

Laparoscopic cholecystectomy in patients with Sickle Cell Disease

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ABSTRACT

Objective: To determine the safety and benefits of laparoscopic cholecystectomy as the standard surgical treatment for gallstones in patients with sickle cell anemia.

Methods: Thirty-six sicklers and 111 non-sickler patients from the eastern province of the Kingdom of Saudi Arabia who were admitted to Qatif Hospital between April 1994 and March 1998 for laparoscopic cholecystectomy, were prospectively compared for their clinical presentation, surgical management and long-term result.

Results: Both groups were comparable from the clinical presentation point of view as well as the operative time. The incidence of choledocholithiasis was higher among

the sicklers, which was managed successfully by endoscopic retrograde cholangiopancreatograph and endoscopic sphincterotomy. Minor postoperative complications were more common in sicklers, but were managed conservatively. There was no mortality in both groups and most of the sickle cell patients were relieved of their symptoms of gallstones.

Conclusion: Laparoscopic cholecystectomy is safe and is a beneficial surgical procedure for the management of cholelithiasis in patients with sickle cell anemia and not associated with increased major morbidity or mortality.

Keywords: Sickle cell anemia, cholecystectomy, laparoscopic.

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Pigment gallstones is an important problem for patients with sickle hemoglobinopathies. Children under the age of 10 years had a 14% prevalence of gallstones, whereas people aged 10-20 years old had a 36% prevalence.¹⁻³ In one series, the incidence was 60% in adults with whom the status of the gallbladder was known⁴ and there is no doubt that gallstones become more prevalent with increasing age.⁵ Despite this high prevalence, the management of this condition in sickle cell disease (SCD) patients is still controversial for the following reasons: 1. The natural history of the gallstones in an asymptomatic patient is unknown so the indications for surgery in the era of minimally invasive surgery is not yet clear. 2. The clinical presentation of gallstones in SCD

patients may be indistinguishable from other causes of right upper quadrant pain and abnormal liver chemistries.^{6,7} Finally, because of the undoubtedly high surgical risk, this risk should be considered in determining the benefit of surgery. Only few recent series have reported the safety of laparoscopic cholecystectomy in SCD patients,⁸⁻¹¹ however, no control study was carried out to compare the surgical outcome of this group of patients with non-sickler patients undergoing laparoscopic cholecystectomy. The aim of this study is to compare the clinical presentation of gallstones, their surgical management and the postoperative morbidity and mortality between SCD patients and normal population in the era of minimally invasive surgery and to find out

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whether cholecystectomy resulted in the relief of their symptoms.

Methods. A total of 147 patients who underwent laparoscopic cholecystectomy between April 1994-March 1998 were included in this study. The preoperative, perioperative and postoperative data was prospectively recorded. There were 111 non-sickler patients (control group) and 36 patients with sickle cell anemia documented by the presence of hemoglobin-S on electrophoresis (Helena Laboratories Super Z electrophoresis kit). Preoperative ultrasonography of the biliary system demonstrated numerous echogenic densities within the gallbladder in all patients, except one who had oral cholecystogram which, showed a non functioning gallbladder. Sickler cell disease patients were admitted 2 days before the planned surgery and baseline investigations were requested. Patients with hemoglobin of less than 10 g/dl were transfused with packed red blood cells to raise their hemoglobin count to at least 10 g/dl. Breathing exercise training was started the day before surgery for all sickler patients using incentive spirometry and they were adequately hydrated the night before the surgery. Deep venous thrombosis prophylaxis in the form of low dose subcutaneous heparin as well as prophylactic antibiotics was given to all patients. Sickler cell disease patients were preoxygenated with 100% oxygen for 5 minutes before the endotracheal intubations. All patients were nursed in general surgical ward with special attentions to the sicklers to be well hydrated and pain relieved with adequate analgesia. Patients were discharged home once they had fully recovered and without any postoperative complications. Patients were followed up in the outpatient clinic for recurrence of the abdominal pain, long term complications of the laparoscopic cholecystectomy as well as the chronic symptoms of the SCD. The first visit of the patient was after one week for sutures removal then monthly for the first postoperative year then every 3 months for 5 years. Statistical testing for differences between the 2 groups was by X² analysis, P<0.05 was considered significant.

Results. Comparing both groups, out of 36 patients with sickle cell disease, there are 22 female (61%), while in the control group 92 were female (86%). The sickler patients were younger, their average age was 25 years old (range 14-52) compared to 36.75 years (range 18-80) for the non-sickler group (p<0.0001). All the patients in both groups were symptomatic. Eleven non-sickler (10%) and 4 sickler patients (11%) were admitted with acute cholecystitis. The signs and symptoms of both groups are shown in Table 1. The mean hemoglobin for sicklers and non-sicklers was 8.9 (range 6.3-11.7

Table 1 - Signs and symptoms of gallstones in all patients.

Signs & Symptoms	SCD group		Non-SCD group	
	n	%	n	%
Upper abdominal pain	36	(100)	111	(100)
Nausea & Vomiting	15	(42)	60	(54)
Fatty dyspepsia	5	(14)	44	(40)
Jaundice	14	(38)	7	(8)
Upper abdominal tenderness	14	(36)	81	(73)
Acute cholecystitis	4	(11)	11	(10)

SCD=sickle cell disease

g/dl) and 12.8 (range 9.5-17.6 g/dl). Twenty-seven SCD patients with hemoglobin less than 10 g/dl received simple transfusion in the form of packed red blood cells. The blood transfusion requirement for SCD patients is shown in Table 2. In the control group, no patients require preoperative or postoperative blood transfusion. Five patients (14%) with sickle cell disease and 33 non-sicklers (30%) needed upper gastro-intestinal endoscopies for atypical clinical presentation of gallstones or suspicion of associated chronic peptic disease. Two sicklers had antral gastritis and a 3rd patient had erosive duodenitis. The remaining 2 patients were reported as normal. In the control group, 6 patients had antral gastritis and 3 had chronic duodenal ulcers. Twelve patients with sickle cell anemia (33%) and 24 patients in the control (22%) required preoperative endoscopic retrograde cholangiopancreatograph (ERCP) for suspected common bile duct (CBD) stones based on clinical

Table 2 - Preoperative blood transfusion in sickle cell anemia patients.

Amount of blood transfused	n	Range of the HB (g/dl)	Mean HB (g/dl)
No blood transfusion	9	10.2-11.6	10.6
Transfused with one unit of PRBCS	13	7.3-9.5	8.8
Transfused with 2 units of PRBCS	13	6.3-9.2	8.2
Transfused with 3 units of PRBCS	1	7.9	-

PRBCS=packed red blood cells, HB=hemoglobin

Table 3 - The indications and findings of the endoscopic retrograde cholangiopancreatography (ERCP) in sicklers and non-sicklers patients.

Indications	Findings							
	Non-SCD group				SCD group			
	CBD stones	CBD dilatation	Normal ERCP	Total	CBD stones	CBD dilatation	Normal ERCP	Total
Abnormal LFTs	1	4	4	9	2	1	1	4
Dilated CBD in the ultrasound	3	2	2	7	1	1	1	3
Abnormal LFTs with dilated CBD	5	3	-	8	3	2	-	5
Total	9	9	6	24	6	4	2	12

CBD=common bile duct, ERCP=endoscopic retrograde cholangiopancreatography, SCD=sickle cell disease, LFTs=liver function tests

suspicion of biliary tract obstruction, ultrasonic CBD dilatation (>6mm) or abnormal liver function tests. The indications and the ERCP findings for both groups are listed in Table 3. Common bile duct stones were detected in 6 sicklers (17%) and 4 patients had CBD dilatation. In the control group, CBD stones were found in 9 patients (8%) and CBD dilatation in 9 patients as well. As can be seen in Table 3, those patients who had dilated CBD in ultrasound and abnormal liver function tests (LFTs) all had CBD stones or dilatation in the ERCP. The mean operative time for SCD was 104 minutes and for the control group 103 minutes. Four cases in sickler anemia group (11%) and 7 from the control group (6%) were converted to open cholecystectomy. The reasons for conversion are shown in Table 4. Postoperatively, 9 patients (25%) with sickle cell anemia and 10 (9%) patients from the control group

developed minor complications Table 5, which were treated conservatively without permanent sequelae. One non-sickler lady operated for acute cholecystitis developed CBD stricture on a few months postoperatively, most probably due to partial occlusion of the CBD with clip applied to the cystic duct. There was no mortality in both groups. The median hospital stay for the SCD group was 3.9 (range 2-7) days and the control group 2.9 (range 1-11) days. A median follow up of 2 years (range 1-56 months) was possible in 33 patients with sickle cell anemia (83%). Eighteen patients (55%) were readmitted during this follow up period with one or more episodes of vasoocclusive crisis (average 4 episodes per patient). The pain mostly involves the limbs and the back. Only 5 patients (15%) had abdominal pain during one of the episodes of the vasoocclusive crisis, which subsided spontaneously.

Table 4 - Reasons for conversion to open cholecystectomy, in all patients.

Reasons	SCD group	Non-SCD group
Difficult anatomy	2	4
Difficult access due to adhesions	1	2
Tense GB difficult to grasp	1	1
Total	4	7

SCD=sickle cell disease, GB=sarin

Table 5 - Minor postoperative complications in all patients.

Complications	SCD group		Non-SCD group	
	n	%	n	%
Bile leakage due to slippage of the cystic duct clip	0	(0)	1	(1)
Wound infection	2	(6)	5	(4.5)
Pulmonary atelectasis	1	(3)	2	(2)
Chest infection	4	(11)	0	(0)
Minor vasoocclusive crisis	2	(6)	0	(0)
Abdominal wall CO ₂ surgical emphysema	0	(0)	1	(1)
Urinary tract infection	0	(0)	1	(1)
Total	9	(26)	10	(9)

SCD=sickle cell disease, CO₂=carbon dioxide

One sickler patient who had had laparoscopic cholecystectomy converted to open, presented 28 months later with acute biliary pancreatitis, most likely due to retained CBD stones. ECRP showed impacted CBD stones that were removed.

Discussion. In this prospective study, we found that the high prevalence of gallstones in females is less pronounced in patients with sickle cell anemia compared to the similar sex in the general population. Ware et al reported a male predominance of 2.4:1 in 27 children with sickle hemoglobinopathies who underwent cholecystectomy.¹² We also noticed that patients with sickle cell anemia developed the signs and symptoms of gallstones at a younger age. These 2 observations may be due to the difference in pathophysiology of gallstones formation in each group, as pigment stones form as a result of accelerated hemolysis, which occurs early in life in both sexes. Gallstones become symptomatic in 75% of patients with sickle cell anemia. In contrast, only 10% of normal adults with cholelithiasis become symptomatic from their gallstones.¹³ The signs and symptoms of cholelithiasis as shown in Table 1 are similar in both groups except that fatty food dyspepsia is less common in sicklers. These observations were also reported by others.^{11,12} Contradictory to what was reported in literature, most of the sickler patients could differentiate the biliary pain from vasocclusive pain and they described the biliary pain as deep intermittent crampy epigastric or right hypochondrium pain which is quite different from the severe continuous generalised pain of vasocclusive crisis.^{6,11-13} Many risks of surgery and anesthesia in patients with sickle hemoglobinopathies result from vascular occlusion by sickled erythrocytes. To minimize these risks, preoperative blood transfusion has been advocated by some authors to reduce the amount of hemoglobin S.¹²⁻¹⁷ Although they reported low morbidity and mortality with simple or exchange transfusion, others have also reported low surgical morbidity and mortality without using preoperative transfusion.¹⁸ Vichinsky et al conducted a multicenter study which showed that conservative transfusion regimen designed to increase the hemoglobin level to 10 g/dl was as effective as an aggressive regimen designed to decrease the hemoglobin S level to less than 30% in preventing perioperative complications in patients with sickle cell anemia and was associated with less transfusion related complications.¹⁹ In this series of sickle cell disease patients, the author adopted a simple transfusion policy with packed blood cells in any patient with preoperative hemoglobin of less than 10 g/dl. The low surgical morbidity and no mortality in this series may also support the benefit of simple blood transfusion. But due to the risks associated with transfusion, a prospective randomized clinical

trial is warranted to define the necessity if any, of preoperative blood transfusion for patients with SCD. Only 5 patients (14%) with sickle cell anemia required upper GI endoscopy for atypical symptoms of gallstones compared to 33 from the control group (30%). Two patients from the first group had antral gastritis and one patient had erosive duodenitis. These findings do not support the high prevalence of duodenal ulceration (30%) that was reported from Jamaica.²⁰ ERCP and endoscopic sphincterotomy (ES) were performed successfully in one 3rd of sickler patients and in one 4th from the control group. If we consider the CBD dilatation detected by endoscopic cholangiography as a sign of previous presence of stones that already passed before the performance of the ERCP which was present in 4 sicklers (11%) and 9 non sicklers (8%), and the presence of CBD stones in sicklers was 17% and non sicklers 8%, then the actual incidence of the choledocholithiasis in patients with sickle cell anemia will be around 28% and 16% in the normal population. This high prevalence of CBD stones in patients with sickle cell anemia supports the previous reports in the literature.²¹⁻²³ The increased prevalence may reflect the smaller size of bilirubinate gallstones which are more likely to move from the gallbladder into the CBD²² so CBD can be identified and safely removed from patients with sickle hemoglobinopathy by means of ERCP and ES.²³ There was no significant difference in the duration of operation between the 2 groups ($p>0.05$) which indicates that laparoscopic surgery in sickle cell anemia patients is not more difficult than in the general population. The conversion rate from laparoscopic to open cholecystectomy is higher in sicklers (11% compared to 6% in the control group). The reason for the higher conversion rate is that 3 out of 4 laparoscopic cholecystectomy in sicklers which were converted to open cholecystectomy have been carried out during the early learning curve of laparoscopic surgery and may also be due to earlier decision for conversion due to fear of complications. The postoperative hospital stay is significantly longer ($p>0.05$) in patients with sickle cell anemia. This is partly due to the fact that these patients need to stay longer for adequate postoperative hydration and observation for complications. There were 9 minor postoperative complications in patients with sickle cell anemia (25%) and 10 minor complications (9%) from the control group. Most of these were chest and wound infections. One patient from the control group had bile duct injury but none in the sicklers group had major complications. Two of the chest infections and one wound infection occurred in the converted to open group. All the minor complications were treated conservatively. Although the complication rate of the laparoscopic cholecystectomy is higher in sickle cell anemia group, it is still less than the reported morbidity associated with open

cholecystectomy that reached 37%.⁸ These complications may be reduced further by preoperative exchange blood transfusion.²⁴ The long term effect of cholecystectomy in patients with sickle cell anemia is difficult to ascertain due to the difficulty in distinguishing the biliary pain from other causes of abdominal pain. Although the follow-up period is relatively short in the series, most of the patients were relieved from their gallstone symptoms after cholecystectomy. This proves beyond doubt the benefit of laparoscopic cholecystectomy in patients with sickle cell anemia. This contradicts what Galloway et al reported that only 50% of patients obtain relief of the biliary pain after surgery.²⁵

In conclusion, laparoscopic cholecystectomy is a safe and beneficial surgical procedure for the management of cholelithiasis in patients with sickle hemoglobinopathies and it is not associated with an increase in major complications or mortality when compared to the general population. Strict adherence to the preoperative preparation protocol, careful anesthesia and surgery and meticulous postoperative management increase the best possible outcome.

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