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Effect of Vitamin D Supplementation on Glycemic Control in Children with Type 1 Diabetes Mellitus at Tertiary Care Centre in North-Western India: A Prospective Observational Study

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Abstract

Introduction: Vitamin D deficiency may influence diabetes risk and management, yet conflicting evidence about its efficacy necessitates further investigation. This study aims to assess the therapeutic benefits of vitamin D supplementation in Type 1 Diabetes Mellitus (T1DM) with vitamin D deficiency.

Method: This prospective hospital-based observational study was conducted in pediatrics department of tertiary care centre over one year. Children ≤14 years old with T1DM and vitamin D deficiency (25-OHD levels <30 ng/ml) were randomly assigned to two groups. Interventional group received 4000 IU of vitamin D daily and calcium intake of 1200 mg/day with insulin therapy for 3 months. Control group continued routine insulin therapy alone. Random Blood Sugar (RBS), glycosylated Hemoglobin (HbA1c), and 25-OHD levels were measured at enrolment and completion. Statistical analysis was performed using appropriate tests.

Results: Out of 60 screened children, 10 were excluded (7 with normal vitamin D levels, 2 lost to follow-up, 1 with abnormal renal function). The baseline characteristics were comparable across groups. The majority of participants (58%) were above 10 years old. Most children (64%) were severely vitamin D deficient. In the interventional group, HbA1c levels decreased significantly in the severely deficient subgroup (p=0.037). RBS values decreased significantly in the severe (p=0.046) and suboptimal (p=0.001) 25-OHD deficiency subgroups, though not in the very severe subgroup (p=0.765).

Conclusion: Vitamin D and calcium supplementation significantly reduce blood glucose and HbA1c levels in T1DM compared to insulin alone. Routine screening and supplementation are advised but should be confirmed by larger randomized controlled trials.

Keywords: Type 1 Diabetes Mellitus (T1DM); Vitamin D Deficiency; Haemoglobin A1c (HbA1c); Vitamin D Supplementation; Children; Glycemic control

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Introduction

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, exists in various forms, with Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM) being the most prevalent. T1DM primarily results from insulin deficiency due to pancreatic beta cell damage, often triggered by autoimmune processes [1]. T1DM predominantly affects children; Its incidence in adults is noteworthy, indicating a global health concern. The prevalence of T1DM has been steadily rising, with substantial numbers being diagnosed annually worldwide. Factors such as genetic predisposition and environmental triggers play pivotal roles in its pathogenesis [2].

The effects of vitamin D on organs other than skeletal system is also known in recent time by finding specific receptors in many tissues, including pancreatic β cells and immune cells. The main action of vitamin D is exerted into the cell nucleus by regulating the transcription of around 3% of the human genome [3]. Studies have implicated that Vitamin D (25-OHD) deficiency as a potential environmental factor contributing to T1DM onset and progression and management [4].

The diagnostic criteria for diabetes mellitus include hyperglycemic symptoms along with elevated plasma glucose levels or Haemoglobin A1c (HbA1C). Despite advances in understanding diabetes patho-physiology, achieving optimal glycemic control remains a challenge, predisposing patients to acute and chronic complications2. Co-morbid conditions like vitamin D deficiency complicate glycemic management, warranting further investigation. Studies have correlated low vitamin D levels with increased insulin resistance, emphasizing

its potential role in diabetes management. Research suggests that vitamin D supplementation could enhance insulin sensitivity and improve glycemic control in diabetic individuals, offering a promising adjunctive therapy [5,6]. Conflicting evidence regarding the efficacy of vitamin D supplementation necessitates comprehensive clinical trials to elucidate its therapeutic benefits in T1DM. So the current study was conducted with the objective to know the impact of vitamin D supplementation on glycemic control in children with type 1 diabetes having low vitamin D status.

Material & Methods

This was a hospital based prospective observational study, conducted at the department of pediatrics of a tertiary care hospital in Northwest India from November 2021 to October 2022. The study was approved by the institutional ethics committee and children/parents were explained about the study in detail and a written informed consent was obtained. The inclusion criteria was children below 14 years with the diagnosis of type 1 Diabetes Mellitus along with low vitamin D status. Children with T2DM or those with history of past or current liver diseases, abnormal renal function, malabsorptive disorders and who were already receiving vitamin D or calcium, were excluded. Sample size was calculated to 60 on the basis of a study conducted by Abdulmoein E Al-Agha et al that 77% of the diabetic patients had reduced the level of vitamin D [7].

All the demographic details along with the detailed history e.g. duration of T1DM, type of insulin with dose and any complication/co-morbid condition were noted in a predesigned proforma. At the initiation of study, baseline Fasting Blood Sugar (FBS), glycosylated hemoglobin (HbA1c) and 25-OH vitamin D (25-OHD) levels were documented. 25-OHD levels were assessed by Chemiluminescent Immunoassay (CLIA) method. HbA1c levels were measured by the High Performance Liquid Chromatography (HPLC) using a variant machine. Patients with vitamin D levels less than 30 ng/ml were considered low and were further subdivided into three subgroups: very severe (<10 ng/ml), severe (10-19 ng/ml) and suboptimal (20-29 ng/ml) vitamin D deficient and were given 4000 IU of 25-OHD daily and a total calcium intake of 1200 mg/day along with their routine insulin therapy for 3 months. After 3 months, FBS and HbA1c were reassessed.

After collecting data, they were entered into excel sheet. All statistical analyses were performed using SPSS version 22.0 (SPSS, Inc., Chicago, IL, USA). Data were expressed as mean± Standard Deviation (SD), or percentages, as appropriate. The Kolmogorov-Smirnov test was used for assessment of normality of data distribution. Because the data were normally distributed, t-test was used to compare differences before and after receiving vitamin D. For continuous variables, differences were compared using nonparametric Mann-Whitney U test and χ^2 test for categorical variables. The difference between groups was considered significant when p value was <0.05.

Results

In the current study total 60 type 1diabetes mellitus children were screened. 25-OH vitamin D was documented to be low in 53 (88%) children. One child was further excluded due to deranged renal profile. During follow up 2 children were lost to follow up (Figure 1). Final analysis was done for 50 children. Maximum 29 (58%) cases were from above 10 years old followed by 18 (36%) from 6 years -10 years age and 3 (6%) from below 5 years age group. Mean age was 10.16 ± 2.8 years and male to female ratio was 1:1.17. Thirty four (68%) were from rural area and 16 (32%) were from urban area (Table 1).

Demographic variable		**Total**	
		No.	**%**
Age Group (in years)	≤5	3	6
	06-Oct	18	36
	>10	29	58
	Mean ± SD	10.16 ± 2.8	
Gender	Female	27	54
	Male	23	46
Geographical location	Rural	34	68
	Urban	16	32
Total		50	

***Table 1*:** The demographic details of the study groups.

Maximum children 32 (64%) were severely 25-OHD deficient, 13 (26%) were with suboptimal 25-OHD levels and 5 (l%) were very severely 25-OHD deficient with mean 25-OHD levels 14.8±5.9ng/ml (Table 2). There was no particular correlation found between severity of vitamin D deficiency and initial HbA1c values (Table 3). There was no correlation found between duration of insulin treatment and initial 25-OH vitamin D levels.

25-OH Vitamin D	**Total**	
(ng/ml)	**No.**	**%**
<10(very severe)	5	10
10-19 (severe)	32	64
20-29 (suboptimal)	13	26
Total	50	
Mean ± SD	14.8 ± 5.09	

***Table 2*:** Number of cases according to severity of Vitamin D deficiency.

25-OH D (mg/ml)	**Initial HbA1c (gm %)**	**After 3 months HbA1c (gm %)**	**P**
	Mean ± SD	**Mean ± SD**	
<10 (very severe)	17.23 ± 2.19	14.77±2.83	0.021*

10-19 (severe)	11.61±3.02	10.16±1.90	0.037*
20-29 (suboptimal)	14.80±1.86	15.27±0.98	0.073
Note: *for p value which was considered significant <0.05.			

***Table 3*:** Comparison of HbA1c at initial and at the end of study.

In very severe 25-OHD deficient children mean HbA1c decreased statistically significant from 17.23 ± 2.19 gm% to 14.77± 2.83 gm% (p=.021) In severely 25-OHD deficient cases, mean HbA1c decreased statistically significant from 11.61 ± 3.02 gm% to 10.16 ± 1.90gm% (p=0.037). In suboptimal 25-OHD children, mean HbA1c did not alter statistically significant from 14.80±1.86 gm % to 15.27 ± .98 gm % (Table 3).

In severe 25-OHD deficient children, mean FBS was significant decreased from 175.56 ± 46.07mg/dl to 154.81 ± 40.53 mg/dl (p=0.002). In suboptimal 25-OHD deficient, mean FBS was statistically significant decreased from 273.33 ± 2.58 mg/dl to 130.33 ± 31.50 mg/dl (P=0.001) while it was increased in FBS from 152.67 ± 33.23 mg/dl to 170.66 ± 0.58 mg/dl (statistically not significant, p=0.454) in very severe 25-OHD deficient cases (Table 4).

25-OH vitamin D (ng/ml)	**Initial FBS (mg/dl)**	**After 3 months FBS (mg/dl)**	**P**
	Mean ± SD	**Mean ± SD**	
<10 (very severe)	152.67 ± 33.23	170.66 ± 0.58	0.454
10-19 (severe)	175.56 ± 46.07	154.81 ± 40.53	0.002*
20-29 (suboptimal)	227.33 ± 2.58	130.33 ± 31.50	0.001*
Note: *for p value which was considered significant <0.05.			

***Table 4*:** Comparison of fasting blood sugar at initial and at the end of study.

Discussion

In our study, out of total 60 cases, 53 (88%) cases were 25-OH vitamin D deficient. Our results are in line with observations reported by Abbas et al who observed that 84% of TIDM children were vitamin D deficient [8].

We found, maximum cases from above 10-year age group. Incidence of T1DM increases with age specially in adolescence age group due to hormonal changes during this period. Similar observations are reported by other authors like Beck-Nielsen and Karvonen et al who also reported diabetes mellitus increases in childhood with age, with highest incidence during the 10-14 years age group [9,10]. However, Engelen et al observed in their study that incidence rate of type 1 diabetes mellitus was highest in 0-4 years age group children [11]. The difference between the studies may be due to the geographical and genetic variations between the study populations.

Gender distribution of patients was almost equal, with a male to female ratio of 1:1.17, indicating no significant gender difference in the incidence of T1DM (p>0.05). This result is consistent with the findings of Dahlquist et al who reported an equal impact of T1DM on both genders [12]. We observed a higher percentage of cases from rural areas (68%), which can be attributed to the study's setting in a government hospital and the predominantly rural population of India. This distribution was similar in both groups.

The most common observation in our study was severe 25-OHD deficiency (64%), followed by suboptimal levels (26%) and very severe deficiency (10%) with mean 25-OHD levels 14.80ng/ml. Our findings align with those of Bener et al [13]. However, our results differ from those of Svoren et al, who observed that 80% of cases had suboptimal levels, while 20% had levels below 20ng/ml [14]. Similarly, Abbas et al found that 64% of cases fell into the suboptimal level group [8].

A significant correlation was observed between vitamin D deficiency and HbA1c levels. Mean HbA1c levels were highest in the very severe deficiency and lowest in the severe deficiency group. This finding highlights the potential impact of vitamin D on glycemic control, although no specific correlation was found between the severity of vitamin D deficiency and HbA1c values. These results align with Buhary et al who reported an inverse correlation between serum 25-OH vitamin D levels and HbA1c values [15].

Significant decreases in mean FBS values were observed after vitamin D, calcium, and insulin supplementation, particularly in the severely deficient and suboptimal groups. These findings support the potential benefit of vitamin D supplementation in improving glycemic control, consistent with the results of Mirhosseni et al [16]. Our results are in line with the study by Foroughi et al that concluded marginally significant decrease in fasting blood glucose values [17]. Our results differ from the observations of Krul-Poel et al a randomized placebo-controlled trial, found no effect on fasting blood sugar values after 6 months supplementation with vitamin D in type 2 diabetes mellitus patients [18].

We observed significant reductions in HbA1c values were noted in the very severe and severely deficient 25-OHD subgroups. This supports the findings of studies by Aljabri et al, Hafez et al and Mohammad et al, who reported improvements in HbA1c after vitamin D supplementation in T1DM children [6,19,20]. Similarly, Buhari et al, observed lowering of HbA1c values after vitamin D supplementation for 3 months in type 1 and type 2 diabetes mellitus patients [15]. Our results also differ from observations reported by Arjumand et al in their randomized controlled double blinded clinical trial, they observed no change in HbA1c value after vitamin D supplementation for 3 months in with vitamin D deficiency [21].

There are some limitations of our study such as small sample size. Beside this the result could have been more impactful if we would have supplemented different dosage of vitamin D based on their base line vitamin D status. Further studies with comparison of the glycemic control after supplementation of

vitamin D versus glycemic control in vitamin D non deficient children are required to know the exact role of vitamin D supplementation.

Conclusion

Vitamin D deficiency is common in children with type 1 diabetes mellitus. Our study confirms that supplementing vitamin D and calcium with insulin significantly reduces blood glucose and HbA1c levels compared to insulin alone. Routine screening and supplementation are recommended but should be validated by larger double-blind randomized trials.

Ethics approval

The ethics committee, Sardar Patel Medical College Bikaner issued approval no15373.

Author's contributions

VS contributed in plan of study, clinical examination, sample & data collection, interpretation. VK analyzed and interpreted the patient data. PK was a major contributor in writing the manuscript. PKD was a major contributor in writing the manuscript and editing. RKS contributed in plan of study, sample & interpretation of data. DM collected and interpreted the patient data with proof reading. All authors read and approved the final manuscript.

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