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Sickle Cell Hepatopathy Among Patients with Sickle Cell Disease in Western Cameroon: Prevalence, Clinical and Biochemical Characteristics, and Associated Factors

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Abstract

Introduction:

Sickle cell disease is a major hemoglobinopathy in sub-Saharan Africa, characterized by acute and chronic complications that can affect multiple organs. Among these, hepatic involvement is a frequent but still insufficiently characterized complication, with heterogeneous clinical and biological manifestations that may influence patient prognosis. This study aimed to determine the frequency, clinical and biological characteristics, and factors associated with sickle cell hepatopathy among patients in Cameroon.

Methods

We conducted an analytical cross-sectional study from November 2025 to May 2026 among 123 patients with sickle cell disease followed at Bafoussam Regional Hospital. Participants were recruited using non-probability consecutive sampling. Sociodemographic, clinical, therapeutic, and transfusion-related data were collected through face-to-face interviews and supplemented by clinical examination. Blood samples were collected for the measurement of transaminases (AST/ALT), gamma-glutamyl transferase (GGT), and alkaline phosphatase (ALP). Data were analyzed using R software. Factors associated with sickle cell hepatopathy were assessed using univariate logistic regression. Associations were expressed as odds ratios (ORs) with 95% confidence intervals (CIs), and statistical significance was set at $p < 0.05$.

Results

Among the 123 patients included, 22 had sickle cell hepatopathy, corresponding to a prevalence of 17.9%. Patients with hepatopathy had significantly higher ALT (53.4 ± 12.9 IU/L; $p = 0.003$), GGT (39.3 ± 25.7 IU/L; $p = 0.012$), and ALP (512 ± 74.7 IU/L; $p < 0.001$) levels. Jaundice (63.6%), right upper quadrant pain (90.9%), and hepatomegaly (81.8%) were significantly more frequent among patients with hepatopathy. The presence of vaso-occlusive crises was strongly associated with hepatopathy (OR = 18.2; 95% CI: 5.53–60.2; $p < 0.001$), as were tachycardia (OR = 14.2; 95% CI: 4.81–41.7; $p < 0.001$) and fever (OR = 60.4; 95% CI: 16.0–228; $p < 0.001$). Previous blood transfusions were also more frequent among patients with hepatopathy (5.82 ± 1.44 vs. 1.96 ± 1.90; $p < 0.001$), while the absence of regular medical follow-up was strongly associated with hepatopathy (OR = 14.0; 95% CI: 3.11–63.4; $p < 0.001$).

Conclusion

Sickle cell hepatopathy was relatively common in this population and was associated with several clinical and biological manifestations as well as exposure-related factors, particularly repeated blood

transfusions and vaso-occlusive crises. Systematic screening for hepatic abnormalities and regular clinical and biological monitoring may contribute to earlier identification of at-risk patients and improve their management.

1. INTRODUCTION

Sickle cell disease (SCD) is an autosomal recessive genetic disorder resulting from a mutation in the *HBB* gene, characterized by the substitution of glutamic acid by valine at the sixth position of the β-globin chain. This abnormality leads to the production of sickle hemoglobin (HbS), whose polymerization under deoxygenated conditions causes red blood cell sickling. This results in impaired red blood cell deformability and lifespan, as well as increased adhesion to the endothelium and other blood cells. These mechanisms sustain a complex pathophysiological process involving chronic hemolysis, endothelial dysfunction, inflammation, oxidative stress, platelet activation, and vaso-occlusion, leading to acute complications and chronic multiorgan involvement [1–3].

Sickle cell disease is currently one of the most important monogenic disorders from a public health perspective. Estimates from the *Global Burden of Disease Study 2021* reported approximately 515,000 annual births of children affected by SCD worldwide in 2021, compared with approximately 453,000 in 2000, representing a 13.7% increase. Approximately 7.7 million people were living with the disease in 2021, and nearly 79% of affected births occurred in sub-Saharan Africa [4–6]. This region therefore bears the greatest share of the global disease burden, in a context marked by persistent inequalities in screening, access to treatment, and specialized care [4,7,8].

Cameroon is part of this high-endemicity region, with the prevalence of the sickle cell trait estimated at 20–30% in some populations [4,9,10]. In this context, improving the management of SCD requires better characterization of its visceral complications, some of which remain underdiagnosed. The liver is particularly vulnerable because of its vascular supply, its role in hemoglobin and bilirubin metabolism, and its involvement in iron metabolism. Hepatic involvement may also be promoted by repeated blood transfusions, iron overload, viral infections, gallstone disease, and biliary tract injury [11–13].

The spectrum of hepatic and biliary manifestations associated with SCD is collectively referred to as sickle cell hepatopathy (SCH). This condition encompasses a heterogeneous clinical and biological spectrum, ranging from transient abnormalities in liver enzymes to potentially fatal acute complications. Acute forms include sickle cell hepatic crisis, acute hepatic sequestration, and sickle cell intrahepatic cholestasis, whereas chronic liver involvement may be associated with iron overload, viral hepatitis, gallstone disease, sickle cell cholangiopathy, and, in advanced cases, fibrosis or cirrhosis [11,13].

The clinical importance of hepatic involvement is now well established. In a cohort of 616 children with SCD, at least one hepatobiliary complication was observed in 37% of patients, while 6% had experienced a severe acute hepatic complication, including hepatic crisis, intrahepatic cholestasis, or acute hepatic sequestration [14]. More recently, a retrospective study of 1,009 patients followed over 30 years reported a high frequency of hepatobiliary complications, particularly gallstones or biliary sludge (42.7%) and

hepatic iron overload (12%). Certain biological abnormalities, particularly elevated ALT levels and marked hyperbilirubinemia, were associated with increased mortality [15]. These findings suggest that hepatic involvement is not only a frequent complication of SCD but may also represent a potential determinant of prognosis.

Repeated blood transfusions are a major contributor to chronic liver complications, particularly through iron overload, which may progress to fibrosis and cirrhosis [13]. Viral infections, gallstone disease, certain treatments, and vaso-occlusive episodes may also contribute to the heterogeneous spectrum of hepatic manifestations [11,13]. From a diagnostic perspective, sickle cell hepatopathy remains difficult to characterize because liver enzyme abnormalities are often mild and intermittent, influenced by the patient's clinical status, and sometimes difficult to distinguish from the effects of hemolysis or concomitant liver diseases. Conversely, some acute forms may rapidly progress to liver failure and multiorgan dysfunction [11,13]. The absence of universally standardized biological criteria further complicates screening and the comparison of findings across studies.

This issue is particularly relevant in sub-Saharan Africa, which carries the majority of the global burden of SCD but remains underrepresented in studies investigating hepatic complications. Differences in genetic background, transfusion exposure, prevalence of hepatic infections, access to treatment, and availability of specialized investigations may influence the profile and severity of hepatic involvement. Data from other regions of the world therefore cannot be directly extrapolated to African populations. Against this background, the present study aimed to better characterize the clinical and biological manifestations of hepatic involvement in Cameroonian patients with SCD and to identify the factors associated with this condition.

2. METHODOLOGY

2.1. Ethical considerations

The study was conducted in accordance with the ethical principles applicable to research involving human participants. Ethical approval was obtained from the Ethics and Quality Assurance Committee of the University of the Mountains (CEAQ-UdM) (authorization No. 2026/031/UdM/PR/CEAQ), as well as administrative research authorization from the Bafoussam Regional Hospital (authorization No. 039/L/MINSANTE/SG/DRSPO/HRB/D). All methods and experiments were performed in accordance with relevant guidelines and regulations including the Declaration of Helsinki.

Written informed consent was obtained from parents or legal guardians and, where applicable, assent was obtained from participants prior to any study procedure. Confidentiality and anonymity of participants' data were maintained throughout the data collection, management, and analysis processes. Participants were informed of their right to access information concerning them and to withdraw from the study at any time without any consequences for their medical care. All collected data and study findings were used exclusively for scientific purposes.

2.2. Study design, setting, and period

This was an analytical cross-sectional study conducted in the pediatric department of Bafoussam Regional Hospital, Cameroon, over a six-month period from November 20, 2025, to May 20, 2026. The study was conducted in the pediatric department of Bafoussam Regional Hospital, located in Bafoussam, in the Western Region of Cameroon. This second-category referral hospital, established in 1963, provides healthcare services to the population of Bafoussam and surrounding health districts. The pediatric department provides diagnostic and therapeutic care for children with various diseases, including sickle cell disease. Laboratory analyses were performed in the laboratory of Bafoussam Regional Hospital.

2.3. Participant recruitment, eligibility criteria, and sampling

Participants were consecutively recruited among patients with sickle cell disease receiving care at the pediatric department of Bafoussam Regional Hospital, Cameroon. A non-probability consecutive sampling method was used, including all eligible patients presenting during the study period until the required sample size was reached.

Patients were eligible if they had a confirmed diagnosis of sickle cell disease and provided informed consent or assent to participate. Patients with known acute or chronic liver disease of causes other than sickle cell disease, severe acute infection, or any other condition likely to significantly influence the biological parameters under investigation were excluded. Patients who had recently received potentially hepatotoxic drugs or medications likely to interfere with the biochemical parameters assessed, as well as those who had undergone a recent blood transfusion that could affect the study results, were also excluded. Hemolyzed or insufficient blood samples for laboratory analysis were not considered. Finally, patients for whom parental informed consent or the required assent had not been obtained, as well as those with insufficient clinical or biological data for analysis, were excluded.

The sample size was estimated using the Daniel Schwartz formula for a single population proportion, assuming a 6% prevalence of acute hepatic complications among patients with sickle cell disease, with a 95% confidence level and a 5% absolute precision [14]. The minimum sample size was estimated at 87 participants. To improve the precision of the estimates and account for potential exclusions or missing data, we aimed to recruit at least 100 participants.

2.4. Administrative procedures and clinical data collection

Following protocol approval, the study was submitted to the Ethics Committee of the University of the Mountains, which granted the corresponding ethical approval. Research authorization was subsequently obtained from the administration of Bafoussam Regional Hospital before the start of data collection.

Patients with sickle cell disease meeting the eligibility criteria were identified during consultations or hospital admissions in the pediatric department. Parents or legal guardians were informed about the

study objectives and procedures, and written informed consent was obtained prior to participation. Participant assent was also obtained when applicable.

Clinical and sociodemographic data were collected using a standardized questionnaire and through clinical examination. The information collected included age, sex, time since diagnosis, treatment with hydroxyurea or other medications, frequency of vaso-occlusive crises, previous blood transfusions, use of herbal medicine, regularity of medical follow-up, and the presence of any associated liver disease.

Vital parameters, including blood pressure and heart rate, as well as anthropometric parameters (weight and height), were measured using standardized procedures. Blood pressure and heart rate were measured after a period of rest using a validated electronic blood pressure monitor (OMRON). Weight was measured in kilograms using a calibrated scale, while height was measured in centimeters using a stadiometer. Body mass index (BMI) was calculated using the formula: weight (kg)/height² (m^2).

A systematic clinical examination was also performed according to the standard steps of inspection, palpation, percussion, and auscultation. Particular attention was paid to clinical signs suggestive of liver involvement, including pallor, jaundice, right upper quadrant pain, and hepatomegaly, as well as any other relevant clinical findings.

2.5. Biological sample collection

A 5 mL venous blood sample was collected from each participant under aseptic conditions and distributed into EDTA tubes for hemoglobin electrophoresis and plain tubes for biochemical analyses. Samples were appropriately labeled and transported to the laboratory under suitable conditions.

Quantitative hemoglobin electrophoresis on alkaline agarose gel was performed for each participant according to the *HELLABIO protocol* to identify and quantify the different hemoglobin fractions. Following electrophoretic migration, the fractions were visualized after Ponceau Red staining and quantified by densitometry.

For biochemical analyses, blood collected in plain tubes was allowed to clot and then centrifuged to obtain serum. The activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) were determined in serum using kinetic spectrophotometric methods with appropriate reagents and a Mindray spectrophotometer. EDTA blood samples were used for the hematological analyses specified in the study protocol.

2.6. Biochemical analysis of liver enzymes

Enzyme activities were determined using kinetic spectrophotometric methods with a Mindray spectrophotometer and expressed in international units per liter (IU/L).

2.6.1. AST and ALT activities

AST and ALT activities were determined using the Accucare kit according to a kinetic enzymatic method. Aminotransferases catalyze the reversible transfer of an amino group between an amino acid and an α-keto acid. AST catalyzes, in particular, the following reaction:

L-aspartate + α-ketoglutarate ⇌ oxaloacetate + L-glutamate.

The enzymatic reactions are coupled to a reaction system involving malate dehydrogenase (MDH) or lactate dehydrogenase (LDH), respectively, with consumption of NADH. The reaction mixture was incubated at 37°C, and the change in absorbance was monitored kinetically at 340 nm. The rate of change in absorbance, which is proportional to enzymatic activity, was used to determine AST and ALT activities, expressed in IU/L.

The reference intervals used were < 42 IU/L for ALT, < 38 IU/L for AST in males, and < 31 IU/L in females [16,17].

2.6.2. Gamma-glutamyl transferase activity

GGT activity was determined using the Carboxy-GPNA kit according to a kinetic spectrophotometric method based on the principles recommended by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). GGT catalyzes the transfer of a γ-glutamyl group from a donor substrate to an acceptor molecule, with glycylglycine serving as the acceptor:

γ-glutamyl donor + acceptor → γ-glutamyl acceptor + reaction product [18].

The reaction system included a γ-glutamyl substrate, glycylglycine, a buffer, and the activators required for enzymatic activity. Following addition of serum to the working reagent and incubation under controlled conditions, formation of the reaction product was monitored spectrophotometrically at 405 nm. The change in absorbance over time was used to calculate GGT activity, expressed in IU/L[19].

The reference intervals used were 5–32 IU/L in females and 10–55 IU/L in males. GGT activity was also considered in conjunction with ALP activity when interpreting potential hepatobiliary involvement.

2.6.3. Alkaline phosphatase activity

Alkaline phosphatase (ALP) activity was determined using the SGM kit according to a kinetic spectrophotometric method. ALP comprises a group of isoenzymes capable of hydrolyzing various phosphate esters under alkaline conditions, particularly *p*-nitrophenyl phosphate, resulting in the formation of *p*-nitrophenol [20].

The working reagent, containing an alkaline buffer and substrate, was brought to 37°C and then mixed with serum. The enzymatic reaction was monitored kinetically by measuring absorbance at 405 nm. The change in absorbance over time, proportional to enzymatic activity, was used to determine ALP activity according to the conversion factor specific to the reagent. Results were expressed in IU/L.

According to the reference values used by the laboratory, the reference interval for ALP was 98–280 IU/L [21].

Interpretation of enzyme activities

Enzyme activities were interpreted according to the laboratory reference intervals. An activity above the upper limit of the reference range was considered abnormal. Results were interpreted in conjunction with other available liver function parameters, particularly bilirubin and prothrombin time. The combination of elevated ALP and GGT was considered compatible with a hepatobiliary origin, whereas isolated elevation of ALP with GGT within the reference range could suggest an extrahepatic, particularly bone, origin [21].

2.7. Data management and statistical analysis

Sociodemographic, clinical, and biological data were checked, coded, and entered into Microsoft Excel, then exported for statistical analysis using R version 4.1.1. Data consistency, completeness, and quality were assessed before statistical analyses. Missing data were identified and their proportion assessed; analyses were performed using available observations when the frequency of missing data was low.

Quantitative variables included age, weight, height, body mass index (BMI), vital signs, time since diagnosis, serum AST, ALT, GGT and ALP activities, as well as the number and duration of vaso-occlusive crises and the number of previous transfusion episodes. Qualitative variables included sex, sickle cell disease genotype, clinical status, treatment with hydroxyurea or other medications, use of herbal medicine or alcohol, family history, and clinical signs including jaundice, pallor, right upper quadrant pain, hepatomegaly, and splenomegaly.

Quantitative variables were described using mean ± standard deviation when their distribution was approximately normal, or median and interquartile range otherwise. Qualitative variables were presented as frequencies and percentages. Enzyme activities were initially analyzed as continuous variables and interpreted according to the laboratory reference intervals. For analyses requiring clinical categorization, enzyme activities were classified as normal or elevated according to the corresponding age- and/or sex-specific upper reference limit, when available.

Definition of liver involvement profiles

In this study, sickle cell hepatopathy (SCH) was defined as hepatobiliary involvement occurring in the context of sickle cell disease and identified on the basis of a concordant set of clinical and laboratory findings, after exclusion of the main alternative causes of liver abnormalities. Given the absence of universally established diagnostic criteria for sickle cell hepatopathy, an operational definition was used, adapted to the data available in our study setting. Classification was primarily based on the presence of clinical manifestations suggestive of hepatobiliary involvement, including jaundice, right upper quadrant pain, and/or hepatomegaly, associated with abnormalities in liver parameters, particularly ALT, GGT, and/or ALP. Isolated AST abnormalities were not considered sufficient to define SCH, given the potential contribution of hemolysis to elevated AST levels in patients with sickle cell disease. Acute liver

involvement was subsequently characterized according to its clinical and biochemical profile. A cytolytic pattern was defined as an elevation of ALT and AST above the upper limit of the reference range. A cholestatic pattern was defined by elevated ALP and GGT levels, whereas a mixed pattern combined abnormalities in transaminases and cholestatic markers. Acute hepatic crisis and acute hepatic sequestration were identified separately based on their respective clinical and laboratory characteristics. This approach is consistent with the current understanding of sickle cell hepatopathy as a spectrum of acute and chronic liver disorders rather than a single diagnostic entity [13,22–24].

The associations between the variables studied and liver involvement profiles were assessed. For comparisons of quantitative variables between two groups, the Student's *t*-test was used when the assumptions of normality and homogeneity of variances were met; otherwise, an appropriate non-parametric test was applied. Qualitative variables were compared using the chi-square test (χ^2) or Fisher's exact test, as appropriate according to the observed frequencies.

Binary logistic regression was used to assess factors associated with sickle cell hepatopathy. Each potential explanatory variable was first analyzed separately in a univariable logistic regression model. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Given the limited number of SCH cases, no multivariable model was fitted.

3. RESULTS

Among the 123 patients included, the mean age was approximately 10 years, with a male predominance and a substantial proportion of underweight patients. Most participants were regularly followed up, had a history of blood transfusions, and experienced recurrent vaso-occlusive crises, while the use of herbal medicine was frequently reported. Clinically, jaundice, right upper quadrant pain, and hepatomegaly were the main manifestations suggestive of liver involvement. Biologically, abnormalities mainly involved AST, ALT, and ALP, whereas GGT elevation was less frequent. Overall, these findings highlight the frequency of hepatic abnormalities among patients with sickle cell disease and support the need for systematic biochemical screening. At the end of the study, 22 of the 123 patients included had sickle cell hepatopathy, corresponding to a prevalence of 17.9%.

3.1. Distribution of sociodemographic parameters and clinical profile of the study population according to sickle cell hepatopathy

3.1.1. Sociodemographic characteristics of the study population according to sickle cell hepatopathy
Table I below describes the sociodemographic characteristics of the study population according to the presence of sickle cell hepatopathy (**SCH**).

Table I: Sociodemographic parameters according to sickle cell hepatopathy

Parameters	*Categories*	*SCH - (N = 101)*	*SCH + (N = 22)*	*Total (N = 123)*	*P value*
		n(%)	*n(%)*	*n(%)*	
Sex	F	35 (34.7)	18 (81.8)	53 (43.1)	< 0.001
	M	66 (65.3)	4 (18.2)	70 (56.9)	
Age (years)	Mean ± SD	10.2 ± 5.12	8.18 ± 5.01	9.80 ± 5.14	0.105
Educational level	None	5 (4.95)	/	5 (4.07)	0.007
	Primary	54 (53.5)	18 (81.8)	72 (58.5)	
	Secondary	40 (39.6)	2 (9.09)	42 (34.1%)	
	Higher education	2 (1.98)	2 (9.09)	4 (3.25)	
Occupation	None	4(5.00)	/	4(4.40)	0.128
	None	5 (4.95)	/	5 (4.07)	
	Student/pupil	94 (93.1)	20 (90.9)	114 (92.7)	
	University student	2 (1.98)	2 (9.09)	4 (3.25)	

SCH + = positive sickle cell hepatopathy; SCH− = negative sickle cell hepatopathy; n = number of participants; N = total number of participants; % = frequency; Mean ± SD = mean ± standard deviation; F = female; M = male.

Table I shows a significant association between sex and the presence of sickle cell hepatopathy ($p < 0.001$), with a higher proportion of females in the SCH+ group (81.8%) compared with the SCH− group (34.7%). A significant difference was also observed according to educational level ($p = 0.007$), with patients in the SCH+ group predominantly having primary-level education (81.8%). In contrast, mean age did not differ significantly between the two groups (8.18 ± 5.01 years in the SH+ group versus 10.20 ± 5.12 years in the SH− group; $p = 0.105$), nor did occupation ($p = 0.128$).

3.1.2. Distribution of the study population according to clinical profile by presence of SCH

3.1.2.1. Disease course, treatment, and medical and family history according to SH status

Table II describes the disease follow-up characteristics, treatment, and medical and family history according to the presence or absence of SCH.

Table II

Distribution of the study population according to disease course, treatment, and medical and family history by SCH status

Parameters	*SCH - (N = 101)*	*SCH + (N = 22)*	*Total (N = 123)*	*P value*
	n(%)	*n(%)*	*n(%)*	
Age at sickle cell disease diagnosis (years), Mean ± SD	2.48 ± 1.95	2.45 ± 1.34	2.47 ± 1.85	0.952
Number of previous blood transfusions, Mean ± SD	1.96 ± 1.90	5.82 ± 1.44	2.65 ± 2.35	< 0.001
Time since last blood transfusion (months), Mean ± SD	11.7 ± 16.7	3.27 ± 1.91	10.2 ± 15.5	< 0.001
Duration of crises (days), Mean ± SD	3.45 ± 2.61	4.73 ± 1.86	3.67 ± 2.53	0.010
Number of crises/year, Mean ± SD	2.90 ± 1.57	6.09 ± 2.60	3.47 ± 2.17	< 0.001
Time since last crisis (weeks), Mean ± SD	27.9 ± 37.3	15.6 ± 16.7	25.7 ± 34.8	0.019
Use of herbal medicine	81 (80.2)	22 (100)	103 (83.7)	0.023
Paracetamol use	8 (7.92)	14 (63.6)	22 (17.9)	< 0.001
NSAID use	13 (12.9)	10 (45.5)	23 (18.7)	0.001
Regular medical follow-up	59 (58.4)	2 (9.09)	61 (49.6)	< 0.001
Hydroxyurea use	6 (5.94)	0 (0.00)	6 (4.88)	0.590
History of gallstones	0 (0.00)	4 (18.2)	4 (3.25)	0.001
Family history of sickle cell disease	22 (21.8)	6 (27.3)	28 (22.8)	0.783

SCH− = negative sickle cell hepatopathy; SCH + = positive sickle cell hepatopathy; n = number of participants; N = total number of participants; SD = standard deviation; NSAIDs = non-steroidal anti-inflammatory drugs.

Table II shows that several parameters related to sickle cell disease progression and treatment practices differed significantly according to the presence of sickle cell hepatopathy. Patients in the SCH+ group had a significantly higher mean number of previous blood transfusions (5.82 ± 1.44 vs. 1.96 ± 1.90; $p < 0.001$) and a more recent last transfusion (3.27 ± 1.91 vs. 11.7 ± 16.7 months; $p < 0.001$). They also experienced a higher annual frequency of vaso-occlusive crises (6.09 ± 2.60 vs. 2.90 ± 1.57; $p < 0.001$), longer crises (4.73 ± 1.86 vs. 3.45 ± 2.61 days; $p = 0.010$), and a more recent last crisis (15.6 ± 16.7 vs. 27.9 ± 37.3 weeks; $p = 0.019$). Herbal medicine use was more frequently reported among SCH+ patients (100% vs. 80.2%; $p = 0.023$), as were paracetamol use (63.6% vs. 7.92%; $p < 0.001$) and NSAID use (45.5% vs. 12.9%; $p = 0.001$). Regular medical follow-up was significantly less common among SCH+ patients (9.09% vs. 58.4%; $p < 0.001$), whereas a history of gallstones was reported exclusively in this group

(18.2% vs. 0%; p = 0.001). In contrast, age at diagnosis, hydroxyurea use, and family history of sickle cell disease did not differ significantly between the two groups.

3.1.2.2. Clinical manifestations according to the presence or absence of SCH

Table III describes the vital and anthropometric parameters, clinical signs, and diagnoses according to the presence or absence of SCH.

Table III

Vital and anthropometric parameters, clinical signs, and diagnoses according to the presence or absence of SCH

Parameters	*Categories*	*SCH - (N = 101)*	*SCH + (N = 22)*	*Total (N = 123)*	*P value*
		n(%)	*n(%)*	*n(%)*	
BMI	Underweight	51 (50.5)	12 (54.5)	63 (51.2)	0.913
	Normal BMI	50 (49.5)	10 (45.5)	60 (48.8)	
Heart rate	Normal	85 (84.2)	6 (27.3)	91 (74.0)	< 0.001
	Increased	16 (15.8)	16 (72.7)	32 (26.0)	
Respiratory rate	Normal	92 (91.1)	14 (63.6)	106 (86.2)	0.003
	Increased	9 (8.91)	8 (36.4)	17 (13.8)	
Temperature	Normal	94 (93.1)	4 (18.2)	98 (79.7)	< 0.001
	Fever	7 (6.93)	18 (81.8)	25 (20.3)	
Bone pain	/	11 (10.9)	6 (27.3)	17 (13.8)	0.080
Pallor	/	10 (9.90)	4 (18.2)	14 (11.4)	0.275
Jaundice	/	4 (3.96)	14 (63.6)	18 (14.6)	< 0.001
Right upper quadrant pain	/	3 (2.97)	20 (90.9)	23 (18.7)	< 0.001
Splenomegaly	/	1 (0.99)	12 (54.5)	13 (10.6)	< 0.001
Hepatomegaly	/	4 (3.96)	18 (81.8)	22 (17.9)	< 0.001
Dyspnea	/	5 (4.95)	2 (9.09)	7 (5.69)	0.607
Vaso-occlusive crisis (VOC)	/	13 (12.9)	18 (81.8)	31 (25.2)	< 0.001
Acute anemia	/	9 (8.91)	4 (18.2)	13 (10.6)	0.247
Infection	/	1 (0.99)	4 (18.2)	5 (4.07)	0.004
Acute chest syndrome (ACS)	/	2 (1.98)	0 (0.00)	2 (1.63)	1.000

SCH− = negative sickle cell hepatopathy; SCH + = positive sickle cell hepatopathy; n = number of participants; N = total number of participants; % = frequency; BMI = body mass index; VOC = vaso-occlusive crisis; ACS = acute chest syndrome.

Table III shows that SCH+ patients more frequently presented with tachycardia (72.7% vs. 15.8%; $p < 0.001$), an increased respiratory rate (36.4% vs. 8.9%; $p = 0.003$), and fever (81.8% vs. 6.9%; $p < 0.001$).

Hepatic manifestations were particularly prominent among SCH+ patients, with a markedly higher frequency of right upper quadrant pain (90.9% vs. 3.0%), hepatomegaly (81.8% vs. 4.0%), and jaundice (63.6% vs. 4.0%), all significantly associated with SCH ($p < 0.001$). Splenomegaly was also more frequent among SCH+ patients (54.5% vs. 1.0%; $p < 0.001$), as were vaso-occlusive crises (81.8% vs. 12.9%; $p < 0.001$) and infections (18.2% vs. 1.0%; $p = 0.004$). In contrast, BMI, bone pain, pallor, dyspnea, acute anemia, and acute chest syndrome did not differ significantly between the two groups.

3.2. Distribution of biological parameters and characterization of hepatic involvement according to SCH

3.2.1. Biological parameters among patients according to SCH status

Table IV presents the different biological parameters of the patients according to SCH status.

Table IV

Distribution of biological parameters among patients according to SCH status.

Parameters	***SCH - (N = 101)*** ***n(%)***	***SCH + (N = 22)*** ***n(%)***	***Total (N = 123)*** ***n(%)***	***P-value***
AST (U/L), Mean ± SD	89.6 ± 19.8	99.2 ± 19.7	91.3 ± 20.0	0.049
AST elevated	101 (100)	22 (100)	123 (100)	/
ALT (U/L), Mean ± SD	43.7 ± 10.3	53.4 ± 12.9	45.5 ± 11.3	0.003
ALT elevated	46 (45.5)	18 (81.8)	64 (52.0)	0.006
ALT normal	53 (52.5)	4 (18.2)	57 (46.3)	
GGT (U/L), Mean ± SD	15.4 ± 8,49	39.3 ± 25,7	18.3 ± 14,1	0.012
ALP (U/L), Mean ± SD	355 ± 113	512 ± 74.7	383 ± 123	< 0.001
ALP normal	30 (29.7)	/	30 (24.4)	< 0.001
ALP elevated	71(69.99)	22(100)	93(75.18)	

Note: *SCH + = patients with sickle cell hepatopathy; SCH− = patients without sickle cell hepatopathy; n = number of participants; N = total number of participants; % = percentage; Mean ± SD = mean ± standard deviation; AST = aspartate aminotransferase; ALT = alanine aminotransferase; GGT = gamma-glutamyl transferase; ALP = alkaline phosphatase.*

The biological profile showed elevated AST levels in all patients, with no difference in the frequency of elevation between the groups, although the mean AST level was slightly higher among patients with SCH+ (99.2 ± 19.7 vs. 89.6 ± 19.8 U/L; $p = 0.049$). ALT levels were also significantly higher in the SCH+

group (53.4 ± 12.9 vs. 43.7 ± 10.3 U/L; p = 0.003), with a higher proportion of elevated values (81.8% vs. 45.5%; p = 0.006). GGT levels were markedly higher among patients with SCH+ (39.3 ± 25.7 vs. 15.4 ± 8.5 U/L; p = 0.012). Finally, ALP showed the most pronounced difference, with mean levels of 512 ± 74.7 U/L in the SH+ group compared with 355 ± 113 U/L in the SCH− group (p < 0.001); all patients with SCH + had elevated ALP levels.

3.2.2. Biological Characterization of Hepatic Involvement According to SCH

Table V presents the distribution of the study population according to the different types of hepatic involvement.

Table V : Biological characterization of hepatic involvement in the study population according to SCH

Parameters	***SCH - (N = 101)*** ***n(%)***	***SCH + (N = 22)*** ***n(%)***	***Total (N = 123)*** ***n(%)***	***P-value***
Hepatic cytolysis	0 (0.0)	22 (100)	22 (17.89)	< 0.001
Cholestasis	1 (0.99)	6 (27.3)	7 (5.69)	< 0.001
Mixed cholestasis	2 (1.98)	16 (72.7)	18 (14.6)	< 0.001
Acute hepatic crisis	/	20 (90.9)	20 (16.3)	< 0.001
Acute hepatic sequestration	/	2 (9.09)	2 (1.63)	0.031
Note: *SCH + = patients with sickle cell hepatopathy; SCH− = patients without sickle cell hepatopathy; n = number of participants; N = total number of participants; % = percentage.*				

Hepatic cytolysis was observed exclusively among SCH+ patients (22/22; 100%). Mixed cholestasis was the most frequent profile among patients with sickle cell hepatopathy (16/22; 72.7%), followed by cholestasis (6/22; 27.3%), with significant differences compared with SCH− patients (p < 0.001). An acute hepatic crisis was identified in 20 SH+ patients (90.9%), whereas acute hepatic sequestration was observed in 2 patients (9.1%). Overall, these findings highlight the predominance of cholestatic patterns, particularly mixed cholestasis, among the hepatic abnormalities identified.

3.3. Factors Associated with Sickle Cell Hepatopathy

Table VI presents the factors associated with sickle cell hepatopathy (SCH) based on univariate analysis.

Table VI

Factors Associated with Sickle Cell Hepatopathy (SH)

Parameters	*Category*	*SCH - (N = 101)* *n(%)*	*SCH + (N = 22)* *n(%)*	*OR*	*IC 95%*	*P-value*
Sex	**F**	35 (34.7)	18 (81.8)	8.49	[2.66;27.0]	< 0.001
	M	66 (65.3)	4 (18.2)	Réf.	Réf.	
Heart rate	**Increased**	16 (15.8)	16 (72.7)	14.2	[4.81;41.7]	< 0.001
	Normal	85 (84.2)	6 (27.3)	Réf.	Réf.	Réf.
Temperature	**Increased**	7 (6.93)	18 (81.8)	60.4	[16.0;228]	< 0.001
	Normal	94 (93.1)	4 (18.2)	Réf.	Réf.	Réf.
Respiratory rate	**Increased**	9 (8.91)	8 (36.4)	5.84	[1.93;17.7]	0.003
	Normal	92 (91.1)	14 (63.6)	Réf.	Réf.	Réf.
Vaso-occlusive crisis	**Yes**	13 (12.9)	18 (81.8)	18.2	[5.53;60.2]	< 0.001
	No	88 (87.1)	4 (18.2)	Réf.	Réf.	Réf.
Hepatic cytolysis	**Yes**	0(0,00)	22(100)	3.84	[0.84;17.5]	0.062
	No	101(100)	0(0,00)	Réf.	Réf.	Réf.
GGT	**Increased**	1 (0.99)	12 (54.5)	120	[14.1;1021]	< 0.001
	Normal	100 (99.0)	10 (45.5)	Réf.	Réf.	Réf.
Regular medical follow-up	**Yes**	59 (58.4)	2 (9.09)	Réf.	Réf.	Réf.
	No	42 (41.6)	20 (90.9)	14.0	[3.11;63.4]	< 0.001
Previous blood transfusions, Mean ± sd	**/**	1.96 ± 1.90	5.82 ± 1.44	1.10	[1.01;1.21]	0.036

Note: *SCH + = patients with sickle cell hepatopathy; SCH− = patients without sickle cell hepatopathy; n = number of participants; N = total number of participants; OR = odds ratio; CI = confidence interval; Ref. = reference category; SD = standard deviation; GGT = gamma-glutamyl transferase.*

Female sex was significantly associated with SCH, with a higher proportion among SCH+ patients than SCH− patients (OR = 8.49; 95% CI: 2.66–27.0; p < 0.001). An increased heart rate was also significantly associated with SCH (OR = 14.2; 95% CI: 4.81–41.7; p < 0.001). Similarly, an increased respiratory rate was more frequently observed among SCH+ patients (OR = 5.84; 95% CI: 1.93–17.7; p = 0.003). Elevated body temperature was strongly associated with SH (OR = 60.4; 95% CI: 16.0–228; p < 0.001). The

presence of a vaso-occlusive crisis was significantly associated with SCH ($p < 0.001$), occurring in 81.8% of SCH+ patients compared with 12.9% of SCH− patients. Elevated GGT levels were also strongly associated with SCH ($p < 0.001$). Finally, the absence of regular medical follow-up was significantly associated with SCH (OR = 14.0; 95% CI: 3.11–63.4; $p < 0.001$).

4. DISCUSSION

The primary objective of this study was to determine the prevalence of sickle cell hepatopathy (SCH) and identify factors associated with its occurrence among patients with sickle cell disease. Hepatic involvement is an important complication of sickle cell disease but is probably underdiagnosed. Indeed, the clinical presentation of sickle cell hepatopathy is highly variable, ranging from isolated biochemical abnormalities to potentially severe acute manifestations such as acute hepatic crisis, hepatic sequestration, or sickle cell intrahepatic cholestasis. This clinical diversity, combined with the overlap between some biochemical abnormalities related to hemolysis and those indicating genuine hepatic injury, makes its diagnosis particularly challenging [25,26]. The literature therefore highlights the lack of a universally accepted definition of sickle cell hepatopathy and the heterogeneity of diagnostic criteria used across studies [27,28]. In our analytical cross-sectional study of 123 patients with sickle cell disease, 22 patients presented with sickle cell hepatopathy, corresponding to a prevalence of 17.9%. This frequency highlights the importance of hepatic involvement in this population and falls within the range of estimates reported in the literature. In their review of sickle cell hepatopathy, Praharaj and Anand emphasized that hepatic involvement is far from uncommon among patients with sickle cell disease, while also highlighting the difficulty of determining its precise frequency because of the diversity of clinical manifestations and diagnostic criteria used [29]. Gardner et al., in their 2014 review, similarly reported that the prevalence of liver dysfunction among patients with sickle cell disease was difficult to establish and had historically been estimated at approximately 10% [30]. The 17.9% prevalence observed in our study is particularly close to that recently reported by Al-Busafi et al. in Oman, who found a prevalence of 17% among adolescents and adults with sickle cell disease [24]. This concordance is noteworthy despite differences in geographical setting and population characteristics. It suggests that hepatic involvement may represent a significant complication of sickle cell disease across different settings, including low-resource countries. Differences in prevalence across studies may, however, be explained by several factors. First, the diagnostic criteria used to define sickle cell hepatopathy are not standardized. Some studies consider only acute clinical manifestations, whereas others include persistent biochemical abnormalities, biliary complications, or radiological findings. This methodological heterogeneity represents an important source of variability in prevalence estimates [27,28]. From a pathophysiological perspective, sickle cell hepatopathy primarily results from erythrocyte sickling and obstruction of the hepatic microcirculation, leading to ischemia, sinusoidal congestion, and hepatocellular injury [3,13]. Recurrent vaso-occlusive crises may therefore promote the development of hepatic lesions, which is consistent with the association observed in our study. Other mechanisms, including repeated blood transfusions and iron overload, as well as biliary complications, may also contribute to hepatic involvement [15,29].

A significant association was observed between sex and the presence of sickle cell hepatopathy, with a predominance of females in the SCH+ group (81.8% vs. 34.7% in the SCH− group; $p < 0.001$). This finding differs from that reported by Al-Busafi et al. in 2025 in Oman [24], who found a male predominance among patients with hepatopathy. This discrepancy may be explained by differences in age, sociodemographic characteristics, disease severity, and recruitment methods between the study populations. The female predominance observed in our study may also be influenced by hormonal factors, as sex hormones can modulate certain hepatic functions and biliary physiology; however, this hypothesis requires confirmation through specifically designed studies [24]. Mean age did not differ significantly between SH + and SCH− patients (8.18 ± 5.01 vs. 10.20 ± 5.12 years; $p = 0.105$). This finding differs from that reported by Al-Busafi et al. [24], in whom patients with hepatopathy were younger than controls. This difference may be related to the markedly different age structures of the study populations, as our study mainly included children, whereas the Omani study involved adolescents and adults.

Previous blood transfusions were significantly more frequent among SCH+ patients (5.82 ± 1.44 vs. 1.96 ± 1.90; $p < 0.001$), and the most recent transfusion had also occurred more recently. This association is consistent with the findings of Deeb et al. [28], who also reported a higher transfusion burden among patients with hepatic involvement. Repeated blood transfusions may promote progressive iron overload, with iron accumulating particularly in the liver and potentially inducing oxidative stress, inflammation, and, ultimately, chronic hepatic injury [26]. However, this association may also indirectly reflect greater disease severity among patients requiring more frequent transfusions.

SCH+ patients also had a higher annual frequency of vaso-occlusive crises (6.09 ± 2.60 vs. 2.90 ± 1.57; $p < 0.001$), longer crises (4.73 ± 1.86 vs. 3.45 ± 2.61 days; $p = 0.010$), and a more recent vaso-occlusive crisis (15.6 ± 16.7 vs. 27.9 ± 37.3 weeks; $p = 0.019$). This relationship may be explained by erythrocyte sickling and obstruction of the hepatic microcirculation during vaso-occlusive episodes, potentially resulting in hypoxia, sinusoidal congestion, and hepatocellular injury [31]. Thus, the frequency and recurrence of vaso-occlusive episodes may contribute to the development or progression of hepatic injury.

The use of herbal medicine was also more frequently reported among SCH+ patients (100% vs. 80.2%; $p = 0.023$). However, this association should be interpreted cautiously, as it does not establish a causal relationship with hepatopathy. Some traditional preparations may contain potentially hepatotoxic substances, but the products used were not characterized in our study. Similarly, paracetamol use (63.6% vs. 7.92%; $p < 0.001$) and NSAID use (45.5% vs. 12.9%; $p = 0.001$) were more frequent among SCH+ patients. This finding may primarily reflect the higher frequency of painful episodes among SCH+ patients, resulting in greater use of analgesic medications. Nevertheless, because paracetamol is primarily metabolized in the liver, repeated use or high doses may represent an additional hepatic stressor [29].

Finally, regular medical follow-up was significantly less frequent among SCH + patients than among SCH – patients (9.09% vs. 58.4%; $p < 0.001$). This association may suggest that inadequate medical follow-up limits the early detection of hepatic complications and delays their management. However, given the cross-sectional nature of our study, a causal relationship between irregular follow-up and the occurrence of hepatopathy cannot be established. Furthermore, a history of gallstone disease was exclusively reported among SCH + patients (18.2% vs. 0%; $p = 0.001$). This finding is consistent with data reported by Deeb *et al.* [28] and Al-Busafi *et al.* [24]. Gallstone disease is a common complication of chronic hemolysis in sickle cell disease. Increased bilirubin production promotes the formation of pigment stones, which may cause biliary obstruction, cholestasis, and secondary hepatobiliary complications [32]. Overall, these findings suggest that hepatopathy in our population was associated with a more active disease profile, characterized notably by a greater transfusion burden, a higher frequency of vaso-occlusive crises, and the presence of biliary complications.

Clinically, fever was significantly more frequent among SCH + patients than among SCH – patients (81.8% vs. 6.9%; $p < 0.001$). This association may reflect the inflammatory state associated with vaso-occlusive episodes or the coexistence of an infectious process, particularly since infection was also more frequent among SCH + patients (18.2% vs. 1.0%; $p = 0.004$). Fever should therefore be interpreted with caution, as it is not specific to hepatic involvement. In contrast, manifestations directly suggestive of hepatobiliary involvement were markedly more frequent among SCH + patients, particularly right upper quadrant pain (90.9% vs. 3.0%), hepatomegaly (81.8% vs. 4.0%), and jaundice (63.6% vs. 4.0%), with each of these manifestations being significantly associated with SCH ($p < 0.001$). These findings are consistent with the manifestations classically described in acute hepatic complications of sickle cell disease [25,33]. Splenomegaly and vaso-occlusive crises were also significantly more frequent among HP+ patients, further supporting an association between disease vaso-occlusive activity and hepatic involvement.

Biologically, AST levels were elevated in all participants, with no difference in frequency between the groups. This generalized elevation should be interpreted cautiously in the context of sickle cell disease, because AST is not liver-specific and is also present in erythrocytes and muscle tissues. Chronic hemolysis may therefore contribute to increased AST levels [34]. In contrast, ALT levels were significantly higher among SCH + patients (53.4 ± 12.9 vs. 43.7 ± 10.3 U/L; $p = 0.003$), with a higher proportion of values exceeding the upper reference limit (81.8% vs. 45.5%; $p = 0.006$). This difference suggests greater hepatocellular injury in the hepatopathy group, as ALT is relatively more specific for hepatic injury than AST. These findings are broadly consistent with those reported by Deeb *et al* [28].

GGT and, particularly, ALP levels were also significantly higher among SCH + patients (39.3 ± 25.7 vs. 15.4 ± 8.5 U/L; $p = 0.012$ and 512 ± 74.7 vs. 355 ± 113 U/L; $p < 0.001$, respectively). The concomitant elevation of ALP and GGT among patients with SCH supports the presence of a hepatobiliary component to the observed abnormalities. In our series, the biochemical profile was dominated by mixed cholestasis (72.7%), followed by pure cholestasis (27.3%) among SCH+ patients. This predominance of cholestatic profiles is compatible with the mechanisms described in sickle cell hepatopathy, including

sinusoidal congestion, intrahepatic vaso-occlusive phenomena, and biliary complications associated with chronic hemolysis [27,28]. However, it is important to emphasize that interpretation of ALP levels in children requires caution, given the physiological contribution of the bone isoenzyme during growth. Nevertheless, the concomitant elevation of GGT in a substantial proportion of SCH + patients further supports a hepatobiliary origin of the observed ALP abnormalities.

Finally, the presence of acute hepatic crisis in 90.9% of SCH + patients and acute hepatic sequestration in 9.1% highlights the predominantly acute nature of the hepatic complications identified in our population. The predominance of acute hepatic crisis may partly explain the marked clinical and biochemical abnormalities observed. These findings also suggest that, in children with sickle cell disease, hepatic manifestations may occur in the context of active vaso-occlusive disease and require prompt clinical and biochemical assessment.

In univariate analysis, female sex was associated with an increased likelihood of sickle cell hepatopathy (OR = 8.49; 95% CI: 2.66–27.0; $p < 0.001$), like some reports describing a female predominance [24]. Tachycardia, increased respiratory rate, and particularly fever were also strongly associated with SCH, probably reflecting the acute clinical context of the hepatic complications observed. The presence of vaso-occlusive crises (VOC) was particularly frequent among SCH + patients (81.8% vs. 12.9%; $p < 0.001$), supporting the hypothesis that recurrent vaso-occlusive phenomena may contribute to the development of hepatic injury. Finally, lack of regular medical follow-up was strongly associated with SCH (OR = 14.0; 95% CI: 3.11–63.4; $p < 0.001$) [35]. This association may reflect delayed detection of hepatic complications among patients receiving less regular medical care [28]. However, the causal interpretation of these associations should remain cautious.

This study has several limitations that should be acknowledged. The relatively short study period and the modest sample size may have limited the statistical power of the study and the generalizability of the findings. In addition, the absence of hepatobiliary imaging prevented the clinical and biochemical findings from being complemented by a morphological assessment of hepatic involvement.

Despite these limitations, this study has several strengths. Overall, our findings show that sickle cell hepatopathy was associated with a constellation of concordant clinical and biological characteristics, including increased vaso-occlusive activity, greater transfusion exposure, biliary complications, clinical signs of hepatic involvement, and a predominance of a cholestatic biochemical profile. These findings support the value of systematic screening for hepatobiliary abnormalities in patients with sickle cell disease, particularly those experiencing frequent vaso-occlusive crises or substantial transfusion exposure.

CONCLUSION

At the end of this study, which aimed to determine the prevalence and factors associated with sickle cell hepatopathy among patients with sickle cell disease in Cameroon, sickle cell hepatopathy was identified in 22 of the 123 participants, corresponding to a prevalence of 17.9%. Clinically, the main manifestations

associated with sickle cell hepatopathy were right upper quadrant pain, hepatomegaly, and jaundice, observed in 90.9%, 81.8%, and 63.6% of SCH + patients, respectively, compared with 3.0%, 4.0%, and 4.0% among SCH − patients. Vaso-occlusive crises were also markedly more frequent among patients with hepatopathy (81.8% vs. 12.9%; $p < 0.001$). Biologically, SH + patients had significantly higher ALT, GGT, and ALP levels, with mean values of 53.4 ± 12.9 U/L, 39.3 ± 25.7 U/L, and 512 ± 74.7 U/L, respectively. The biochemical profile was predominantly characterized by mixed cholestasis (72.7%), followed by pure cholestasis (27.3%), while acute hepatic crisis was identified in 90.9% of SCH + patients. In univariate analysis, several factors were significantly associated with sickle cell hepatopathy, including male sex (OR = 8.49; 95% CI: 2.66–27.0; $p < 0.001$), increased heart and respiratory rates, fever, the presence of vaso-occlusive crises (OR = 18.2; 95% CI: 5.53–60.2; $p < 0.001$), elevated GGT levels, and lack of regular medical follow-up (OR = 14.0; 95% CI: 3.11–63.4; $p < 0.001$). The number of previous blood transfusions was also significantly higher among SCH + patients (5.82 ± 1.44 vs. 1.96 ± 1.90; $p = 0.036$). This study highlights the substantial occurrence of sickle cell hepatopathy in our setting and underscores the importance of regular clinical and biochemical monitoring, particularly among patients experiencing recurrent vaso-occlusive crises, substantial transfusion exposure, or clinical and biological features suggestive of hepatobiliary involvement.

Declarations

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding the publication of this manuscript.

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None

Author Contribution

RTDM, PNT, Julie MMS, IWSYong, and MSN contributed to data collection, data interpretation, and manuscript drafting. JSL performed the statistical analysis of the extracted data. PDCD supervised the study. PDCD critically reviewed the manuscript. All authors read and approved the final version of the manuscript. RTDM had full access to all data included in the study and takes full responsibility for the integrity of the data and the accuracy of the data analysis.

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Transparency Statement

The lead author, Romaric Tuono De Manfouo, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

References

1. Kato GJ, Piel FB, Reid CD, Gaston MH, Ohene-Frempong K, Krishnamurti L, et al. Sickle cell disease. Nat Rev Dis Prim [Internet]. Macmillan Publishers Limited; 2018;4:1–22. https://doi.org/10.1038/nrdp.2018.10
2. G. DG. ⁂⁂⁂⁂⁂⁂ HHS Public Access. Physiol Behav. 1965;176:139–48. https://doi.org/10.1146/annurev-pathmechdis-012418-012838.Pathophysiology
3. Simo JL. Hepatic Enzyme Abnormalities and Their Association With Hematological Parameters in Sickle Cell Disease : A Case - Control Study in Cameroon. 2026; https://doi.org/10.1002/hsr2.72649
4. Thomson AM, McHugh TA, Oron AP, Teply C, Lonberg N, Vilchis Tella VM, et al. Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000–2021: a systematic analysis from the Global Burden of Disease Study 2021. Lancet Haematol. 2023;10:e585–99. https://doi.org/10.1016/S2352-3026(23)00118-7
5. Louokdom J, Romaric S, Tuono DM, Seuko M, Claude N, Tayou T. Oxidative Stress , Antioxidant Capacity , Dyslipidemia and Cardiovascular Risk in Sickle Cell Disease : A Systematic Review and Meta-Analysis. 2026;1–19. https://doi.org/10.1155/tswj/8864775
6. Tuono RDM. Inflammation and Iron Profile in Children With Sickle Cell Disease in Cameroon : Frequency and Associated Factors , an Analytical Cross - Sectional Study. 2025; https://doi.org/10.1002/hsr2.70773
7. Hay SI, Gupta S, Weatherall DJ, Williams TN. Global Burden of Sickle Cell Anaemia in Children under Five , 2010 – 2050 : Modelling Based on Demographics , Excess Mortality , and Interventions. 2013;10. https://doi.org/10.1371/journal.pmed.1001484
8. Tuono RDM, Simo JL, Njopwouo MS, Tayou CT. Abnormalities of hemostasis in sickle cell patients and predisposition to thrombotic risk : a systematic review and meta-analysis. 2025;
9. Manfouo RT De, Louokdom JS, Pieme CA, Claude B, Prosper C, Biapa C, et al. Homozygote drepanocytosis : Ferric status and inflammation in world and Africa : Review article and meta analysis. 2023;1–9. https://doi.org/10.1002/hsr2.1609

10. Manfouo RT De, Louokdom S, Chedjou JP, Cabral P, Nya B, Mbatcham W, et al. Iron , Oxidative Stress , and Haptoglobin Gene Polymorphism in Sickle Cell Disease Patients With Inflammation in Cameroon : An Analytical Cross-Sectional Study. 2025;2025:1–8. https://doi.org/10.1155/bri/5303373
11. Suddle AR. Management of liver complications in sickle cell disease. 2019;345–50.
12. Porter J, Garbowski M. Consequences and management of iron overload in sickle cell disease. 2013;447–56.
13. Shah R, Taborda C, Chawla S. Acute and chronic hepatobiliary manifestations of sickle cell disease: A review. World J Gastrointest Pathophysiol. 2017;8:108. https://doi.org/10.4291/wjgp.v8.i3.108
14. Allali S, Montalembert M De, Brousse V, Heilbronner C, Taylor M, Brice J, et al. Hepatobiliary Complications in Children with Sickle Cell Disease : A Retrospective Review of Medical Records from 616 Patients. 2019;
15. Deeb M, Kuo KHM, Leung KK, Ward R, Feld JJ, Hirschfield GM. Hepatobiliary complications in patients with sickle cell disease : A 30-year review of 1009 patients Hepatobiliary complications in patients with sickle cell disease : A 30-year review of 1009 patients. https://doi.org/10.1097/HC9.0000000000000712
16. Elevated Liver Enzymes. Am Fam Physician. 2017;96:2017.
17. Mohammad M, Alaoui-Ismaili Z, Arvig MD, Barzanji AF. Forhøjede levertransaminaser ved rabdomyolyse hos rekrut efter felttur. Ugeskr Laeger. 2023;185:1431–2.
18. Savage K, Porter C, Bunnett E, Hana M, Keegan A, Ogden E, et al. Liver and inflammatory biomarker relationships to depression symptoms in healthy older adults. Exp Gerontol. Elsevier Inc.; 2023;177:112186. https://doi.org/10.1016/j.exger.2023.112186
19. Xuan Y, He F, Liu Q, Dai D, Wu D, Shi Y, et al. Elevated GGT to HDL ratio as a marker for the risk of NAFLD and liver fibrosis. Sci Rep. 2025;15:1–17. https://doi.org/10.1038/s41598-024-84649-w
20. Siller AF, Whyte MP. Alkaline Phosphatase: Discovery and Naming of Our Favorite Enzyme. J Bone Miner Res. 2018;33:362–4. https://doi.org/10.1002/jbmr.3225
21. Sekaran S, Selvaraj V, Thangavelu L. The physiological and pathological role of tissue nonspecific alkaline phosphatase beyond mineralization. Biomolecules. 2021;11:1–21. https://doi.org/10.3390/biom11111564
22. Anderson GJ, Frazer DM. Current understanding of iron homeostasis. Am J Clin Nutr. 2017;106:1559S-1566S. https://doi.org/10.3945/ajcn.117.155804
23. Nsiah K, Dzogbefia VP, Ansong D, Akoto AO, Boateng H, Ocloo D. Clinical Medicine Insights : Blood Disorders Pattern of AST and ALT Changes in Relation to Hemolysis in Sickle Cell Disease. 2011;1–9. https://doi.org/10.4137/CMBD.S3969
24. Al-Busafı SA, Al-Zaabi F, Al-Kindi S. Prevalence, risk factors, and demographic insights of sickle cell hepatopathy in Omani adolescents and adults: A retrospective analysis. Saudi J Gastroenterol. 2025;31:301–12. https://doi.org/10.4103/sjg.sjg_177_25

25. Rodrigues L, Almeida S, Salgado C, Gonçalves C. Pediatric Acute Liver Failure in Sickle Cell Disease. GE Port J Gastroenterol. 2022;29:192–6. https://doi.org/10.1159/000515469
26. Mohamed KA, Nephew LD, Kaur H. Sickle cell hepatopathy: An underrecognized and undertreated cause of chronic liver disease. Clin Liver Dis. 2023;22:229–32. https://doi.org/10.1097/CLD.0000000000000092
27. Papafragkakis H, Ona MA, Changela K, Anand S, Sadanandan S, Jelin A, et al. Acute liver function decompensation in a patient with sickle cell disease managed with exchange transfusion and endoscopic retrograde cholangiography. Therap Adv Gastroenterol. 2014;7:217–23. https://doi.org/10.1177/1756283X14530781
28. Deeb M, Leung KK, Ward R, Feld JJ, Kuo KHM, Hirschfield GM. Hepatobiliary complications in patients with sickle cell disease: A 30-year review of 1009 patients. Hepatol Commun. 2025;9. https://doi.org/10.1097/HC9.0000000000000712
29. Praharaj DL, Anand AC. Sickle Hepatopathy. J Clin Exp Hepatol. Elsevier Ltd; 2021;11:82–96. https://doi.org/10.1016/j.jceh.2020.08.003
30. Gardner K, Suddle A, Kane P, O'Grady J, Heaton N, Bomford A, et al. How we treat sickle hepatopathy and liver transplantation in adults. Blood. 2014;123:2302–7. https://doi.org/10.1182/blood-2013-12-542076
31. Lynch K, Mega A, Daves M, Sadiq A, Fogarty H, Piccin A. Liver Disease and Sickle Cell Disease: Auto-Immune Hepatitis more than a Coincidence; A Systematic Review of the Literature. Mediterr J Hematol Infect Dis. 2023;15:1–11. https://doi.org/10.4084/MJHID.2023.060
32. Ghosh JB. Sickle Cell Intrahepatic Cholestasis with Acute Liver Failure and Acute Kidney Injury: Favorable Outcome with Exchange Transfusion: Correspondence. Indian J Pediatr. The Indian Journal of Pediatrics; 2021;88:200–1. https://doi.org/10.1007/s12098-020-03368-y
33. Pathophysiology G. Acute and chronic hepatobiliary manifestations of sickle cell - WJGH - 2017. 2017;5330.
34. Surapaneni PK, Mills K, Renelus BD. A Rare Complication of Sickle Cell Anemia. Gastroenterology. Elsevier, Inc; 2021;161:45–6. https://doi.org/10.1053/j.gastro.2020.11.025
35. Novelli EM, Gladwin MT. Crises in sickle cell disease. Chest [Internet]. Elsevier Inc; 2016;149:1082–93. https://doi.org/10.1016/j.chest.2015.12.016