***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 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, platelets, and differential counts). The threshold for statistical significance was p < 0.05.

**Results**:  
Compared to controls (13.13 ± 1.06 g/dL and 39.64 ± 2.86%, respectively; p = 0.000), SCD patients had significantly lower Hb (7.75 ± 2.17 g/dL) and PCV (22.42 ± 5.74%). Among SCD patients, there was an increase in WBC (11.37 ± 6.57 ×10⁹/L vs. 5.64 ± 1.79 ×10⁹/L) and platelet counts (351.62 ± 153.96 ×10⁹/L vs. 233.04 ± 59.95 ×10⁹/L) (p = 0.000). The counts of neutrophils, lymphocytes, monocytes, eosinophils, and basophils did not differ significantly (p > 0.05). There was a significant negative connection between Hb and WBC (r = -0.198, p = 0.029) and PCV and WBC (r = -0.209, p = 0.021). The number of eosinophils was higher in males (2.98 ± 2.88 vs. 1.84 ± 1.40; p = 0.007).

**Conclusion**:  
Steady-state SCD is marked by anemia, leukocytosis, and thrombocytosis, with potential thrombotic and inflammatory risks. Routine monitoring of these parameters is essential for early intervention and improved clinical outcomes.

**Keywords**: Sickle Cell Disease, Haematological 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 aberrant hemoglobin S (HbS) to be produced, 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).

About 150,000 children are born with sickle cell disease (SCD) each year in Nigeria, which has the highest prevalence of the condition worldwide, contributing to a considerable amount of pediatric morbidity and mortality (3). Patients with sickle cell disease (SCD) still frequently experience infections, acute chest syndrome, stroke, and renal impairment despite improvements in therapy. Patients spend the majority of their lives in what is known as the "steady state," which is characterized as a period of at least four weeks without recent transfusion, infection, or acute crisis, even if acute episodes frequently necessitate hospitalization (4).

Even in the steady state, haematological changes offer important information about the pathophysiology of the disease and the possibility of consequences. In steady state, SCD patients usually have thrombocytosis, high white blood cell (WBC) levels, and chronic anemia (5). These anomalies may put patients at risk for thrombotic episodes and organ damage since they are frequently associated with splenic dysfunction, chronic inflammation, and persistent endothelial activation (6).

It is essential to comprehend these haematological characteristics in order to monitor and manage diseases effectively. For example, severe anemia may require transfusion and affect overall quality of life, whereas leukocytosis and high platelet counts have been linked to an increased risk of stroke and vaso-occlusion (7). Haematological indicators in the steady state are frequently under-assessed in normal treatment, despite their clinical significance.

This study sought to examine the haematological changes in SCD patients during steady state, given the substantial health burden that the disease places on Nigeria and the continuous difficulties in managing it. The study aims to demonstrate the impact of these deviations on clinical outcomes and the significance of routine haematological monitoring for the early detection of complications by contrasting these findings with those of healthy controls.

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

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

This study employed a cross-sectional, case-control design to evaluate haematological parameters among individuals with sickle cell disease (SCD) in a steady state compared to healthy controls. The research was conducted at the Haematology 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 a 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 haematological 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 a steady state and 45 healthy controls. The sample size was determined based on previous studies assessing haematological 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 Haematology 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 ethylenediaminetetraacetic acid (EDTA) anticoagulated tubes for haematological analysis.

#### **2.6.2 Haematological Analysis**

Complete blood count (CBC) parameters, including hemoglobin concentration (Hb), packed cell volume (PCV), total white blood cell (WBC) count, and platelet count, were measured using an automated hematology analyzer (e.g., Sysmex KX-21N, Sysmex Corporation, Kobe, Japan). The analyzer was calibrated daily, and quality control measures were strictly adhered to, ensuring accuracy and reliability of results.

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

Hemoglobin electrophoresis was performed to confirm the hemoglobin genotype of all participants. This was conducted 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 maintained throughout the study.

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

Data collected were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (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. Independent sample t-tests were used to compare mean haematological parameters between SCD patients and controls. A p-value of less than 0.05 was considered statistically significant.

**3. RESULTS**

**3.1 COMPARISON OF HAEMATOLOGICAL PARAMETERS AMONG GROUPS**

There were significant differences between the Haematological Parameters (Hb, PCV, WBC and Platelets counts) of sickle cell patients compare to those who were normal (p=0.000) as shown in table 1; with sickle cell patients having a higher mean WBC and platelet counts respectively. Also, sickle cell patients had a lower mean PCV and Hb concentrations respectively. However, there were no significant differences between the Haematological Parameters (Neutrophylls, Lymphocytes, Monocytes, Eosinophil and Basophil) of sickle cell patients compared to those who were normal (p>0.05).

**TABLE 1: COMPARISON OF MEAN±SD HAEMATOLOGICAL PARAMETERS OF STUDY SUBJECTS (TEST/CASES AND CONTROL)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **SICKLE CELL PATIENTS (n=122)** | **NORMAL PEOPLE/CONTROL (n=45)** | **t-test** | **p-value** | **Remark** |
| **Haematological parameters** | **Mean**±SD | **Mean**±SD |  |  |  |
| Hb | 7.75 ± 2.17 | 13.13 ± 1.06 | 15.947 | 0.000\* | Significant |
| Packed Cell Volume (PCV) | 22.42 ± 5.74 | 39.64 ± 2.86 | 19.247 | 0.000\* | Significant |
| WBC (10^3) | 11.37 ± 6.57 | 5.64 ± 1.79 | 5.757 | 0.000\* | Significant |
| PLATELET | 351.62 ± 153.96 | 233.04 ± 59.95 | 5.020 | 0.000\* | Significant |
| NEUTROPHYLLS | 49.31 ± 14.83 | 46.31 ± 9.94 | 1.257 | 0.211 | Not Significant |
| LYMPHOCYTES | 39.55 ± 14.71 | 41.73 ± 10.14 | 0.917 | 0.360 | Not Significant |
| MONOCYTES | 7.28 ± 3.57 | 7.82 ± 2.93 | 0.914 | 0.362 | Not Significant |
| EOSINOPHIL | 2.44 ± 2.36 | 2.88 ± 2.17 | 1.107 | 0.270 | Not Significant |
| BASOPHIL | 1.47 ± 1.97 | 1.00 ± 0.93 | 1.536 | 0.127 | Not Significant |

\*p<0.05 (i.e. Significant).

**3.2 CORRELATION OF AGE WITH HAEMATOLOGICAL PARAMETERS OF TEST SUBJECTS**

The table below showed no significant correlations between Age and Haematological parameters of test subjects (p>0.05). The table also showed a strong statistically significant positive correlation between PCV and Hb (r =0.847, p=0.000) of test subjects. Also, there were significant positive correlation between the Platelet count and Basophill (r= 0.178, p=0.050). More so, a significant strong negative correlations were observed between PCV and WBC (r= -0.209, p=0.021); Hb and WBC (r= -0.198, p=0.029); Platelet count and Lymphoctes (r= -0.195, p=0.031); Neutrophyl and Lymphocytes (r= -0.944, p=0.000); Neutrophyl and Monocytes (r= -0.248, p=0.006); and Lymphocytes and Eosinophyl (r= -0.231, p=0.010).

**TABLE 2: CORRELATION OF AGE WITH HAMATOLOGICAL PARAMETERS OF TEST SUBJECTS (n=122)**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Variables (r values**  **(p values)** | **Age (years)** | **Hb** | **PCV** | **WBC** | **Platelet** | **Neutro** | **Lymphocytes** | **Monocytes** | **Eosinophil** | **Basophil** |
| Age | 1 |  |  |  |  |  |  |  |  |  |
| Hb | 0.075 (0.412) | 1 |  |  |  |  |  |  |  |  |
| PCV | 0.012 (0.899) | **0.847 (0.000\*)W** | 1 |  |  |  |  |  |  |  |
| WBC (10^3) | 0.073 (0.422) | **-0.198 (0.029\*)** | **-0.209 (0.021\*)** | 1 |  |  |  |  |  |  |
| Platelets | -0.074 (0.419) | -0.136 (0.134) | -0.118 (0.194) | 0.009 (0.922) | 1 |  |  |  |  |  |
| Neutrophylls | 0.100 (0.274) | -0.021 (0.817) | -0.065 (0.478) | -0.128 (0.160) | 0.152 (0.095) | 1 |  |  |  |  |
| Lymphocytes | -0.097 (0.290) | 0.064 (0.486) | 0.120 (0.189) | 0.157 (0.083) | **-0.195 (0.031\*)** | **-0.944 (0.000\*)** | 1 |  |  |  |
| Monocytes | -0.103 (0.260) | -0.118 (0.195) | -0.108 (0.235) | -0.086 (0.348) | 0.105 (0.251) | **-0.248 (0.006\*)** | 0.005 (0.953) | 1 |  |  |
| Eosinophil | 0.136 (0.134) | -0.057 (0.531) | -0.113 (0.216) | -0.107 (0.240) | 0.026 (0.778) | 0.034 (0.707) | **-0.231 (0.010\*)** | 0.061 (0.502) | 1 |  |
| Basophil | 0.017 (0.855) | -0.003 (0.978) | -0.033 (0.718) | 0.068 (0.459) | **0.178 (0.050\*)** | -0.024 (0.794) | -0.104 (0.255) | -0.096 (0.293) | 0.153 (0.092) | 1 |

\*p<0.05 (i.e. Significant).

**3.3 RELATIONSHIP BETWEEN SEX AND HAMATOLOGICAL PARAMETERS OF TEST SUBJECTS**

The table below showed that there was a significant difference between the Haematological Parameters (Eosinophil) of sickle cell patients in relation to sex (p=0.007) as shown in table 3; with male sickle cell patients having a higher mean Eosinophil value. However, there were no significant differences between the Hamatological Parameters (PCV, Hb, WBC, Platelets counts, Neutrophils, Lymphocytes, Monocytes and Basophil) of sickle cell patients in relation to sex of these patients (p>0.05).

**TABLE 3: RELATIONSHIP BETWEEN SEX AND HAMATOLOGICAL PARAMETERS OF TEST SUBJECTS (n=122)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Hematological Parameters** | **SEX** | | **t-test** | **p-value** | **Remark** |
|  | Male (n=64) | Female (n=58) |  |  |  |
|  | Mean (±SD) | Mean (±SD) |  |  |  |
| Age | 32.86 ± 7.74 | 30.41 ± 7.53 | 1.765 | 0.080 | Not Significant |
| Hb | 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 (10^3) | 11.60 ± 8.04 | 11.11 ± 4.48 | 0.412 | 0.681 | Not Significant |
| Platelets | 360.53 ± 154.67 | 341.79 ± 153.90 | 0.670 | 0.504 | Not Significant |
| Neutrophylls | 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 |
| Eosinophil | 2.98 ± 2.88 | 1.84 ± 1.40 | 2.732 | 0.007\* | Significant |
| Basophil | 1.77 ± 2.24 | 1.12 ± 1.57 | 1.836 | 0.069 | Not Significant |

\*p<0.05 (i.e. Significant).

**4.0 Discussion**

Significant haematological changes in sickle cell disease (SCD) patients during steady state are highlighted by the study's findings, which offer crucial new information about the enduring pathophysiological processes that go on even when there are no acute crises. The chronic hemolytic character of sickle cell disease (SCD), where sickle hemoglobin polymerization causes erythrocyte destruction and reduced red blood cell survival, is reflected in the severe anemia seen (mean hemoglobin 7.75 ± 2.17 g/dL; PCV 22.42 ± 5.74%) [8]. Significant clinical repercussions of this level of anemia include decreased oxygen transport to tissues, elevated heart workload, and a decline in quality of life [9]. SCD patients have considerable hematological compromise even during clinical stability, which calls for continuous monitoring and therapy, as seen by the significantly lower hemoglobin and hematocrit values compared to healthy controls (p = 0.000) [10].

The significant leukocytosis in steady-state SCD patients was one of the most noteworthy findings (mean WBC 11.37 ± 6.57 ×10⁹/L versus 5.64 ± 1.79 ×10⁹/L in controls; p = 0.000). The chronic inflammatory state that characterizes sickle cell disease (SCD) that is fueled by endothelial activation, ischemia-reperfusion damage, and recurrent vaso-occlusion is probably reflected in this persistent rise of white blood cells [11]. WBC count and hemoglobin (r = -0.198, p = 0.029) and hematocrit (r = -0.209, p = 0.021) have negative relationships, which implies that inflammation may exacerbate anemia by suppressing erythropoiesis or increasing hemolysis [12].

These results are consistent with the increasing understanding that inflammation, especially in times of clinical stability, plays a significant role in the pathogenesis of SCD [6]. The prothrombotic state that is present in steady-state SCD is further highlighted by the higher platelet counts (351.62 ± 153.96 ×10⁹/L versus 233.04 ± 59.95 ×10⁹/L in controls; p = 0.000), which may put patients at risk for silent vascular consequences [13].

Male SCD patients had significantly higher eosinophil counts than females (2.98 ± 2.88 versus 1.84 ± 1.40; p = 0.007), however the study also found some intriguing sex-based differences. This study raises the possibility of sex-specific variations in immune modulation or inflammatory responses in SCD, but more research is needed to determine its clinical importance [14]. The fact that there are no appreciable variations in other differential counts between SCD patients and controls suggests that the leukocytosis seen is a broad rise in white blood cells rather than an expansion of a particular component [15].

These results have significant therapeutic ramifications for the treatment of SCD. This period shouldn't be regarded as completely asymptomatic, according to the chronic hematological abnormalities seen throughout steady state [7]. Early management may be possible if routine monitoring is used to identify people who are more likely to experience difficulties [16]. The persistent use of these straightforward assays for monitoring is supported by the significant connection between PCV and hemoglobin (r = 0.847, p = 0.000) [17]. The results also call into question whether controlling thrombocytosis or inflammation in the steady state could alter the course of the disease [18].

Future longitudinal research would more effectively establish prognostic value, and the cross-sectional form of the study restricts the ability to draw conclusions about causality [19]. Novel treatment targets may be found by investigating the mechanisms underlying these changes [2].

**5.0 Conclusion**

Significant haematological changes in sickle cell disease (SCD) patients during steady state are highlighted by the study's findings, which offer crucial new information about the enduring pathophysiological processes that go on even when there are no acute crises. The chronic hemolytic character of sickle cell disease (SCD), where sickle hemoglobin polymerization causes erythrocyte destruction and reduced red blood cell survival, is reflected in the severe anemia seen (mean hemoglobin 7.75 ± 2.17 g/dL; PCV 22.42 ± 5.74%) (8). Significant clinical repercussions of this level of anemia include decreased oxygen transport to tissues, elevated heart workload, and a decline in quality of life (9). SCD patients have considerable hematological compromise even during clinical stability, which calls for continuous monitoring and therapy, as seen by the significantly lower hemoglobin and hematocrit values compared to healthy controls (p = 0.000) (10).

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Male SCD patients had significantly higher eosinophil counts than females (2.98 ± 2.88 versus 1.84 ± 1.40; p = 0.007), however the study also found some intriguing sex-based differences. This study raises the possibility of sex-specific variations in immune modulation or inflammatory responses in SCD, but more research is needed to determine its clinical importance (14). The fact that there are no appreciable variations in other differential counts between SCD patients and controls suggests that the leukocytosis seen is a broad rise in white blood cells rather than an expansion of a particular component (15).

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Future longitudinal research would more effectively establish prognostic value, and the cross-sectional form of the study restricts the ability to draw conclusions about causality (19). Novel treatment targets may be found by investigating the mechanisms underlying these changes (2).

**6.0 Recommendation**

Future research should investigate targeted anti-inflammatory and antithrombotic therapies during steady state to potentially modify disease progression and improve clinical outcomes. Based on the study findings, we recommend routine hematological monitoring for sickle cell disease (SCD) patients in steady state, with particular attention to hemoglobin levels, white blood cell counts, and platelet indices. These parameters reflect ongoing disease activity and potential risk for complications, and healthcare providers should consider incorporating these assessments into standard follow-up protocols to enable early detection of abnormalities and timely intervention. Furthermore, the observed sex-based variations in eosinophil counts highlight the significance of individualized care approaches for this complicated hematologic illness and point to the necessity of gender-specific considerations in SCD management techniques.

**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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