Emerging Medical Science (EMS)
Available at: *https://emspub.com*

Original Article

OPEN ACCESS

Perioperative Events of Laparoscopic Cholecystectomy in Patients with Hemoglobinopathies

Jyotiranjan Mohapatra *[1], Bhagyalaxmi Das [2], Snehasis Pradhan [3]

[1]Assistant Professor, Department of General Surgery, Shri Jagannath Medical College and Hospital, Puri, Odisha, India.
[2]Lecturer in Zoology, Maharishi College of Natural Law, Bhubaneswar, Odisha, India.
[3]Associate Professor, Department of Surgical Oncology, IMS & SUM Hospital, Bhubaneswar, Odisha, India.

*Corresponding Author: Dr. Jyotiranjan Mohapatra; *drjrm.mkcg@gmail.com*

Received: 09 April 2025; **Revised:** 15 May 2025; **Accepted:** 19 May 2025; **Published:** 23 May 2025

Abstract

Background: Hemoglobinopathies represent a prevalent category of inherited genetic disorders characterized by disruptions in the biosynthesis of one or more globin polypeptide chains constituting the hemoglobin molecule. While laparoscopic cholecystectomy is the established surgical intervention for symptomatic cholelithiasis in individuals with normal hemoglobin profiles, the safety and feasibility of this procedure in the context of underlying hemoglobinopathies remains a subject of ongoing investigation and clinical uncertainty. ***Aims:*** To assess the safety of laparoscopic cholecystectomy in patients with hemoglobinopathies and to characterize the spectrum of perioperative events encountered during the preoperative, intraoperative, and postoperative periods. ***Methods:*** This retrospective comparative study conducted over a period of 5 years, involved 31 hemoglobinopathic patients and 75 patients with normal hemoglobin variant. All underwent laparoscopic cholecystectomy and comparison done regarding perioperative events. ***Results:*** The overall complication rate was 56.5% in hemoglobinopathic patients and 21.6% in the other group and the difference was statistically significant (P- value <0.001). Vaso-occlusive crisis occurred in 2 patients (%), respiratory complications (atelectasis and bronchitis) in (9.7%), acute chest syndrome in (4.8%) and hemolysis in (4.8%). ***Conclusions:*** Laparoscopic cholecystectomy can be considered a safe surgical approach in well-prepared patients with hemoglobinopathies. However, this patient population exhibits a significantly elevated risk of disease-specific complications, notably acute chest syndrome, hemolysis, and vaso-occlusive crises. These findings underscore the necessity for specialized and multidisciplinary pre-, intra-, and postoperative management, involving the surgeon, physician, and anesthetist, to optimize outcomes in hemoglobinopathic patients undergoing laparoscopic cholecystectomy.

Keywords: ***hemoglobinopathies, laparoscopic cholecystectomy, sickle cell disease, complications.***

Introduction

Hemoglobinopathies constitute a significant global health burden as common autosomal recessive disorders. These disorders manifest as either qualitative defects, such as HbS resulting from a valine-to-glutamine substitution at the sixth position of the β-globin chain, or quantitative defects involving the reduced production or deletion of α- or β-globin chains. These molecular aberrations lead to dysfunctional hemoglobin, resulting in chronic morbidity. Compound heterozygous conditions, like HbS-β-thalassemia, can exacerbate disease severity compared to individual hemoglobinopathic conditions [1,2]. The widespread global prevalence and increasing international mobility have heightened the importance of managing hemoglobinopathies. Advancements in transfusion and chelation therapy have significantly improved survival rates in conditions such as thalassemia. Consequently, surgical interventions may become necessary for these patients, underscoring the need for surgical and anesthesia teams to possess a comprehensive understanding of their unique physiological vulnerabilities and increased risk of perioperative complications. The incidence of cholelithiasis varies considerably across different hemoglobinopathies, ranging from 4% to 85% in sickle cell anemia, 29% in sickle cell trait, 12% in HbS-β-thalassemia, and 30% to over 80% in β-thalassemia major [3]. Globally, hemoglobinopathies affect a substantial number of individuals, with over 30 million reported cases of sickle cell disease across 163 countries and approximately 1.5% of the world's population carrying β-thalassemia traits. Recent data indicate a significant annual incidence of serious hemoglobin disorders in newborns, estimated between 300,000 and 400,000. Given the potential requirement for surgical procedures and the inherent risks associated with general anesthesia in this patient population, meticulous pre-, intra-, and postoperative management is crucial. This includes the prevention of hypoxia, maintenance of adequate hydration and normothermia, and correction of anemia [5-8]. Cholecystectomy is one of the most frequently required surgical procedures for these patients. This investigation aims to elucidate the perioperative characteristics and outcomes across a spectrum of inherited hemoglobin disorders in comparison to individuals without these conditions.

Methods

This retrospective comparative study was conducted at two tertiary care hospitals located in Puri and Cuttack. A total of 210 patients were enrolled between January 2019 and December 2024, comprising 62 patients with hemoglobinopathies and 148 patients

with normal hemoglobin. The two groups were matched for age and gender. Surgical indications included chronic calculous cholecystitis and biliary colic. Patients with acute cholecystitis, obstructive jaundice, or severe comorbidities rendering them unsuitable for general anesthesia were excluded. Hemoglobinopathies were diagnosed via hemoglobin electrophoresis. All patients underwent preoperative investigations including a complete blood count, liver function tests, bleeding profile, blood glucose levels, renal function tests, screening for hepatitis and HIV, electrocardiography, chest X-ray, and abdominal ultrasonography. Echocardiography and respiratory function tests were performed when clinically indicated. Following outpatient assessment, all patients were admitted one day prior to surgery, except for those with a hemoglobin level below 9 g/dL, who were admitted earlier for blood transfusion. Upon admission, patients received intravenous hydration (1000-1500 ml of 4% dextrose in 0.18% normal saline in the evening before surgery) and prophylactic antibiotics. All patients underwent laparoscopic cholecystectomy under general anesthesia using the standard four-port technique. Operative time was recorded from the insertion of the primary port to wound closure. Gallbladder dissection was performed using the critical view of safety technique. Drain tubes were inserted at the surgeon's discretion. Postoperatively, patients were managed in the surgical wards (with a few cases requiring intensive care unit admission), receiving intravenous fluids, antibiotics, and analgesia. Discharge occurred when patients achieved full ambulation and tolerated an oral diet. Postoperative follow-up was conducted for three weeks. Data analysis was performed using the Statistical Package for Social Sciences (SPSS) software version 23, employing the chi-square test or Fisher's exact test where appropriate. A p-value of less than 0.05 was considered statistically significant.

Results

The study cohort comprised 106 participants, with 31 individuals diagnosed with hemoglobinopathies and 75 with normal hemoglobin profiles. The overall male to female ratio was 1:3.6, and the mean age of the cohort was 30.6 years (± 8.58). Age and gender distributions were comparable between the hemoglobinopathy and control groups (**Table 1**).

Table 1: Sociodemographic characteristics, preoperative work-up, and indications for surgery in patients with hemoglobinopathies versus patients with normal hemoglobin.

Age (years)		**Hemoglobinopathic (N=31)**	**Patients with normal hemoglobin (N=75)**	**P value**
Age (years)	<30	17	32	0.275
	30-39	10	32	
	≥40	4	1	
Sex	Male	7	16	0.506
	Female	24	59	
Hepatitis	Hepatitis B	1	0	0.08
	Hepatitis C	2	0	0.007
No. of Stones (U/S)	Single	6	11	0.278
	Multiple	25	64	
Blood parameters	Hemoglobin(g/dl) (mean)	9.34	12.23	<0.001
	Preoperative Transfusion (mean)	21	1	<0.001
	Total Serum Bilirubin (mg/dl)(mean)	3.63	0.85	<0.001
Indication for Surgery	Chronic Calculous Cholecystitis	26	65	0.095
	Biliary Colic	5	9	
	Conversion Rate	1	1	0.06
	Mean Operative Time	42.73 ±8.57	38.22 ±8.57	0.523
Complain	Joint Pain	5	0	<0.001
	Chest Pain	2	2	0.027
	Acute Chest Syndrome	2	0	0.025
	Hemolysis	2	0	0.025
	Respiratory complications	3	5	0.149
	Fever	3	4	0.194
	Diffuse abdominal pain	2	4	0.335
	Bile leak	0	1	0.496
	Bleeding	0	2	0.244
	Wound infection	0	3	0.119
	Overall complications rate	9	16	<0.001
Hospital Stay (days)	Mean ± SD	2.27±79	1.31±0.55	<0.001

Among the hemoglobinopathic patients, the most prevalent subtype was Beta Thalassemia Minor (54.6%), Sickle Cell Disease (23.2%) and Sickle Cell Trait (22.2%), Preoperative screening for viral hepatitis revealed a significantly higher prevalence of Hepatitis C markers in the hemoglobinopathy group (6.5%) compared to the control group, while the prevalence of Hepatitis B markers (3.2% in the hemoglobinopathy group) did not differ significantly between the groups. Surgical indications were similar in both cohorts; however, significant differences were observed in mean hemoglobin levels, total serum bilirubin concentrations, and the requirement for preoperative blood transfusion between the hemoglobinopathy and control groups.

Intraoperative analysis indicated a significantly higher frequency of drain placement in the hemoglobinopathy group compared to the control group. Conversely, no significant

differences were found in mean operative time or the rate of conversion to open surgery.

The incidence of overall complications was significantly higher in the hemoglobinopathy group. Specifically, acute chest syndrome, joint pain, hemolysis, and chest pain occurred more frequently in patients with hemoglobinopathies. The mean duration of postoperative hospitalization was also significantly longer for the hemoglobinopathy group.

Among the 31 hemoglobinopathic patients, (56.5%) experienced postoperative complications. Acute chest syndrome (n=3) and hemolysis (n=3) were observed in patients with Sickle Cell Disease, Sickle Cell Trait, and Thalassemia trait (n=1 each for hemolysis). Chest pain (n=4), diffuse abdominal pain, and respiratory complications (atelectasis or bronchitis) were also documented within the hemoglobinopathy group.

Discussion

While laparoscopic cholecystectomy is an established surgical intervention for gallstone disease in individuals with typical hemoglobin profiles [9], its safety and feasibility in patients with hemoglobinopathies remain subjects of ongoing investigation [10,11]. The perioperative management of hemoglobinopathic patients presents distinct challenges, including a high prevalence of anemia secondary to hemolysis, immunocompromise, and susceptibility to vaso-occlusive crises. Improved medical care has led to increased survival into adulthood for these patients, consequently increasing the incidence of disease-related complications. The optimal preoperative hemoglobin threshold and the necessity of prophylactic blood transfusion to mitigate perioperative morbidity and mortality are areas of continued debate. Surgeons must also consider the patient's history of prior transfusions, which may indicate potential iron overload sequelae. A large multicenter study by Vichinsky *et al.* (n=604 sickle cell anemia patients undergoing various surgical procedures, with over one-third undergoing cholecystectomy) found no significant difference between aggressive and conservative transfusion protocols [12]. Conversely, a retrospective analysis in Bahrain (n=85 sickle cell disease patients undergoing diverse surgeries) comparing exchange transfusion, simple transfusion, and no transfusion did not demonstrate the superiority of exchange transfusion in preventing postoperative sickle cell-related complications [13], while Maigatari *et al.* reported that preoperative transfusion reduced the risk of postoperative sickle-related complications in low- and medium-risk surgical procedures [14]. Vaso-occlusive crisis, a primary cause of readmission in sickle cell anemia, is characterized by ischemic pain, predominantly affecting bones, joints, and the abdomen, resulting from microvascular sickling [15]. Management focuses on hydration, analgesia, and transfusion. In this study, vaso-occlusive crisis, manifested as bone pain, joint pain, and backache, was the most frequent postoperative complication (14.5%) in hemoglobinopathic patients, despite adequate pre- and intraoperative hydration, and was managed with intravenous fluids and analgesia within 1-2 days. Respiratory complications (atelectasis and bronchitis) were the second most common sequelae (9.7%), consistent with findings from a study by Meshikhes *et al.* in Saudi Arabia [16]. Restrictive lung disease is a common respiratory abnormality in β-thalassemia major [17], with potential contributing factors including pulmonary fibrosis and interstitial edema secondary to iron overload [18], as well as anesthetic challenges and increased infection susceptibility. Acute chest syndrome occurred in 4.8% of the hemoglobinopathic cohort, particularly in sickle cell disease patients, a rate significantly higher than in patients with normal hemoglobin. All cases were successfully managed in the intensive care unit, aligning with a French retrospective study on sickle cell disease patients undergoing cholecystectomy, which reported higher mortality after laparoscopic versus open cholecystectomy due to a greater incidence of acute chest syndrome in the laparoscopic group (8.5% vs. 1.1%) [19]. Acute chest syndrome is a significant cause of postoperative mortality in sickle cell disease, characterized by fever, dyspnea, cough, chest pain, and new pulmonary infiltrates on radiography, excluding atelectasis [20]. Postoperative hemolysis, characterized by pallor, dark urine, and a hemoglobin drop below 9 g/dL, occurred in 4.8% of hemoglobinopathic patients (one with sickle cell disease, one with sickle cell trait, and one with sickle cell β-thalassemia), all successfully treated with red blood cell transfusion. Preoperative screening in this study revealed a notable prevalence of viral hepatitis B (3.2%) and hepatitis C (6.5%) in the hemoglobinopathic group, highlighting the risk of iatrogenic viral transmission, consistent with a high rate of hepatitis C antibodies (67.3%) reported in multiply transfused thalassemic patients in an Iraqi study [21]. The mean operative time was 42.73 minutes for hemoglobinopathic patients and 38.22 minutes for those with normal hemoglobin, within the range reported in other studies [19,22,23]. Conversion to open cholecystectomy occurred in 3.2% of hemoglobinopathic patients due to limited surgical field from hepatosplenomegaly and difficulty in Calot's triangle dissection, compared to 1.4% in the normal hemoglobin group due to fibrosis. This conversion rate is similar to that reported in another study [23], although lower than some and higher than others [22]. Abdominal drains were used more frequently in hemoglobinopathic patients due to challenging dissection in the presence of hepatosplenomegaly and the difficulty in clinically differentiating early postoperative complications in this population, despite the ongoing debate regarding drain use in laparoscopic cholecystectomy [24]. The mean hospital stay was significantly longer for hemoglobinopathic patients (2.27 days) compared to those with normal hemoglobin (1.3 days), consistent with other studies showing variable lengths of stay [19,22,23] and a Sri Lankan study indicating higher perioperative complications in thalassemic patients [11]. A study comparing laparoscopic and open cholecystectomy in sickle cell disease patients reported a lower complication rate in the laparoscopic group [25].

Conclusions

Despite the relative safety of laparoscopic cholecystectomy in optimized hemoglobinopathic patients, they are at a significantly elevated risk for disease-specific complications (acute chest syndrome, hemolysis, vaso-occlusive crises), underscoring the critical need for specialized multidisciplinary perioperative care.

Declarations

Ethical Approval and Consent to participate

Not applicable as retrospective nature of study.

Consent for publication

Not applicable as retrospective nature of study.

Availability of supporting data

Upon request to the corresponding author.

Competing interests

Nil

Funding Statement

Nil

Authors contributions

All authors made substantial contributions to the reported work, including in the areas of conception, study design, execution, data collection, analysis, and interpretation. They participated in drafting, revising, and critically reviewing the article, gave final approval for the version to be published, agreed on the journal for submission, and accepted responsibility for all aspects of the work.

References

[1] Sanctis VD, Kattamis C, Canatan D, Soliman AT, Elsedfy H, Karimi M, *et al.* β-Thalassemia Distribution in the Old World: an Ancient Disease Seen from a Historical Standpoint. Mediterr J. Hematol Infect Dis. 2017; 9(1): e2017018.

[2] Hamamy HA, Al-Alawi NAS. Epidemiological profile of common haemoglobinopathies in Arab countries. J Community Genet. 2013 Apr; 4(2): 147–167.

[3] Wilson M, Forsyth P, Whiteside J. Haemoglobinopathy and sickle cell disease. Continuing education in anaesthesia Critical care and pain 2010; 10(1): 24-28.

[4] Staikou, C, Stavriolakis, E, Karmaniolou, I. A narrative review of Per-operative management of patients with thalassemia. Anesthesia 2014, 69: 494-510.

[5] Abdullah UYH, Jassim H M, Baig A A, *et al.* Gallstones in patients with inherited hemolytic diseases. International Journal of Pharmacy and Pharmacetical Sciences Volume 7, Issue 7, 2015.

[6] Adjepong KO, Otegbeye F, Adjepong YA. Perioperative management of sickle cell disease. Mediterr J Hematol Infect Dis 2018; 10(1): e2018032.

[7] Kountouris P, Lederer CW, Fanis P, Feleki X, Old J, Kleenthous M. Itha Gene: An interactive database for hemoglobin variations and epidemiology. PLoS one 2014; 9(7):e1030.

[8] Alkasab FM, Al-Alusi FA, Adnani MS, Alkafajei AM, Al-Shakerchi NH, Noori SF. The revalence of sickle cell disease in AbuAL-Khasib district of southern. Iraq J Trop Med Hyg 1981; 84(2):77-80.

[9] Ansaloni L, Pisano M, Coccolini F *et al.* 2016 WSES guidelines on acute calculous cholecystitis. World J Emerg Surg 2016, 11:25.

[10] Al-Mulhim AS, Al-Mulhim AA. Laparoscopic cholecystectomy in 427 adults with sickle cell disease: A single-center experience. Surg Endosc 2009, 23:1599-1602.

[11] Anuja P., *et al.* Place for elective cholecystectomy for patients with severe thalassaemia: a retrospective case control study. BMC Res Notes 2019; 12:245.

[12] Vichinsky EP, *et al.* A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. The Preoperative Transfusion in Sickle Cell Disease Study Group. N Engl J Med.1995.

[13] Al-Samak ZM,Al-Falaki MM,Pasha AA. Assessment of perioperative transfusion therapy and complications in sickle cell disease patients undergoing surgery. Middle East J. Anaesthesiol 2008; 19(5):983-995.

[14] Maigatari DM, Abdulrasheed I, Lawal DI, Hassan A, Augustine B, Muhammad PK. Preoperative blood transfusion in adults with sickle cell disease undergoing elective surgical procedures: A survey of practice and outcome in Zaria, Nigeria. Arch Int Surg 2017; 7: 17-21.)

[15] Yale S, Nagib N, Guthrie T. Approach to Vaso-occclusive Crisis in Adults with Sickle Cell Disease. Am Fam Physician 2000; 16 (5):1349-1356.

[16] Meshikhes AWN, Al-Abkari HA, Al-Faraj AA, Al-Dhrais SA, Al-Saif O. The Safety of laparoscopic Cholecystectomy in Sickle Cell Disease: An Update. Annals of Saudi Medicine 1998; 18:12-14.

[17] Tai DY, Wang YT, Lou J, Wang WY, Mak KH, Cheng HK. Lungs in thalassemia major patients receiving regular transfusion. European Respiratory Journal 1996; 9:1389-1394.

[18] Carnelli V, D'Angelo E, Pecchiari M, Ligorio M, D'Angelo E. Pulmonary Dysfunction in Transfusion Dependent Patients with Thalassemia Major. Am J Respir Crit Care Med2003; 168:180-184.

[19] Meshikhes AW. Comment on cholecystectomy in sickle cell disease patients: is there more acute chest syndrome after laparoscopy? A case-controlled study. International Journal of Surgery 2008; 6:422-423.

[20] Ruhl AP, Sadreameli SC, Allen JL, Bennett DP, Campbell AD, Coates TD. Identifying Clinical and Research Priorities in Sickle Cell Lung Disease. An Official American Thoracic Society Worshop Report. Ann Am Thorac Soc 2019; 16(9): e17-e32.

[21] Al-Kubaisy WA1, Al-Naib KT, Habib M. Seroprevalence of hepatitis C virus specific antibodies among Iraqi children with thalassaemia. East Mediterr Health J 2006 12(1-2):204-210.

[22] Dan D, *et al.* Laparoscopic cholecystectomy in sickle cell disease patients: Does operating time matter? Int J Srg. 2009

[23] Rachid S, Diddier LJ, Bade MA, Chaibou Sani CM, Habibou A. Laparoscopic cholecystectomy in sickle cell patients in Niger. Pan Afr Med J, 2009; 3:19.

[24] Gurusamy KS, Samraj K, Mullerat P, Davidson BR. Routine abdominal drainage for uncomplicated laparoscopic cholecystectomy. Cochrane Database Syst Rev 2007 Oct 17; (4):CD006004.

[25] Leandros E, ymionis GD, Konstadoulakis MM, Albanopoulos K, Dmitrakis K, Gomatos I, *et al.* Laparoscopc or open cholecystectomy in patients with sickle cell disease: which approach is superior? Eur J Surg. 2000; 166(11):856-861.