



CO-MORBIDITY IN CHILDREN WITH SICKLE CELL DISEASE AND ITS RELATION TO THE VIT D STATUS: A HOSPITAL BASED STUDY.

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ABSTRACT

Aim: The present study was undertaken to find the prevalence of VDD among sickle cell children and to assess the association of co-morbidities with VDD.

Materials and Methods: Cross sectional study on 89 children who were attending a sickle cell clinic/admitted to paediatric wards of Medical college, Rajnandgaon were enrolled in this study. After their history, clinical examination, samples were taken for serum 25-hydroxy vitamin D ng/mL and calcium level assessment. The outcome was morbidity in sickle cell children in terms of number of pain episodes, number of febrile episodes, number of blood transfusions and total number of admissions.

Results: Out of 89 cases, 58 (65.17%) cases were deficient in vitamin D (<20 ng/dL), 22 (24.72%) cases had insufficiency (20-30 ng/dL) and 9 (10.11%) cases had normal vitamin D levels (>30 ng/dL). The mean vitamin D level was 19.42ng/dL. Morbidity in SCD was more in VDD children compared to vitamin D sufficient children with significance in the number of pain episodes and the total number of hospital admissions but not in the number of admissions for acute febrile illness or the total number of blood transfusions.

Conclusion: VDD was prevalent in 65.17% of children with SCD. Children between 4-12 years were more affected with a male predominance. As this study involved children with SCD alone, future studies need to be carried out involving children without SCD to establish a better possible link between vitamin-D and SCD morbidity.

Keywords: Sickle cell Disease (SCD), vitamin D deficiency (VDD), co-morbidities, Pain episodes.

INTRODUCTION

SCD is caused by a mutation in the beta-globulin haemoglobin gene, which results from an exchange of nitrogenous bases at the sixth codon, leading to the formation of abnormal haemoglobin known as haemoglobin S (HbS) (1). SCD is highly prevalent in India, particularly in the central and western regions, and carries a significant health burden (2). According to an Indian Council of Medical Research survey, approximately 20% of children with SCD die before the age of two, and 30% of children with SCD in the tribal community do not survive past adulthood (2,3). Children with sickle cell anaemia (SCA) face a higher risk of developing nutritional deficiencies, often linked to poor dietary intake, infectious complications, and other associated issues (4). Among these, vitamin D deficiency (VDD) is of particular concern in children with SCA, as they are more prone to developing VDD compared to healthy controls (6). This is attributed to factors such as high melanin content in

the skin, low physical activity levels, and reduced food intake (5). Calcium and vitamin D are essential for maintaining proper bone metabolism; inadequate calcium intake can lead to lower bone mass in children and adolescents with SCA, contributing to growth failure (7). VDD is also associated with an increased occurrence of respiratory infections, muscle weakness, and a heightened risk of falls and micro lesions (8). Additionally, SCD is a genetic disorder characterised by serious complications affecting multiple organ systems, such as periodic vaso-occlusive crises, chronic haemolysis, jaundice, infarcts, and acute chest syndrome (1). These vaso-occlusive crises arise from interactions between sickle red blood cells, inflammatory cytokines, and the endothelium. VDD may contribute to the pathogenesis of SCD due to its impact on endothelial dysfunction and cytokine activity (6). Patients with SCD often display elevated white blood cell counts, abnormal activation of granulocytes, monocytes, and endothelial cells, along with increased levels of various inflammatory mediators. Importantly, SCD is an inflammatory condition, and vitamin D binding protein levels tend to decline in inflammatory states. Recent studies suggest a link between VDD and increased anaemia in patients with chronic anaemia (9). Individuals with SCD are at risk of these complications, although it remains unclear to what extent VDD is a contributing causal factor. VDD is commonly observed in patients with SCD and has recently become a focus of public health concern due to its role in adverse skeletal and non-skeletal manifestations (10).

MATERIAL AND METHOD:

The cross-sectional study was conducted on 89 children between 2-18 years with SCD with “SS” and “SA” patterns, diagnosed by high-performance liquid chromatography, who were attending a sickle cell clinic or admitted to the paediatric ward of Government Medical College, Rajnandgaon.

Exclusion criteria includes hydroxyurea therapy, sickle cell children with chronic diseases, or those on vitamin D supplementation

Ethical clearance and approval were obtained from the Institutional Ethical Committee, and written informed consent was taken from the parents of the patients.

A detailed history, clinical examination, and anthropometry were performed, and data were collected using structured data collection forms.

Blood samples were taken in plain vial for 25-OH-vitamin D [25(OH)D] and serum calcium. The estimation of vitamin D was done by radio-immune assays using chemiluminescent protein binding assay.

The classification of vitamin D deficiency (VDD) based on serum levels of vitamin D, according to Indian paediatrics guidelines, is as follows: 1) deficiency < 20 ng/dL, 2) insufficiency 20-30 ng/dL, and 3) sufficiency ≥ 30 ng/dL. Calcium was estimated by the Arsenazo III method.

The morbidity in sickle cell children includes the frequency of pain episodes, the number of admissions for acute febrile illness, the number of blood transfusions, and the total number of admissions.

RESULT

A total of 89 children with SCD (SS-88 children and SA-1 child) were enrolled in this study, of whom 50 (56%) were males and 39 (44%) were females. The majority of cases were in the age group of >4-8 years (40.45%), followed by >8-12 years (34.83%), 2-4 years (13.48%), and >12-18 years (11.24%). The mean age of patients was 7.32 ± 3.27 years, ranging from 2.5 to 16 years.

Vitamin D deficiency (VDD) was reported in 58 (65.17%) children, with 24 (27.0%) having insufficient levels and 9 (10.11%) having normal levels. The mean vitamin D level was 19.42 ng/dL, ranging from 5.12 to 62.05 ng/dL. It is divided into two class undernutrition and normal nutrition by WHO and CDC criteria.

Out of 89 cases, 26 children had normal nutrition and 63 children were undernourished. VDD was more common among undernourished children than those with normal nutrition, with a p-value of 0.001, which was statistically significant.

1. Vitamin D deficiency in SCD children was associated with increased pain episodes compared to vitamin D sufficient children ($p=0.001$).

2. Number of hospital admissions for acute febrile illness had an inverse relationship with vitamin D levels with a p-value of 0.152, which was not statistically significant. Thus, VDD was associated with an increased risk for admissions for acute febrile illness but not significantly.

3. Number of blood transfusions had an inverse relationship with vitamin D level with a p-value=0.728, which was not statistically significant.

4. Decrease in vitamin D levels increases the number of total admissions in the deficient group > insufficient group > normal vitamin D level with a p-value=0.018.

The comparisons of mean values of co-morbidities (number of pain crises, acute febrile illness, blood transfusions, and total number of admissions) between VDD and vitamin D sufficiency groups are show below:

Morbidity	Vit D deficiency	Vit D Sufficiency	P value
No of pain episodes	5.60±3.25	2.22±1.64	0.01
No. of acute febrile illness	3.48±1.76	2.66±1.93	0.09
No. of Blood transfusion	3.00±5.25	1.55±1.81	0.4
Total hospital admission	9.01±5.30	5.11±3.01	0.02

The mean number of pain episodes, admissions for acute febrile illness, and total number of admissions were significantly higher in the VDD group compared to the vitamin D sufficient group.

DISCUSSION

In the present study, the most common age group of SCD patients was 4 to 8 years, similar to that reported in the Garrido et al. (12) study. It was observed more amongst male than female due to better utilisation of healthcare facilities (13). Vit D deficiency is one of the most common nutrient deficiencies among children with sickling disease. The prevalence of VDD in young children is around 50-90% in the Indian subcontinent (14). The study shows that 90% of children were below 30 ng/dL and 65.17% were deficient. These results are similar to previous such studies (12,15,16). Rovner et al. (6) defined VitD deficiency as a vitamin D level less than 11 ng/mL and Vit D insufficiency as a vitamin D level between 11 to 30 ng/mL. The mean vitamin D level was 19.2 ng/dL, which is consistent with the study of Winters Et al. It is comparable. (17) They found that the mean [25(OH)D] level Was 17.2 ± 9.5 ng/dL.

There was no association between vitamin D levels and sex of an individual. With the age vitD level decreases in the body but this was not statistically significant ($p = 0.688$). Similar results were reported in study by Adewoye et al. Reported. (18) and AlJama et al. (19). VDD in malnourished children was higher. Jackson et al. (20) Reported vitamin D levels were not significantly correlated with BMI percentile ($p=1.00$)/BMI z-score ($p=0.53$). Ozen Et al. (21) found that vitamin D levels were significantly lower in children with height and/or weight greater than 2 standard deviations above the mean. Existing research Found that decreased vitamin D levels were associated with increased chances of painful crises. The vaso-occlusive crisis occurs due to interactions between sickle cells, inflammatory cytokines, and the endothelium. VDD affects endothelial dysfunction and cytokines, leading to the development of SCD (7). Serum [25(OH) D] ng/ml is a negative acute phase reactant that affects acute and chronic inflammatory diseases.

Serum [25(OH)D] ng/ml is an unreliable biomarker of Vitamin D status after an acute episode of inflammation (22). This may be the cause of increased bone pain severity and hospitalization due to vascular occlusion.

Lee et al (16) found similar results that serum [25(OH) D] ng/ml was associated with pain, but there was no significant association between serum [25(OH) D] ng/ml and acute Chest syndrome. Osonwo et al. (23) also found a significant association between VDD and painful crises. Shams et al. (2) Found that vitamin D administration was associated with lower postoperative analgesic requirements and postoperative complications.

Children with sickle cell anemia with vitamin D deficiency had an increased risk of hospitalization compared to children without vitamin D deficiency, but this was not statistically significant ($p=0.220$). Children with lower vitamin D levels had an increased number of transfusions by but this value was

not statistically significant ($p=0.728$). These results Are consistent with previous studies (25,26). Total number of hospitalizations was inversely associated with vitamin D levels ($p = 0.018$) with Cases. Macaskill et al. (27) also found similar results in Cases in which serum vitamin D levels were inversely associated with hospitalizations reported in the medical records of Visits ($p=0.0$).

CONCLUSION

The prevalence rate of Vitamin D deficiency found in this study was 65.17%, found to be one of the most common nutrient deficiencies among children with sickle cell disease (SCD. There should be routine monitoring of vitamin D levels in SCD patients and the use of supplements to manage morbidity like pain, anaemia, and lower the need for hospitalization. There is need of comparative study among children with SCD and vit D deficiency and children with SCD and without vit D deficiency for finding out SCD related morbidity and vit D status.

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