

Research Article

Advances in Hematology and Oncology Research

Evaluation of Hemoglobin Variants among Patients with Sickle Cell Anemia in Khartoum State, Sudan

Mohammed Osman Ali Mohammed¹, Hadeel Ali², Ibrahim Bakhit³ and Ghanem Mohammed Mahjaf^{4*} 

¹PhD, Department of Hematology, Faculty of Medical Laboratory Sciences, Shendi University Sudan

²MSc, Department of Hematology, Faculty of Medical Laboratory Sciences, Shendi University, Sudan

³PhD, Department of Histopathology, Faculty of Medical Laboratory Sciences, Shendi University, Sudan

⁴Department of Medical Microbiology, Faculty of Medical Laboratory Sciences, Shendi University, Sudan

***Corresponding Author**

Ghanem Mohammed Mahjaf, Department of Medical Microbiology, Faculty of Medical Laboratory Sciences, Shendi University, Sudan.

Submitted: 2026, Sep 26; **Accepted:** 2026, Oct 19; **Published:** 2026, Oct 26

Citation: Mohammed, M. O. A., Ali, H., Bakhit, I., Mahjaf, G. M. (2026). Evaluation of Hemoglobin Variants among Patients with Sickle Cell Anemia in Khartoum State, Sudan. *Adv Hema Onco Res*, 9(2), 01-05.

Abstract

Background: Sickle cell anemia (SCA) is one of the most common inherited hemoglobin disorders in Sudan, with a particularly high prevalence among populations originating from western regions of the country. The disease is characterized by abnormal hemoglobin S (HbS), which leads to chronic hemolytic anemia and recurrent vaso-occlusive complications. Assessment of hemoglobin variants is essential for disease diagnosis, monitoring, and evaluating treatment response, particularly to hydroxyurea therapy.

Methods: A hospital-based case-control study was conducted between November 2022 and March 2023 at the Sickle Cell Clinic of Gaafar Ibn Auf Specialized Hospital and Omdurman Children's Emergency Hospital, Khartoum State, Sudan. A total of 75 participants were enrolled, including 50 patients diagnosed with sickle cell anemia and 25 healthy controls. Venous blood samples were collected in EDTA tubes, and hemoglobin variants (HbA, HbA₂, HbS, and HbF) were measured using the CAPILLARYS 2 FLEX PIERCING system. Statistical analysis was performed using SPSS software, with a p-value <0.05 considered statistically significant.

Results: The mean percentages of HbS, HbA, HbA₂, and HbF among patients with SCA were 78%, 7.2%, 3.0%, and 10.0%, respectively, compared with 0.0%, 97.0%, 2.5%, and 0.0% among healthy controls. Significant differences were observed between cases and controls in HbS, HbA, and HbF levels ($p < 0.001$), whereas HbA₂ levels did not differ significantly ($p = 0.40$). Among patients receiving hydroxyurea therapy, the mean HbF level was markedly higher (14%) than among those not receiving hydroxyurea (1%) ($p < 0.001$). No significant associations were found between hemoglobin variants and patients' age or sex.

Conclusion: Patients with sickle cell anemia demonstrated significantly elevated HbS and HbF levels and reduced HbA levels compared with healthy individuals. Hydroxyurea therapy was associated with a substantial increase in fetal hemoglobin (HbF), supporting its beneficial role in the management of sickle cell anemia.

Keywords: Sickle Cell Anemia, Hemoglobin Variants, Hemoglobin S, Fetal Hemoglobin, Hydroxyurea, Sudan

List of Abbreviations

SCA: Sick Cell Anemia

SCD: Sick Cell Disease

HbS: Hemoglobin S

HbA: Hemoglobin A

HbA₂: Hemoglobin A₂

HbF: Fetal Hemoglobin

HU: Hydroxyurea

EDTA: Ethylenediaminetetraacetic Acid

SPSS: Statistical Package for the Social Sciences

SD: Standard Deviation

β-globin: Beta-globin

1. Introduction

Sickle cell disease (SCD) is one of the most common inherited hemoglobin disorders worldwide. It is an autosomal recessive disease caused by a single point mutation in the β-globin gene, resulting in the production of abnormal hemoglobin S (HbS). Under deoxygenated conditions, HbS polymerizes, causing red blood cells to become rigid and assume a characteristic sickle shape. These abnormal erythrocytes exhibit reduced deformability, increased fragility, and a shortened lifespan, leading to chronic hemolytic anemia and recurrent vaso-occlusive episodes that contribute to progressive organ damage and reduced life expectancy [1,2]. Globally, approximately 300,000–400,000 infants are born annually with sickle cell disease, with the highest burden occurring in sub-Saharan Africa. The clinical manifestations of SCD are highly variable and include recurrent painful vaso-occlusive crises, acute chest syndrome, stroke, severe infections, splenic dysfunction, and chronic complications affecting the kidneys, liver, lungs, and other organs. Early diagnosis and appropriate therapeutic interventions are essential for reducing disease-related morbidity and mortality. Current treatment strategies include supportive care, blood transfusion, hydroxyurea therapy, and hematopoietic stem cell transplantation [3].

Sudan is among the countries with a high prevalence of sickle cell disease, particularly in western regions such as Kordofan and Darfur. The disease is especially common among the Messiria, Baggara, Hausa, Fulani, and Blue Nile tribes because of the high frequency of the sickle cell gene within these populations. Previous studies have reported carrier rates reaching up to 30% in some communities of western Sudan, making SCD a significant public health concern [4]. Hydroxyurea is currently considered the cornerstone pharmacological therapy for patients with sickle cell anemia. It increases fetal hemoglobin (HbF) production, thereby reducing HbS polymerization, decreasing the frequency of vaso-occlusive crises, and improving overall clinical outcomes. Measurement of hemoglobin variants, including HbA, HbA₂, HbF, and HbS, provides valuable information for confirming the diagnosis, monitoring disease severity, and evaluating therapeutic response [5,6]. Although several studies have investigated sickle cell disease in Sudan, data describing the distribution of hemoglobin variants among Sudanese patients remain limited. Therefore, this study aimed to evaluate hemoglobin variants among patients with sickle cell anemia in Khartoum State, Sudan, and to assess the

influence of hydroxyurea therapy on fetal hemoglobin levels.

2. Materials and Methods

2.1. Study Design

A hospital-based case-control study was conducted between November 2022 and March 2023 to evaluate hemoglobin variants among patients with sickle cell anemia in Khartoum State, Sudan.

2.2. Study Area

The study was carried out at the Sick Cell Clinic of Gaafar Ibn Auf Specialized Hospital and Omdurman Children's Emergency Hospital, both located in Khartoum State, Sudan.

2.3. Study Population

The study included 75 participants of both sexes and different age groups. Fifty patients with confirmed sickle cell anemia were recruited as the case group, while 25 apparently healthy individuals without sickle cell disease were enrolled as the control group.

2.4. Inclusion Criteria

- Patients with confirmed sickle cell anemia.
- Individuals of both sexes.
- Participants who agreed to participate in the study and provided informed consent.

2.5. Exclusion Criteria

- Individuals with incomplete clinical information.
- Patients with other known hemoglobinopathies or hematological disorders.
- Participants who declined to participate.

2.6. Sample Collection

Approximately 2–3 mL of venous blood was collected aseptically from each participant into ethylenediaminetetraacetic acid (EDTA) anticoagulant tubes. The samples were gently mixed and analyzed according to standard laboratory procedures.

2.7. Laboratory Analysis

Hemoglobin variants, including HbA, HbA₂, HbF, and HbS, were analyzed using the Capillary's 2 Flex Piercing automated capillary electrophoresis system following the manufacturer's instructions. This technique separates hemoglobin fractions based on their electrophoretic mobility and provides quantitative measurements of each hemoglobin variant.

2.8. Data Collection

Demographic and clinical information, including age, sex, and hydroxyurea treatment status, was collected using a structured questionnaire administered through face-to-face interviews with the participants or their guardians.

2.9. Statistical Analysis

The collected data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) software. Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and

percentages. Differences between groups were assessed using the appropriate statistical tests, and a p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 75 Sudanese participants were enrolled in this study, including 50 patients diagnosed with sickle cell anemia (cases)

and 25 apparently healthy individuals (controls). The mean age of the case group was 6 ± 0.57 years (range: 1–15 years), whereas the mean age of the control group was 8 ± 0.64 years (range: 2–17 years). Males represented 54% of the cases and 52% of the controls Table 1.

Variable	Cases (n=50)	Controls (n=25)
Age range (years)	1–15	2–17
Mean age (years)	6 ± 0.57	8 ± 0.64
Male, n (%)	27 (54%)	13 (52%)
Female, n (%)	23 (46%)	12 (48%)

Table 1: Demographic Characteristics of the Study Participants

The comparison of hemoglobin fractions between patients and healthy controls is presented in Table 2. Patients with sickle cell anemia showed significantly higher HbS and HbF levels and

significantly lower HbA levels than healthy controls. However, HbA₂ levels did not differ significantly between the two groups.

Hemoglobin variant	Cases (Mean ± SD)	Controls (Mean ± SD)	P-value
HbA (%)	7.2 ± 0.18	97.0 ± 0.10	<0.001
HbA ₂ (%)	3.0 ± 0.50	2.5 ± 0.10	0.40
HbS (%)	78.0 ± 0.18	0.0 ± 0.00	<0.001
HbF (%)	10.0 ± 0.80	0.0 ± 0.00	<0.001

Table 2: Comparison of Hemoglobin Variants between Cases and Controls

Among patients with sickle cell anemia, 35 (70%) were receiving hydroxyurea therapy, whereas 15 (30%) were not. There were no statistically significant differences in HbA, HbA₂, or HbS

levels between patients receiving and not receiving hydroxyurea. However, HbF levels were significantly higher among patients receiving hydroxyurea therapy (Table 3).

Hemoglobin variant	Hydroxyurea (n = 35)	No hydroxyurea (n = 15)	P-value
HbA (%)	6.6 ± 0.19	8.4 ± 0.19	0.70
HbA ₂ (%)	2.9 ± 0.10	4.4 ± 0.10	0.50
HbS (%)	76 ± 0.16	86 ± 0.20	0.07
HbF (%)	14 ± 0.70	1 ± 0.10	<0.001

Table 3: Association between Hydroxyurea Therapy and Hemoglobin Variants among Patients with Sickle Cell Anemia

The relationship between gender and hemoglobin variants among patients with sickle cell anemia is presented in Table 4. No statistically significant differences were found between male and

female patients with respect to HbA, HbA₂, HbS, or HbF levels (all *p* > 0.05).

Hemoglobin variant	Male	Female	P-value
HbA (%)	9.2 ± 0.22	4.8 ± 0.10	0.40
HbA ₂ (%)	2.7 ± 0.10	4.1 ± 0.80	0.30
HbS (%)	77 ± 0.19	80 ± 0.16	0.60
HbF (%)	10.0 ± 0.70	10.3 ± 0.90	0.90

Table 4: Association between Gender and Hemoglobin Variants among Patients with Sickle Cell Anemia

Correlation analysis between age and hemoglobin variants is shown in Table 5. No statistically significant correlations were identified between age and HbA, HbA₂, HbS, or HbF levels (all $p > 0.05$).

Variable	Correlation coefficient (r)	P-value
Age vs HbA	0.16	0.09
Age vs HbA ₂	0.06	0.50
Age vs HbS	0.08	0.09
Age vs HbF	0.08	0.40

Table 5: Correlation between Age and Hemoglobin Variants among Patients with Sickle Cell Anemia

4. Discussion

The present study evaluated hemoglobin variants among Sudanese patients with sickle cell anemia using capillary electrophoresis. The findings demonstrated significantly increased HbS and HbF levels and markedly decreased HbA levels among patients compared with healthy controls, while HbA₂ levels showed no statistically significant difference between the two groups. The current study demonstrated that the mean HbS level was 78%, indicating that HbS was the predominant hemoglobin fraction among patients with sickle cell anemia. This finding is expected because HbS is the characteristic abnormal hemoglobin responsible for the pathophysiology of sickle cell disease through polymerization under hypoxic conditions, resulting in erythrocyte sickling and chronic hemolytic anemia.

Similarly, HbA was markedly reduced among patients compared with healthy controls, reflecting the replacement of normal adult hemoglobin by HbS in individuals with homozygous sickle cell anemia. These findings are consistent with the well-established pathophysiology of sickle cell disease described by Stuart and Nagel, and Rees et al [1,2]. A statistically significant increase in HbF was observed among patients with sickle cell anemia compared with healthy controls. The elevated HbF level is likely attributable to hydroxyurea therapy, which was received by 70% of the study participants. Hydroxyurea is known to stimulate fetal hemoglobin synthesis, thereby reducing HbS polymerization and improving clinical outcomes. These findings are consistent with the report of Khair, who demonstrated HbF levels of approximately $7 \pm 5.6\%$ among Sudanese patients with sickle cell disease, and with the study by Akinsheye et al., who identified fetal hemoglobin as one of the strongest genetic modifiers influencing the hematological and clinical manifestations of sickle cell disease [7,8]. The present study further demonstrated that patients receiving hydroxyurea therapy had significantly higher HbF levels (14%) than untreated patients (1%). This observation supports the established therapeutic role of hydroxyurea in increasing HbF production and reducing disease severity.

Similar findings were reported by Kotila and Shokunbi, who emphasized that elevated HbF levels are associated with reduced clinical severity and fewer vaso-occlusive complications in patients with sickle cell disease [9]. No statistically significant difference in HbA₂ levels was observed between patients and healthy controls. This finding agrees with the observations reported by Embury et

al., who demonstrated that HbA₂ is generally within the normal range in patients with homozygous sickle cell anemia and is primarily elevated in patients with sickle β -thalassemia rather than classical sickle cell anemia [10]. The present study also found no statistically significant association between hemoglobin variants and patients' gender. Likewise, correlation analysis demonstrated no significant relationship between age and HbA, HbA₂, HbS, or HbF levels. These findings suggest that the distribution of hemoglobin variants is primarily determined by the underlying genetic mutation and treatment status rather than demographic characteristics. Overall, the findings of this study support the clinical usefulness of hemoglobin variant analysis for the diagnosis and monitoring of sickle cell anemia. Furthermore, the significant increase in HbF among patients receiving hydroxyurea provides additional evidence supporting the routine use of hydroxyurea therapy in the management of sickle cell disease.

4.1. Limitations

This study had several limitations. First, the relatively small sample size may limit the generalizability of the findings. Second, participants were recruited from two hospitals in Khartoum State, which may not fully represent the Sudanese population. Third, the study did not evaluate the relationship between hemoglobin variants and clinical outcomes such as vaso-occlusive crises, transfusion requirements, or hospitalization. Finally, genetic analysis of β -globin haplotypes and molecular characterization were not performed.

5. Conclusion

Patients with sickle cell anemia exhibited significantly increased HbS and HbF levels together with markedly reduced HbA levels compared with healthy individuals. HbA₂ remained within the normal range and showed no significant difference between study groups. Hydroxyurea therapy was significantly associated with increased fetal hemoglobin levels, highlighting its therapeutic value in the management of sickle cell anemia.

Recommendations

Routine hemoglobin variant analysis should be incorporated into the standard clinical management of patients with sickle cell disease to facilitate diagnosis and treatment monitoring. Hydroxyurea therapy should be encouraged for eligible patients because of its demonstrated ability to increase fetal hemoglobin (HbF) levels and improve disease outcomes. In addition, early

diagnosis through neonatal and premarital screening programs should be strengthened in Sudan to reduce the burden of sickle cell disease. Future multicenter studies with larger sample sizes are recommended to provide more representative data on hemoglobin variants across different Sudanese populations and to further investigate the relationship between HbF levels and the clinical severity of sickle cell disease.

Declarations Section

Ethical Approval

Ethical approval was obtained from the appropriate institutional ethics committee before commencement of the study. Written informed consent was obtained from all participants before enrollment. All collected data were treated confidentially and used exclusively for research purposes in accordance with the principles of the Declaration of Helsinki.

Consent

The patient's written consent has been collected

Author Contributions

Mohammed Osman Ali Mohammed conceived and designed the study, participated in data collection, laboratory investigations, and interpretation of the findings. Hadeel Ali contributed to data collection, laboratory analysis, and data management. Ibrahim Bakhit contributed to the study design, laboratory investigations, interpretation of results, and critical revision of the manuscript. Ghanem Mohammed Mahjaf contributed to study conception and methodology, statistical analysis, interpretation of the data, and drafting, reviewing, and editing the manuscript. All authors contributed to the revision of the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

References

1. Stuart, M. J., & Nagel, R. L. (2004). Sickle-cell disease. *The Lancet*, 364(9442), 1343-1360.
2. Rees, D. C., Williams, T. N., & Gladwin, M. T. (2010). Sickle-cell disease. *The Lancet*, 376(9757), 2018-2031.
3. Kato, G. J., Piel, F. B., Reid, C. D., Gaston, M. H., Ohene-Frempong, K., Krishnamurti, L., ... & Vichinsky, E. P. (2018). Sickle cell disease. *Nature reviews Disease primers*, 4(1), 18010.
4. Lauder, J. R., & Ibrahim, S. A. (1970). Sickling in south-west Kordofan. *Sudan Medical Journal*, 8(4), 206-214.
5. Lichtman, M. A., Kipps, T. J., Seligsohn, U., Kaushansky, K., Prchal, J. T., & editors. (2007). *Williams Hematology*. 7th ed. New York: McGraw-Hill, 285-377.
6. Hoffbrand, A. V., & Moss, P. A. (2011). *Essential Haematology (Essentials)*. Wiley-Blackwell.
7. Khair, F. M. (2002). The Genetic Origin of Sickle Cell Disease in Sudan: Haplotype Determination of Homozygous Patients [MD thesis]. Khartoum (Sudan): University of Khartoum.
8. Akinsheye, I., Alsultan, A., Solovieff, N., Ngo, D., Baldwin, C. T., Sebastiani, P., ... & Steinberg, M. H. (2011). Fetal hemoglobin in sickle cell anemia. *Blood, The Journal of the American Society of Hematology*, 118(1), 19-27.
9. Kotila, T. R., & Shokunbi, W. A. (2003). Haemoglobin F levels in healthy Nigerian adults. *West African Journal of Medicine*, 22(2), 143-145.
10. Embury, S. H., Vichinsky, E. P., Mahoney, D. H. Jr. Diagnosis of sickle cell syndromes. In: UpToDate [Internet]. Waltham (MA): UpToDate Inc.

Copyright: ©2026 Ghanem Mohammed Mahjaf, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.