

Prophylactic Laparoscopic Cholecystectomy in Adult Sickle Cell Disease Patients with Cholelithiasis: A Prospective Cohort Study**Rashmita Panigrahi¹, Samarendra Satpathy², Mukti Prasad Mishra³, Swagat Satpathy⁴, Rajat Kumar Dash⁵**¹Assistant Professor, Department of Transfusion Medicine, MKCG, Berhampur²Assistant Professor, Department of General Surgery, VIMSAR, Burla³Assistant Professor, Department of General Surgery, JKMCH, Jajpur⁴Assistant Professor, Department of General Surgery, JKMCH, Jajpur⁵Junior Resident, Department of General Surgery, VIMSAR, Burla

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Conflict of interest: Nil

Abstract

Introduction: The value of prophylactic laparoscopic cholecystectomy for asymptomatic gallstones remains a point of debate, particularly in high-risk populations like patients with chronic haemolytic conditions. Sickle cell disease (SCD) is frequently associated with gallstone formation, and subsequent complications can significantly increase patient morbidity. This study aimed to evaluate the effectiveness of prophylactic cholecystectomy in SCD patients presenting with asymptomatic gallbladder stones.

Methods: We retrospectively analysed 50 SCD patients who underwent laparoscopic cholecystectomy at VIMSAR Burla between January 2021 and June 2024. Twenty-six patients with asymptomatic cholelithiasis were prospectively enrolled and underwent prophylactic cholecystectomy with intraoperative cholangiography. A comparison group of 24 patients who underwent cholecystectomy for symptomatic cholelithiasis was studied retrospectively. All patients received standardized perioperative care, including intravenous hydration, prophylactic antibiotics, oxygen therapy, intravenous analgesics, and subcutaneous low-molecular-weight heparin. We compared postoperative mortality, morbidity, and length of hospital stay between the two groups.

Results: No postoperative deaths or bile duct injuries occurred in either group. The asymptomatic group experienced 3 postoperative complications (11.53%), while the symptomatic group experienced 7 (29.16%).

Discussion: Considering SCD related complications, acute chest syndrome occurred in 1 patient (3.8%) in the asymptomatic cholelithiasis group and in 2 patients (8.33%) in the symptomatic group. Vaso-occlusive crisis was observed in 1 patient (3.8%) with asymptomatic cholelithiasis and in 2 patients (8.33%) in the symptomatic group. The mean hospital stay was 5.8 days for the prophylactic cholecystectomy group compared to 7.96 days for the symptomatic group.

Conclusions: Laparoscopic prophylactic cholecystectomy in asymptomatic SCD patients was associated with a lower incidence of postoperative SCD-related complications. When combined with appropriate perioperative management, this intervention appears safe and may prevent emergency operations for acute complications such as cholecystitis, choledocholithiasis, and cholangitis. Prophylactic cholecystectomy in SCD patients also reduces the duration of hospital stays.

Keywords: Cholecystectomy, SCD (Sickle Cell Disease), CBD (Common Bile Duct), ERCP (Endoscopic Retrograde Cholangiopancreatography).

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Introduction

Asymptomatic cholelithiasis is typically considered a benign condition, with only 6-20% of patients developing symptoms over a 4-20 year follow-up period, and less than 5% experiencing complications [1]. Consequently, a 1993 NIH Consensus Conference Report advised against prophylactic cholecystectomy for individuals with silent gallstones [2]. However, this recommendation may not be appropriate for high-

risk subgroups, including those with sickle cell disease, diabetes mellitus, asymptomatic cholelithiasis with common bile duct stones, suspected malignancy, or porcelain gallbladder [1,3,4]. Prophylactic cholecystectomy is often considered for SCD patients with asymptomatic cholelithiasis for several reasons. First, vaso-occlusive crises and biliary complications can present with similar symptoms (fever, abdominal

pain, leucocytosis, and jaundice), making accurate diagnosis and management challenging. Second, the natural history of cholelithiasis differs significantly in patients with chronic haemolytic anaemia compared to the general population, where cholelithiasis affects approximately 10% of adults, increasing with age from 10-15% in men and 20-40% in women after age 60 [1]. In contrast, cholelithiasis is observed in up to 70% of adults with SCD over 30 years old [5,6]. The incidence of pigmented stones is also higher in chronic haemolytic diseases, including in paediatrics patients, increasing with age: 14% for those under 10 years, 22% for those between 10 and 14 years, 36% for those between 15 and 18 years, and 50% for patients over 22 years [7-9]. Third, while only 2-5% of the general population develops biliary complications over a 5-20 year follow-up, this risk is significantly elevated in SCD patients, with approximately 50% developing complications within 3-5 years of diagnosis [1]. Emergency surgery in this group carries a higher risk of morbidity and mortality [10-13]. This study aims to demonstrate that laparoscopic prophylactic cholecystectomy is associated with lower morbidity compared to cholecystectomy performed for symptomatic lithiasis.

Methodology

The study was conducted at the Department of General Surgery VIMSAR Burla for managing patients with major sickle cell disease (SCD). Beginning in January 2021, a prospective evaluation was initiated, in collaboration with Department of Transfusion Medicine and anaesthesiologists, to determine the efficacy of prophylactic elective laparoscopic cholecystectomy for adult SCD patients with asymptomatic cholelithiasis. The prospective management of these patients spanned 4 years, from 2021 to 2024. Up to June 2024, all 26 adult SCD patients diagnosed with asymptomatic cholelithiasis via ultrasound underwent prophylactic cholecystectomy with routine intraoperative cholangiography. Concurrently, records of 24 other SCD patients who underwent elective laparoscopic cholecystectomy for symptomatic cholelithiasis were reviewed.

All patients in both groups underwent ultrasound examination to confirm gallbladder cholelithiasis without stones in the common bile duct (CBD), and no patients had preoperatively diagnosed common duct stones. Among the 26 patients with asymptomatic cholelithiasis, 21 had homozygous sickle cell haemoglobin HbSS, 2 had heterozygous sickle cell haemoglobin HbSC, 3 had sickle-beta cell disease. The patients ranged in age from 18 to 53 years, with a mean age of 26.5 years, and included 21 females. The mean preoperative haemoglobin level was 8.5 g/dL (range, 6.1-12.6).

The symptomatic patient group consisted of 19 homozygous sickle cell haemoglobin HbSS patients, 3 heterozygous sickle cell haemoglobin HbSC patients, and 2 sickle beta cell disease patients. Their mean age was 25.4 years (range, 18-46), with 18 females. The mean preoperative haemoglobin level was 8.6 g/dL (range, 6-11). All patients undergoing surgery received comprehensive perioperative management involving a multidisciplinary team of haematologists, anaesthesiologists, and surgeons. Patients were admitted to the Department of Surgery one day prior to cholecystectomy. Initially all patients with a haemoglobin level below 10 g/dL received a blood transfusion to achieve a preoperative haemoglobin level above 10 g/dL. Later on, exchange transfusion was reserved for patients with a haemoglobin level below 7 g/dL. Upon admission, all patients received intravenous hydration, continued until they could independently consume 2 L of water per day.

Intravenous antibiotic prophylaxis, using amoxicillin or penicillin, was initiated 1 hour before cholecystectomy and continued for 5 days post-operation. Additional interventions included oxygenation, incentive spirometry use, intravenous painkillers transitioned to oral administration, subcutaneous administration of low-molecular-weight heparin in preventive doses postoperatively, and early mobilization. During the same study period, two emergency patients, one with acute cholecystitis and the other with cholangitis and CBD stones, were also operated on. The latter was the only patient preoperatively diagnosed with CBD stones via ultrasound.

This patient was excluded because this study aimed to evaluate the treatment of asymptomatic gallbladder lithiasis without complications, and emergency procedures were not included. Laparoscopic cholecystectomy was performed under general anaesthesia, with a thermal cover applied at 40°C throughout the operative period. Pneumoperitoneum was established through an umbilical incision or in the left hypochondrium, followed by the insertion of a 10-mm trocar for carbon dioxide insufflation at a pressure of 12 mmHg. A standard 4-port technique was employed for laparoscopic cholecystectomy.

Cholangiography was routinely performed by injecting iodinated contrast (Hexabrix 320 mg/mL) into the biliary tract through a percutaneous catheter with a 20-F-diameter rigid tip (Applied Medical, USA), introduced into the cystic duct via a cutaneous incision in the right hypochondrium. Opacification of the CBD and contrast passage into the duodenum were confirmed using intraoperative radiology. CBD stones, if present, were removed using a Dormia basket or saline solution jets under high pressure after choledochotomy, to flush the

stones from the cystic duct. Conversion to open cholecystectomy and choledochotomy were performed only if CBD stone extraction was impossible, and a T-tube was left in place. The study compared postoperative mortality, morbidity, and length of hospital stay between the two elective surgery groups. Outcomes were correlated in both

groups, and preoperative and postoperative characteristics were compared using a chi-squared (χ^2) test. P-values less than 0.05 were considered statistically significant. This observational study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

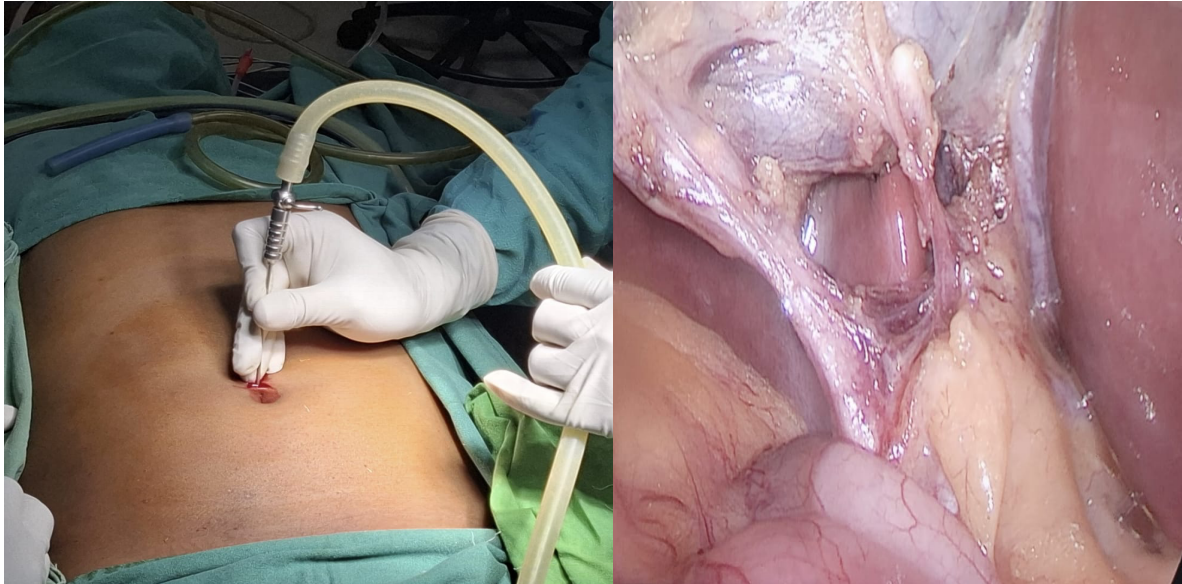


Figure 1: LAP Cholecystectomy

Result

Asymptomatic Cholelithiasis Group: Preoperative blood transfusions were administered to 6 patients (23%), with 2 patients (7.6%) undergoing exchange transfusions before surgery. Postoperatively, 2 patients (7.6%) received blood transfusions. Gallstones were found in the common bile duct (CBD) in one patient (3.8%), necessitating conversion to open cholecystectomy with choledochotomy for the removal of 4 stones. Postoperative complications occurred in 3 patients (11.5%). One patient required re-intervention via a right subcostal incision for hemoperitoneum. One case was attributed to anticoagulation therapy for a mitral valve prosthesis. The hemoperitoneum cases were attributed to high bleeding risk (cardiac valve prosthesis). Other complications included one case each of acute chest syndrome, *Klebsiella pneumoniae* infection, abdominal vaso-occlusive crisis, and postoperative jaundice (investigated with EUS, which revealed no stones, suggesting spontaneous migration). There were no bile duct injuries or deaths. The mean hospital stay was 5.8 days (range: 4-17 days).

Symptomatic Cholelithiasis Group: Two patients had a history of acute cholecystitis, and one had

acute pancreatitis, all managed medically before elective surgery. Two patients (8.33%) received preoperative blood transfusions, and 3 patients (12.5%) underwent exchange transfusions preoperatively. Postoperatively, 3 patients (12.5%) received blood transfusions. Intraoperative cholangiography revealed CBD stones in 4 cases. Two cases were managed via laparoscopic stone extraction.

The remaining 3 required conversion to open cholecystectomy with choledochotomy for stone removal. A T-tube was left in 2 cases. Postoperative complications occurred in 6 patients (25%). Medical complications included 2 cases of acute chest syndrome, 1 case of *K. pneumoniae* pneumonia with acute respiratory failure, 2 cases of abdominal vaso-occlusive crisis and 1 case of fever without a identified source. Surgical complications included one case requiring percutaneous drainage of a gallbladder fossa abscess and one case of abdominal wall hematoma. Two patients required intensive care unit monitoring. There were no bile duct injuries or deaths. The mean hospital stay was 7.9 days (range: 4-18 days).

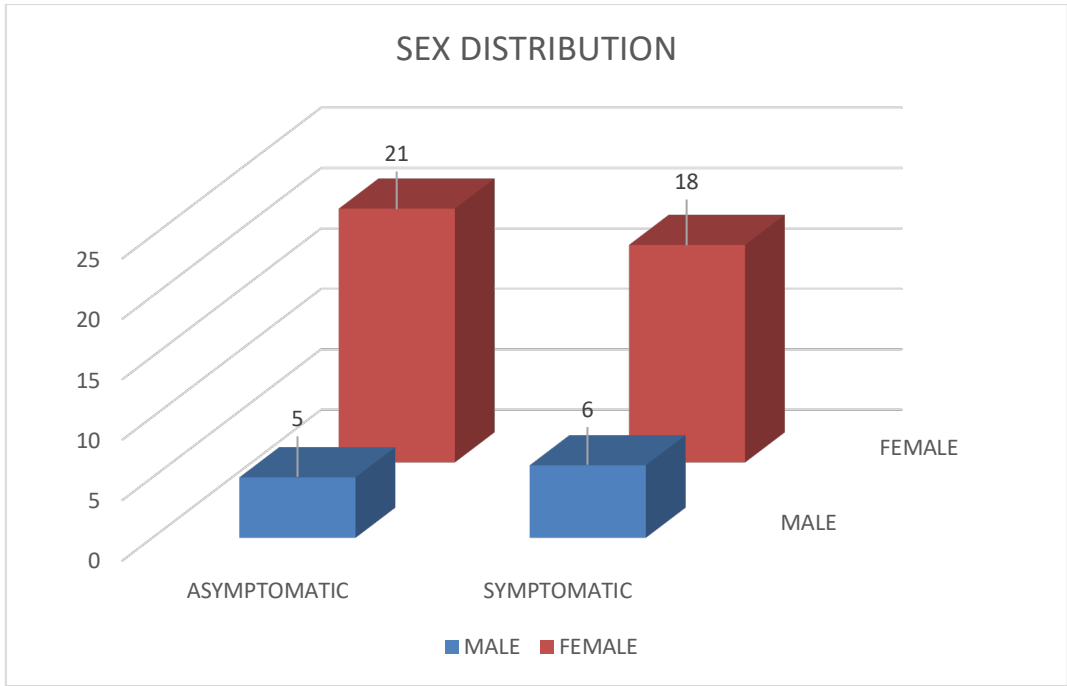


Figure 2: For Sex Distribution

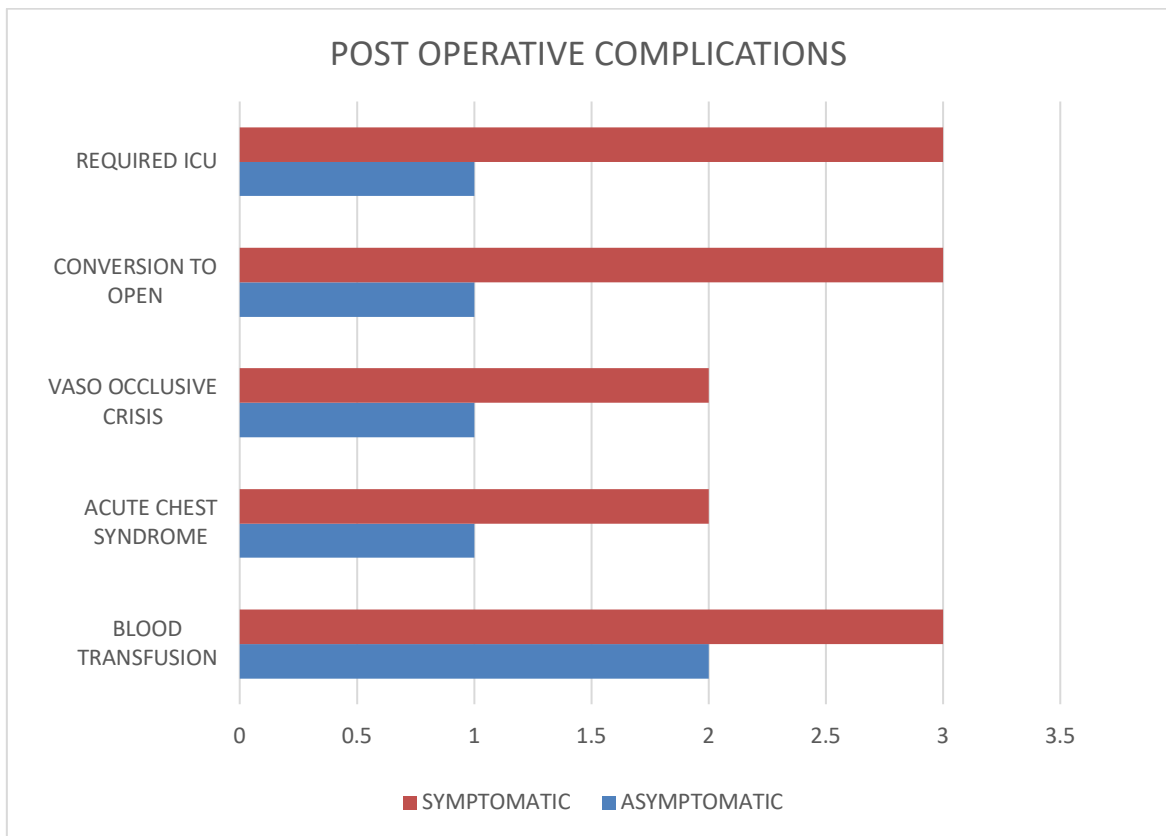


Figure 3: Post-Operative Complications

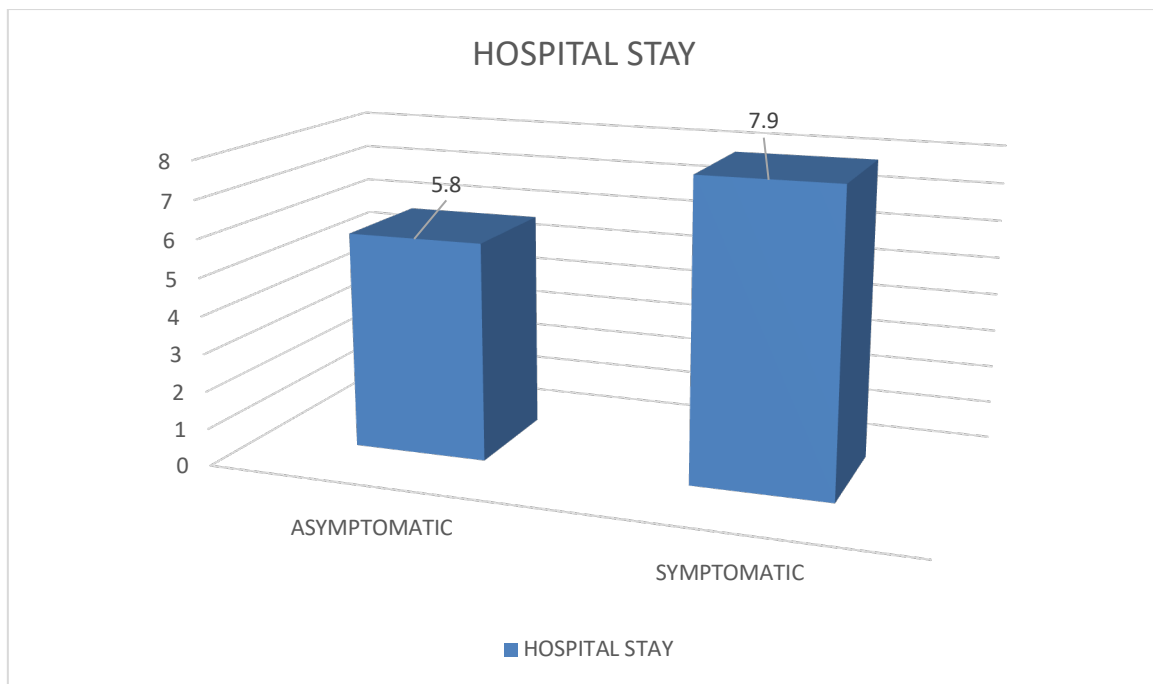


Figure 4: Hospital Stay

Discussion

Laparoscopic cholecystectomy for cholelithiasis in adult patients with sickle cell disease (SCD) is well-documented in the literature, primarily for symptomatic cases. While some studies include a small number of asymptomatic patients (ranging from 1 to 5) [17, 18], these cases are rarely analysed separately. In contrast, several authors have advocated for prophylactic laparoscopic cholecystectomy in asymptomatic children with SCD and cholelithiasis [5, 23]. Notably, in France, the High Authority of Health has recommended cholecystectomy for children with SCD and gallstones, regardless of symptoms, since 2005. However, a lack of guidelines exists for managing asymptomatic cholelithiasis in adults with SCD. To our knowledge, our study represents the first prospective analysis of a large cohort of adult SCD patients undergoing laparoscopic cholecystectomy specifically for asymptomatic cholelithiasis. The natural history of cholelithiasis in SCD differs from the general population, with earlier onset and a higher likelihood (70%) of asymptomatic gallstones becoming symptomatic, leading to delayed surgical intervention [12, 13]. Our hypothesis was that prophylactic cholecystectomy could reduce SCD-related complications seen in patients undergoing elective or emergency surgery for symptomatic gallstone disease. Importantly, we observed no postoperative deaths in either group, likely due to our perioperative management strategies. This contrasts with some reports in the literature regarding symptomatic and complicated cholelithiasis, which cite mortality rates of 1-6% [10, 18, 22]. Emergency cholecystectomy in SCD

patients is known to be associated with increased complications and postoperative risk [24, 25]. In our study, we selectively employed intraoperative cholangiography, performing it routinely for SCD patients while utilizing a validated multifactorial scoring system [26, 27] to guide its use in non-SCD patients. This strategy was primarily implemented to differentiate symptoms of residual choledocholithiasis from sickle cell crises in the early postoperative period [28], thereby avoiding unnecessary bile duct explorations in emergency situations involving post-cholecystectomy jaundice. This approach aligns with findings by Nickkholgh et al. [29], which support routine intraoperative cholangiography during laparoscopic cholecystectomy for accurate identification of biliary tract stones.

Cholangiography revealed a significantly higher rate (16%, $P = 0.02$) of associated choledocholithiasis in the symptomatic group compared to the general population (5%) [30]. This indicates that symptomatic SCD patients with gallstones have a threefold higher risk of concurrent choledocholithiasis. Other studies suggest even higher incidences of CBD stones in SCD patients, reaching up to 30% [31, 32], suggesting a unique presentation of gallstone disease. We frequently observed microlithiasis with pigmented gallstones, potentially explaining the increased migration of stones into the common bile duct. In contrast, the choledocholithiasis rate in asymptomatic patients was only 2%, despite a similar mean age in both groups, suggesting that age, by itself, is not necessarily predictive [26, 27]. For managing associated choledocholithiasis, we

opted for open surgical exploration if laparoscopic removal was not feasible, rather than postoperative ERCP. This decision was based on our preference to avoid potential ERCP-related complications such as pancreatitis, bleeding, cholecystitis, perforation, and stenosis. Some studies have demonstrated that laparoscopic CBD exploration has a lower morbidity and mortality compared to a two-stage approach with ERCP and sphincterotomy. An advantage of converting to an open procedure, rather than performing ERCP, is avoiding a second anaesthetic induction for subsequent CBD stone extraction via ERCP, which poses risks for SCD patients. Laparoscopic cholecystectomy offers benefits over open surgery, including improved postoperative pulmonary function [34], reduced pain [35], shorter hospital stays, and faster recovery. The extended postoperative stays in both groups can be attributed to our protocol of intravenous hydration, oxygenation, and 5-day prophylactic antibiotics, along with heightened caution for SCD patients requiring close monitoring for early SCD complications. Notably, all cases of acute chest syndrome and vaso-occlusive crisis occurred during the first postoperative week. French guidelines recommend penicillin prophylaxis for SCD children undergoing surgery. While prophylactic penicillin is accepted to reduce pneumococcal infection risk in SCD patients, the optimal duration remains undefined [36, 37]. Medical complications linked to SCD were more frequent in symptomatic patients (Table 2), with 2 acute chest syndrome cases compared to one in the asymptomatic group. Similarly, sickle cell crisis occurred once in asymptomatic patients versus two times in the symptomatic group. The groups were similar in age (26.5 vs 25.4 years), sex distribution (5M/21F vs 6M/18F), and preoperative haemoglobin levels (8.5 vs 8.6 g/dL). All patients underwent elective procedures with perioperative management. Although mean Hb levels were similar (8.5 vs 8.6 g/dL), asymptomatic patients received more preoperative or exchange transfusions (8/26 vs 5/24), reflecting greater caution due to the elective nature of their surgery, potentially explaining their lower morbidity. The need for preoperative transfusions in SCD patients before cholecystectomy is debated. Aziz et al. demonstrated safe laparoscopic cholecystectomy without routine transfusions [38]. However, a 2013 Lancet study by Howard et al. indicated that preoperative transfusions in homozygous SCD patients undergoing low- to medium-risk surgery significantly reduced postoperative complications, particularly acute chest syndrome [39]. Our practice involves transfusing or performing exchange transfusions for patients with haemoglobin levels below 7 g/dL. The SCD-related morbidity rate was 4% in asymptomatic patients, lower than reported rates for symptomatic patients

[22,39,40], in which SCD-related morbidity was 14%. The higher complication rate in symptomatic patients may reflect longer operative times. Each group had two surgical complications, without biliary injuries, but those in the asymptomatic group were less severe, including two laparotomies for haemostasis, without subsequent chest syndrome or vaso-occlusive crisis.

Conclusions

This series of 50 elective cholecystectomies included 26 asymptomatic adults with SCD and cholelithiasis, representing, to our knowledge, the largest such group studied post-cholecystectomy. Our results indicate that prophylactic cholecystectomy for asymptomatic lithiasis is safe and associated with fewer postoperative medical complications.

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