

Vitamin D Deficiency and Its Hematological Correlates in Patients with Sickle Cell Disease at a Ugandan Clinic

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Purpose: To determine the prevalence of vitamin D deficiency (VDD), evaluate its correlation with key hematological parameters, and identify associated factors among patients attending the Sickle Cell Clinic at Mengo Hospital (Kampala, Uganda).

Patients and Methods: This cross-sectional study enrolled 213 patients with sickle cell disease (SCD) at Mengo Hospital, serum 25-hydroxyvitamin D levels were measured. Levels were classified as deficient (<20 ng/mL) or sufficient (≥20 ng/mL). Hematological indices, red blood cell (RBC) count, hemoglobin (Hb), and red cell distribution width-coefficient of variation (RDW-CV) were assessed using an automated analyzer, and Spearman correlation was used to assess correlations with vitamin D levels. Multivariable Poisson regression identified variables associated with vitamin D deficiency (VDD), reporting outcomes as adjusted prevalence ratios (aPR).

Results: The median age was 10 years (IQR 5–13); 50.7% were male. The prevalence of vitamin D deficiency (VDD) was 47.4% (95% CI 40.8–54.2%). Weak but significant positive correlations were observed between serum vitamin D levels and RBC count ($\rho = 0.170$, $p = 0.013$) and Hb concentration ($\rho = 0.157$, $p = 0.022$), while a negative correlation was noted with RDW-CV ($\rho = -0.162$, $p = 0.018$). Adolescents and adults had a higher prevalence of VDD compared to younger children (12–17 years; aPR 1.96, $p = 0.002$) and (≥ 18 years; aPR 3.20, $p < 0.001$) respectively. Additionally, folic acid and hydroxyurea were associated with a lower risk of VDD (aPR 0.69, $p = 0.028$).

Conclusion: Nearly half of the patients with sickle cell disease had vitamin D deficiency. Older age increased the risk. VDD is weakly but significantly associated with lower Hb/RBC and higher RDW, suggesting a possible contributory role in the hematologic profile of Ugandan SCD patients.

Keywords: prevalence, vitamin D deficiency, sickle cell disease, anemia, hematological parameters

Introduction

Sickle cell disease (SCD) is an inherited hemoglobinopathy characterized by defective hemoglobin structure, leading to chronic hemolysis, vaso-occlusive crises, and systemic inflammation. These processes predispose patients to multi-organ damage, including significant bone-related morbidity.^{1,2}

Vitamin D deficiency (VDD), defined as serum 25-hydroxyvitamin D <20 ng/mL,³ is a critical comorbidity in SCD.⁴ A recent meta-analysis estimated a pooled VDD prevalence of 48.5% among SCD patients.⁵ Regional studies report VDD in SCD rates of 65% in the US,⁶ 31% in Canada,¹ 88.5% in Nigeria.⁷ Across Sub-Saharan Africa, lower levels of vitamin D have been reported among SCD patients in comparison to non-SCD patients^{8,9} being compounded by many other factors including malnutrition.¹⁰

The high prevalence of VDD in SCD is multifactorial, arising from mechanisms such as chronic hemolysis, renal dysfunction, nutritional insufficiencies, and persistent inflammatory states¹¹ Consequently, SCD patients with VDD face a greater burden of complications, including an increased incidence of acute chest syndrome, stroke, vaso-occlusive crises, osteomyelitis, and a vascular necrosis.^{12,13}

Beyond the immunomodulatory roles the emerging evidence further suggests that vitamin D directly regulates erythropoiesis, providing a biological plausibility for an association with hematological indices in SCD. The active metabolite 1,25-dihydroxyvitamin D promotes the proliferation and maturation of burst-forming unit-erythroid (BFU-E) and colony-forming unit-erythroid (CFU-E) cells acting synergistically with erythropoietin to enhance red cell production.¹⁴ High levels of vitamin D3 reduce circulating hepcidin, an inhibitor of gut enterocyte iron transport, thereby altering pro-inflammatory cytokine levels, thereby improving iron availability for hemoglobin synthesis.¹⁵ With these pathways relevant to SCD in which chronic inflammation and hepcidin-mediated functional iron restriction already constrain erythropoiesis in VDD, which compounds the hematological burden.¹¹

Impacting erythropoiesis and hemoglobin synthesis vitamin D has major effect on primary red cell indices including RBC count and hemoglobin concentration.¹⁴ RDW_CV primarily reflects the degree of anisocytosis, which arises from heterogeneous and infective erythropoiesis and VDD is independently associated with heightened inflammatory and oxidative states, which further widen the red cell size variability.¹⁶ Correlation between adequate serum vitamin D levels and normalized hematological parameters, with studies reporting significant associations between vitamin D sufficiency and healthier values for mean platelet volume (MPV), platelet distribution width (PDW), red blood cell counts, and mean corpuscular volume (MCV).¹⁷

The situation is particularly concerning in sub-Saharan Africa, the epicentre of the SCD burden, where patients face a heightened risk of general malnutrition,¹⁸ which may exacerbate micronutrient deficiencies like VDD. In Nigeria, for example, the clinical significance of vitamin D deficiency is evident from its prevalence of 79% among SCD patients who experienced complications necessitating blood transfusion, versus only 18% among those without such complications.¹⁹ Therefore, the serum Vitamin D levels would positively associate with RBC count and hemoglobin concentration, while inversely associated with RDW-CV, reflecting its supportive role for erythropoietic output and red cell heterogeneity in this population.

Despite this burden, vitamin D status is not routinely assessed at the Mengo Hospital Sick Cell Clinic. Consequently, deficiencies remain undiagnosed, and the relationship between vitamin D and hematological health has not been characterized in this cohort. This study therefore aimed to determine the local prevalence of VDD, its correlation with hematological indices, and associated factors, to generate evidence for potentially integrating vitamin D screening into standard care.

Material and Methods

Study Setting

The study was conducted at the Sick Cell Clinic of Mengo Hospital, a private faith-based hospital located in Kampala, Uganda. The clinic operates weekly and provides routine care and follow-up for patients with confirmed sickle cell disease. Approximately 30–50 patients attend the clinic each week, including 2–8 newly diagnosed cases. The hospital laboratory confirms suspected sickle cell disease before patients are enrolled for follow-up at the clinic.

Study Design

This was a cross-sectional study conducted to determine serum vitamin D levels, its correlation to hematological indices and associated factors among sickle cell patients with SCD at Mengo Hospital. The study was carried out from May to June 2025 at Mengo Hospital.

Study Population and Sampling

Non-probability convenience sampling was used to recruit adolescents and children with confirmed sickle cell disease who attended the sickle cell clinic. Patients with SCD who visited the Mengo clinic for review and the newly diagnosed on the day of the clinic visit were recruited for this study.

Inclusion Criteria

- Children and adolescents with a confirmed diagnosis of SCD.
- Newly diagnosed SCD patients presenting on the day of recruitment.
- Provision of informed assent (participant) and consent (parent/guardian).
- Use of food supplements, including vitamin D.

Exclusion Criteria

- Patients with SCD who received a blood transfusion within the last three months.

Sample Size Determination

The sample size was calculated using the Kish-Leslie (1965) single population proportion formula to estimate the prevalence of vitamin D deficiency among patients with SCD.

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

Where:

n = Study sample size

z = Standard normal deviate corresponding to 95% confidence interval (= 1.96)

p = Prevalence of vitamin D deficiency among patients with SCD (Prevalence of 34.8% in Uganda.²⁰)

d = margin of error on P (set at 5%)

Calculation:

$$n = \frac{1.96^2 0.348(1 - 0.348)}{0.05^2}$$

$$n = 348$$

Given that the total number of active SCD patients regularly attending the Mengo clinic at the time of this study was 480, the Cochran (1977) finite population correction formula was subsequently applied to reduce the sample size accordingly.

$$n = \frac{no}{1 + \frac{no-1}{N}}$$

Where;

$$no = 348$$

$$n = \frac{348}{1 + \frac{348-1}{480}}$$

$$n = 213$$

The study therefore recruited 213 study participants.

Data Collection Tools and Procedures

A semi-structured questionnaire was used to gather sociodemographic and clinical data from patients, including medication duration, history of sickle cell crises, blood transfusions, medication adherence, and comorbidities such as hypertension, diabetes, kidney disease, cardiovascular diseases, and tuberculosis. Lifestyle factors like physical activity, smoking, and alcohol use were also documented. Patients' height and weight were measured for Body Mass Index calculation per WHO standards, and blood pressure was assessed using a digital sphygmomanometer with two readings taken 5 minutes apart to calculate the mean.

Venous blood samples (3 mL) were drawn into EDTA (purple-top) and serum-separator (red-top) tubes for hematological parameters and 25-hydroxyvitamin D measurement respectively, and tested within 24 hours. Samples not tested within two hours of collection were stored at -20°C until analysis.

To ensure data quality and reliability, the questionnaire was pre-tested among 10% of the target sample at Rubaga Hospital, and data collectors were trained on the study procedures and ethical considerations. All laboratory analyses followed standard operating procedures, with daily instrument calibration/verification, two levels of quality control materials, preventive maintenance, and lot-validated reagents. All assays were performed by qualified laboratory technologists.

Laboratory Procedures

Serum 25-hydroxyvitamin D was quantified via electrochemiluminescence immunoassay on a Cobas e-411 Analyzer (Roche Diagnostics). Levels <20 ng/mL were classified as deficient. Additionally, red blood cell count, hemoglobin, red cell distribution width, and platelet count were assessed using the Mindray BC-6200 Automated hematology analyzer.

Data Analysis

Data were checked for completeness and consistency before being double-entered into Microsoft Excel and subsequently analyzed using STATA version 17. Continuous variables underwent a normality assessment via the Shapiro–Wilk test; mean $\pm$ standard deviation was reported for normally distributed variables, while non-normally distributed variables were summarized using median (interquartile range). Comparisons of these variables between participants with and without vitamin D deficiency were conducted using Student's *t*-test or Mann–Whitney *U*-test as appropriate. Categorical variables were presented as frequencies and proportions, evaluated through Chi-square or Fisher's exact test, with statistical significance set at $P < 0.05$. The prevalence of vitamin D deficiency was calculated with 95% Confidence Intervals and depicted in a pie chart. Correlations between serum vitamin D levels and hematological indices were determined using Spearman correlation coefficients, with significance at $P < 0.05$.

Because the outcome prevalence exceeded 10%, Poisson regression with robust variance was used to estimate prevalence ratios directly.

Variables with a *p*-value ≤ 0.2 in univariable analysis were included in a multivariable Poisson regression model with robust variance to estimate adjusted prevalence ratios (aPR). Model fit was assessed using the Hosmer–Lemeshow test *p* value 0.29 and multicollinearity was assessed before running the final model. Variables with high multicollinearity were not included in the final model. Associations in the final model were considered statistically significant at a *p*-value < 0.05 .

Ethical Approval

Ethical approval was granted by Mbarara University of Science and Technology Research Ethics Committee (Ref. MUST-REC-2025-301) and institutional permission by Mengo Hospital. The study adhered to the Declaration of Helsinki. Written informed consent was obtained from all study participants prior study commencement. Participant data were kept confidential; hard copies were stored under lock and key, and soft copies were password-protected.

Results

Socio-Demographic, Economic, and Lifestyle Characteristics of the Study Participants

The median age of participants was 10 years (interquartile range [IQR]: 5–13), with the majority (61.5%) under 12 years of age. Slightly more than half of the cohort were male (50.7%). Socioeconomic data indicated that over half of the participants (56.3%) belonged to families with a monthly income exceeding 800,000 Ugandan Shillings (UGX). In terms

of dietary patterns, most participants reported consuming fruits and vegetables on fewer than four days per week (72.8%) and consumed meat 2–3 times per month (48.8%). The median BMI was 17.3 kg/m² (IQR 15.1–21.9), with 59.6% of participants classified as underweight (BMI <18.5) (Table 1).

Table 1 Socio-Demographic, Economic and Lifestyle Characteristics of the Study Participants

Variable	Category	Frequency (N = 213)	Percentage (%)
Age categories	<12	131	61.5
	12–17	69	32.4
	≥18	13	6.1
Sex	Male	108	50.7
	Female	105	49.3
Residence	Rural	55	25.8
	Urban	158	74.2
Family income per month (UGX)	<500,000	18	8.5
	500,000–800,000	75	35.2
	>800,000	120	56.3
Vegetable and fruit intake	<5 servings per day	176	82.6
	≥5 servings per day	37	17.4
Fruit/vegetable intake days per week: ≤4 days/>4 days	≤4days	155	72.8
	>4days	58	27.2
Meat consumption per month	None	27	12.7
	2–3times	104	48.8
	≥4times	82	38.5
Dinner time	Before 8 pm	28	32
	After 8 pm	60	68
Physical activity (MET min/week) Median (IQR)	456 (209–953)		
Physical activity (MET min/week)	<600	132	62.0
	600–3000	64	30.0
	>3000	17	8.0
Body mass index (kg/m ²): Median (IQR)	17.28395 (15.11–21.89)		
Body mass index (kg/m ²)	<18.5	127	59.6
	18.5–24.9	50	23.5
	25–29.9	13	6.1
	≥30	23	10.8
Sleep duration	≤7hours	50	23.5
	>7hours	163	76.5

Hematological Parameters of the Study Participants by Serum Vitamin D Level Status

Most of hematological parameters, including WBC parameters and platelet parameters did not differ significantly between participants with and without vitamin D deficiency. The red cell parameters were significantly different between the two groups. Red cell count and Hb concentration were significantly lower in participants with vitamin D deficiency compared to those without vitamin D (median $2.63 \times 10^{12}/L$, IQR 2.32–2.98) versus ($2.79 \times 10^{12}/L$, IQR 2.43–3.36) $p = 0.020$ and (median 7.80 g/dL, IQR 6.90–8.80) versus (median 7.9 g/dL, IQR 7.35–9.6), $p=0.037$ respectively while RDW was higher among those with vitamin D deficiency than those without ((median 25.20%, IQR 20.70–30.60) versus (median 22.4%, IQR 19.75–26.45), $p = 0.012$) (Table 2).

The Proportion of SCD Patients with Vitamin D Deficiency

The Overall Prevalence of VDD Was 47.4% (95% CI: 40.8–54.2%) (Figure 1).

Correlation Between Vitamin D Deficiency and the Hematological Indices of Patients with SCD

Significant correlations were observed between serum vitamin D levels and red cell indices (Table 3). A modest but statistically significant positive correlation was found with red blood cell (RBC) count ($p = 0.170$, $p = 0.013$) and hemoglobin concentration (Hb) ($p = 0.157$, $p = 0.022$). Although hematocrit demonstrated a trend toward a positive association, it did not reach statistical significance ($p = 0.133$, $p = 0.053$). Conversely, a weak yet significant inverse

Table 2 Hematological Parameters of the Study Participants by Serum Vitamin D Level Status

Hematological Parameter	Total N=213	Absent N=112	Present N=101	p-Value
WBC ($\times 10^9/L$): Median (IQR)	9.58 (6.55–13.69)	9.49 (6.47–13.43)	9.6 (6.56–14.50)	0.53
Neut ($\times 10^9/L$): Median (IQR)	1.65 (0.59–4.66)	1.63 (0.53–4.13)	1.76 (0.73–4.88)	0.22
Eos ($\times 10^9/L$): Median (IQR)	0.26 (0.11–0.59)	0.27 (0.115–0.695)	0.24 (0.09–0.56)	0.39
Bas ($\times 10^9/L$): Median (IQR)	0.1 (0.06–0.15)	0.1 (0.07–0.15)	0.1 (0.06–0.16)	0.92
Lymph ($\times 10^9/L$): Median (IQR)	5.41 (3.81–7.73)	5.25 (3.66–7.55)	5.44 (3.97–8.3)	0.40
Mon ($\times 10^9/L$): Median (IQR)	0.65 (0.37–1.01)	0.64 (0.37–1.05)	0.67 (0.36–1)	0.76
RBC ($\times 10^{12}/L$): Median (IQR)	2.71 (2.35–3.17)	2.79 (2.43–3.36)	2.63 (2.32–2.98)	0.020
Hgb (g/dL): Median (IQR)	7.9 (7.1–9.1)	7.9 (7.35–9.6)	7.80 (6.90–8.80)	0.037
MCV (fL): Mean (SD)	89.06 (11.60)	87.68 (10.68)	90.59 (12.41)	0.068
MCH (pg): Mean (SD)	29.48 (4.19)	29.15 (3.74)	29.84 (4.64)	0.23
MCHC (g/dL): Median (IQR)	33.2 (32.1–34.1)	33.20 (32.20–34.10)	33 (31.80–34)	0.21
RDW-CV (%): Median (IQR)	23.4 (20–28.2)	22.4 (19.75–26.45)	25.20 (20.70–30.60)	0.012
PCT (%): Median (IQR)	0.363 (0.241–0.5)	0.35 (0.25–0.480)	0.367 (0.22–0.53)	0.45
PDW: Median (IQR)	15.6 (15.3–16.1)	15.6 (15.3–16)	15.70 (15.30–16.20)	0.21
PLT ($\times 10^9/L$): Median (IQR)	369 (254–515)	364.0 (245.5–489.0)	381 (259–537)	0.32
PLR: Median (IQR)	62.3 (41.34–111.92)	62.09 (43.64–102.51)	63.46 (39.21–117.27)	0.83
HCT (%): Median (IQR)	24 (21.6–27.1)	24.20 (21.75–28.80)	23.8 (21.30–26.60)	0.11
MPV (fL): Median (IQR)	9.8 (8.9–10.7)	9.95 (8.75–10.8)	9.80 (9–10.40)	0.81
Hb RR: Median (IQR)	0.34 (0.25–0.43)	0.37 (0.28–0.47)	0.31 (0.23–0.40)	0.005

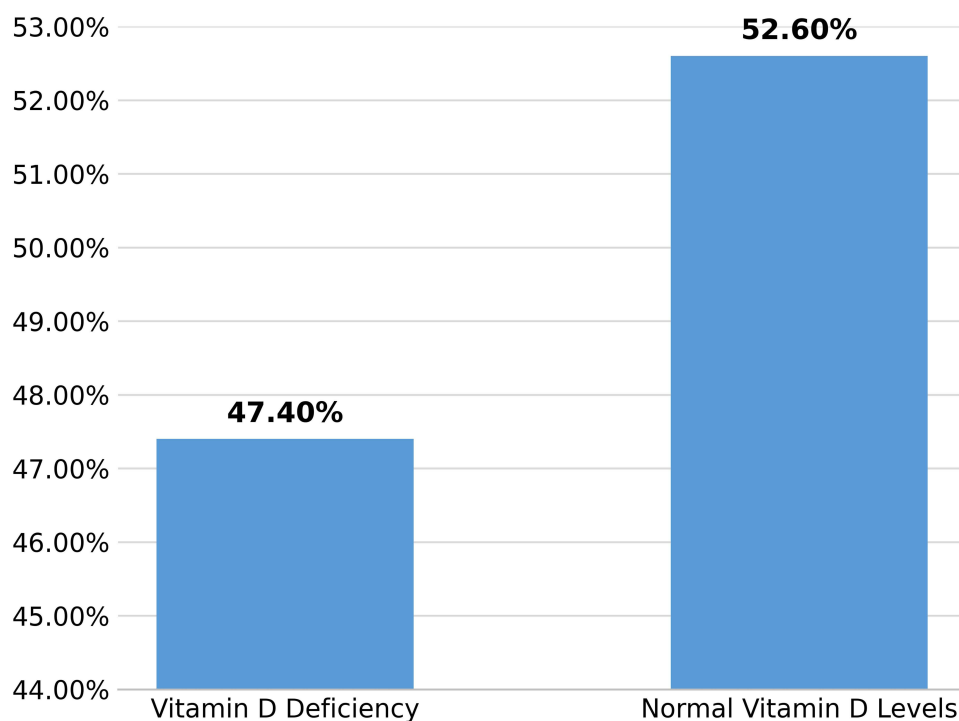


Figure 1 A bar chart showing the proportion of patients with SCD with vitamin D deficiency.

correlation was noted between vitamin D levels and red cell distribution width–coefficient of variation (RDW-CV) ($\rho = -0.162$, $p = 0.018$). While total white blood cell, neutrophil, lymphocyte, monocyte, and basophil counts were slightly elevated in one group, these differences did not reach statistical significance between the two groups.

Table 3 Correlation Between Serum Vitamin D Levels with Hematological Indices Among Sickle Cell Patients

Hematological Indices	Spearman Correlation Coefficient (ρ)	p-Value
RBC ($\times 10^{12}$)/L	0.1704	0.0127
Hb (g/dL)	0.1570	0.0219
MCV (fL)	−0.0869	0.2066
MCH (pg)	−0.0505	0.4637
MCHC (g/dL)	0.0746	0.2784
RDW-cv (%)	−0.1622	0.0179
PCT (%)	−0.0801	0.2445
PDW	−0.0922	0.1800
PLT ($\times 10^9$)/L	−0.0971	0.1580
HCT (%)	0.1328	0.0530
MPV (fL)	0.0113	0.8696
Total WBC count	−0.0619	0.3686

(Continued)

Table 3 (Continued).

Hematological Indices	Spearman Correlation Coefficient (rho)	p-Value
Neutrophil count	−0.0815	0.2365
Lymphocyte count	−0.0452	0.5115
Monocyte count	−0.0362	0.5992
Eosinophil count	0.0641	0.3522
Basophil count	−0.0253	0.7137

Abbreviations: MCV, Mean Cell Volume; MCH, Mean Hemoglobin Concentration; MCHC, Mean Cell Hemoglobin Concentration; MPV, Mean Platelet Volume; PDW, Platelet distribution width.

Factors Associated with Vitamin D Deficiency Among Patients with SCD

At the bivariate level, age emerged as a significant predictor of vitamin D deficiency. Compared to children under 12 years, adolescents aged 12–17 years (cPR = 1.59, 95% CI: 1.18–2.14, $p = 0.002$) and adults aged ≥ 18 years (cPR = 2.26, 95% CI: 1.64–3.11, $p < 0.001$) exhibited a significantly higher prevalence of deficiency. Rural residence (cPR = 1.332, 95% CI: 1.00–1.77, $p = 0.049$), Hb concentration (cPR = 0.97, 95% CI: 0.83–0.98, $p = 0.017$), hematocrit (cPR = 0.97, 95% CI: 0.95–1.00, $p = 0.037$), RDW-CV (cPR = 1.01, 95% CI: 1.00–1.01, $p = 0.001$) and MPV (cPR = 1.00, 95% CI: 1.00–1.00, $p = <0.001$) were significant. Participants with less than 7 hours of sleep also had higher odds of vitamin D deficiency (cPR = 1.58, 95% CI: 1.21–2.07, $p = 0.001$). Variables with a p -value ≤ 0.2 in univariable analysis were subsequently entered into the multivariable model.

After adjusting for potential confounders, age remained an independent predictor of vitamin D deficiency among SCD patients. Individuals aged 12–17 years (aPR = 2.19, 95% CI: 1.33–3.62, $p = 0.002$) and those aged ≥ 18 years (aPR = 3.34, 95% CI: 1.61–6.93, $p < 0.001$) were significantly more likely to be vitamin D deficient than the reference group (<12 years). Additionally, RDW-CV (aPR = 1.01, 95% CI: 1.00–1.01), $p = 0.005$, was associated with the likelihood of vitamin D deficiency. None of the WBC parameters showed an association with VDD (Table 4).

Table 4 Factors Associated with Vitamin D Deficiency Among Patients with SCD

Variable	Bivariate		Multivariate	
	cPR (95% CI)	P Value	aPR (95% CI)	P Value
Age groups				
<12	I		I	
12–17	1.59 (1.18–2.14)	0.002	2.19 (1.33–3.62)	0.002
≥ 18	2.26 (1.64–3.11)	<0.001	3.34 (1.61–6.93)	0.001
Gender				
Male	I			
Female	0.93 (0.70–1.24)	0.63		
Residence				
Rural	1.332 (1.00–1.77)	0.049	1.1 (0.82–1.48)	0.540
Urban	I			

(Continued)

Table 4 (Continued).

Variable	Bivariate		Multivariate	
	cPR (95% CI)	P Value	aPR (95% CI)	P Value
Hypertension				
No	1			
Yes	0.86 (0.48–1.55)	0.611		
Vegetable and fruit intake				
<5 servings per day	1.31 (0.84–2.03)	0.234		
≥5 servings per day	1			
No of days of vegetable and fruit intake				
≤4 days	1.27 (0.89–1.81)	0.188		
>4 days	1			
Meat consumption per month				
None	1			
2–3times	1.20 (0.73–1.98)	0.464	1.15 (0.67–1.96)	0.610
≥4times	1.17 (0.70–1.94)	0.552	1.18 (0.68–2.04)	0.549
Physical activity (MET mins/week)				
<600	0.88 (0.64–1.20)	0.418	1.08 (0.77–1.52)	0.659
600–3000	1			
>3000	1.29 (0.84–1.99)	0.239	1.47 (0.93–2.33)	0.101
Body mass index (kg/m ²)				
<18.5	0.80 (0.59–1.08)	0.149	0.87 (0.63–1.2)	0.396
18.5–24.9	1			
25–29.9	0.66 (0.32–1.37)	0.269	0.99 (0.46–2.13)	0.973
≥30	0.60 (0.33–1.10)	0.100	0.79 (0.43–1.46)	0.454
Blood pressure(mmHg)				
Normal	1			
High	1.41 (0.63–3.19)	0.405	0.88 (0.39–1.97)	0.757
Sleep duration(hours)				
≤7	1.58 (1.21–2.07)	0.001	1.12 (0.8–1.58)	0.509
>7	1	1		
Family history of hypertension				
No	1			
Yes	0.93 (0.62–1.38)	0.702		

(Continued)

Table 4 (Continued).

Variable	Bivariate		Multivariate	
	cPR (95% CI)	P Value	aPR (95% CI)	P Value
Family history of kidney disease				
No	I			
Yes	0.52 (0.09 2.88)	0.456		
Family history of cardiovascular disease				
No	I			
Yes	0.90 (0.46 1.67)	0.735		
Family history of dyslipidemia				
No	I			
Yes	0.62 (0.24 1.62)	0.331		
Duration on SCD medication				
≤10years	I	I		
>10years	1.30 (0.98 1.74)	0.072	0.66 (0.42–1.05)	0.079
SCD medication				
Folic acid only	I	I		
Hydroxyurea only	1.04 (0.38 2.84)	0.944	0.98 (0.34–2.87)	0.975
Both folic acid and hydroxyurea	0.97 (0.73 1.30)	0.835	0.75 (0.51–1.09)	0.131
SCD crisis				
Yes	2.65 (0.95 7.45)	0.064	1.95 (0.7–5.47)	0.204
No	I	I		
Always do lab monitoring tests				
Yes	1.11 (0.60 2.08)	0.735		
No	I	I		
Total WBC Count	1.01 (1–1.02)	0.216	1.01 1.02	0.216
Neutrophil count	1.02 (0.98–1.05)	0.363	1.03 (0.99–1.07)	0.191
Lymphocyte count	1.01 (0.99–1.03)	0.298	1.01 (0.97–1.06)	0.575
Monocyte count	0.91 (0.73–1.14)	0.425	0.91 (0.68–1.21)	0.528
Eosinophil count	0.91 (0.65–1.27)	0.585	1.06 (0.77–1.46)	0.736
Basophil count	1.32 (0.54–3.22)	0.547	0.52 (0.08–3.58)	0.510
Total RBC count	0.77 (0.63–0.94)	0.009	0.93 (0.61–1.41)	0.728
Hemoglobin concentration	0.9 (0.83–0.98)	0.017	0.97 (0.82–1.15)	0.721
Hematocrit	0.97 (0.95–1.00)	0.037		
MCV (fL)	1.01 (1–1.02)	0.056		

(Continued)

Table 4 (Continued).

Variable	Bivariate		Multivariate	
	cPR (95% CI)	P Value	aPR (95% CI)	P Value
MHC (pg)	1.02 (0.99–1.06)	0.226		
MCHC g/dL	0.93 (0.85–1.01)	0.076		
RDW-CV	1.01 (1.00–1.01)	0.001	1.01 (1.00–1.01)	0.005
Total Platelet Count	1.00 (0.99–1.00)	0.094	0.74 (0.32–1.74)	0.496
MPV fL	1.00 (1.00–1.00)	<0.001	1.13 (0.91–1.39)	0.268
PDW	1.08 (0.88–1.32)	0.484	1.08 (0.92–1.39)	0.491
Plateletcrit	1.44 (0.7–2.97)	0.320	0.74 (0.32–1.74)	0.013

Notes: cPR = crude prevalence ratio; aPR = adjusted prevalence ratio, adjusted for all variables shown in the multivariate column. Model adjusted for age, gender, residence, meat consumption, physical activity, BMI, blood pressure, sleep duration, duration on SCD medication, SCD medication type, SCD crisis, and lab monitoring. High blood pressure is defined as systolic/diastolic >90th percentile for age/sex or $\geq 130/80$ mmHg in adults.

Abbreviations: MCV, Mean Cell Volume; MCH, Mean Hemoglobin Concentration; MCHC, Mean Cell Hemoglobin Concentration; MPV, Mean Platelet Volume; PDW, Platelet distribution width.

Discussion

The prevalence of vitamin D deficiency (VDD) among children with SCD in this study was 47.4%. This figure is notably lower than those reported in other African studies, such as 88.5% in Nigeria and 83.3% in Egypt.^{7,21} These discrepancies may be attributable to differences in study populations. For instance, one investigation reported a higher prevalence of 72.5% among older children receiving care at a tertiary SCD center.²² In contrast, much lower rates have been documented, including a prevalence of only 1.6% in a study that predominantly enrolled younger, less severely affected children.²² Highlighting the role of contextual factors such as inadequate dietary intake and poor supplementation practices. Together, these findings underscore the need to integrate routine vitamin D screening and supplementation into standard SCD care.

However, the prevalence observed in the current study is higher than the 34.8% reported by Atutta (2019) among children with SCD at Mulago National Referral Hospital in Uganda.²⁰ The current study included a substantial proportion of adolescents and adults (32.4% aged 12–17 years and 6.1% aged ≥ 18 years), while Atutta (2019) enrolled predominantly younger children below 12 years old. Older age is a strong independent risk factor for vitamin D deficiency in SCD, likely due to cumulative organ damage, reduced sun exposure, and higher metabolic demands. A higher median age in the current cohort would explain the increased prevalence. These differences may reflect variations in age distribution, dietary habits, sunlight exposure, and supplementation practices.

The observed prevalence of vitamin D deficiency (VDD) in the current study (47.4%) is consistent with findings from Saudi Arabia (52.8%) and South America (46.7%)^{23,24} as well as a systematic review that reported a pooled prevalence of 50.49%,⁵ suggesting shared factors and similar populations may contribute to these results, particularly among individuals with darker skin and limited dietary intake of vitamin D.²⁵

In the present study, serum vitamin D concentrations showed statistically significant positive correlations with red blood cell (RBC) count and hemoglobin concentration, together with a negative correlation with red cell distribution width (RDW). Vitamin D is known for its function as a proinflammatory cytokine, which reduces hepcidin levels in chronic inflammations and improving erythropoiesis. Its deficiency may impact Hb concentration and RBC count,¹⁴ however, the associations observed in this study were weak ($\rho \approx 0.15$ – 0.17), indicating that vitamin D status accounted for only a small proportion of the variability in these hematological parameters. For that reason, vitamin D may not be the only factor influencing erythropoiesis or the severity of anemia among patients with sickle cell disease. Therefore, the observed association between vitamin D status and erythrocyte-related parameters should be interpreted cautiously.

The observed weak associations are broadly consistent with previous studies reporting lower hemoglobin levels or higher RDW among individuals with vitamin D deficiency, although the magnitude of these relationships has generally been modest.^{26,27} The modest correlation coefficients observed in our study may suggest that other established determinants of anemia in sickle cell disease, such as chronic hemolysis, inflammation, nutritional status, renal dysfunction, hydroxyurea use, and disease severity, are likely to have substantially greater influence on RBC indices than vitamin D status alone.

In the multivariate model, age and RDW-CV remained independently associated with VDD with adolescents and adults being more likely to have VDD compared to younger children. This finding aligns with previous research indicating that vitamin D levels decrease with age, particularly in children with sickle cell disease (SCD).^{24,28} Contributing factors include chronic organ damage and systemic inflammation that develop with age, which disrupt vitamin D metabolism.^{29,30} Additionally, factors such as low dietary intake and increased metabolic demand associated with ageing are noted as contributors to VDD in SCD patients.³⁰ This age-dependent increase in VDD prevalence suggests that routine screening should begin no later than early adolescence.

RDW-CV was the only red cell parameter that remained significantly associated with vitamin D status after multivariate regression and showed an inverse correlation in the correlation analysis. This may reflect the effects of anisocytosis, chronic hemolysis, reticulocytosis, and overall disease burden in SCD.¹⁶ Although the cross-sectional design does not allow causal conclusions, the independent association suggests that RDW-CV may be a useful, low-cost marker of hemolytic severity and could help identify patients who may benefit from vitamin D screening.

Given the high prevalence of vitamin D deficiency observed in this study, particularly among patients aged ≥ 12 years, systematic assessment of vitamin D status should be considered, especially for adolescents and adults with SCD. However, the cross-sectional design does not establish the clinical benefits, safety, or effectiveness of empirical vitamin D supplementation without laboratory confirmation. Therefore, supplementation should be guided by confirmed vitamin D status and established local protocols for dosing and monitoring. Prospective and interventional studies are needed to determine whether vitamin D supplementation improves hematological outcomes and to inform evidence-based clinical recommendations.

Vitamin D deficiency was not significantly associated with neutrophil, lymphocyte, monocyte, or basophil counts, despite the biological plausibility of an anti-inflammatory role in SCD. The significant findings clustered instead around red cell parameters (RBC, Hgb, RDW-CV), suggesting vitamin D status may be more tightly linked to hemolysis-related pathology than to the leukocyte-driven inflammatory pattern of SCD in this population.

Limitations of the Study

Several limitations should be acknowledged. First, the cross-sectional design precludes any causal interpretation of the associations observed between vitamin D status and hematological parameters. Second, all laboratory measurements were based on single time-point assessments, which may not accurately represent individuals' long-term vitamin D or hematological profiles. Third, the absence of inflammatory biomarker data limited our ability to explore the interplay between vitamin D status and immune or inflammatory responses, despite their recognized relevance in sickle cell disease pathophysiology. Fourth, the convenience sampling approach may have introduced selection bias, thereby restricting the generalizability of our prevalence findings. Additionally, the lack of dietary vitamin D intake data represents a potential source of residual confounding. Nevertheless, despite these constraints, our findings offer valuable preliminary data on the burden of vitamin D deficiency and its hematological associations within this population, and they provide a foundation for future prospective and interventional studies.

Conclusion

In this study, almost half of the SCD patients in this study exhibited vitamin D deficiency, which was weakly associated with lower red blood cell counts, reduced hemoglobin concentrations, and elevated red cell distribution width. Older age and higher RDW-CV values were also found to correlate with a greater prevalence of deficiency. However, given the cross-sectional nature of the study, these findings do not imply causality or support therapeutic efficacy. To better

elucidate these relationships and to inform evidence-based guidelines for vitamin D screening and supplementation in SCD management, further longitudinal and interventional research is warranted.

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Disclosure

The author(s) report no conflicts of interest in this work.

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