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Original Research Article

Status of Vitamin D Level in Children with Sickle Cell Disease: A Hospital Base Case Control Study

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Abstract:

Background: Sickle cell disease (SCD) is one of the most prevalent genetic disease in several countries. Individuals living with sickle cell disease (SCD) reportedly have a high prevalence of vitamin D deficiency. Vitamin D is a group of fat soluble secosteroids responsible for increasing intestinal absorption of calcium, magnesium, & phosphate & having multiple other biological effects. For better understanding the magnitude of vitamin D deficiency among children populations with SCD, and whether the prevalence is higher among those with SCD compared with similar children without SCD, present study was carried out to know the status of vitamin D level in children having sickle cell disease and the impact of deficiency in the affected children.

Methods: This was a hospital-based analytic study carried out over 12 months from June 2018 to –May 2019 in the department of pediatrics, of a tertiary care hospital, Assam. For Cases, all Diagnosed case of Sickle Cell Disease by HPLC who fulfill the inclusion criteria, after taking informed, written consent was selected and detailed history, clinical examination and relevant laboratory investigations was done. For Controls, Children without Sickle Cell & other haemolytic disease & who is age, sex & nutritional status matched as controls was taken and the Case control ratio is 1:2. The received data like age, gender, and socioeconomic status, age of diagnosis of disease, number of times blood transfusion received, presenting features, and anthropometric findings was recorded in predesigned proforma.

Results: Out of 50 cases of sickle cell children, 42% (21) were sufficient vitamin D level (≥30 ng/mL), 24% (12) were insufficient vitamin D level (20-29 ng/mL) and 34% (17) were having deficient vitamin D level (<20ng/mL) While 90% (90) of the controls showed sufficient vitamin D level, 10% (10) showed insufficient vitamin D level. None of the cases or controls showed toxic level of vitamin D. The difference of vitamin D level between the sickle cell disease patient and controls was statistically significant with p value of<0.001, with the mean value of vitamin D among cases being 31.02±16.54 ng/mL and among controls being 48.05±14.45 ng/mL

Conclusion: The study demonstrates a significant level of vitamin D deficiency in SCD children as compare to the control. So it is recommended that vitamin D supplementation should be given to these patients in an adequate dose and for adequate duration. As most of these patients belong to the lower socioeconomic class so the vitamin D solutions should be supplied to these patients free of cost.

Keywords: Sickle Cell Disease, Vitamin D Deficiency.

Introduction

Sickle cell disease (SCD) is one of the most prevalent genetic disease in several countries. [1,2] SCD occurs when a person inherits two abnormal copies of haemoglobin gene in chromosome 11, one from each parent. Several subtypes exist depending upon the exact mutation in each haemoglobin gene.

Sickling of Red Blood Cell set off by the temperature changes, stress, dehydration & high altitude. At present, the majority of patients with SCD live at least until mid-adulthood. Although life expectancy in India is unknown, it is likely to be around 40 to 50 years, which is similar to that described in other countries. [3] In addition, many advances achieved in recent years in the management of these patients have increased significantly their quality of life. [4,5] Thus, different lines of research in this disease are open today to move forward in providing the best care for patients and decreasing their morbidity and mortality.

Vitamin D is a group of fat soluble secosteroids

responsible for increasing intestinal absorption of calcium, magnesium, & phosphate & having multiple other biological effects. Vitamin D (25-hydroxyvitamin D) deficiency has emerged as a public health focus in recent years for its contribution to adverse skeletal and extra-skeletal manifestations. [6] Moreover, individuals living with sickle cell disease (SCD) reportedly have a high prevalence of vitamin D deficiency. [7] Race, age, body mass index (BMI), latitude, diet, sunlight exposure, and skin pigmentation are all factors influencing vitamin D status.8 In addition to its effects on bone health vitamin D deficiency has been linked to multiple health conditions including cardiovascular disease, asthma, nephropathy and chronic pain. [9-15] Patients with SCD are susceptible to all of these complications although it is unclear to what extent vitamin D deficiency is a contributing causal factor [16,17]. Vitamin D deficiency is now recognized as one of the most common nutritional conditions among persons with SCD [18]. For better understanding the magnitude of vitamin D deficiency among children populations with SCD, and whether the prevalence is higher among those with SCD compared with similar children without SCD, is that vitamin D can be reliably and inexpensively treated, making it a prime intervention to potentially improve health outcomes. So this present study is carried out to know the status of vitamin D level in children having sickle cell disease and the impact of deficiency in the affected children.

Material and Methods

This was a hospital-based analytic study carried out over 12 months from June 2018 to –May 2019 in the department of pediatrics, of a tertiary care hospital, Assam. The study was conducted after the approval from the Institutional Ethics Committee.

For Cases, all Diagnosed case of Sickle Cell Disease by HPLC attending Department of Paediatrics, Assam Medical College & Hospital during study period who fulfill the inclusion criteria, after taking informed, written consent was selected and detailed history, clinical examination and relevant laboratory investigations was done.

For Controls, Children without Sickle Cell & other haemolytic disease & who is age, sex & nutritional status matched as controls was taken and the Case control ratio is 1:2. The received data like age, gender, and socio economic status, age of diagnosis of disease, number of times blood transfusion received, presenting features, and anthropometric findings was recorded in predesigned proforma.

Blood was obtained by venipuncture & collected in dry tube (CLOT ACCTIVATOR VIAL for serum vitamin D & serum ferritin estimation, & K3 EDTA vial for haemoglobin percentage). Vitamin D level was estimated using the ELISA kit for vitamin D (BioDetect, cat# 1073) Reference value of Vitamin D was taken as per US Endocrine Society Classification 2015: Deficiency < 20 ng/ml , Insufficiency 20-29 ng/ml , Sufficiency ≥30 ng/ml, Toxicity >150 ng/m.

The statistical analysis of data was performed using the computer program, Statistical Package for Social Sciences (SPSS for Windows, version 20.0. Chicago, SPSS Inc.) and Microsoft Excel 2010. Results on continuous measurements are presented as mean ± standard deviation are compared using student t test. Discrete data are expressed as number (%) and are analysed using Chi square test and Fischer‘s exact test (where the cell counts were <0.05)

Results and Observations

The present study comprised of 50 cases of sickle cell disease children & 100 controls which fulfill the inclusion criteria. The study was conducted in the Department of Pediatrics, Assam Medical College and Hospital, Dibrugarh, for a duration of 1 (one) year, from June 2018 to May 2019. The study was undertaken to determine the status of Vitamin D in children with sickle cell disease and to find out the factors involved in the variability of Vitamin D levels in that population.

Out of the 50 sickle cell disease children included, 64% (32) of the cases were males, 36% (18) of the cases were females. Out of 100 controls, 58% (58) of the controls were males and 42% (42) of controls were females with male: female ratio of cases 1.78:1 and that of controls were 1.38:1 (fig-1).

Although there is no sex preponderance seen in sickle cell disease, there is a slight male preponderance seen in this study as 64% (32) of the included cases were males and 36% (18) of the included cases were females. In the study group , 2% (1) of the cases were in the age group <5 years and 98%(49)cases were in the age group 5-12 years and in control 3%(3) were in the age group <5 years and 97%(97) were in the age group 5-12 years . The mean age group of cases included in the study was 8.64±2.64 years and that of control was 8.56±2.64 years. Hence, majority of sickle cell disease children were belonged to age group of 5-12 years 62% (31) of the cases were diagnosed after 5 years of age, 38% (19) were diagnosed between 1-5 years of age and no cases were diagnosed before 1 year of age. Hence, majority of sickle cell cases in this study were diagnosed after 5 years of age with mean age of diagnosis being 6.48 ± 2.52 years.

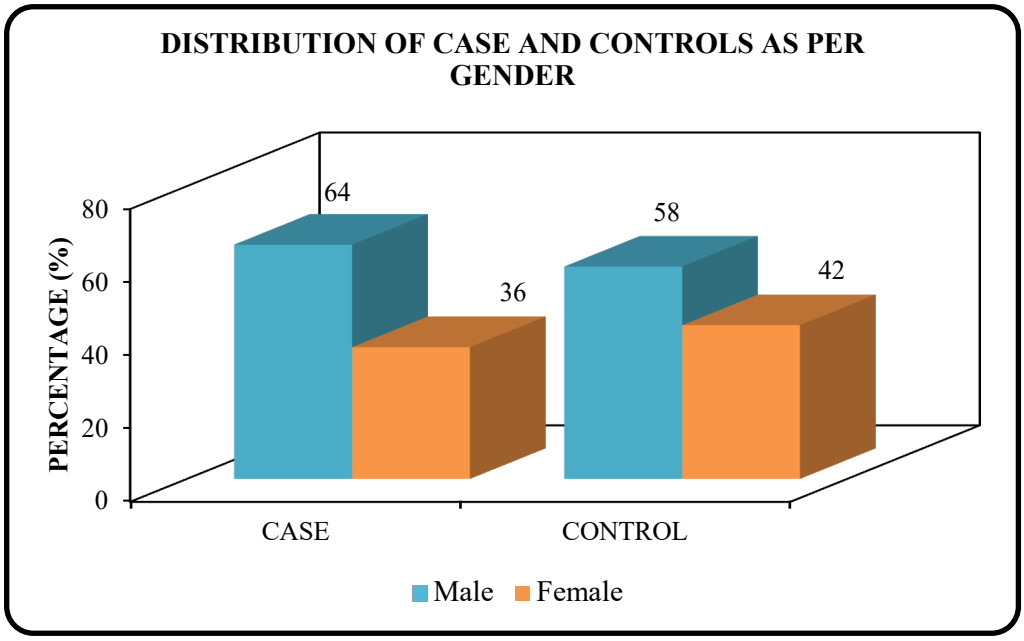

Figure 1: Distribution of case and controls as per gender

Out of 50 cases of sickle cell children, 42% (21) were sufficient vitamin D level (≥30 ng/mL), 24% (12) were insufficient vitamin D level (20-29 ng/mL) and 34% (17) were having deficient vitamin D level (<20ng/mL) While 90% (90) of the controls showed sufficient vitamin D level, 10% (10) showed insufficient vitamin D level. None of the cases or controls showed toxic level of vitamin D. The difference of vitamin D level between the sickle cell disease patient and controls was statistically significant with p value of<0.001, with the mean value of vitamin D among cases being 31.02±16.54 ng/mL and among controls being 48.05±14.45 ng/mL. (Table 1)

Table 1: Vitamin D level among Cases and Controls

Vitamin D Level(ng/mL)		Case		Control		P Value
		n	%	n	%	
Deficiency	<20	17	34.00	0	0.00	<0.001
Insufficiency	20–29	12	24.00	10	10.00	
Sufficiency	≥30	21	42.00	90	90.00	
Toxicity	>150	0	0.00	0	0.00	
TOTAL		50	100.00	100	100.00	
Mean±SD		31.02	16.54	48.05	14.45	

Out of 50 cases, 37.50% (12) of the males and 50% (9) females showed sufficient vitamin D level, 34.38% (11) of males and 33.33% (6) of the females showed deficient vitamin D status and 28.13% (9) of the males and 16.67% (3) of the females showed insufficient vitamin D level. None of the male or female showed toxic level of vitamin D. Mean vitamin D level among male was 31.01±16.86 ng/mL and among female was 31.04±16.43 ng/mL. The difference in the level of vitamin D among male and female was not statistically significant. (Table 3)

Table 3: Showing vitamin D level in both male and female in case and control

Vitamin D Level(ng/mL)		Females				P value
		Case		Control		
		n	%	n	%	
Deficiency	<20	6	33.33	0	0.00	0.000185
Insufficiency	20–29	3	16.67	4	9.52	
Sufficiency	≥30	9	50.00	38	90.48	
Toxicity	>150	0	0.00	0	0.00	
TOTAL		18	100.00	42	100.00	
Mean±SD		31.04	16.43	49.33	14.59	
Vitamin D Level(ng/mL)		Males				P value
		Case		Control		

		n	%	n	%	
Deficiency	<20	11	34.38	0	0.00	<0.001
Insufficiency	20–29	9	28.13	6	10.34	
Sufficiency	≥30	12	37.50	52	89.66	
Toxicity	>150	0	0.00	0	0.00	
TOTAL		32	100.00	58	100.00	
Mean±SD		31.01	16.86	47.12	14.40	

Out of 32 male cases, 34.38% (11) showed deficient level of vitamin D, whereas 37.5% (12) showed sufficient level of vitamin D and the rest 28.13% (9) showed insufficient level of vitamin D. Out of 58 male controls, none showed deficient level of vitamin D, whereas 89.66% (52) showed sufficient level of vitamin D and the rest 10.34% (6) showed insufficient level of vitamin D. The mean value of vitamin D among male cases was 31.01±16.86 ng/mL and that of male controls was 47.12±14.40 ng/mL. The difference between the levels of vitamin D among male participants (in cases and controls) was statistically significant with a p value of <0.001

Out of 18 female cases, 33.33% (6) showed deficient level of vitamin D, whereas 50% (9) had sufficient level of vitamin D and the rest 16.67% (3) had insufficient level of vitamin D. Out of 42 female controls, none showed deficient level of vitamin D, whereas 90.48% (38) showed sufficient level of vitamin D and the rest 9.52% (4) had insufficient level of vitamin D. The mean value of vitamin D among female cases was 31.04±16.43 and that of female controls was 49.33±14.59. The difference between the levels of vitamin D among female participants (in cases and controls) was statistically significant with a p value of 0.000185

We have study the association between vitamin D level and serum ferritin. We found that out of 50 cases, 31 cases (62%) showed serum ferritin level of <1000ng/ml the rest 19 cases (38%) showed serum ferritin level between 1000-2000 ng/ml. The overall mean level of serum ferritin among cases was 948.53±257.93 ng/mL. The mean value of vitamin D level among the group who showed serum ferritin level of < 1000 ng/ml was 36.34±17.88 ng/ml and that of the group who showed serum ferritin level of ≥1000 ng/mL was 22.35±9.15ng/mL. This difference between the mean values of vitamin D amongst these two groups was statistically significant p value of 0.012. (Fig – 2)

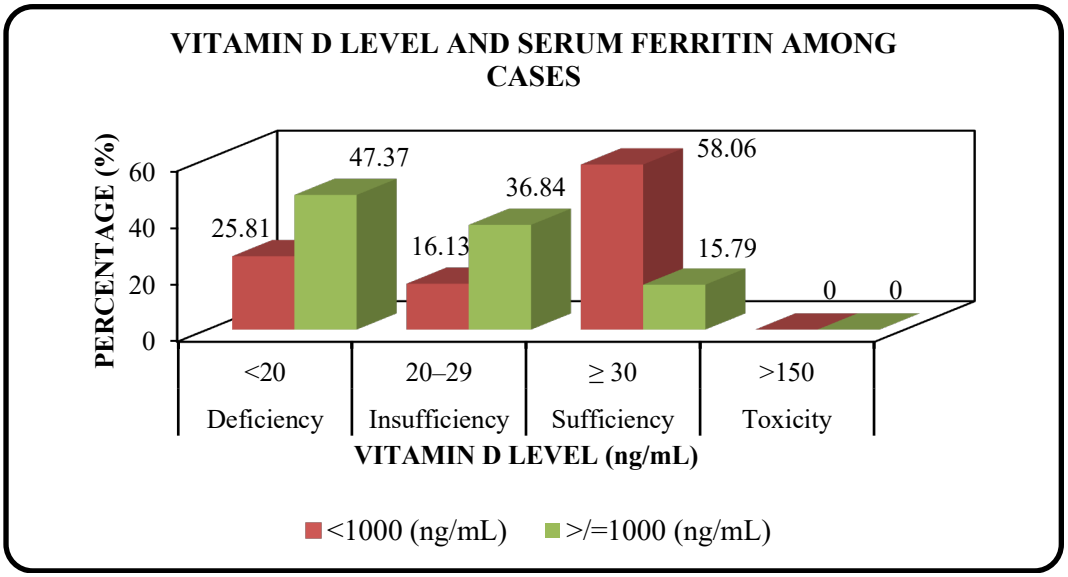

Figure 2: Vitamin D level and serum ferritin among cases

Discussion

The study evaluates the prevalence of vitamin D deficiency in 50 SCD children. Out of the all the cases taken 64% (32 cases out of 50) were males and 36% (18 cases out of 50) were females. Out of 100 controls taken 58% (58 controls out of 100) were males and 42% (42 cases out of 100) were females.

The ratio of male: female in case group was 1.78:1 and the ratio was 1.38:1 in the control group. In the study of Ahmed F et al the males constituted 55% of all cases and 87.5% of all controls. Whereas the females constituted 45% among the cases and 12.5% among the controls. [20] In our study out of 50 cases of sickle cell disease children, 42% (21) had sufficient vitamin D level (≥30 ng/mL), 24% (12) had insufficient vitamin D level (20-29

ng/mL) and 34% (17) had deficient level of vitamin D (<20ng/ml) but in controls 90% (90) showed sufficient vitamin D levels, whereas 10% (10) showed insufficient level of vitamin D. But none of the control showed deficient vitamin D level. None of the cases or controls showed toxic level of vitamin D. This result (vitamin D level between the sickle cell patients and controls) was statistically significant with a p value of <0.001.The mean value of vitamin D level was 31.02±16.54 ng/mL in cases and 48.05±14.45 ng/mL in controls. Similar Study by Buison et al, [21] found that children with sickle cell disease had significantly lower serum vitamin D concentrations than healthy children. Study by Mohammed et al. [22] also found that vitamin D levels were significantly lower in participants with SCD compared to healthy controls.

In our study, among cases, 37.50% (12 out of 32 cases) of the males and 50% (9 out of 18 cases) of the females showed sufficient vitamin D level. 34.38 % (11 out of 32 cases) of the males and 33.33% (6 out of 18 cases) of the females showed deficient vitamin D status and 28.13% (9 out of 32 cases) of the males and 16.67% (3 out of 18 cases) of the females showed insufficient vitamin D level. Mean vitamin D level among male cases was 31.01±16.86 ng/mL and among female was 31.04±16.43 ng/mL. The difference in level of vitamin D in males and females were not statistically significant in the case group. Among the controls, 89.66% (52 out of 58 controls) of males and 90.48% (38 out of 42 controls) of females were having sufficient level of vitamin D, 10.34% (6 out of 58 controls) of males and 9.52% (4 out of 42 controls) of females were having insufficient level of vitamin D. Mean vitamin D level among male control was 47.12±14.40 ng/mL and that of female control was 49.33±14.59 ng/mL. The difference in level of Vit D among males and females were not statistically significant in control group.

But when this was compared between case and control group taking same gender in consideration, it showed a significant difference. Out of 32 male cases, 34.38% showed deficient level of vitamin D, whereas 37.5% showed sufficient level of vitamin D and the rest 28.13% showed insufficient level of vitamin D. Out of 58 male controls, none showed deficient level of vitamin D, whereas 89.66% showed sufficient level of vitamin D and the rest 10.34% (6 of 58 controls) showed insufficient level of vitamin D. None of the male participant showed toxic level of vitamin D. The mean value of vitamin D among male cases was 31.01±16.86 ng/mL and that of male controls was 47.12±14.40 ng/mL. The difference between the levels of vitamin D among male participants (among case and control group) was statistically was statistically significant with a p value of <0.001.

When this was seen among females, almost similar results were obtained. Out of 18 female cases, 33.33% showed deficient level of vitamin D, whereas 50% had sufficient level of vitamin D and the rest 16.67% had insufficient level of vitamin D. Out of 42 female controls, none showed deficient level of vitamin D, whereas 90.48% showed sufficient level of vitamin D and the rest 9.52% had insufficient level of vitamin D. The mean value of vitamin D among female cases was 31.04±16.43 and that of female controls was 49.33±14.59. The difference between the levels of vitamin D among female participants (in cases and controls) was statistically significant with a p value of 0.000185. None of participant in the case or control group showed toxic level of vitamin D. In our study it was seen that the mean level of vitamin D was slightly in the higher range among cases of females as compared to males.

There were no previous studies showing the difference between vitamin D level among male and female participants.

The relationship between vitamin D level and serum ferritin level was studied among the cases. Out of total 50 cases, 62% (31 of 50 cases) showed serum ferritin level of <1000ng/mL of which 58.06% (18 cases) showed sufficient level of vitamin D, 25.81% (8cases) showed deficient level of vitamin D and 5 patients were having insufficient level of vitamin D. 19 patients of 50 cases showed serum ferritin level ≥1000ng/mL, out of which 47.37% (9cases) showed deficient level of vitamin D, 36.84% (7cases) showed insufficient levels and 15.79% (3cases) showed sufficient level of vitamin D.

The mean value of vitamin D between these two groups (serum ferritin of <1000ng/mL and ≥1000ng/mL) were 36.34±17.88ng/mL and 22.35±9.15ng/mL respectively. This result showed statistical significance with p value of 0.012. So as the transfusion load increases, the adverse effects related to iron overload also increases. Skin pigmentation due to iron deposition among these patients decreases the sunlight exposure and hence the vitamin D synthesis. So frequent blood transfusion leading to iron overload and increase in serum ferritin can be related to a deficient vitamin D status among sickle cell disease patients.

Conclusion

In this study we have found that the vitamin D levels are significantly low in sickle cell disease patients compared to those of controls. There is a clear difference of vitamin D levels among the different ethnic groups and those receiving more blood transfusions also showed lower vitamin D levels. Complications like abdominal pain, fever etc. are also more in those with low vitamin D levels.

So it is recommended that vitamin D supplementation should be given to these patients in an adequate dose and for adequate duration. As most of these patients belong to the lower socioeconomic class so the vitamin D solutions should be supplied to these patients free of cost. Also vitamin D level estimation cost should be decreased or made free.

Further stress should be given on the nutritional status of these children as poor nutrition is also believed to be a cause of vitamin D deficiency in these children. More studies should be conducted on this topic to evaluate other parameters associated with vitamin D deficiency in sickle cell disease patients.

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