

## Original Research Article

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# Observational study of cholelithiasis and its complications in sickle cell disease: experience from a tertiary care hospital in central India

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## ABSTRACT

**Background:** Sickle cell disease (SCD) is a genetic hemoglobinopathy associated with chronic hemolysis and vaso-occlusive crises. Pigment gallstone formation is among its most common hepatobiliary complications, causing cholelithiasis and resulting morbidity. Gallstones in patients with SCD have variable prevalence worldwide and are determined by genetic, hematologic, and environmental variables. Indian data are meager, and prospective hospital-based studies on clinical profiles, complications, and outcomes of management are minimal. This research sought to assess the prevalence, clinical spectrum, and prognosis of cholelithiasis among SCD patients presenting at a tertiary care center in central India.

**Methods:** This prospective observational study was conducted from August 2023 to January 2025 at a tertiary care hospital. A total of 91 adult patients with confirmed SCD presenting with symptoms of cholelithiasis were enrolled after ethical clearance and informed consent. Demographic, clinical, laboratory, and imaging data were collected. Management included laparoscopic cholecystectomy, ERCP, common bile duct (CBD) exploration, or conservative treatment. Data were analyzed using SPSS v27, with  $p < 0.05$  considered statistically significant.

**Results:** Gallstones were found in 26 patients (28.57%). Mixed stones (38.46%) were most frequent, followed by pigment (34.62%) and cholesterol stones (26.92%). Patients with gallstones had much lower hemoglobin ( $8.17 \pm 1.36$  g/dl) and higher bilirubin ( $2.29 \pm 0.28$  mg/dl) than those without ( $p < 0.001$ ). Complications were choledocholithiasis (53.85%), acute cholecystitis (46.15%), and acute pancreatitis (42.31%). Laparoscopic cholecystectomy was the most frequent intervention (42.31%), with a 9.09% conversion rate. All patients were recovered and discharged without in-hospital mortality.

**Conclusions:** Cholelithiasis is prevalent in SCD and strongly correlated with hemolysis-related indices. Early screening, aggressive surgical intervention, and mindful perioperative optimization are essential to minimize morbidity in this high-risk population.

**Keywords:** Cholelithiasis, Gallstones, Hemolysis, Laparoscopic cholecystectomy, Sickle cell disease

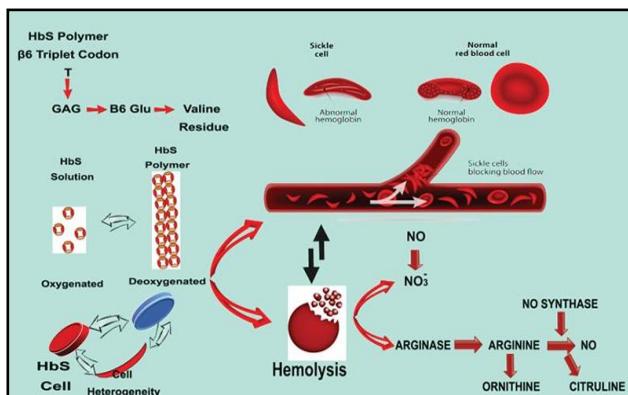
## INTRODUCTION

Sickle cell disease (SCD) is one of the most common monogenic disorders worldwide, affecting more than 20 million people and responsible for considerable morbidity and mortality, particularly in malaria-endemic region.<sup>1,2</sup> It

results from a point mutation in the  $\beta$ -globin gene leading to the substitution of valine for glutamic acid at the sixth position of the hemoglobin  $\beta$ -chain. This molecular defect yields hemoglobin S (HbS) that polymerizes in hypoxia, distorting red cells into their characteristic sickle

shape (Figure 1).<sup>3</sup> The result is chronic hemolytic anemia, frequent vaso-occlusive crises, and multi-organ damage.

Globally, SCD is most prevalent in sub-Saharan Africa, the Middle East, and the Indian subcontinent.<sup>1,3,4</sup> The World Health Organization (WHO) recognizes it as a major public health issue. In India, the prevalence of sickle cell trait (SCT) ranges from 5% to 40% among tribal populations, with the central Indian states of Maharashtra, Madhya Pradesh, Chhattisgarh, and Odisha bearing the highest burde.<sup>5</sup> With improved survival due to better supportive care, the prevalence of chronic complications has concurrently increased.<sup>2,3</sup>



**Figure 1: Pathophysiology of SCD.**

Of the numerous systemic complications associated with SCD, hepatobiliary manifestations are frequent and clinically relevant. Chronic hemolysis causes overproduction of bilirubin, making these patients susceptible to the development of pigment gallstones.<sup>6,7</sup> Several studies have demonstrated that the incidence of gallstones in patients with SCD varies widely, from 25% to 60% in African and Middle Eastern populations,<sup>4,8-11</sup> while meta-analyses have estimated a pooled global prevalence of around 25%.<sup>12</sup> In contrast, the prevalence of gallstones in the general Indian population is reported to be only 3-6%,<sup>13</sup> reinforcing the hemolysis-driven pathophysiology in SCD. Early epidemiologic work from Europe documented appreciable gallstone prevalence in SCD cohorts, highlighting that this complication is not confined to traditionally endemic regions.<sup>14</sup>

Clinically, cholelithiasis can remain asymptomatic for years; however, in SCD patients, even silent stones carry a higher risk of complications due to recurrent hemolysis and biliary sludge formation.<sup>15,16</sup> Symptomatic gallstones may present with right-upper-quadrant pain, jaundice, fever, or pancreatitis and can be mistaken for vaso-occlusive crises, complicating diagnosis.<sup>7,17</sup> Surgery in these patients is challenging because SCD increases perioperative risks, including acute chest syndrome, vaso-occlusive episodes, and postoperative infection.<sup>18,19</sup> Hence, careful perioperative optimization hydration, oxygenation, temperature maintenance, and tailored transfusion strategies is essential.<sup>19</sup>

The role of prophylactic cholecystectomy in asymptomatic SCD patients remains controversial. Some authors advocate for elective laparoscopic removal to prevent emergent complications, whereas others prefer a conservative approach unless symptoms develop.<sup>6,8,20-22</sup> Nevertheless, multiple studies confirm that laparoscopic cholecystectomy in SCD patients is safe and effective when proper optimization protocols are followed.<sup>18-20</sup>

Although ample data are available from Africa, the Middle East, and Western countries, Indian studies on the prevalence and clinical presentation of cholelithiasis in SCD remain sparse.<sup>13,17,23,24</sup> The central Indian belt, particularly Maharashtra, contributes a major portion of India's SCD burden, yet hepatobiliary complications in this population have not been systematically characterized.<sup>5,13</sup> Variations in genetic background, nutritional status, and healthcare access may influence the presentation and outcomes of SCD-related cholelithiasis compared to global cohorts.

The present study was undertaken with the objective of determining the prevalence, clinical profile, complications, and outcomes of cholelithiasis among adult patients with SCD attending a tertiary care hospital in central India. By analyzing clinical, biochemical, radiological, and operative findings, this study aimed to establish correlations between hemolysis-related parameters and gallstone formation, assess the safety and efficacy of laparoscopic cholecystectomy, and generate region-specific evidence to guide screening and management protocols for SCD patients at risk of gallstone disease.

## METHODS

### Study design and setting

This was a prospective observational study done in the Department of General Surgery in Government Medical College and Hospital, Nagpur, which is a central Indian tertiary referral center. The study was performed over a period of 18 months from August 2023 to January 2025. The institution is a prominent referral center for patients from tribal and rural areas of Maharashtra state, whose rate of sickle cell disease (SCD) is very high.

### Ethical approval and consent

The study protocol was approved by and read at the Institutional Ethics Committee (IEC) of Government Medical College and Hospital, Nagpur. All participants gave written informed consent before enrolment. Patients were guaranteed confidentiality, voluntary participation, and the right to withdraw at any time without compromising their level of care. The study complied with the tenets of the Declaration of Helsinki (2013 revision).

### **Study population**

We studied adult patients ( $\geq 18$  years) with documented SCD who attended the surgical outpatient department or emergency with clinical features of cholelithiasis. Confirmation of SCD diagnosis by hemoglobin electrophoresis or HPLC report in the medical record was done.

### **Inclusion criteria**

Age  $\geq 18$  years, both sexes, documented diagnosis of SCD (HbSS or HbAS genotypes), clinical suspicion of cholelithiasis (e.g., recurrent right upper quadrant pain, jaundice, nausea, vomiting), patients who are willing to give written informed consent were included.

### **Exclusion criteria**

Patients with unconfirmed SCD, pregnant women (because of changed physiology and possibility of confounders in gallstone disease), and patients who refuse or are incapable of giving consent were excluded.

### **Sample size calculation**

The sample size was approximated utilizing the formula for prevalence studies:

$$n = Z^2 \times p \times (1-p) / d^2$$

Where,  $Z = 1.96$  (95% confidence interval),  $p =$  previously estimated prevalence of cholelithiasis in SCD from Indian/Nigerian studies ( $\sim 22.5\%$ ),  $d =$  error margin (10%).

Minimum calculated sample size was 91 patients, and this was met during the study duration. Convenience sampling was adopted with all the patients fulfilling the inclusion criteria presenting within the study period.

### **Data collection**

At the time of enrolment, a structured proforma was employed in order to gather the following data:

**Demographic parameters:** It includes age, sex, residential background.

**Clinical history:** It includes nature of SCD, presenting symptoms (abdominal pain, jaundice, fever, pallor, bone pain, fatigue), history of previous vaso-occlusive crises or blood transfusions.

**Physical examination:** It includes pallor, icterus, hepatosplenomegaly, abdominal tenderness.

**Laboratory investigations:** It includes complete blood count, liver function tests (total bilirubin, AST, ALT, ALP), renal function tests.

**Radiological findings:** It includes abdominal ultrasonography and CT scan where necessary.

**Intraoperative findings:** It includes nature of gallstones, complications, necessity for conversion to open cholecystectomy.

**Treatment modality:** It includes laparoscopic cholecystectomy, ERCP, CBD exploration, or conservative treatment.

**Postoperative course:** It includes duration of hospital stay, morbidity, and mortality results.

### **Imaging and diagnostic criteria**

**Ultrasound (USG):** Transabdominal USG was done in all the patients with a 3.5-5.0 MHz curvilinear probe. Diagnosis of gallstones was done by observing echogenic foci in the gallbladder lumen producing posterior acoustic shadows. Acute cholecystitis was diagnosed by gallbladder wall thickening, pericholecystic fluid, or sonographic Murphy's sign.

**CT Abdomen:** Utilized in selected instances to further characterize stones or complications like pancreatitis or abscess formation.

**ERCP:** Used in patients with suspected choledocholithiasis on the basis of laboratory and imaging results

Types of gallstones were classified intraoperatively as pigment stones, cholesterol stones, or mixed stones on the basis of gross appearance.

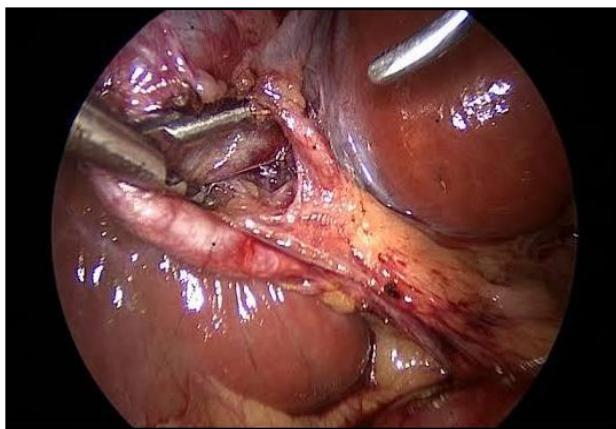
### **Management protocol**

Conservative management was offered to asymptomatic patients or those found unfit for surgery.

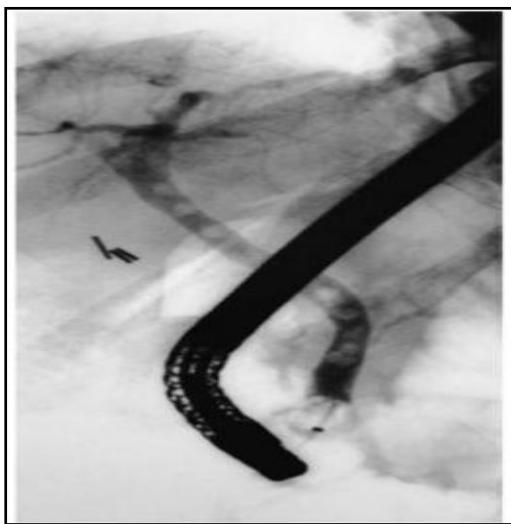
Laparoscopic cholecystectomy was done in symptomatic cholelithiasis patients. Standard 4-port technique was employed, with emphasis on attaining the Critical View of Safety (CVS) (Figure 2) prior to clipping the cystic duct and artery. Conversion to open surgery was done in case of unclear anatomy or suspected complications.

**Endoscopic retrograde cholangiopancreatography (ERCP):** Employed for common bile duct stone removal before or after cholecystectomy (Figure 4).

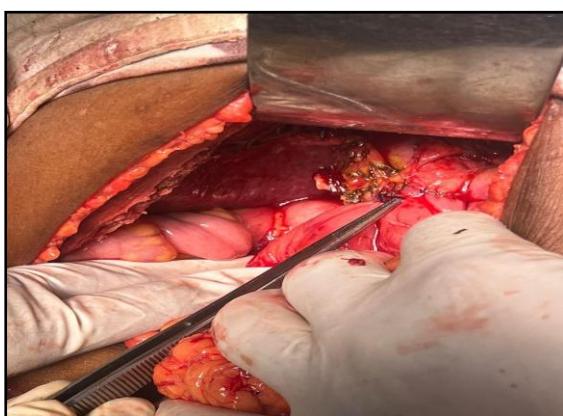
**CBD exploration:** Open or laparoscopic exploration was performed in selected patients with multiple ductal stones or failed ERCP (Figure 3).



**Figure 3: Intraoperative image of Calot's triangle and critical view of safety in laparoscopic cholecystectomy.**



**Figure 3: ERCP image of duct with multiple stones.**



**Figure 4: Intraoperative image of CBD exploration showing clipped gall bladder and sutured CBD.**

All patients received perioperative special care focused on hydration, oxygenation, normothermia, and transfusion modalities to minimize the risk of vaso-occlusive crises or acute chest syndrome.

### Outcome measures

Primary outcome was prevalence of cholelithiasis among adult SCD patients. Secondary outcomes were 1) Type of gallstones, 2) Clinical presentation and complications (choledocholithiasis, cholangitis, pancreatitis, acute cholecystitis), 3) Management modalities and conversion rate, 4) Hospital stay duration, and 5) Outcomes of treatment (discharge, death).

### Statistical analysis

Data were typed in Microsoft Excel and analyzed with SPSS v27 (IBM, Armonk, NY, USA). The continuous variables (e.g., age, hemoglobin, bilirubin) were reported as mean $\pm$ SD and compared by the independent sample t-test. The categorical variables (e.g., gender, the presence of gallstones, the gallstones' type) were presented as frequencies and percentages and compared by the Chi-square test or Fisher's exact test where necessary. A p-value  $<0.05$  was taken to be statistically significant

## RESULTS

A total of 91 patients with confirmed sickle cell disease (SCD) presenting with symptoms suggestive of cholelithiasis were enrolled during the study period. Of these, 26 patients (28.57%) were diagnosed with gallstones on ultrasonography and/or intraoperative findings, while the remaining 65 patients (71.43%) did not have gallstones.

### Demographic profile

The demographic profile of the study participants is summarized in Table 1. The mean age of the study cohort was  $38.6\pm13.4$  years (range: 18-70 years). Most gallstone-positive patients were in the 21-30-year age group (38.5%), followed by 31-40 years (26.9%). There was a slight female predominance (57.7%), though the difference was not statistically significant ( $p=0.71$ ). A majority of patients (65.9%) were from rural areas, reflecting the hospital's catchment population. Gallstone-positive patients had significantly lower hemoglobin levels and higher bilirubin values than gallstone-free patients ( $p<0.001$ ), reaffirming the strong association between chronic hemolysis and gallstone formation.

### Genotypic distribution and types of gallstones

The genotypic distribution and gallstone characteristics are summarized in Table 2. Most patients in both groups had the HbAS genotype (82.4% overall), while HbSS patients constituted 17.6%. There was no statistically significant association between genotype and the presence of gallstones ( $p=0.57$ ). Among gallstone-positive patients, mixed stones (38.5%) were most common, followed by pigment stones (34.6%) and cholesterol stones (26.9%), indicating a predominant hemolytic etiology consistent with SCD pathophysiology.

**Table 1: Demographic characteristics of the study population.**

Parameter	Gallstone-Positive (n=26)	Gallstone-Negative (n=65)	Total (n=91)	P value
<b>Age (years)</b>	35.0±13.2	39.7±13.4	38.6±13.4	0.11
<b>Age group (years), N (%)</b>				
<20	2 (7.7)	7 (10.8)	9 (9.9)	-
21-30	10 (38.5)	18 (27.7)	28 (30.8)	-
31-40	7 (26.9)	15 (23.1)	22 (24.2)	-
41-50	4 (15.4)	13 (20.0)	17 (18.7)	-
>50	3 (11.5)	12 (18.4)	15 (16.4)	-
<b>Gender, N (%)</b>				
Male	11 (42.3)	31 (47.7)	42 (46.1)	0.71
Female	15 (57.7)	34 (52.3)	49 (53.9)	-
<b>Residence, N (%)</b>				
Rural	18 (69.2)	42 (64.6)	60 (65.9)	0.66
Urban	8 (30.8)	23 (35.4)	31 (34.1)	-
<b>Mean hemoglobin (g/dl)</b>	8.17±1.36	9.48±1.13	9.13±1.25	<0.001
<b>Mean bilirubin (mg/dl)</b>	2.29±0.28	0.69±0.41	1.10±0.60	<0.001

**Table 2: Genotypic distribution and types of gallstones among SCD patients.**

Parameter	Gallstone-Positive (n=26)	Gallstone-Negative (n=65)	Total (n=91)	P value
<b>Genotype, N (%)</b>				
HbAS (sickle cell trait)	20 (76.9)	55 (84.6)	75 (82.4)	0.57
HbSS (sickle cell disease)	6 (23.1)	10 (15.4)	16 (17.6)	-
<b>Type of gallstones* N (%)</b>				-
Pigment stones	9 (34.6)	-	9 (9.9)	-
Mixed stones	10 (38.5)	-	10 (11.0)	-
Cholesterol stones	7 (26.9)	-	7 (7.7)	-

**Table 3: Association of signs and symptoms with presence of gallstone.**

Symptoms	Presence of gallstones		P value
	Present (n=26)	Absent (n=65)	
<b>Pain in bone</b>	18 (69.23)	33 (50.77)	0.1709
<b>Abdominal pain</b>	8 (30.77)	19 (29.23)	1.0000
<b>Pallor</b>	16 (61.54)	18 (27.69)	0.0055
<b>Jaundice</b>	4 (15.38)	9 (13.85)	1.0000
<b>Fever</b>	16 (61.54)	40 (61.54)	1.0000
<b>Fatigue</b>	6 (23.08)	20 (30.77)	0.6334

### Clinical presentation

Pallor was the sole symptom with a statistically significant correlation with gallstones. Other symptoms, though prevalent, failed to portray significant disparity in the two groups.

### Complications

Cholelithiasis among SCD patients had a high rate of complications as shown in Table 3.

### Treatment modalities

Of the 26 gallstone-positive patients, the most frequent treatment was laparoscopic cholecystectomy (42.3%).

ERCP was done in 26.9% for choledocholithiasis. Exploration of CBD was needed in 11.5%. Conservative treatment was taken in 19.2% because of patient comorbidities or surgical refusal (Table 5).

**Table 4: Distribution of complications observed in patients with gallstones.**

Complications	Number	Percent
<b>Choledocholithiasis</b>	14	53.85
<b>Acute pancreatitis</b>	11	42.31
<b>Acute cholecystitis</b>	12	46.15
<b>Cholangitis</b>	8	30.77
<b>Cholangitic liver abscess</b>	2	7.69
<b>Gall bladder adenocarcinoma</b>	1	3.85

**Table 5: Distribution of patients according to treatment modalities.**

Treatment modalities	Number	Percent
<b>Laparoscopic cholecystectomy</b>	11	42.31
<b>ERCP</b>	7	26.92
<b>Exploration of CBD</b>	3	11.54
<b>Conservative</b>	5	19.23

In the patients who underwent laparoscopic cholecystectomy, 9.1% (1 out of 11) were converted to open surgery. The reason for conversion was dense adhesions and incoherent anatomy in Calot's triangle.

#### Length of hospital stay and outcomes

Most of the gallstone-positive patients (61.5%) were hospitalized for a stay of five or more days, whereas 38.5% were discharged in fewer than five days. This longer stay demonstrated the severity of biliary complications and the necessity of perioperative optimization in SCD patients.

Notably, all patients were successfully discharged after treatment, and no in-hospital mortality was noted in either group.

#### DISCUSSION

The present prospective study offers critical insights into the prevalence, clinical spectrum, and management of cholelithiasis in patients with sickle cell disease (SCD) in central India. The observed prevalence of 28.6% corroborates international trends and confirms gallstone formation as a major hepatobiliary manifestation of chronic hemolysis. The study also highlights a significant association between low hemoglobin, elevated bilirubin, and gallstone formation strengthening the pathophysiological link between sustained hemolysis and pigment gallstone development. Additionally, the outcomes of surgical management demonstrate that, with proper optimization, laparoscopic cholecystectomy is both feasible and safe in this vulnerable group.

#### Prevalence of cholelithiasis

The 28.6% prevalence of cholelithiasis found in our study corresponds closely with global estimates. Oguntayo et

al reported a prevalence of 25-37% in Nigeria, while Mohamed et al reported a pooled prevalence of ~25% in their meta-analysis.<sup>10,12</sup> Comparable findings were also documented by Martins et al in Brazil (30%).<sup>9</sup> By contrast, Al-Salem et al reported higher rates approaching 60% in the Middle East, possibly due to earlier onset of disease and more severe hemolytic phenotypes in those populations.<sup>8</sup> Indian data remain limited but consistent with Mukherjee et al and Jain et al reported prevalence rates between 25-30%, similar to our results.<sup>17,24</sup> This cross-regional consistency underscores the universal role of hemolysis in gallstone pathogenesis among SCD patients.

#### Demographic characteristics

Gallstones were most common in the 21-40-year age group, with a mild female predominance (57.7%). These findings align with Walker et al and Diagne et al, who reported similar age and sex distributions.<sup>4,25</sup> The higher female incidence likely reflects estrogen-mediated changes in bile composition and gallbladder motility. The clustering of cases in early adulthood corresponds to the cumulative duration of hemolysis, leading to progressive bilirubin supersaturation of bile.

#### Hematological and biochemical correlation

The marked differences in hemoglobin (8.17±1.36 g/dl vs 9.48±1.13 g/dl) and bilirubin (2.29±0.28 mg/dl vs 0.69±0.41 mg/dl,  $p<0.001$ ) between gallstone-positive and gallstone-free patients reinforce the role of hemolytic intensity as a predictor of gallstone formation. Hamza et al and Aliyu et al reported similar findings, establishing that elevated bilirubin is the single most consistent biochemical risk factor for gallstone formation in SCD.<sup>15,21</sup> The absence of significant variation in WBC and platelet counts suggests that gallstone formation in SCD is not inflammatory in origin but a direct consequence of hemolysis.

#### Stone composition

Our study found mixed stones (38.5%) and pigment stones (34.6%) to be predominant. This composition mirrors findings from Martins et al (42% pigment, 36% mixed) and Mukherjee et al (40% pigment).<sup>9,24</sup> The predominance of pigment stones underscores hemolysis-driven lithogenesis, while the presence of mixed stones reflects the chronicity of disease and the interplay between bilirubin and cholesterol metabolism. Regional nutritional factors and hepatic enzyme polymorphisms may also contribute to minor variations in stone type between populations.

#### Clinical presentation and complications

Complications were frequent and clinically significant in this cohort, with choledocholithiasis (53.8%), acute cholecystitis (46.2%), and acute pancreatitis (42.3%)

dominating the clinical picture. These rates parallel those reported by Aranda-Narváez et al and Ebert & Nagar, who found complication frequencies between 30-50%.<sup>7,16</sup> Indian data by Jain et al revealed a 48% complication rate, nearly identical to ours.<sup>17</sup> The overlapping symptoms of biliary pain and vaso-occlusive crisis often delay diagnosis, explaining why SCD patients frequently present late with advanced complications. This emphasizes the need for early imaging and surgical referral in all SCD patients presenting with upper abdominal pain or jaundice. Radiologic studies such as Baheti et al have emphasized that hepatobiliary complications in SCD are often multifactorial, and ultrasonographic findings may underestimate early biliary sludge or microstones.<sup>26</sup>

#### **Management and surgical outcomes**

Laparoscopic cholecystectomy remains the gold standard for symptomatic gallstones, and our results confirm its safety and efficacy in SCD patients when performed under optimal conditions. Early pediatric and surgical series have emphasized that elective cholecystectomy reduces emergency morbidity in this population.<sup>2</sup> In this series, 42.3% of gallstone-positive patients underwent laparoscopic cholecystectomy, with a conversion rate of 9.1% and zero perioperative mortality.

Comparable outcomes have been documented by Muroni et al, who reported 2% conversion and no mortality in a prospective cohort of adult SCD patients undergoing elective laparoscopic cholecystectomy.<sup>20</sup> Similarly, the National Preoperative Transfusion Study (Haberkern et al) demonstrated low morbidity when patients were adequately transfused preoperatively.<sup>18</sup> The absence of mortality in our study can be attributed to meticulous perioperative optimization including hydration, oxygenation, avoidance of hypothermia, and individualized transfusion regimens consistent with recommendations by Howard et al in the TAPS trial.<sup>19</sup> In our cohort, ERCP was required in 26.9% of cases for choledocholithiasis and was successfully performed prior to or following cholecystectomy. The use of combined endoscopic and surgical approaches aligns with international best practices, as supported by Aranda-Narváez et al and Ebert & Nagar.<sup>7,16</sup> CBD exploration (11.5%) was reserved for patients with multiple ductal stones or failed ERCP, and conservative management (19.2%) was applied in medically unfit or unwilling cases. These results collectively demonstrate that, with a multidisciplinary approach, laparoscopic cholecystectomy in SCD patients is not only feasible but also confers outcomes comparable to those in non-SCD populations. Our findings reinforce the growing consensus that elective laparoscopic cholecystectomy should be preferred over emergency surgery, which carries higher morbidity due to inadequate preoperative optimization.

#### **Prophylactic cholecystectomy: revisiting the controversy**

Whether to perform cholecystectomy in asymptomatic SCD patients remains debated. Al-Salem et al and Muroni et al advocate prophylactic cholecystectomy to prevent emergent complications, while Aliyu et al and Ware et al recommend a conservative approach based on symptomatology.<sup>8,20-22</sup> Singhal et al demonstrated that up to 70% of asymptomatic SCD patients developed biliary symptoms or complications within five years, lending further support to a proactive, prophylactic cholecystectomy strategy.<sup>28</sup> Our findings showing that more than half of the gallstone-positive patients eventually developed complications support a selective prophylactic strategy, particularly in high-risk patients (recurrent pain, rising bilirubin, or poor access to tertiary care).

The present study has certain limitations that warrant consideration. First, as a single-center investigation, the findings may not be generalizable to other populations or geographic regions. Second, the sample size, although adequate to estimate prevalence, limits the statistical power for subgroup analyses and may restrict the robustness of broader inferences. Third, the relatively short duration of follow-up precluded the assessment of long-term outcomes such as recurrence of symptoms, late complications, or quality of life measures. Finally, genetic stratification was not performed; therefore, the potential influence of different HbS haplotypes or other genetic modifiers on disease presentation and outcomes could not be evaluated.

#### **CONCLUSION**

This prospective study demonstrates that cholelithiasis is a common and clinically significant hepatobiliary complication of sickle cell disease in central India, affecting nearly one-third of adult patients. The predominance of mixed and pigment stones confirms the central role of hemolysis in gallstone pathogenesis, while the strong correlation between low hemoglobin and elevated bilirubin highlights their predictive value for biliary disease. Importantly, our findings establish that laparoscopic cholecystectomy, when performed with meticulous perioperative optimization, is a safe and effective intervention with minimal morbidity in this high-risk population. By providing region-specific epidemiological and surgical outcome data, this study bridges a critical gap in Indian literature and strengthens the global understanding of gallstone disease in SCD. It underscores the importance of early ultrasonographic screening, timely elective surgery, and the need for multicentric trials to refine evidence-based guidelines for prophylactic cholecystectomy in resource-limited settings.

### Recommendations

Our data support the use of routine ultrasound screening for adult patients with SCD even when asymptomatic. Identification early in the disease process permits pre-surgical counseling and surgical planning. Elective laparoscopic cholecystectomy, being safely executed in optimized perioperative conditions, is protective against the high morbidities of emergency surgery.

Since recurrent vaso-occlusive pain episodes often mimic biliary colic, careful differential diagnosis and early imaging are crucial, as highlighted by Ballas et al in his discussion of overlapping pain syndromes in SCD.<sup>29</sup>

Future studies must emphasize large multicenter studies with follow-up for many years in Indian patients to establish evidence-based guidelines for prophylactic cholecystectomy. Further studies using genetic and biochemical markers of hemolysis may identify patients at highest risk of developing gallstones.

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*Ethical approval: The study was approved by the Institutional Ethics Committee of Government Medical College and Hospital, Nagpur, India*

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