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Prevalence and Predictors of Low Packed Cell Volume among Sickle Cell Disease Patients in Northwestern Nigeria

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ABSTRACT

Background: Among Sickle cell disease (SCD) patients, the levels of Steady state packed cell volume (SSPCV) can reflect the extent of the anemia, and several factors have been linked with low SSPCV. However, in Northwestern Nigeria, the burden and the associated factors remained unexplored; therefore, this study aimed to determine the prevalence and predictors of low SSPCV in this environment.

Method: A cross-sectional study was conducted at the Department of Hematology of Usmanu Danfodiyo University teaching UDUTH, Sokoto, among patients with sickle cell disease attending clinic visits. A total of 206 patients were recruited via systematic sampling. The SSPCV was assessed from routine clinical investigations and the case file. Statistical analysis was conducted with SPSS version 25.

Results: The mean steady-state packed cell Volume (SSPCV) of the respondents was **24.00**±4.70%, and about one in two (45.6%) had a low SSPCV below 24%. There was a statistically significant association between a lower steady-state packed cell volume and lower socio-economic status, lower levels of education, participants from the Hausa/Fulani tribe, and hemoglobin S homozygosity (HBSS). However, only educational level and socio-economic status remained predictors of low SSPCV.

Conclusion: The burden of low SSPCV is substantial, with about half of the participants having low SSPCV. Low level of education and Socioeconomic disadvantage were identified as the main predictors. Therefore, there is a need for targeted social interventions as well as health education and community awareness to mitigate this burden.

Keywords: *Sickle cell disease, Steady state, Packed cell volume, Nigeria, PCV.*

Introduction

Historically, Sickle cell disease (SCD) was first described in 1910, and since then, it has been the most common inherited disease globally. (1,2) It affects multiple organ systems in the body with widespread hemolysis, inflammatory changes, and vascular compromise. (3–5) A point mutation stemming from the beta-globin gene is the culprit implicated with the consequent sickling of the red blood cell, hence the name Sickle Cell Disease. (3,6) Globally, about 25 million individuals are living with this

clinical condition. (1,2) Even though not all manifest the disease clinically because sickle cell trait (SCT) is a carrier state, not the disease. (7) In contrast, homozygosity for the sickle gene (HbSS) manifests the clinical symptoms, hence it is the disease state. (8) There are multiple variants of the disease; however, Hemoglobin S (HbS) and Hemoglobin C (HbC) are the most common. (8) The majority of sickle-cell haemoglobinopathies are in Africa, 40% having the disease in some part of the continent. (9) Nigeria has the highest prevalence of the disease globally. SCD is characterized by recurrent crises called Vaso-occlusive crises, which are the hallmark of the disease (10).

The normal range of PCV among non-SCD healthy individuals ranges from 35 to 50%, which is much higher than what is obtained among SCD patients. (11) Despite this, in a clinical state called the steady state, or baseline, or stable state, a sickle cell individual is free from crisis despite possible low hematocrit. (12) Having low SSPCV indicates chronic anemia from an ongoing hemolysis of the erythrocytes, which can lead to reduced perfusion to the tissues, leading to easy fatigability, weakness of the body, and poor exercise tolerance. (13) There is also a heightened risk of vascular complications like pulmonary hypertension, bone infarction, recurrent crisis, chronic kidney disease, sickle cell retinopathy, and leg ulcer. (14–16)

Multiple factors have been reported from previous studies to affect the levels of steady state PCV among SCD, with some reporting gender as a factor in favor of males, age, social class, ethnicity, and geographical location (17–20). Furthermore, the use of hydroxyurea, present of comorbidities like chronic kidney disease, as well as the genotype, have also been implicated. (21–23) Assessing the steady-state PCV level in our environment and the factors that affect it is paramount, as preventive measures can be taken to minimize the complications of the clinical condition. This study serves as a background study for others, as there was little to no study in this part of the country.

Methodology

This cross-sectional study was conducted at the Department of Hematology of Usmanu Danfodiyo University teaching UDUTH, Sokoto, among patients with sickle cell disease attending clinic visits. A total of 206 patients were recruited via

systematic sampling. Informed consent was taken from patients who were at least 18 years of age, had clinical diagnoses of sickle cell disease, and did not have any severe mental or physical conditions that made participation difficult. Ethical clearance was obtained from UDUTH, Sokoto (UDUTH/HREC/2022/1151/V2). All patients have a routine packed cell volume at the clinic, while some steady-state PCV was obtained from case notes and, in some cases, volunteered historically. The mean PCV was used as a cut-off to dichotomize the SSPCV into low and high. Statistical analysis was conducted with SPSS version 25 (IBM SPSS Statistics for iOS, Version 25.0, Armonk, NY: IBM Corp.). Chi-square and binary logistic regression were used to test for the association as well as the determinants of low SSPCV

Results

The Genotype and the Mean serum steady-state packed cell Volume of the respondents

From Table 1 below, the mean steady-state packed cell Volume (SSPCV) of the respondents, based on their genotype, shows that the overall mean SSPCV was 24.00 ± 4.70%**.** The respondents with Hemoglobin SC disease (HbSC) had a higher mean SSPCV of 29.34±4.25% compared with those with hemoglobin SS (HbSS), 23.42%±4.39 %**.**

Table 1. The Genotype and the Mean serum steady-state packed cell Volume of the respondents

Hemoglobin Type (Genotype)	**Mean SSPCV**
HbSC	**29.34%** (SD ±4.25)**.**
HbSS	**23.42%** (SD ±4.39)**.**
Both (HbSS+HbSC)	**24.00 %** (SD ±4.70)**.**

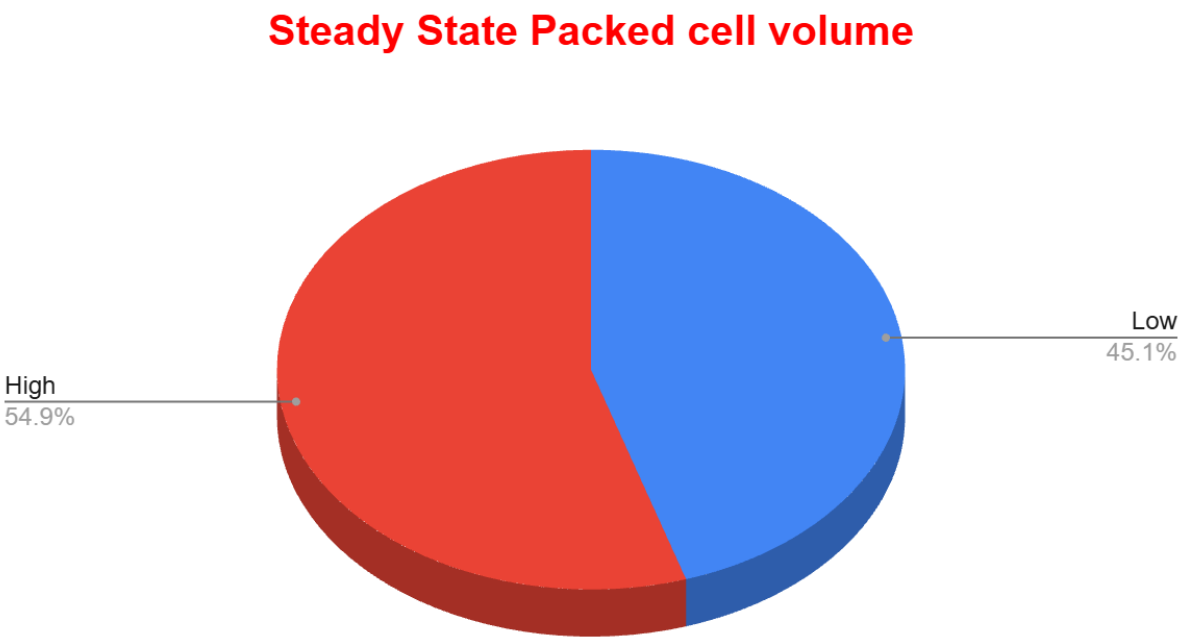

Figure 1: Dichotomized Steady State Packed Cell Volume

About one in two respondents (45.6%) had a PCV below 24%.

Sociodemographic Factors Associated with Low Steady State Packed Cell Volume

From Table 2 below, there was a statistically significant association between steady-state packed cell volume and socio-economic status, with participants from lower social classes having lower packed cell volume. Similarly, education level was associated with SSPCV: respondents with lower levels of education had lower SSPCV. The patients' tribe was also statistically significant, with respondents from the Hausa/Fulani tribe having lower SSPCV.

Table 2: Sociodemographic Factors Associated with Low Steady State Packed Cell Volume

Variable	**Low Steady state PCV (%)**	**High Steady State PCV (%)**	**X^2**	**df**	**P-value**
Age Category					
18–32	91.3%	90.2%	1.676	2	0.607
33–47	8.7%	8.0%			
48–62	0.0%	1.8%			
Gender					
Male	41.3%	34.8%	0.903	1	0.385
Female	58.7%	65.2%			
Marital status					

Single	76.1%	62.5%	4.752	2	0.101
Married	21.7%	35.7%			
Divorced	2.2%	1.8%			
Tribe					
Hausa/Fulani	96.7%	88.4%	8.385	3	**0.022**
Yoruba	0.0%	2.7%			
Igbo	2.2%	0.9%			
Others	1.1%	8.0%			
Religion					
Islam	96.7%	92.9%	1.492	1	0.351
Christianity	3.3%	7.1%			
Socioeconomic status					
Low	52.2%	43.8%	6.229	2	**0.046**
Medium	39.1%	34.8%			
High	8.7%	21.4%			
Employment					
Employed	7.6%	14.3%	4.085	4	0.415
Retired	0.0%	1.8%			
Unemployed	20.7%	17.9%			
Business	10.9%	9.8%			
Student	60.9%	56.2%			
Level of education					
Secondary and below	65.2%	41.1%	11.798	1	**0.001**
Above secondary	34.8%	58.9%			
Family type					
Monogamous	48.9%	39.3%	1.904	1	0.202
Polygamous	51.1%	60.7%			

Social support					
Poor	5.4%	0.9%	4.252	2	0.118
Moderate	10.9%	15.2%			
Good	83.7%	83.9%			

P< 0.05

Clinical Factors Associated with Low Steady State Packed Cell Volume

From Table 3 below, there was a statistically significant association between the level of steady state packed cell volume and the genotype of patients with hemoglobin S homozygous (HBSS) having low SSPCV.

Table 3 Clinical Factors Associated with Low Steady State Packed Cell Volume

Variable	**Low Steady state PCV (%)**	**High Steady State PCV (%)**	**X^2**	**df**	**P-value**
Comorbid condition					
Yes	52.2%	42.0%	2.116	1	0.160
No	47.8%	58.0%			
Insurance coverage					
Yes	20.7%	25.0%	0.538	1	0.507
No	79.3%	75.0%			
Type of hemoglobin					
HbSS	100.0%	80.4%	20.256	1	**<0.001**
HbSC	0.0%	19.6%			
Hydroxyurea use					
Yes	29.3%	33.9%	0.488	1	0.547
No	70.7%	66.1%			

P< 0.05

Predictors of low Packed Cell Volume

From Table 4 below, Variables that were statistically significantly associated at the bivariate level of analysis, i.e., socio-economic status, levels of education, tribe, and genotype of the patients, were entered into a binary logistic regression; however,

only the level of education and the socio-economic status remained as predictors for low SSPCV

Table 4: Predictors of low Packed Cell Volume

Determinant*	**Wald**	**Sig.**	**Exp(B)**	**95% Confidence Interval**	
				Lower	**Upper**
Level of education	13.659	0.000	0.288	0.149	0.558
Socioeconomic Status (1)	11.802	0.001	0.178	0.067	0.477
Socioeconomic Status (2)	9.153	0.002	0.212	0.078	0.579
Tribe	3.035	0.082	0.144	=.016	1.274
Hemoglobin Type	0.000	0.998	0.000	0.000	0.000

Discussion

The steady-state PCV of SCD patients is generally lower than that of healthy non-sickle cell individuals. (24) From this study, the steady state PCV was found to be **24.00**±4.70**%. This is similar to what Akinbami and colleagues reported among patients with sickle cell disease attending a teaching hospital in the southern part of Nigeria, where they reported an SSPCV of 24.46 ± 4.76%**. (24) The study also revealed that the homozygous state, i.e., HbSS, with the mean SSPCV of **23.42**±4.30%, has a lower SSPCV than the heterozygous state, HbSC. With an SSPCV of **29.34**±4.25%**.** Similarly, another Nigerian researcher found the SSPCV for the homozygous state to be ~24.44 ± 4.68%. (17) The mean SSPCV reported in the current study also falls within the **15.6%–27.6%** PCV reference interval of SSPCV among young adult Nigerian SCD patients, as well as several other studies done globally. (12,25–28). The steady-state PCV is lower than that of the general population, regardless of geographical location. This may be explained by the fact that SCD, anywhere, inherently has continuous or recurrent hemolysis, which the bone marrow cannot compensate for, as well as chronic inflammation that further compromises erythropoiesis, thereby lowering the PCV even at steady state. (24,29)

Furthermore, this research identified several factors associated with low SSPCV, including Tribe, level of education, social class, and genotype. Similarly, Animasahun in Lagos, Nigeria, found that lower socioeconomic status, which has been associated with malnutrition, is associated with lower SSPCV. (18) Some Brazilian researchers also found low levels of education among not only the patients but also their informal caregivers to be linked to low SSPCV, possibly due to poor health-seeking habits, lack of awareness, and poor compliance with treatment. (19)

Conclusion

The steady-state packed cell volume among SCD patients is lower than the reference packed cell volume of healthy individuals, and several sociodemographic and clinical factors are associated with low steady-state packed cell volume, including lower levels of education, lower socioeconomic status, ethnicity, and genotype. Therefore, targeted interventions in our environment can be channeled towards these identified factors to mitigate the detrimental consequences of the persistent low SSPCV. However, the study is cross-sectional and limited to a single institution, making generalizability to the community difficult and the causal relationship between low SSPCV and the identified factor unclear. Therefore, future research could improve on this by following up with patients to assess causality and by recruiting community patients to enhance generalizability.

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