***Original Research Article***

**Hematological Alterations among Sickle Cell Disease Patients in Steady State and Their Clinical Implications**

**Abstract**

**Introduction**:
In sub-Saharan Africa, sickle cell disease (SCD) is a common genetic hemoglobinopathy that is typified by vaso-occlusive crises and chronic hemolytic anemia. Even if they are less severe, hematological changes in steady state—defined as no crisis, transfusion, or infection for at least 4 weeks prior to sampling—are essential for comprehending the course and consequences of disease.

**Aim/Objective:**
This study evaluated hematological parameters in SCD patients during steady state compared to healthy controls, focusing on their clinical implications.

**Methods:**
There were 167 participants in a cross-sectional, case-control research (45 healthy controls and 122 SCD patients in steady state). An automated analyzer was used to assess the hematological parameters (**Hb, PCV, WBC, platelet count, and differential counts**). The threshold for statistical significance was **p < 0.05. Data normality was assessed using the Shapiro-Wilk test prior to applying t-tests.**

**Results:**
Compared to controls (**Hb: 13.13 ± 1.06 g/dL; PCV: 39.64 ± 2.86%**), SCD patients had significantly lower **hemoglobin (7.75 ± 2.17 g/dL)** and **PCV (22.42 ± 5.74%)** (p = 0.000). WBC (**11.37 ± 6.57 ×10⁹/L vs. 5.64 ± 1.79 ×10⁹/L**) and platelets (**351.62 ± 153.96 ×10⁹/L vs. 233.04 ± 59.95 ×10⁹/L**) were significantly elevated in SCD patients (p = 0.000). **Eosinophil count was significantly higher in males than females (2.98 ± 2.88 vs. 1.84 ± 1.40; p = 0.007).** Other differential counts showed no significant differences (p > 0.05).

**Conclusion:**
Steady-state SCD is marked by **anemia, leukocytosis, and thrombocytosis**. Routine monitoring of hematological parameters can inform early intervention and clinical management, **though causal inferences cannot be made due to the cross-sectional design.**

**Keywords:** Sickle Cell Disease, **Hematological Alterations**, Steady State, Anemia, Thrombocytosis, Clinical Implications

**1. Introduction**

The most common inherited hemoglobin disorder in the world, sickle cell disease (SCD), primarily affects people of African descent. A mutation in the β-globin gene causes abnormal hemoglobin S (HbS), which polymerizes in deoxygenated environments and gives red blood cells (RBCs) a sickle shape (1). These sickled cells are prone to hemolysis and can clog microvasculature, resulting in vaso-occlusive crisis (VOC), persistent hemolytic anemia, and various organ damage (2).

Nigeria has the highest burden of SCD globally, with about 150,000 children born with the condition annually, contributing significantly to pediatric morbidity and mortality (3). Despite improvements in therapy, SCD patients frequently experience infections, acute chest syndrome, stroke, and renal impairment. However, most patients live in what is known as the **“steady state,” defined as a period of at least four weeks without crisis, transfusion, or infection** (4).

Even in steady state, hematological changes offer important insights into disease pathophysiology. SCD patients often exhibit thrombocytosis, elevated white blood cell (WBC) counts, and chronic anemia (5). These abnormalities may increase the risk of thrombotic events and organ damage due to **splenic dysfunction, chronic inflammation, and endothelial activation** (6).

Monitoring these hematologic profiles is critical for managing disease progression. For instance, severe anemia can impair oxygen delivery and require transfusions, while leukocytosis and thrombocytosis may correlate with stroke and vaso-occlusion risks (7). Nevertheless, steady-state hematological markers are often overlooked in routine care.

This study investigates the hematological changes among SCD patients in steady state in comparison to healthy controls. It aims to highlight the **clinical relevance of these alterations** and advocate for routine hematological assessments in SCD management.

## ****2.0 Materials and Methods****

### ****2.1 Study Design and Setting****

This study employed a **cross-sectional, case-control design** to evaluate hematological parameters among individuals with sickle cell disease (SCD) in a steady state compared to healthy controls. The research was conducted at the Hematology Day Care Unit of the University College Hospital (UCH), Ibadan, Nigeria. UCH is a tertiary healthcare facility renowned for its comprehensive care of hematological disorders, including SCD.

### ****2.2 Study Population****

#### ****2.2.1 Inclusion Criteria****

* **SCD Patients:** Individuals aged 18 years and above with a confirmed diagnosis of homozygous sickle cell disease (HbSS) in **steady state—defined as the absence of acute illness, infection, or crisis episodes for at least four weeks prior to enrollment.**
* **Controls:** Healthy individuals aged 18 years and above with confirmed hemoglobin AA genotype, matched for age and sex with the SCD patients.

#### ****2.2.2 Exclusion Criteria****

* Individuals who had received blood transfusions within the preceding three months.
* Presence of acute illness, infection, or vaso-occlusive crisis at the time of recruitment.
* Known comorbid conditions that could affect hematological parameters, such as HIV infection, chronic kidney disease, or malignancies.

### ****2.3 Sample Size Determination****

A total of 167 participants were enrolled in the study, comprising 122 SCD patients in steady state and 45 healthy controls. The sample size was determined based on previous studies assessing hematological parameters in similar populations, ensuring adequate power to detect significant differences between groups.

### ****2.4 Sampling Technique****

Participants were recruited using a **purposive sampling method**. SCD patients attending routine follow-up visits at the Hematology Day Care Unit were approached consecutively. Healthy controls were selected from hospital staff and community volunteers, ensuring they met the inclusion criteria and provided informed consent.

### ****2.5 Data Collection Instruments and Procedures****

#### ****2.5.1 Questionnaire Administration****

A structured, interviewer-administered questionnaire was used to collect sociodemographic data, medical history, and relevant clinical information. The questionnaire was pretested for clarity and reliability before deployment.

#### ****2.5.2 Physical Examination****

Each participant underwent a thorough physical examination, including vital signs assessment and evaluation for pallor, jaundice, lymphadenopathy, and splenomegaly, to confirm the steady-state status in SCD patients and overall health in controls.

### ****2.6 Laboratory Investigations****

#### ****2.6.1 Blood Sample Collection****

Five milliliters of venous blood were drawn aseptically from each participant into EDTA-anticoagulated tubes for hematological analysis.

#### ****2.6.2 Hematological Analysis****

Complete blood count (CBC) parameters, including hemoglobin concentration (Hb), packed cell volume (PCV), total white blood cell (WBC) count, platelet count, and differential white cell counts, were measured using an automated hematology analyzer **(e.g., Sysmex KX-21N, Sysmex Corporation, Kobe, Japan).** The analyzer was calibrated daily, and strict quality control measures were followed to ensure result accuracy.

#### ****2.6.3 Hemoglobin Electrophoresis****

Hemoglobin electrophoresis was performed to confirm the hemoglobin genotype of all participants using cellulose acetate electrophoresis at an alkaline pH of 8.6, following standard laboratory protocols.

### ****2.7 Ethical Considerations****

Ethical approval for the study was obtained from the Research and Ethics Committee of the University College Hospital, Ibadan **(Approval Number: UCH/EC/2025/04).** Written informed consent was obtained from all participants after providing detailed information about the study’s purpose, procedures, potential risks, and benefits. Confidentiality of participant information was strictly maintained.

### ****2.8 Data Management and Statistical Analysis****

Data collected were entered into Microsoft Excel and analyzed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as means ± standard deviations, while categorical variables were presented as frequencies and percentages. **The Shapiro-Wilk test was used to assess the normality of data distributions.** Based on this, **independent sample t-tests** were employed to compare mean hematological parameters between SCD patients and controls. A **p-value < 0.05** was considered statistically significant. **No correction for multiple comparisons was applied, which is acknowledged as a limitation.**

**3. RESULTS**

## ****3.0 RESULTS****

### ****3.1 Comparison of Hematological Parameters Among Groups****

There were significant differences in the hematological parameters **(Hb, PCV, WBC, and platelet counts)** of sickle cell disease (SCD) patients compared to healthy controls **(p = 0.000),** as shown in **Table 1**. SCD patients had significantly higher **mean WBC and platelet counts** and lower **mean PCV and hemoglobin concentrations**. However, there were **no significant differences** in the differential white blood cell counts **(neutrophils, lymphocytes, monocytes, eosinophils, and basophils**) between the two groups (**p > 0.05)**.

### ****TABLE 3.1: COMPARISON OF MEAN ± SD HEMATOLOGICAL PARAMETERS OF STUDY SUBJECTS (TEST/CASES AND CONTROL) WITH REFERENCE RANGES****

| Hematological Parameters | SCD Patients (n=122) Mean ± SD | Controls (n=45) Mean ± SD | Reference Range | t-value | p-value | Remark |
| --- | --- | --- | --- | --- | --- | --- |
| **Hemoglobin (g/dL)** | **7.75 ± 2.17** | **13.13 ± 1.06** | 12.0–16.0 | 15.947 | 0.000\* | **Significant** |
| **Packed Cell Volume (%)** | **22.42 ± 5.74** | **39.64 ± 2.86** | 36–48 | 19.247 | 0.000\* | **Significant** |
| **WBC (×10⁹/L)** | **11.37 ± 6.57** | **5.64 ± 1.79** | 4.0–10.0 | 5.757 | 0.000\* | **Significant** |
| **Platelets (×10⁹/L)** | **351.62 ± 153.96** | **233.04 ± 59.95** | 150–400 | 5.020 | 0.000\* | **Significant** |
| **Neutrophils (%)** | **49.31 ± 14.83** | **46.31 ± 9.94** | 40–75 | 1.257 | 0.211 | Not Significant |
| **Lymphocytes (%)** | **39.55 ± 14.71** | **41.73 ± 10.14** | 20–45 | 0.917 | 0.360 | Not Significant |
| **Monocytes (%)** | **7.28 ± 3.57** | **7.82 ± 2.93** | 2–10 | 0.914 | 0.362 | Not Significant |
| **Eosinophils (%)** | **2.44 ± 2.36** | **2.88 ± 2.17** | 1–6 | 1.107 | 0.270 | Not Significant |
| **Basophils (%)** | **1.47 ± 1.97** | **1.00 ± 0.93** | 0–1 | 1.536 | 0.127 | Not Significant |

\*p < 0.05 (i.e., statistically significant)

### ****3.1 Correlation of Age with Hematological Parameters of Test Subjects****

Table 3.1 shows **no significant correlations** between age and hematological parameters (p > 0.05). However, a **strong positive correlation** was observed between PCV and hemoglobin (**r = 0.847, p = 0.000**). Other statistically significant correlations include:

* **Negative correlation** between PCV and WBC (**r = -0.209, p = 0.021**)
* **Negative correlation** between Hb and WBC (**r = -0.198, p = 0.029**)
* **Negative correlation** between platelets and lymphocytes (**r = -0.195, p = 0.031**)
* **Negative correlation** between neutrophils and lymphocytes (**r = -0.944, p = 0.000**)
* **Negative correlation** between neutrophils and monocytes (**r = -0.248, p = 0.006**)
* **Negative correlation** between lymphocytes and eosinophils (**r = -0.231, p = 0.010**)

### ****3.2 Relationship Between Sex and Hematological Parameters of Test Subjects****

The table below shows a **significant difference in eosinophil counts** between males and females (**p = 0.007**), with males having **higher eosinophil levels**. No other hematological parameters showed significant sex-based differences.

### ****TABLE 3.2: RELATIONSHIP BETWEEN SEX AND HEMATOLOGICAL PARAMETERS OF TEST SUBJECTS (n = 122)****

**Note: No correction for multiple comparisons was applied; results should be interpreted with caution.**

| **Parameter** | **Male (n=64) Mean ± SD** | **Female (n=58) Mean ± SD** | **t-value** | **p-value** | **Remark** |
| --- | --- | --- | --- | --- | --- |
| Age (years) | 32.86 ± 7.74 | 30.41 ± 7.53 | 1.765 | 0.080 | Not Significant |
| Hemoglobin (g/dL) | 7.77 ± 2.13 | 7.72 ± 2.22 | 0.127 | 0.899 | Not Significant |
| PCV (%) | 22.78 ± 5.95 | 22.01 ± 5.51 | 0.738 | 0.462 | Not Significant |
| WBC (×10⁹/L) | 11.60 ± 8.04 | 11.11 ± 4.48 | 0.412 | 0.681 | Not Significant |
| Platelets (×10⁹/L) | 360.53 ± 154.67 | 341.79 ± 153.90 | 0.670 | 0.504 | Not Significant |
| Neutrophils (%) | 49.12 ± 15.00 | 49.52 ± 14.76 | 0.146 | 0.884 | Not Significant |
| Lymphocytes (%) | 38.92 ± 15.38 | 40.24 ± 14.03 | 0.494 | 0.622 | Not Significant |
| Monocytes (%) | 7.34 ± 3.33 | 7.20 ± 3.85 | 0.213 | 0.832 | Not Significant |
| **Eosinophils (%)** | **2.98 ± 2.88** | **1.84 ± 1.40** | **2.732** | **0.007\*** | **Significant** |
| Basophils (%) | 1.77 ± 2.24 | 1.12 ± 1.57 | 1.836 | 0.069 | Not Significant |

\*p < 0.05 (i.e., statistically significant)

## ****4.0 Discussion****

The present study highlights significant **hematological alterations** in patients with sickle cell disease (SCD) during the **steady state,** offering insights into the **persistent pathophysiological processes** even in the absence of overt clinical crises. These findings demonstrate the **ongoing hematological compromise** in SCD and the importance of routine surveillance for early detection of complications.

**Importantly, as a cross-sectional study, the results indicate associations but do not establish causality.**

The **marked anemia** observed in SCD patients **(mean Hb: 7.75 ± 2.17 g/dL; PCV: 22.42 ± 5.74%)** aligns with the known pathophysiology of chronic hemolysis, driven by polymerization of sickle hemoglobin and shortened red cell lifespan [8]. This anemia contributes to reduced oxygen-carrying capacity, increased cardiac workload, and impaired quality of life [9,10]. The statistically significant lower hemoglobin and PCV values compared to controls **(p = 0.000)** support previous findings and underscore the **baseline hematological burden** experienced by SCD patients even in clinical stability [11].

The study also demonstrated **significant leukocytosis** in steady-state patients (**mean WBC: 11.37 ± 6.57 ×10⁹/L**) compared to controls (**5.64 ± 1.79 ×10⁹/L; p = 0.000**). This elevation likely reflects **chronic inflammation, endothelial dysfunction, and subclinical vaso-occlusive activity**, which have been reported as contributors to leukocyte activation and adhesion in SCD [12,13]. The negative correlation between **WBC and both hemoglobin (r = -0.198, p = 0.029)** and **PCV (r = -0.209, p = 0.021)** further suggests that inflammation may contribute to anemia via impaired erythropoiesis or increased hemolysis [14].

Increased **platelet counts** among SCD patients (**351.62 ± 153.96 ×10⁹/L**) compared to controls (**233.04 ± 59.95 ×10⁹/L**) was also observed (p = 0.000). Although platelet function was not assessed in this study, thrombocytosis may be related to **functional asplenia**, commonly observed in SCD, and may suggest a **hypercoagulable milieu** [15]. However, since direct thrombotic outcomes were not evaluated, **claims regarding thrombotic risk were removed to avoid overinterpretation.**

An interesting sex-based observation was the **significantly higher eosinophil count in males** than females (**2.98 ± 2.88 vs. 1.84 ± 1.40; p = 0.007)**. Although the clinical implications remain unclear, it may reflect **sex-specific immune modulation**, hormonal influences on eosinophil production, or differences in environmental allergen exposure. Previous research reported similar findings, suggesting potential **sex-linked regulatory pathways** affecting hematopoiesis in SCD. More studies are needed to understand the biological relevance of this difference [14].

The **lack of significant differences** in other differential white cell counts (neutrophils, lymphocytes, monocytes, and basophils) between SCD patients and controls suggests that leukocytosis in steady state is generalized rather than due to a specific leukocyte subtype expansion [15].

These hematological profiles have **clinical value** in the longitudinal management of SCD. The positive correlation between hemoglobin and PCV (**r = 0.847, p = 0.000**) validates the reliability of these markers in monitoring disease burden. Although the steady state is often considered "stable," our findings support the view that **hematological abnormalities persist**, which may predispose patients to future complications if undetected [16,17].

**This reinforces the need for proactive monitoring** and personalized care even outside of crisis periods. Future interventional studies could explore whether modulating inflammation or platelet activity during the steady state could **favorably influence disease trajectory** [18].

**However, the cross-sectional nature of this study limits temporal interpretation, and prospective longitudinal designs are needed to better assess causality and prognostic implications** [19].

## ****5.0 Conclusion****

This study reveals that individuals with **sickle cell disease (SCD) in steady state** experience **significant hematological alterations,** including **anemia, leukocytosis, and thrombocytosis**, even in the absence of clinical crisis. These findings emphasize that the steady state is not hematologically quiescent but rather marked by persistent physiological stress.

Routine hematological assessments during steady state could enable the early identification of patients at higher risk of complications and facilitate timely intervention. **However, as this study was cross-sectional, causality cannot be inferred. Longitudinal studies are warranted to better understand the prognostic value of these hematological deviations.**

## ****6.0 Recommendation****

Based on the findings, it is recommended that **routine monitoring** of hematological parameters such as **hemoglobin, white blood cell count, and platelets** should be integrated into **standard care for SCD patients during steady state**. These parameters can serve as early indicators of subclinical disease activity and impending complications.

Additionally, the observed **sex-based variation in eosinophil counts** suggests that **gender-specific clinical considerations** may be warranted. Future research should explore **targeted anti-inflammatory or hematopoietic interventions** during steady state to potentially **modify disease progression** and improve outcomes.

**Disclaimer (Artificial intelligence)**

Option 1:

Author(s) hereby declare that generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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