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# PATTERNS OF ERYTHROCYTE MORPHOLOGICAL INDICES AMONG PATIENTS WITH SICKLE CELL DISEASE: IMPLICATIONS FOR ANAEMIA SEVERITY AND CLINICAL MANAGEMENT

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## ABSTRACT

**Background:** Sickle cell disease (SCD) is associated with chronic haemolysis, anaemia, and progressive alterations in erythrocyte morphology. This study assessed the patterns of erythrocyte morphological indices among patients with SCD in steady state and vaso-occlusive crisis and compared them with healthy controls.

**Materials and Methods:** This comparative study involved 180 participants aged 5–40 years in Bayelsa State, Nigeria, comprising 67 patients with SCD in vaso-occlusive crisis, 53 patients in steady state, and 60 healthy controls. Three millilitres of venous blood were collected into EDTA containers and analysed for packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC). Data were analysed using SPSS version 27.0. One-way analysis of variance with Tukey's post-hoc test was used to compare groups, with statistical significance set at $p<0.05$.

**Results:** Significant differences were observed in PCV, MCV, MCH, and MCHC among the three groups ($p<0.001$). PCV was significantly higher in controls (41.47±3.64%) than in steady-state (24.96±2.85%) and crisis (22.94±2.93%) SCD patients. MCV, MCH, and MCHC were also significantly reduced in both SCD groups compared with controls. The lowest PCV observed during crisis indicated greater anaemia severity associated with acute disease exacerbation.

**Conclusions:** SCD is associated with significant alterations in erythrocyte morphological indices, with greater abnormalities during vaso-occlusive crisis. Routine assessment of PCV, MCV, MCH, and MCHC may provide simple, affordable biomarkers for assessing anaemia severity and monitoring disease activity, particularly in resource-limited settings.

**Keywords:** Sickle cell disease; Erythrocyte morphological indices; Packed cell volume; Mean corpuscular volume; anaemia; Vaso-occlusive crisis; Haemolysis.

## 1 INTRODUCTION

One of the most common hereditary hemoglobinopathies in the world, sickle cell disease (SCD) continues to be a serious public health concern, especially in sub-Saharan Africa where it significantly increases morbidity and early mortality. It is caused by a single point mutation in the β-globin gene, which produces aberrant hemoglobin S (HbS). HbS polymerizes in hypoxic, dehydrated, or oxidatively stressed environments, giving erythrocytes the distinctive sickle shape. Repeated rounds of sickling and unsickling cause persistent hemolysis, vaso-occlusion, tissue ischemia, organ destruction, and severe anemia in these inflexible, poorly deformable red blood cells [1-4].

Nigeria has the highest global burden of sickle cell disease, with roughly 150,000 infants with SCD each year, accounting for nearly one-third of all new cases worldwide. Despite advances in newborn screening, hydroxyurea therapy, vaccination, and thorough clinical care, vaso-occlusive crises and chronic anaemia continue to be the predominant causes of hospitalization and decreased quality of life among those affected(5-9). Frequent haemolysis and inefficient erythropoiesis constantly modify red blood cell morphology, making routine haematological examination an essential component of illness monitoring.

Automated haematologyanalysers generate erythrocyte morphological indices such as packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC), which provide valuable information about erythrocyte size, haemoglobin content, and overall red blood cell morphology. These measures are commonly used to classify anemia, assess erythropoietic activity, monitor treatment response, and determine illness severity in a variety of haematological disorders [10-13]. Alterations in these indices in sickle cell disease patients may indicate chronic haemolysis, reticulocytosis, dietary deficits, hydration status, and bone marrow compensatory responses, making them important predictors of disease progression.

Previous research has shown that patients with sickle cell disease have significantly lower packed cell volume and altered erythrocyte indices than healthy people, though the magnitude of these differences varies according to disease phenotype, treatment status, and clinical condition[14-15]. During vaso-occlusive crises, rapid haemolysis, inflammatory activation, oxidative stress, and enhanced erythrocyte destruction can aggravate anaemia and alter red blood cell morphology. As a result, assessing erythrocyte indices during both steady-state and crisis stages might help clinicians better understand disease dynamics and give objective laboratory markers for monitoring patient status.

In low- and middle-income countries, where access to advanced molecular diagnostics and specialized biomarkers may be limited, routine evaluation of erythrocyte morphological indices is especially beneficial. Automated full blood count analysis is affordable, easily accessible, and offers quick quantitative information that can help clinicians identify disease deterioration, assess the severity of anemia, monitor therapeutic interventions, and make timely clinical decisions[16.] These parameters may also have prognostic value when interpreted in conjunction with clinical findings, improving patient management in settings with limited resources.

Relatively few studies have precisely compared erythrocyte morphological indices among patients in vaso-occlusive crisis, those in steady state, and healthy controls within the Nigerian population, despite the fact that many have examined haematological abnormalities in sickle cell disease. Haematological profiles may be influenced by regional differences in nutritional status, environmental factors, healthcare access, genetic modifiers, and disease management techniques. This emphasizes the necessity for locally produced evidence to direct clinical practice. Improved patient monitoring, diagnostic interpretation, and customized management approaches all depend on this kind of data.

Therefore, this study intends to investigate the patterns of erythrocyte morphological indices among patients with sickle cell disease in crisis, steady state, and healthy controls, and to identify their consequences for anaemia severity and therapeutic care. The findings are expected to give additional evidence to support the use of regular erythrocyte indices as feasible biomarkers for monitoring disease severity and enhancing clinical management of sickle cell disease. The study is based on observed differences in packed cell volume, mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration across the three study groups.

## 2 MATERIAL AND METHODS

### 2.1 Study area

This analysis focused on communities in Bayelsa State, with coordinates of 4.8678°N, 5.8987°E. Bayelsa State, located in Southern Nigeria's central Niger Delta Region between Delta and River States, with a total surface area of approximately 10,773 km2 (4,159 sq mi). Yenagoa, the capital, is at 4°55'29"N, 6°15'51"E. English is the official language, however Ijaw is the most widely spoken. The state was founded in 1996 from a piece of Rivers State, and its

population is expected to be 1,704,515 according to the 2006 census. Yenagoa is the capital of Bayelsa State, which has eight local government districts. The study was conducted between June 2025 and February 2026.

### 2.2 Study population

The study population consisted of 180 male and female participants ranging in age from 5 to 40 years old, including 67 sickle cell subjects in crisis and 53 stable sickle cell subjects who were either admitted or attended their clinic days at Federal Medical Centre Yenagoa, Kaiama General Hospital, Diete Koki Memorial Hospital, and Niger Delta University Teaching Hospital Okolobiri during the study period. Controls consisted of 60 AA participants.

### 2.3 Selection Criteria

This was done using questionnaire and consent form.

#### 2.3.1 Inclusion Criteria

Participants in the study were confirmed sickle cell patients and AA controls, both male and female, aged 5 to 40 years, as determined by laboratory screening.

#### 2.3.2 Exclusion Criteria

This study excludes

- Co-morbidities among sickle cell patients and controls included hypertension, diabetes mellitus, chronic renal disease, and known coagulation problems.
- Individuals who refused to give informed consent.

### 2.4 Sample size

The prevalence of sickle cell disease in Nigeria's south-south region was estimated to be 3.7% [17]. The sample size was obtained using the formula presented by Oladimeji[18],

$$N=Z^2PQ/d^2$$

Where:

- N = required sample size
- $Z^2$ = critical value at 95% confidence level = 1.96
- P = estimated prevalence = 0.037
- Q = 1 − P = 0.963
- $d^2$ = absolute sampling error tolerated = 0.05

The calculations were done as follows:

- $Z^2 = 1.96^2 = 3.8416$
- P =3.7% =0.037
- Q =1-0.037 =0.963
- $d^2$=5% =0.05 =0.0025
- N =3.8416 X 0.037 X0.963 / 0.0025 =54.7
- The minimum sample size for this study was 55.

Using 10% attrition rate, the sample size increased to 60 participants each.

### 2.5 Collection of sample

Using a 5 mL syringe, 3 mL of venous blood was collected and dispensed into an EDTA tube for haematological examination. To prevent haemolysis, analyses were performed within 2 hours of sample collection using whole blood.

### 2.6 Ethical approval

The Bayelsa State Ministry of Health, which oversees all Bayelsa State health facilities, and the Federal Medical Center Yenagoa research committee both provided ethical clearance. Respect for participants' rights was observed, including the right to refuse participation with a reason via the participant information form.

### 2.7 Statistical analysis

Data were entered, cleaned, and analyzed with SPSS version 27.0. Continuous data were reported as mean ± SD, with a p-value of less than 0.05 indicating statistical significance. One-way ANOVA was used to compare the crisis, stable, and control groups.

### 2.8 Method ofLaboratory analysis

Packed Cell volume and Red Cells Indices were evaluated using a 5-part Haematology Analyzer (wincom HA8520), and electrophoresis was done with the Model Techmel and Techmel 300 (USA) systems.

Table 1 presents a comparison of full blood count parameters among control, stable sickle cell disease (SCD), and crisis SCD groups using one-way ANOVA with Tukey's post hoc test. Packed cell volume (PCV) differed significantly across the groups ($F = 583.054$, $p < 0.001$), with values highest in the control group (41.47 ± 3.64), followed by the stable group (24.96 ± 2.85), and lowest in the crisis group (22.94 ± 2.93). Mean cell volume (MCV) also showed a statistically significant difference ($F = 36.794$, $p < 0.001$), with the control group having higher values (86.98 ± 3.93) compared to both stable (78.14 ± 7.12) and crisis (79.40 ± 6.50) groups. Similarly, mean cell haemoglobin (MCH) varied significantly among the groups ($F = 56.655$, $p < 0.001$), with the control group showing higher values (27.16 ± 3.10) than the stable (21.40 ± 2.24) and crisis (24.26 ± 3.18) groups. Mean cell haemoglobin concentration (MCHC) also differed significantly ($F = 46.755$, $p < 0.001$), with the control group (31.77 ± 3.07) being higher than both SCD groups.

**Table 1: Comparison of packed cellvolume and red cells indices amongst crisis, stable and control subjects.**

| Parameter | Control | Stable | Crisis | F | p-value |
|---|---|---|---|---|---|
| **PCV (%)** | 41.47 ± 3.64 | 24.96 ± 2.85[a] | 22.94 ± 2.93[ab] | 583.054 | 0.000 |
| **MCV (fL)** | 86.98 ± 3.93 | 78.14 ± 7.12[a] | 79.40 ± 6.50[a] | 36.794 | 0.000 |
| **MCH (pg)** | 27.16 ± 3.10 | 21.40 ± 2.24[a] | 24.26 ± 3.18[ab] | 56.655 | 0.000 |
| **MCHC(g/dL)** | 31.77 ± 3.07 | 27.02 ± 2.27[a] | 29.40 ± 2.37[ab] | 46.755 | 0.000 |

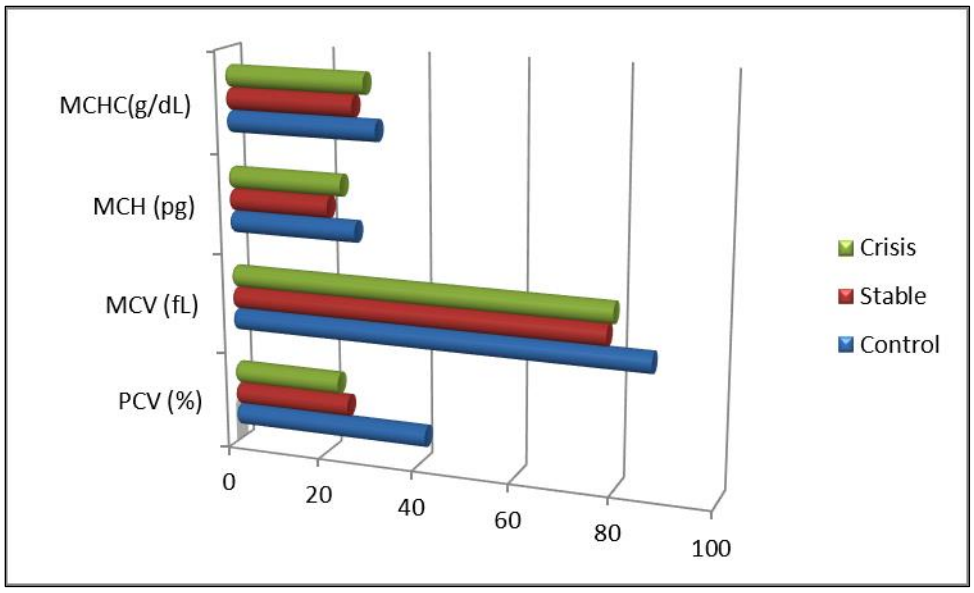


**Figure 1: Comparative Patterns of Erythrocyte Morphological Indices among Healthy Controls, Steady-State Sickle Cell Disease Patients, and Patients during Vaso-Occlusive Crisis**

Figure 1 illustrates the comparative distribution of packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) among healthy controls, patients with sickle cell disease (SCD) in steady state, and those experiencing vaso-occlusive crisis. The graphical representation demonstrates a marked decline in all erythrocyte morphological indices among patients with SCD compared with healthy controls. Packed cell volume exhibited the greatest reduction in patients during vaso-occlusive crisis, reflecting worsening anaemia associated with increased haemolysis. Mean corpuscular volume remained consistently lower in both SCD groups than in controls, while MCH and MCHC were also significantly reduced, indicating impaired erythrocyte haemoglobinization and altered red cell morphology. Overall, the figure demonstrates a

progressive deterioration in erythrocyte integrity from healthy individuals to steady-state disease and finally to vaso-occlusive crisis, highlighting the dynamic effects of chronic haemolysis on red cell morphology.

## 3 DISCUSSION

The current study shows that sickle cell disease patients have significantly different erythrocyte morphological indices, which become increasingly more noticeable during vaso-occlusive crises. The idea that chronic hemolysis is a dynamic process rather than a static pathological event is reinforced by the combined interpretation of Table 1 and Figure 1, which shows a distinct continuum of deteriorating erythrocyte morphology from healthy controls through steady-state SCD to crisis. The graphical presentation in this study offers an integrated visualization of disease progression, allowing for the simultaneous appreciation of changes in erythrocyte volume, hemoglobin content, and overall red cell integrity, whereas earlier studies have reported reductions in individual red cell indices.This integrated approach represents an important contribution to laboratory interpretation of SCD, particularly in settings where advanced biomarkers are unavailable.

Packed cell volume (PCV) decreased the most of all examined indices, with values dropping from healthy controls to steady-state patients and after a vaso-occlusive crisis. This gradual drop represents faster erythrocyte destruction caused by repeated sickling, oxidative membrane injury, splenic sequestration, and decreased erythrocyte survival. The extra drop seen during the crisis shows that acute inflammatory stress exacerbates chronic haemolyticanaemia by increasing tissue hypoxia and metabolic demand. These findings are consistent with the observations of Rees et al[14] and Kato et al[3], who found that deteriorating haemolysis during vaso-occlusive episodes directly correlates to a decrease in haematocrit and increased clinical severity.

The study also found that both SCD groups had significantly lower mean corpuscular volume (MCV) than healthy controls, with only minor variations observed between steady-state and crisis patients. This study implies that chronic disease processes, rather than acute vaso-occlusive events, have the greatest influence on erythrocyte size. Persistent haemolysis, inefficient erythropoiesis, recurrent oxidative damage, and nutritional deficits may all contribute to low erythrocyte count. The relative stability of MCV during a crisis suggests that acute vaso-occlusion largely affects erythrocyte survival rather than cellular dimensions, validating previous studies that MCV reflects chronic marrow adaptability and treatment status rather than acute disease activity [13].

Similarly, decreases in mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) indicate poor hemoglobinization of circulating erythrocytes. Reduced intracellular haemoglobin content can be caused by persistent erythrocyte destruction, accelerated turnover of immature red cells, chronic inflammation, and erythropoiesis-related dietary deficiencies[19]. Surprisingly, patients in vaso-occlusive crisis had somewhat higher MCH and MCHC than those in steady state, while having lower PCV. This trend may indicate enhanced reticulocytosis during acute haemolytic events, as reticulocytes are normally larger and have a higher hemoglobin concentration than mature erythrocytes. Rather than merely deteriorating anemia, the crisis state appears to involve a compromise between rapid haemolysis and compensatory bone marrow response[20].

One of the most innovative findings of this study is that the collective assessment of erythrocyte morphological indices provides a more comprehensive picture of disease progression than any single parameter. Rather than evaluating PCV, MCV, MCH, or MCHC independently, the integrated graphical pattern demonstrates that SCD progression is characterized by coordinated deterioration in erythrocyte morphology, reflecting the combined effects of chronic haemolysis, oxidative stress, ineffective erythropoiesis, and inflammatory activation. This multidimensional interpretation enhances the diagnostic value of routine full blood count analysis and may improve clinical assessment of disease severity.

Another important contribution is the demonstration that routine erythrocyte indices generated by automated haematologyanalysers can function as affordable surrogate biomarkers of anaemia severity in resource-limited healthcare settings. Unlike molecular biomarkers, measurements such as PCV, MCV, MCH, and MCHC are readily available through routine complete blood count analysis and require no additional laboratory infrastructure. Their consistent relationship with disease severity suggests that they may be incorporated into routine monitoring algorithms to identify patients at increased risk of severe anaemia, guide transfusion decisions, and evaluate therapeutic response. This finding is particularly relevant in sub-Saharan Africa, where access to specialized laboratory investigations remains limited despite the high burden of SCD [16]

Overall, the evidence presented in Table 1 and Figure 1 supports the increasing idea that erythrocyte morphological indices are dynamic indications of disease activity and bone marrow adaptability, rather than just descriptive laboratory characteristics. The graphical development from healthy controls to steady-state disease and vaso-occlusive crisis demonstrates the changing form of erythrocyte injury in SCD and emphasizes the clinical significance of including

several red cell indicators into routine patient monitoring. Such an approach may allow for earlier detection of disease progression, improved risk classification, and more personalized care options.

## 4 CONCLUSION

This study demonstrated significant alterations in erythrocyte morphological indices among patients with sickle cell disease, with the greatest abnormalities observed during vaso-occlusive crisis. Packed cell volume, mean corpuscular volume, mean corpuscular haemoglobin, and mean corpuscular haemoglobin concentration were significantly reduced in patients with SCD compared with healthy controls, reflecting chronic haemolysis and worsening anaemia. The further decline in packed cell volume during crisis highlights the dynamic progression of erythrocyte destruction during acute disease exacerbation. These findings indicate that routine erythrocyte indices are valuable, inexpensive biomarkers for assessing anaemia severity and disease activity. Their integration into routine clinical practice could improve patient monitoring, therapeutic decision-making, and overall clinical management, particularly in resource-limited settings.

The significance of the study

It shows that erythrocyte morphological indices (PCV, MCV, MCH, MCHC) are significantly altered in sickle cell disease patients, especially during vaso-occlusive crisis, reflecting the severity of anaemia and ongoing haemolysis.

- The study establishes that these routine, low-cost haematological parameters can serve as affordable biomarkers for monitoring disease activity and anaemia severity in resource-limited settings.
- It provides locally generated evidence from Nigeria, filling a gap in regional data and supporting context-specific clinical management strategies.
- By integrating multiple indices, the study offers a comprehensive framework for patient monitoring, guiding transfusion decisions and improving individualized care.

In brief, the study is significant because it identifies simple, accessible laboratory markers that can enhance the diagnosis, monitoring, and management of sickle cell disease, ultimately improving patient outcomes.

### *Recommendations*

- Routine evaluation of packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) should be incorporated into the standard clinical monitoring of patients with sickle cell disease.
- Clinicians should use erythrocyte morphological indices alongside clinical findings to identify patients at risk of severe anaemia and vaso-occlusive complications, thereby facilitating timely intervention and individualized patient management.
- Healthcare facilities in resource-limited settings should strengthen access to automated full blood count analysis, as these routine erythrocyte indices provide reliable and cost-effective biomarkers for monitoring disease progression.
- Future multicentre longitudinal studies should investigate the prognostic value of erythrocyte morphological indices in predicting hospitalization, transfusion requirements, organ damage, and long-term clinical outcomes among patients with sickle cell disease.
- Further studies should evaluate the influence of hydroxyurea therapy, nutritional status, iron metabolism, and genetic modifiers on erythrocyte morphological indices to improve understanding of disease heterogeneity and optimize patient-specific treatment strategies.

### *Contribution to Knowledge*

- This study provides evidence that erythrocyte morphological indices differ significantly between healthy individuals, patients with steady-state sickle cell disease, and those experiencing vaso-occlusive crisis, reflecting progressive deterioration in red cell morphology with increasing disease severity.
- The study demonstrates that the combined assessment of PCV, MCV, MCH, and MCHC offers a more comprehensive evaluation of anaemia severity than reliance on a single erythrocyte parameter.
- It establishes that routine erythrocyte morphological indices generated by automated haematologyanalysers can serve as simple, affordable, and readily available surrogate biomarkers for monitoring disease activity and guiding clinical management in sickle cell disease.
- The study highlights the usefulness of graphical analysis of erythrocyte indices in illustrating the continuum of red cell deterioration from healthy controls to steady-state disease and vaso-occlusive crisis, thereby enhancing interpretation of disease progression.

- The findings provide locally generated evidence from Nigeria supporting the integration of routine erythrocyte morphological indices into the assessment and management of patients with sickle cell disease, contributing to improved laboratory-based clinical decision-making in resource-constrained environments.

## STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of ethical approval*

Ethical clearance was obtained from Bayelsa State Ministry of Health which control activities of all Bayelsa State health facility and from the Federal Medical Center Yenagoa research committee.

### *Statement of informed consent*

Respect to participants' rights was observe including the right to refuse participation with explanation through participant's information form.

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