



# Hematological Profile of Adult Haemoglobin SS and SC Sickle Cell Patients in Stationary Phase: Evidences from National Teaching Hospital of Cotonou in Benin

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## Authors' contributions

*This work was carried out in collaboration among all authors. All authors contributed to the paper. All authors helped to conceptualise ideas, interpret the findings and contributed to the revision of the manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

**Background and Objective:** Sickle cell disease is a major public health problem. The aim of this study was to determine the hematological parameters in the inter-critical period of adult sickle cell patients at the National Teaching Hospital CNHU-HKM of Cotonou.

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**Materials and Methods:** This is a descriptive study with analytical aims carried out from July 2021 to December 2021 in the hematology department of the National Teaching Hospital CNHU-HKM of Cotonou. An hemogram was performed using Sysmex XT 4000i on a total of 181 sickle cell patients including 119 Hb SS and 62 Hb SC. Data were analyzed using R software.

**Results:** Patients studied had a mean age of  $32 \pm 13$  years. The mean of hemoglobin level was  $7.7 \pm 1.9$  g/dL in Hb SS patients versus  $11.27 \pm 1.79$  g/dL in Hb SC patients ( $p = 0.001$ ). The mean leukocyte count was  $13.2 \pm 4.4$  G/L in Hb SS patients versus  $7.3 \pm 3$  G/L in Hb SC patients ( $p = 0.003$ ); the mean neutrophil count was  $6.93 \pm 3.24$  G/L in Hb SS patients versus  $3.96 \pm 1.72$  G/L in Hb SC patients ( $p = 0.001$ ). Platelet counts averaged  $426 \pm 213$  G/L in Hb SS patients versus  $223 \pm 103$  G/L in Hb SC patients ( $p = 0.001$ ).

**Conclusion:** This study revealed a higher mean hemoglobin level, mean leukocyte count and mean platelet count in Hb SS patients compared to Hb SC patients in the stationary phase.

*Keywords: Sickle cell disease; hemogram; stationary phase; Benin.*

## 1. INTRODUCTION

Sickle cell disease is the most prevalent genetic disorder in the African region of the World Health Organization [1,2]. In 2006, the WHO recognized it as a public health priority. In Benin, the prevalence of sickle cell disease is estimated at 4.8% [3]. The clinical course of major sickle cell disease can be categorized into three phases: the stationary phase, acute complications, and chronic complications. The stationary phase is defined by the absence of fever, bone or abdominal pain, and acute hemolysis, whereas the critical phase is marked by acute pain, infectious episodes, and anemic crises. The presence of hemogram abnormalities during these different phases underscores the importance of a comprehensive understanding of hemogram parameters for the overall management of sickle cell disease, which includes regular and systematic follow-up [4]. The hemogram standards during the stationary period in sickle cell disease differ from those of a healthy subject. Documenting these standards is crucial for accurate hemogram interpretation. In Benin, the existing literature in this area reveals a significant lack of knowledge regarding the hematological parameters of sickle cell patients in the stationary phase. This study aims to analyze the hematological parameters of sickle cell patients during the inter-critical period. The findings of this study will not only enhance the existing literature but also provide reference values for biologists, serving as a basis for comparison with sickle cell patients in crisis.

## 2. MATERIALS AND METHODS

**Settings and participants of the study:** This study is prospective descriptive research

conducted from July 2021 to December 2021 at the Hematology Teaching Hospital, located at CNHU-HKM in Cotonou. The study population comprised 181 sickle cell patients, with 119 having Hb SS and 62 having Hb SC. These patients were under regular and comprehensive monitoring, with a minimum of 3 consultations per year. Additionally, they met the criteria of being aged 18 years or older, being in the stationary phase for a minimum of 3 months, and receiving care at the outpatient clinic. Importantly, the patients had not undergone any blood transfusions within the last 3 months, nor were they currently on hydroxyurea treatment.

**Sampling and Hematological analysis:** For each patient, a sample was collected using tubes containing tripotassium ethylene diamine tetraacetic (EDTA-K3) and immediately sent to the hematology laboratory at the same center. Hematological analysis was conducted using the Sysmex XT 4000i automated system, employing hydro-focusing and flow cytometry techniques. Various methods were used for different hemogram parameters: spectrophotometry for hemoglobin determination, impedance-based hematologic analyzers for red cell, leukocyte, and platelet counts, and flow cytometry for leukocyte count, reticulocyte count, and erythroblast count. The blood count parameters measured included hemoglobin level (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), platelet count (Plat), white blood cell count (WBC), and the differential blood count for identifying the number of neutrophils (Neut), lymphocytes (Ly), eosinophils (Eo), basophils (Baso), and monocytes (Mono). Furthermore, internal quality controls

(combination of commercial three levels controls) for the blood count were conducted daily, and the results were systematically validated by a biologist. An external QC program was performed (Probioqual, Lyon, France). Blood smears were also routinely examined after fixation and staining with May-Grünwald Giemsa. The patients' values were compared against the laboratory's reference interval [5].

**Statistical investigation:** The data collected were entered and processed using Excel 2016 software, and further analyzed and compared using R. Means for each parameter were presented along with standard deviations, considering a 95% confidence interval. Decisions regarding means comparison were determined through t-tests at the same confidence level.

### 3. RESULTS

During the study duration, a total of 181 sickle cell patients were enrolled, with a breakdown of 119 individuals having Hb SS and 62 individuals having Hb SC. The gender distribution revealed a higher representation of females, accounting for 56.36% of the total participants, resulting in a male-to-female (M/F) sex ratio of 0.8. Table 1 illustrates the distribution of patients based on their sex and hemoglobin profile.

The average age of patients was  $32 \pm 13$  years, with a range spanning from 18 to 95 years. The mean age for individuals with Hb SS was 29 years, while those with Hb SC had a slightly higher mean age of 37 years.

Among the Hb SS sickle cell population, anemia was evident, with an average hemoglobin level of  $7.70 \pm 1.90$  g/dL, whereas Hb SC sickle cell patients had a higher mean hemoglobin level of  $11.27 \pm 1.79$  g/dL. In subjects with SS genotype, the average hemoglobin level stood at  $7.6 \pm 1.6$  for males and  $7.6 \pm 1.7$  g/dL for females ( $p = 0.79$ ). Among subjects with SC genotype, the

average hemoglobin level was  $10.4 \pm 1.3$  g/dL or females and  $11.8 \pm 1.7$  for males ( $p = 0.0001$ ).

In the Hb SS group, normocytic anemia was observed in 62.4% of cases, while 37.6% exhibited either microcytic or macrocytic anemia. In contrast, Hb SC patients showed normocytic anemia in 8.1% of cases and microcytic anemia in 91.9%.

Regarding the mean corpuscular hemoglobin concentration, it was  $33.86\% \pm 1.88$  in the Hb SS sickle cell population, while it measured  $34.81\% \pm 2.17$  in the Hb SC sickle cell population.

Microscopic examination of blood smears unveiled a plethora of qualitative abnormalities in red blood cells, predominantly characterized by aniso-poikilocytosis, sickle cells, Jolly bodies, and target cells.

In individuals carrying the Hb SS sickle cell trait, the mean platelet count stood at 426 G/L, as opposed to 223 G/L in those with the SC sickle cell trait.

Hyperleukocytosis manifested universally in Hb SS patients, with a mean value of  $13.2 \pm 4.4$  G/L. For SC patients, the mean white blood cell count registered  $7.3 \pm 3.0$  G/L. Among SS individuals, the mean neutrophil count measured  $6.93 \pm 3.24$  G/L, whereas in the SC cohort, it was  $3.96 \pm 1.72$  G/L. The average eosinophil count in SS subjects reached  $0.35 \pm 0.44$  G/L, compared to  $0.17 \pm 0.26$  G/L in the SC group. SS patients exhibited a mean monocyte count of  $0.71 \pm 0.58$  G/L, whereas SC patients showed  $0.37 \pm 0.34$  G/L. Lastly, the mean lymphocyte count was  $4.94 \pm 2.13$  G/L among SS individuals, in contrast to an average of  $2.62 \pm 1.22$  G/L in SC individuals.

Table 2 provides a summary of the mean values for hemogram parameters according to hemoglobin type.

**Table 1. Sample distribution by gender and hemoglobin profile**

	Hb SS patients		Hb SC patients		Total
	N	%	N	%	
Female	70	58.8	32	51.6	102
Male	49	41.2	30	48.4	79
Total	119	100	62	100	181

**Table 2. Mean values of blood count parameters in our study sample**

Parameters	Reference interval adult AA in our laboratory [5]		Hb SS Sickle cell patients			Hb SC Sickle cell patients			p
	Male	Female	M	SD	CI	M	SD	CI	
HBC (g/dL)	12 - 16	11.5 - 14	7.70	1.90	6.50 – 8.80	11.27	1.79	9.95 – 2.28	0.001
HCT (%)	36 - 49	30 - 40	23	5	19 - 26	33	5	29 - 37	0.001
MCV (fL)	80 - 90		84	9	78 - 91	72	8	69 - 75	0.001
MCH (pg)	25 - 32		28.5	3.5	26.6 – 30.6	25.5	2.8	23.4 – 26.9	0.001
MCHC (%)	30 - 36		33.86	1.88	33 - 35	34.81	2.17	34 - 36	0.006
PLT (G/L)	150 - 400		426	213	295 - 492	223	103	154 - 270	0.001
WBC (G/L)	3 - 8		13.2	4.4	10.8 - 14	7.3	3	6.2 – 8.5	0.003
NEUT (G/L)	1.5 - 6		6.93	3.24	5.04 – 8.05	3.96	1.72	3.02 – 4.45	0.001
EO (G/L)	0.15 à 0.4		0.35	0.44	0.00 – 0.49	0.17	0.26	0.00 – 0.23	0.001
BASO (G/L)	0.05 à 0.15		0.04	0.12	0.00 – 0.00	0.04	0.15	0.00 – 0.02	0.8
LY (G/L)	1.5 - 4		4.94	2.13	3.55 – 5.81	2.62	1.22	1.72 – 3.26	0.001
MONO (G/L)	0.2 à 0.8		0.71	0.58	0.30 – 1.03	0.37	0.34	0.00 – 0.60	0.001

HBC: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin MCHC: Mean corpuscular hemoglobin concentration, PLT: Platelets, WBC: White blood cell count, NEUT: Neutrophils, EO: Eosinophils, BASO: Basophils, LY: Lymphocytes, MONO: Monocytes, M: Mean, SD: Standard deviation, CI: Confidence interval

#### 4. DISCUSSION

The characteristics of our study sample closely align with those described in the existing literature. Similar trends in gender distribution were observed in studies by Doupa et al. in Senegal [6], Kocko et al. in Congo [7], Elisangela et al. in Brazil [8], Omoti et al. in Nigeria [9], and Nacoulma et al. in Burkina Faso [10], all of which reported a predominance of females, with sex ratios of 0.7, 0.9, 0.9, 0.8, and 0.9, respectively. On the other hand, authors such as Mounkaila et al. in Niger [11] and Dahmani et al. in Morocco [12] found a predominance of males in their series, with sex ratios of 1.1 and 1.2, respectively. The age distribution also corresponds to the literature, with the average age being 32, consistent with previous reports [7].

Anemia was a prevalent feature in the majority of Hb SS patients in our sample (96.6%). Normocytic anemia constituted 62.4% of cases, which is comparable to the findings reported by Dahmani et al. [12], who observed 88.5% anemia with 67.8% being normocytic. Normocytic normochromic anemia in Hb SS homozygotes reflects the ongoing hemolysis characteristic of these patients, even during the stationary phase. Cases of microcytic anemia could be attributed to possible iron deficiencies and/or concurrent thalassemia. Hb SC patients exhibited microcytic anemia in 91.9% of cases. It's noteworthy that hemoglobinopathy C often presents with microcytosis with or without anemia, and in cases of chronic hemolysis, this microcytosis may transition to normocytosis [13].

In the white blood cell line, hyperleukocytosis was consistently observed in all patients in our stationary phase SS cohort. This finding corroborates existing literature, indicating that in homozygous SS sickle cell patients, hyperleukocytosis is present even in the absence

of infections [13]. This hyperleukocytosis is linked to the chronic hypercoagulable state seen in sickle cell disease, with associated alterations in hemostasis and inflammation [14-15]. In contrast, double heterozygotes SC in the stationary period did not show significant changes in their blood counts [12].

SS homozygotes exhibited a mean platelet count of 426 G/L. The thrombocytosis observed in SS homozygotes can also be attributed to the changes in hemostasis and hypercoagulability seen in these patients [15].

Table 3 summarizes data from various studies on the main hemogram parameters' characteristics in stationary sickle-cell patients in sub-Saharan Africa.

The interpretation of hemogram counts must consider the reference intervals specific to the relevant populations [16]. To ensure accurate technical and biological validation of blood counts, it is essential to establish the reference ranges for sub-Saharan African populations. This holds true, especially for sickle-cell patients, where interpretation varies based on whether the disease is in the stationary or critical phase. Three key points emerge: the basal hemoglobin level and knowledge of the baseline hemoglobin level during the stationary phase is crucial for both patients and the medical community. It serves as a fundamental parameter for monitoring and making informed therapeutic decisions, particularly in the context of blood transfusions; Microcytosis investigation and if microcytosis is identified, a thorough investigation should be conducted to assess the potential presence of iron deficiency or associated thalassemia. This diagnostic step is essential for understanding the underlying causes of microcytic anemia in sickle-cell patients and hyperleukocytosis definition which

**Table 3. Comparison of mean adult hemogram parameters in different studies**

	Our study		Congo	Senegal	Burkina-Faso		Maroc	Niger		Nigeria
	SS	SC	SS	SS	SS	SC	SS	SS	SC	SS
Frequency (N)	119	62	122	100	20	20	87	73	24	162
HBC (g/dL)	7.70	11.27	6.48	8.2	7.8	9.8	7.59	7.8	10.7	7.54
MCV (fL)	84	72	81.97	83.2	86.3	82.28	80.81	79	75	79.38
WBC (G/L)	13 ;2	7.3	16.22	12.35	15.24	9.82	13.55	12.72		12.72
PLT (G/L)	426	223	180.5	439	323	339	335.9	511	389	342

*HBC: Hemoglobin, MCV: Mean corpuscular volume, WBC: White blood cells, PLT: Platelets*

should consider the elevated white blood cell counts already observed in sickle-cell SS patients during the inter-critical phase. This context-specific understanding ensures a proper assessment of white blood cell levels in sickle cell disease. By incorporating these considerations into the interpretation of hemogram counts, healthcare professionals can enhance the accuracy of diagnosis, monitoring, and decision-making for sickle-cell patients. It underscores the importance of utilizing reference intervals specific to the population and the disease phase to provide the most meaningful clinical insights.

## 5. CONCLUSION

This study is preliminary and a first in Benin. It concerns the hemogram profile of adult SS and SC sickle cell patients in stationary phase at the National Teaching Hospital CNHU-HKM in Cotonou. The results are similar to those reported in the literature, with a significant difference in hemoglobin, leukocyte and neutrophil counts according to hemoglobin type. They should be taken into account in the interpretation and technical and biological validation of blood tests on sickle cell patients in stationary phase. They can also be used as a basis for comparison during critical episodes and for monitoring treatment.

## 6. STUDY BIASES AND LIMITATIONS

Sample size was a limiting factor in the power of our study. Further work with a larger sample size will enable us to refine the reference values of the blood count in this patient profile.

The cross-sectional nature of our study may constitute a bias due to the variation in erythrocyte constants resulting from the existence of several factors likely to modify them (parasitosis, nutritional deficiencies, iron deficiency anemia, etc.).

## CONSENT AND ETHICAL APPROVAL

This study received approval from the Institutional Committee of Ethics and Research at the University of Parakou (Authorization 0397/CLERB-UP/P/SP/R/SA). Prior to the study commencement, participants were provided with detailed information through a newsletter, which included the study's objectives, benefits, and associated risks, in order to obtain informed consent. The confidentiality of research results

was maintained by utilizing a unique code for each patient.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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