International Journal of Contemporary Pediatrics
Srinivas CNS et al. Int J Contemp Pediatr. 2022 Sep;9(9):834-838
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20222122

Original Research Article

Evaluation of serum vitamin D levels in diabetic children and the effect of vitamin D supplementation on glycemic control (Hba1C) in vitamin D deficient diabetic children

Chandana Nanjaiah Shetty Srinivas*, Savitha Mysore Ramaraj

Department of Pediatrics, Mysore Medical College and Research Institute, Mysore, Karnataka, India

Received: 25 July 2022
Accepted: 12 August 2022

***Correspondence:**
Dr. Chandana Nanjaiah Shetty Srinivas,
E-mail: chandanas776@gmail.com

ABSTRACT

Background: It has been estimated that around 96,000 children under 15 years are found to develop type 1 diabetes annually all over the world. Vitamin D deficiency is more common in paediatric diabetic population and vitamin D supplementation is known to improve glycemic control in Diabetic children. The objectives of the study being, to compare serum vitamin D levels of diabetic children aged less than 18 years with non-diabetic children aged <18 years and to study the effect of oral vitamin D supplementation on glycemic control in vitamin D deficient diabetic children.
Methods: Present study was a cross sectional study conducted in Cheluvamba hospital, Mysuru. 60 diabetic children and 60 healthy (control) children were enrolled for the study. Serum 25(OH)D was assessed by ELISA in both groups. HbA1c levels were assessed by HPLC among vitamin D deficient diabetic children before and after supplementation of Vitamin D.
Results: In current study, study group (diabetic children) mean vitamin D levels were found to be 21.667±7.9 ng/ml which were statistically significant compared to control group that is 25.90±10.06 ng/ml (p=0.012) but there was no clinical significance. Among diabetic children the mean HbA1c before and after supplementation of vitamin D among vitamin D insufficient children was 11.78±2.22% vs. 11.73±0.141% (p=0.141) respectively and in vitamin D deficient children was 11.74±1.18% vs 11.72±1.17% (p=0.662).
Conclusions: Mean serum vitamin D levels were comparable among diabetic children and control group. The mean HbA1c levels were comparable before and after supplementation of vitamin D among vitamin D deficient diabetic children thus indicating that there is no role of vitamin D in glycemic control among diabetic children.

Keywords: Type 1 Diabetes, HbA1c, Vitamin D

INTRODUCTION

Type 1 diabetes mellitus is a common endocrine disorder in children and are at high risk of complications like diabetic ketoacidosis if not managed well.[1] Diabetes mellitus is one of the leading public health concerns in the current times. The prevalence of diabetes mellitus in children has also increased specially in developed countries.[2] It is estimated that around 96,000 children develop diabetes mellitus every year.[3] It is estimated that India harbours around 97,700 children living with type 1 diabetes mellitus.[4] Evidences have revealed that 1,25(OH)2D3 is closely related to the occurrence of autoimmune diseases. It has been shown that vitamin D inhibits inflammatory and immune reaction, enhances the synthesis, secretion of insulin and insulin sensitivity.

Studies have revealed that vitamin D deficiency has an influence on T1DM occurrence, progression to complications.[5] There has been evidence that vitamin D helps in prevention of pancreatic islet cell death and it modifies beta cell function.[6]

Vitamin D deficiency is prevalent among diabetic children and known to have an impact on glycaemic control which suggests the possible role of vitamin D supplementation to diabetic children to have a better glycaemic control.[7] Although the role of vitamin D in T1DM and the association between vitamin D supplementation on glycaemic control has been extensively studied among many population groups, not many studies are available regarding this in India particularly in south India. So, this study is of relevance that is evaluating the levels of vitamin D among paediatric patients with T1DM in comparison with age and gender matched controls in general paediatric population and effect of vitamin D supplementation on glycaemic control among vitamin D deficient diabetic children.

METHODS

A comparative study conducted at Cheluvamba hospital, a tertiary care centre in Mysuru for a period of 14 months from March 2020 to July 2021. Children aged less than 18 years of age diagnosed as Diabetes Mellitus according to ISPAD 2018[3] were included as cases and non-diabetic children aged less than 18 years admitted to Cheluvamba hospital were included as controls. Children who were on vitamin D supplementation, antiepileptic drugs and has taken vitamin D in the past one year and children with chronic liver and kidney disease were excluded from the study. Serum vitamin D levels, renal function tests and liver function tests were done in all children. Serum 25(OH) D levels are interpreted as Per IAP guidelines as >20 ng/ml sufficient, 12-20 ng/ml insufficient, <12 ng/ml deficient.[8] Serum vitamin D deficient and insufficient study population are supplemented with oral vitamin D (granules) of 60,000 IU weekly for 6 doses followed by daily maintenance dose of 600 IU/day for a period of 3 months.[8] HbA1c levels were done in diabetic children who are vitamin D deficient and insufficient. Vitamin D is supplemented as mentioned above for 3 months. HbA1c levels are repeated after 3 months after the completion of the treatment. Compliance of insulin injections during the period of vitamin D supplementation is ensured by Insulin chart provided to the patient and periodic phone call. A sample size of 60 Diabetic children were taken up for the study which is calculated based on the prevalence of 4% of diabetes amongst children attending Cheluvamba hospital, at 0.05 significance level. Written informed consent were taken from parents. Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Chi-square test or Fischer's exact test (for 2X2 tables only) was used as test of significance for qualitative data. Independent t test was used for qualitative data.

RESULTS

The mean age of diabetic children was 12.4±4.46 years with a male to female ratio of 1:0.8. Among diabetic children, there were 16 children who belonged to the age group of 1-9 years and 44 children belonged to age group of 10-18 years. Among non-diabetic children, there were 16 children who belonged to the age group of 1-9 years and 44 children belonged to the age group 10-18 years (p value=1.00) (Table 1).

Table 1: Distribution of subjects according to age among diabetic children and non-diabetic children.

Variables		Age (years)		
		1-9	10-18	Total
Diabetic	N	16	44	60
	%	50.0	50.0	50.0
Non diabetic	N	16	44	60
	%	50.0	50.0	50.0
Total	N	32	88	120
	%	100.0	100.0	100.0

The mean age at presentation of diabetes among diabetic children with normal vitamin D levels were 11.62±3.8 years whereas in children with low vitamin D levels were 13.52±4.44 years (p value 0.08) (Table 2).

Table 2: Comparison of mean age at presentation (years) of diabetes according to vitamin D levels.

Vitamin D		Age (years)
Normal vitamin D	Mean	11.62
	SD	3.822
Low vitamin D	Mean	13.52
	SD	4.44
Total	Mean	12.42
	SD	4.462

Among Diabetic children, 65% (39) had normal vitamin D levels and 35% (21) had low vitamin D levels. Among non-diabetic children, 75% (45) had normal vitamin D levels and 25% (15) had low vitamin D levels (p value 0.231).

Table 3: Distribution of subjects according to vitamin D levels among diabetic children and non-diabetic children.

Variables		Status		
		Diabetic	Non-diabetic	Total
Normal vitamin D	N	39	45	84
	%	65.0	75.0	70.0
Low vitamin D	N	21	15	36
	%	35.0	25.0	30
Total	N	60	60	120
	%	100.0	100.0	100.0

Among diabetic children mean vitamin D levels were found to be 21.667±7.9 ng/ml which were statistically significant compared to the control group that is 25.90±10.06 ng/ml (p=0.012) but there was no clinical significance (Table 4). Among the diabetic children the mean dose of insulin requirement in vitamin D deficient children was 1.170±0.28 u/kg/day and 1.17±0.33 u/kg/day among children with normal vitamin D levels (p value=0.861) (Table 5).

Table 4: Comparison of mean vitamin D levels among diabetic children and non-diabetic children.

Variables	Mean	SD
Diabetic children	21.661667	7.9757916
Non-Diabetic children	25.906667	10.0677513
Total	23.784167	9.2917239

Table 5: Comparison of mean insulin dose according to vitamin D levels.

Vitamin D		Insulin Dose (U/kg/day)
Normal vitamin D	Mean	1.17
	SD	.33
Low vitamin D	Mean	1.17
	SD	0.28

The mean duration of Diabetes among children with normal vitamin D levels was 47.21±39.77 months and among vitamin D deficient children was 64.5±37.9 months (p value=0.10) (Table 6).

Table 6: Comparison of duration of DM in months according to vitamin D levels.

Vitamin D		Duration of DM
Normal Vitamin D	Mean	47.21
	SD	39.779
Low Vitamin D	Mean	64.5
	SD	37.9
Total	Mean	53.27
	SD	37.522

Among the diabetic children the mean HbA1c before supplementation of vitamin D was 11.782±2.22% and 11.73±2.19% among vitamin D insufficient diabetic children (p=0.141). And the mean HbA1c after supplementation of vitamin D were 11.74±1.18% and 11.71±1.17% (p=0.662) among vitamin D deficient children (Table 7).

Table 7: HBa1c levels among diabetic children before vs after vitamin D supplementation.

Levels	Before		After		P value
	Mean	SD	Mean	SD	
Sufficient	11.78	2.22	11.73	2.19	0.141
Deficiency	11.74	1.18	11.71	1.17	0.662

Among vitamin D deficient diabetic children, mean insulin dose requirement before vitamin D supplementation was 1.17 ±0.18 and after supplementation was 1.17±0.18 (p=0.9) (Table 8). Among diabetic children with normal vitamin D levels, 2.6% (1) had less than 30 minutes of sunlight exposure per day, 97.4% (38) had more than 30 minutes of sunlight exposure per day. Among diabetic children with low vitamin D levels 100% (21) had less than 30 minutes of sunlight exposure per day (p=0.00) (Table 9).

Table 8: Mean insulin dose requirement among vitamin D deficient children before and after supplementation of vitamin D.

Variable	Before supplementation		After supplementation		P value
	Mean	SD	Mean	SD	
Mean insulin dose (U/kg/day)	1.17	0.18	1.17	0.18	0.9

Table 9: Duration of sunlight exposure among diabetic children with normal and low vitamin D levels.

Variables		Status		
		Normal vitamin D	Low vitamin D	Total
<30	N	1	21	22
	%	2.6	100	36
>30	N	38	0	38
	%	97.4	0.0	63.3
Total	N	39	21	60
	%	100	100	100

DISCUSSION

In our study, the study group (diabetic children) mean vitamin D levels were found to be 21.66±7.97 ng/ml which were statistically significant compared to the control group that is 25.90±10.06 ng/ml (p=0.012) but there was no clinical significance. According to IAP guidelines the cut off for vitamin D insufficiency was 20 ng/ml. since in our study, mean vitamin D levels were 21.66 ng/ml which was clinically not significant. In our study vitamin D deficiency was not prevalent among diabetic children compared to the healthy children and among the diabetic children 35% (21) were vitamin D deficient and 65% (39) had normal vitamin D status. Another study conducted by Nwosu et al[9] 2014, showed mean vitamin D level 21.5l±5.8 ng/ml (p<0.001), although this result was similar to our study, in this study the cut off considered for vitamin D sufficiency, insufficiency and deficiency were different from our study. In this study vitamin D supplementation was done to all the diabetic children with vitamin D levels <30 ng/ml. Hence this showed that there was increased prevalence of vitamin D deficiency among diabetic

children. Glycemic control is the main stem in the management of Diabetes Mellitus and knowing the various factors that would influence the glycemic control is of paramount importance in our clinical practice. We studied the effect of vitamin D supplementation on glycemic control in vitamin D Deficient Diabetic children. The mean HbA1c was 11.7±1.18% and 11.71±1.17% before and after vitamin D supplementation (p=0.66), it did not show any improvement in HbA1c following vitamin D supplementation once a week for 6 weeks at a dose of 60,000 IU. There are many factors that influence the HbA1c levels in diabetic children. The most important one being duration of diabetes. If child is in the initial part of the disease, there may be residual beta cell function and function of insulin secretion may be still present and some children may be in the later stage of the disease spectrum where beta cells are already been destroyed and requiring relatively high exogenous insulin, which could be influencing the glycemic control and the categorization of such subjects would be difficult. Another being presence of various insulin preparations in the market. In our set up, insulin preparations were prescribed as per the child and respective parents preference considering age and child's attendance to school. So non standardized insulin regimen would be a confounding factor that may influence the glycemic control. Non standardized insulin dose and insulin preparations could be the reason in current study for no improvement in glycemic control. In our study we also assessed other parameters such as, mean duration of Diabetes, number of hospitalizations for glycemic control, age at presentation and insulin dose requirement in relation to low vitamin D levels. However, in the current study none of these parameters were statistically significant when compared to the Diabetic children with normal vitamin D levels.

A similar study conducted by Silvia et al[7], A cross sectional study which involved 141 T1DM patients. The mean HbA1c levels before supplementation was 11.4±2.1% and after supplementation was 8.3±1.3%. This study suggested that the complications such as DKA was more in vitamin D deficient children and children with low vitamin D showed higher daily requirement and thus proving that low vitamin D has generalized impact on metabolic status and glycemic homeostasis, thus considering vitamin D supplementation is helpful. Another study conducted by Sharma et al conducted at JIPMER a tertiary care hospital, Southern India which included 52 children aged 1-18 years with T1DM with 26 participants each in the intervention and standard of care arm.[10] Oral Vitamin D therapy was given once in a month for six months along with insulin in intervention arm while only insulin was given to the other arm. Oral vitamin D therapy was administered once a month for 6 months in addition to insulin. The mean HbA1c levels before supplementation was and after supplementation of vitamin D was 10.2±2.5% and 9.8±1.8% respectively (p=0.147) thus indicating that there is no significant decrease in HbA1c levels following vitamin D supplementation. This result was consistent with present study result that there is no role of vitamin D in glycemic control in vitamin D deficient diabetic children. Further prospective studies in India are required to evaluate the long term effect of vitamin D supplementation on glycemic control in diabetic children with a standardized insulin regimen and standardized vitamin D cut off criteria and vitamin D supplementation regimen and long term follow up of such patients in order to confirm the benefits of supplementation of vitamin D in these children as glycemic control is an important aspect in management of Diabetes and thus helping in preventing long term complications and mortality associated with it. Also, vitamin D therapy is an inexpensive and cost-effective tool which would be helpful especially in developing countries like India.

Limitations

Limitations of current study were use of different types of insulin analogues by the diabetic children, further follow up for 6-9 months may have provided more insights into the glycemic control.

CONCLUSION

There was no increased prevalence of vitamin D deficiency among children with type 1 diabetes mellitus as compared to age and sex matched controls. There was no decrease in mean HbA1c levels following vitamin D supplementation among vitamin D deficient type1 diabetes mellitus children.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Patterson CC, Karuranga S, Salpea P. Worldwide estimates of incidence, prevalence and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019;157:107842.
2. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020;10(1):14790.
3. Mayer-Davis EJ, Kahkoska AR, Jefferies C. ISPAD clinical practice consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents. Pediatr Diab. 2018;19(27):7-19.
4. Kumar KM. Incidence trends for childhood type 1 diabetes in India. Indian J Endocrinol Metab. 2015;19(1):S34-5.
5. Liu C, Wang J, Wan Y. Serum vitamin D deficiency in children and adolescents is associated with type 1

diabetes mellitus. Endocr Connect. 2018;7(12):1275-9.
6. Daljabri KS, Bokhari SA, Khan MJ. Glycemic changes after vitamin D supplementation in patients with type 1 diabetes mellitus and vitamin D deficiency. Ann Saudi Med. 2010;30(6):454-8.
7. Savastio S, Cadario F, Genoni G. Vitamin D deficiency and glycemic status in children and adolescents with type 1 diabetes mellitus. PLoS One. 2016;11(9):e0162554.
8. Khadilkar A, Khadilkar V, Chinnappa J. Prevention and Treatment of Vitamin D and calcium deficiency in children and adolescents: Indian academy of pediatrics (IAP) Guidelines. Indian Pediatr. 2017;54(7):567-73.
9. Nowasu BU, Maranda L. The effects of vitamin D supplementation on hepatic dysfunction, vitamin D status, vitamin D status, and glycemic control in children and adolescents with vitamin D deficiency and either type 1 or type 2 diabetes mellitus. PLOS one. 2014:9(6):e99646.
10. Sharma S, Biswal N, Bethou A. Does Vitamin D supplementation improve glycaemic control in children with type 1 diabetes mellitus? - a randomized controlled trial. J Clin Diagn Res. 2017;11(9):SC15-7.

Cite this article as: Srinivas CNS, Ramaraj SM. Evaluation of serum vitamin D levels in diabetic children and the effect of vitamin D supplementation on glycemic control (Hba1C) in vitamin D deficient diabetic children. Int J Contemp Pediatr 2022;9:834-8.