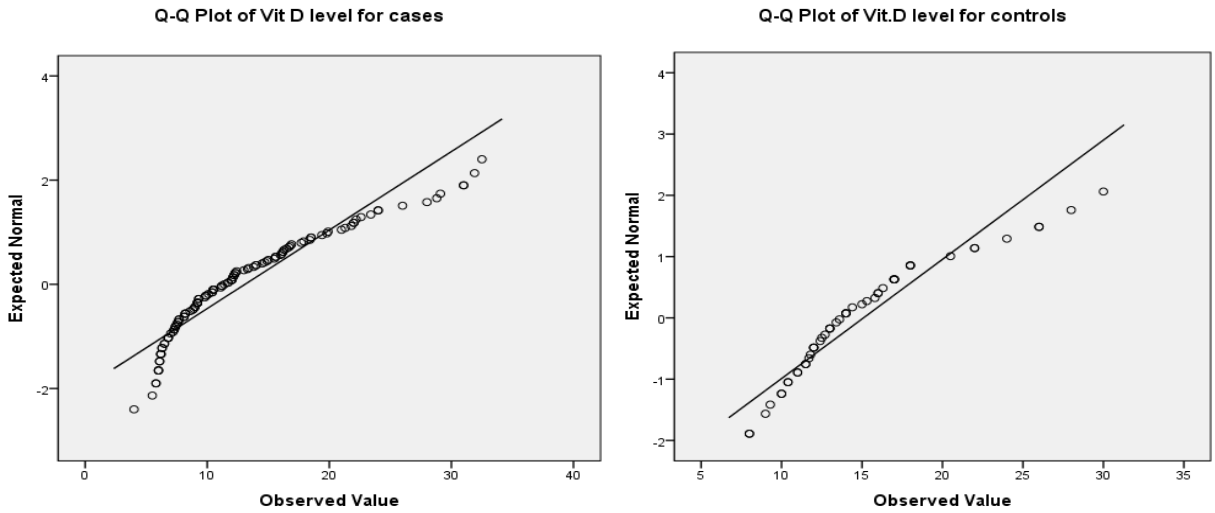

Figure2. Case-control Q-Q Plot of Vitamin-D level

Table3. Ranks

	N	Mean Rank	Sum of Ranks
Case	121	78.86	9542.50
Control	50	103.27	5163.50
Total	171		

Table 4. Test Statistics

	Vit.D level
Mann-Whitney-U	2161.500
Wilcoxon W	9542.500
Z	-2.933
Asymp. Sig. (2-tailed)	.003

Table 5. Case-control severe vitamin-D deficiency distribution

		Cases	Controls
severe deficiency	N	51	6
	%	42%	12%
normal and mild deficiency	N	70	44
	%	57%	88%

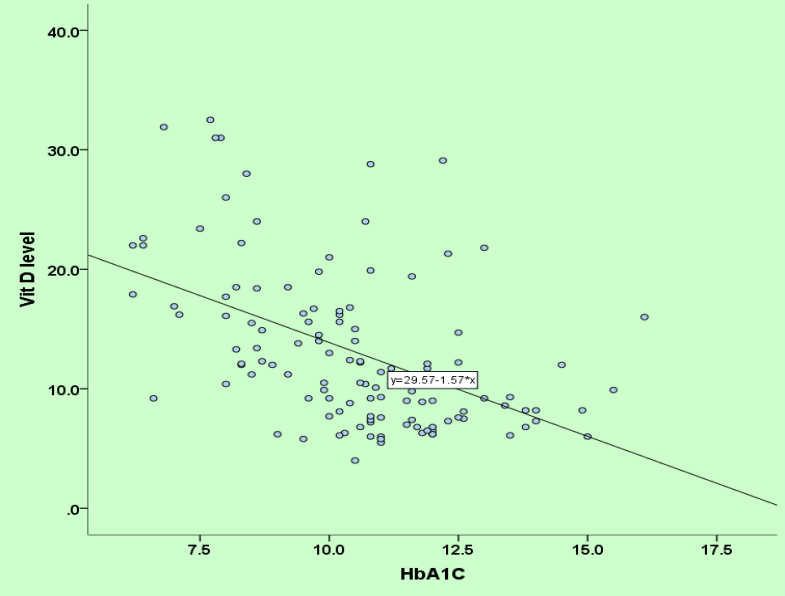

Figure3. "Person Correlation" between vitamin-D level (ng/ml) and HbA1C(%)

Discussion

Diabetes causes major metabolic effects in many tissues including liver, muscles and fatty tissue. These changes will affect the equilibrium of other endocrine and metabolic maintaining systems including cholesterol, lipids and vitamin-D metabolism. These effects have been of concern for new researches to determine the mutual relation between vitamin-D deficiency and diabetes. We found in this study that vitamin-D deficiency was higher in children and teenagers with T1DM than non-diabetic controls. We also found that severe deficiency of vitamin-D with levels lower than (10 ng/ml) in T1DM cases (42%) was higher than non-diabetic controls (12%). These results agree with other studies in Europe; Littorin et al., Janner et al., Vojtkova et al. [9–11], in solar

rich countries; by Aljabri et al., Bin-Abbas et al., Bener et al., Zhang et al., and Hassan et al. [12–16] and in Hispanic population by Gomez-Meade et al. [17]. All found higher prevalence of vitamin-D deficiency affecting diabetic children. Despite Iraq is a sunshine rich area throughout the year, there is high prevalence of vitamin-D deficiency among children and teenagers with T1DM. "Epidemiological studies suggest possible associations between vitamin D deficiency and a variety of conditions, but a causal relationship has not been established and the mechanism for the associations is not clear. These include certain immunological conditions such as type 1 diabetes" [18]. Evidence has shown the Expression of 25-hydroxyvitamin D3-1alpha-hydroxylase in pancreatic islets [19]. Our study did not agree with Slavcheva et al., which showed that vitamin-D level is similar in diabetic patients and non-diabetic controls [20]. Deficiency of vitamin-D differs between nations and races. This is due to geographical environment, skin color, dietary intake, social and genetic effects. We found strong negative correlation between HbA1c and vitamin-D level, which agrees with Elsayed et al. and Wulandari et al. studies [21,22]. (Vitamin D Receptor) found on pancreatic beta cells may play role in insulin production and secretion which may affect glycemic control in children [22]. Supplementation with vitamin D in vitro influence on both the secretion and biosynthesis of Insulin in islets B cells of animals [23].

Conclusion

Children and teenagers withT1DM are more vulnerable to vitamin-D deficiency than non-diabetics are. Severity of vitamin-D deficiency is more among T1DM children and teenagers. We recommend measuring level of vitamin-D for all T1DM children and teenagers as well as effective treatment for deficient patients.

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