# ASSESSMENT OF PERIOPERATIVE TRANSFUSION THERAPY AND COMPLICATIONS IN SICKLE CELL DISEASE PATIENTS UNDERGOING SURGERY

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## Abstract

*Background:* Perioperative blood transfusion is usually given to sickle cell disease patients to reduce or prevent perioperative morbidity. Assessment of such a practice was the subject of our study.

*Methods:* A retrospective one year survey of sickle cell disease patients undergoing surgery at Salmaniya Medical Complex, Bahrain was conducted. The medical records were reviewed to characterize the surgical procedure, transfusion management and perioperative complications.

*Results:* 85 sickle cell disease patients who underwent surgery were studied. Preoperatively, 21.2% had exchange transfusion (ETX), 24.7% had simple transfusions (STX) and 54.1% had no transfusion (NTX). 14.1% of all patients had postoperative complications, and 50% of those, had complications from the laparoscopic cholecystectomy group. The incidence of sickle cell crisis postoperatively was 22.2% in ETX group, 9.5% in STX group and 4.34% in the NTX group. The incidence of acute chest syndrome postoperatively was found to be 5.55% in the ETX group, 4.76% in the STX group and 4.34% in the NTX group. No intraoperative complications were recorded in all groups.

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All patients who had postoperative complications had a preoperative HBSS > 40%.

*Conclusion:* Exchange transfusion does not prevent perioperative complications of sickle cell disease patients. HBSS > 40% carries a higher risk of postoperative complications.

**Keywords:** Sickle cell disease patients, perioperative transfusion therapy, complications.

## Introduction

Sickle cell disease (SCD) is one of the most common inherited diseases in the world. It is most commonly seen in individuals whose genetic origins are in sub-Saharan Africa, southern India, and the Mediterranean. Approximately 1 in 350 African Americans are born with HBS, whereas 1 in 835 have HBSC and 1 in 1700 have HBSβ-thalassemia[1].

Pathophysiologicaly, SCD is a hemoglobin structure disorder in which glutamic acid at the sixth residence of the β chain of hemoglobin is substituted by valine, resulting in the formation of a poorly soluble hemoglobin tetramer ($\alpha 2/\beta 2$ S)[2]. Homozygote (SS) will show clinical symptoms and heterozygote (AS) or traits are usually asymptomatic.

The hallmarks of SCD are anemia and vasculopathy. The major sources of morbidity and mortality in SCD are acute painful syndromes, severe anemia, infections, acute chest syndrome and organ failure.

Surgical procedures are often required. Preoperative blood transfusions are frequently given to prevent perioperative complications. There is no consensus, however. on the best regimen for transfusion for this purpose. Blood transfusion can be life saving and can ameliorate some of the complications of SCD. Nevertheless, blood transfusions, even when correctly used, are not without complications[3].

The aim of this study was to assess the relative risks and benefits of preoperative blood transfusion regimens in patients with sickle cell disease undergoing surgery of any type in any setting.

## Patients and Methods

A retrospective one year survey of sickle cell disease patients undergoing surgery at Salmaniya Medical Complex, Bahrain was conducted. Patients were eligible for enrollment in the study if they had a diagnosis of sickle cell disease documented by the presence of hemoglobin SS on electrophoresis.

The patients were grouped into three categories, exchange transfusion (EXT), simple transfusion (STX), and no transfusion (NTX). Patients' data were collected from the medical records and reviewed preoperatively and through 30-days postoperative follow up period to characterize the surgical procedure, transfusion management and perioperative complications. The medical history, anesthetic management and recovery period were also recorded.

Each patient's anesthetic risk (ASA physial status) was determined, and extensive periopertive laboratory information was obtained.

Data on patients' characteristics, transfusion, perioperative management and complications are expressed as number and means ± SD.

## Results

By reviewing the medical records of all surgical cases during the calendar 2005, there were 85 sickle cell disease patients who underwent surgery. Diagnosis of sickle cell disease was documented by the presence of hemoglobin SS on electrophoresis. All patients received preoperative hydrations, premedicated with tranquilizers and prophylactic antibiotics and were monitored intraoperatively.

Table 1 shows the details of the patients where both sexes were involved (51 males and 34 females) with a mean age of 21 (range from 1-50) years. The surgeries that were done were laparoscopic cholecystectomy, splenectomy, ENT procedures, orthopedic surgeries like total hip replacement, and minor surgical procedures.

*Table 1*

*Details of the patients*

| Variable | | Postoperative | complications |
|---|---|---|---|
| | | Sickle cell crisis | Acute chest syndrome |
| Number | 85 | 8(9.4%) | 4(4.7%) |
| Age (year): | | | |
| Range | 1-50 | | |
| Mean ± SD | 21.3 ± 15.7 | | |
| 1-10 year | 21 | 1 (4.7%) | 2 (9.5%) |
| 11-12 year | 19 | 1 (5.2%) | 1 (5.2%) |
| 21-30 year | 17 | 3 (17.6%) | 0 (0%) |
| 31-40 year | 25 | 2 (8%) | 1 (4%) |
| 41-50 year | 3 | 1 (33.3%) | 0 (0%) |
| Sex: | | | |
| Male | 51 | 6 (11.7%) | 4 (7.8%) |
| Female | 34 | 2 (5.8%) | 0 (0%) |
| Surgery: | | | |
| Lap. Chole. | 20 | 5 (25%) | 1 (5%) |
| Ay, Ty | 17 | 1 (5.8%) | 2 (11.7%) |
| Orthopedic | 15 | 1 (6.6%) | 1 (6.6%) |
| Miscellaneous | 33 | 1 (3.0%) | 0 (0%) |
| Transfusion therapy: | | | |
| No transfusion | 46 (54.1%) | 2 (4.34%) | 2 (4.34%) |
| Simple transfusion | 21 (24.7%) | 2 (9.50%) | 1 (4.76%) |
| Exchange transfusion | 18 (21.2%) | 4 (22.2%) | 1 (5.55%) |
| Pre-transfusion HBA: | | | |
| Range (gm/dl) | 6.5 – 15.2 | | |
| Mean ± SD | 8.4 ± 4.2 | | |
| Post-transf. HBA: | | | |
| Range (gm/dl) | 9.5 – 15.8 | | |
| Mean ± SD | 12.4 ± 2.9 | | |
| Pre-transfusion HBS: | | | |
| Range (gm/dl) | 40.0 – 86.3 | | |
| Mean ± SD | 71.5 ± 13.4 | | |
| Post-transf. HBS: | | | |
| Range (gm/dl) | 37.9 – 63.7 | | |
| Mean ± SD | 46.7 ± 8.9 | | |

Data are expressed as a number.

Lap. Chole: Laparoscopic cholecystectomy.

Ay, Ty: Adenotonsillectomy.

*Fig. 1*
*The most common types of surgery and its relationship to postoperative complication*

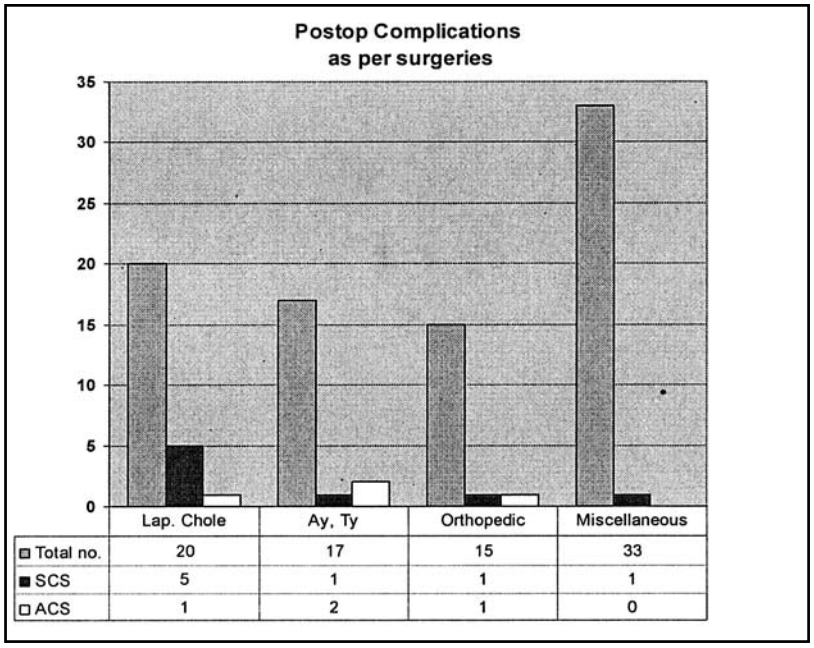



Fig. 1 shows that 23.5% of SCD patients underwent a laparoscopic cholecystectomy where 25% of them developed sickle cell crisis and 5% developed acute chest syndrome postoperatively. 20% of the SCD patients endured adenotonsillectomy operations where 5.8% of them developed sickle cell crisis and 11.7% developed acute chest syndrome.

The orthopedic operations usually done patients (17.6% of SCD patients), 6.6 of them developed sickle cell crisis and same percentage developed acute chest syndrome. The remaining 38.8% of the sickler patients underwent different types of surgery: splenectomy 4 patients, incision and drainage for different types of abscesses 7 patients, ERCP (Endoscopic retrograde cholangiopancreogram) 4 patients, gynecological procedures 5 patients, anal surgery 6 patients and other types of surgery 7 patients.

The most common minor complication was a brief fever. Only serious

or life – threatening complications were analyzed. The overall postoperative complication rate was 14.1%, 9.4% of which developed sickle cell crisis and 4.7% developed acute chest syndrome. (Table 1). No other serious complications were noticed on reviewing their medical records.

Fig. 2, shows the complications percentage in relation to age group. Fig. 3 shows complication (%) in relationship to sex.

*Fig. 2*
*Complications percentage in relation to the age group*

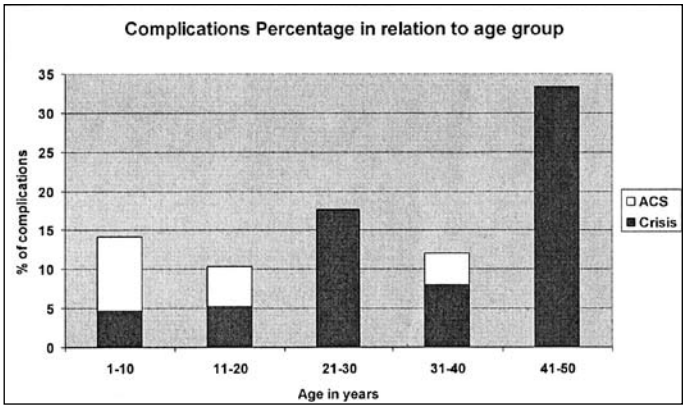
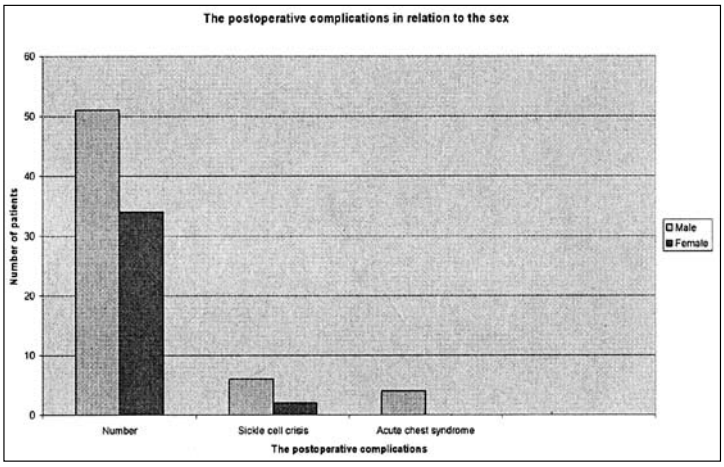



*Fig. 3*
*The complications percentage in relation to sex*



Preoperatively 54.1% of patients did not receive any blood transfusion (NTX), 24.7% managed conservatively by simple transfusion (STX) and exchange transfusion (ETX) was done for 21.2% of patients (Fig. 4). Pre-transfusion, the means HB A, and HB S were 8.4 (g/dl) and 71.5 percent respectively. Post-transfusion, the means of HBA, and HBS became 12.4 (g/dl) and 46.7 percent respectively.

*Fig. 4*

*The complications percentage in relation to transfusion therapy*

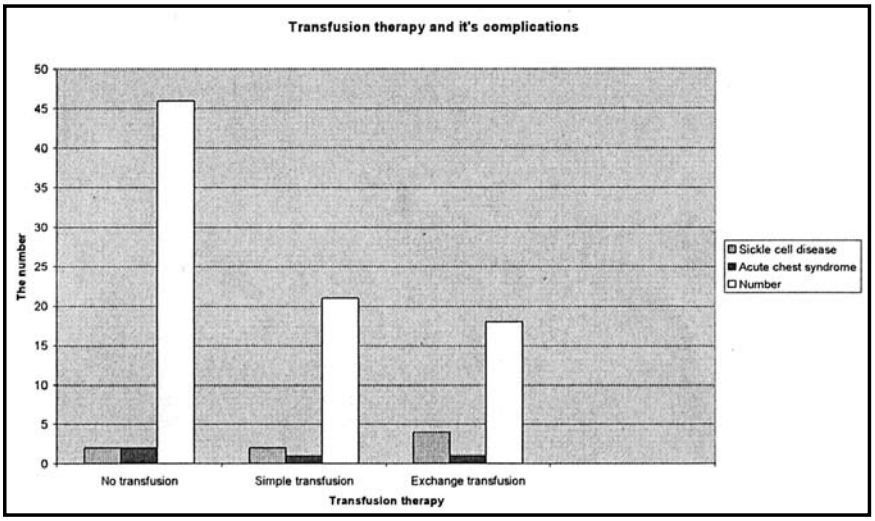



Table 2 shows details of patients who developed postoperative complications.

## Discussion

Persons with sickle cell disease (SCD) are more likely to undergo surgery than are the general population during their lifetime[4]. Because surgery exposes patients to many of the factors that are known to precipitate red blood cell sickling, persons with SCD undergoing surgery require meticulous clinical care to prevent perioperative sickle cell-related complications. Even with meticulous care, approximately 25% - 30% of patients will have postoperative complications[5].

*Table 2*

*Details of patients who developed postoperative complications*

| | | | Pre-Transfusion | | Post-Transfusion | | | |
|---|---|---|---|---|---|---|---|---|
| | No. | | Hb A1 level (g/dL) | Hb S level (%) | Hb A1 level (g/dL) | Hb S level (%) | Transfusion Status | Post-Crisis & ACS Hb |
| | 1 | Ay, Ty | 11.30 | 64.80 | *Not transfused* | *Not transfused* | NTX | 8 |
| | 2 | Lap. Chole | 10.30 | 78.80 | 12.30 | 48.10 | ETX | |
| Sickle | 3 | Lap. Chole | 9.80 | 71.00 | 14.00 | 53.80 | ETX | 10.6 |
| Cell | 4 | Lap. Chole | 9.70 | 62.70 | 11.10 | 50.80 | STX | 10.8 |
| Crisis | 5 | Lap. Chole | Not done | Not Done | 11.90 | 59.50 | STX | 10.5 |
| | 6 | Ev. Of uterus | 9.30 | 43.60 | *Not transfused* | *Not transfused* | NTX | 6.9 |
| | 7 | Lap. Chole | 11.10 | 83.70 | *13.00* | *61.80* | ETX | 10 |
| | 8 | THR | 7.60 | 76.00 | 12.90 | 42.90 | ETX | 9 |
| Acute | 1 | Ay, Ty | 9.6 | 80.70 | *Not transfused* | *Not transfused* | ETX | 11 |
| Chest | 2 | Arthroscopy | 10.0 | 40.00 | *Not transfused* | *Not transfused* | NTX | 6.7 |
| Syndrome | 3 | Ay, Ty | 11.3 | 64.80 | *Not transfused* | *Not transfused* | NTX | 10.1 |
| | 4 | Lap. Chole | 11.7 | 72.9 | 13.4 | 57.80 | STX | 12.2 |

Data are expressed as a number.

Lap. Chole: Laparoscopic cholecystectomy.

Ay, Ty: Adenotonsillectomy.

THR: Total hip replacement.

Ev: Evacuation.

In many parts of the developed world, patients with SCD often have blood transfusion before surgery, because it is believed this will lower their risk for postoperative complications. This procedure may be an exchange transfusion, which is given to lower the level of HbS, usually to around 30%, or a simple transfusion of 1 or 2 units of blood to raise the overall hemoglobin level to approximately 10 g/dl[6], improving the overall oxygen-carrying capacity.

Although preoperative blood transfusion is routine practice in many centers, the role of blood transfusion before surgery remains a topic of debate among clinicians caring for patients with SCD because it has never been fully researched[7]. The case for preoperative transfusion is based on improving oxygen delivery, because most patients with SCD are chronically anemic, although they develop compensatory mechanisms to ensure reasonable functioning at low hemoglobin levels. In addition, by lowering the level of HbS and the number of sickled red blood cells, whole blood viscosity should fall, reducing the risk of vaso-occlusion. Some reports have suggested a low perioperative complication rate among transfused patients[8].

In reality, many hospitals and sickle cell centers have policies that err on the side of caution and advocate giving a transfusion to patients before surgery. Many centers have adopted a more conservative policy following the publication of the study by the preoperative transfusion in sickle cell disease group[9]. This showed that this policy was as safe as exchange transfusion.

Some centers do not routinely transfuse patients before surgery but rely heavily on the delivery of excellent care from a wide multidisciplinary team to prevent the development of postoperative sickle cell events[10]. In a recent national survey of practice in the United Kingdom, it was shown that most patients undergoing cholecystectomy and adenoidectomy do so without preoperative blood transfusion, whereas almost all patients undergoing hip arthroplasty are prepared by an exchange transfusion. There was no difference in the rate of postoperative complications in patients who received a transfusion and those who did not, suggesting a growing trend in the United Kingdom to avoid transfusion when possible[11].

Abdominal operations, particularly cholecystectomy and splenectomy, are the most frequent type of surgery in patients with SCD. Cholecystectomy is often necessary as a result of cholelithiasis, a condition more frequent in patients with SCD than in the general population owing to chronic hemolytic anemia[12]. During the early 1990s, laparoscopic cholecystectomy superseded open cholecystectomy, and the procedure is now widely used in patients with SCD[13].

In our study, the sickle cell disease patients who underwent laparoscopic cholecystectomy were liable to develop sickle cell crisis than other operation where 25% of them developed crisis and 5% developed acute chest syndrome. 50% of laparoscopic cholecystectomy patients received exchange transfusion (ETX), and 50% received simple transfusion (STX).

In 1997 Haberkern *et al.* published the results of a study of 364 SCD patients undergoing cholecystectomy[14]. This study compared 110 patients randomized to aggressive transfusion, 120 patients randomized to conservative transfusion, 37 patients nonrandomized to nontransfusion, and 97 patients nonrandomized to transfusion. This confirmed the previous findings of Vichinsky *et al.*[9] of no improved prophylactic benefit from an aggressive transfusion compared with conservative transfusion.

By reviewing the files of sickle cell disease patients, we noticed that the exchange blood transfusion did not prevent occurrence of postoperative complications if HbS was more than 40% regardless the level of HbA. 22.2% of those patients developed sickle cell crisis and 5.5% developed acute chest syndrome. The exchange transfusion can be performed manually or automated erythrocytaphresis. When used acutely, exchange transfusion has the advantage of reducing the concentration of HbS while limiting the volume administered and minimizing hyperviscosity[15]. Although some clinicians advocate maintaining the HbS level around 30%, others argue that HbS concentration below 50% is adequate to prevent stroke.

The sickle cell disease children who underwent adenotonsillectomy were more liable to develop acute chest syndrome especially if HbS was more than 40% where 11.7% of them developed acute chest syndrome and 5.8% developed sickle cell crisis. Adenotonsillectomy is a common

surgical procedure in children with sickle cell disease owing in part to adenotonsillar hypertrophy, probably associated with early functional hyposplenism[5]. Obstructive sleep apnea secondary to enlarged adenoids is frequently observed and often precipitates the need for adenotonsillectomy[16]. Pre operative complications can be specific to SCD or nonspecific. SCD-specific complications include sickle cell crisis and acute chest syndrome (ACS). This occurs with a high frequency in the perioperative period.

Blood transfusion carry their own complications like, red cell allo immunization, development of non-ABO erythrocyte antibodies, transmission of infections like Hepatitis C, iron overload, and transfusion reaction. None of the patients in our study were found to develop any such complications.

The acute chest syndrome, one of the most frequent clinical complications, developed in 4.7% of the patients in our study. It is an acute pneumonia-like complication of SCD, is defined on the basis of the finding of a new pulmonary infiltrate involving at least one complete lung segment on chest radiograph, consistent with alveolar consolidation, but excluding atelectasis. An additional diagnostic feature includes chest pain, pyrexia greater than 38.5°C, tachypnea, wheezing, or cough[14].

All sickler patients who developed postoperative complications in our retrospective study had HbS more than 40% regardless of the level of preoperative HbA. The postoperative complications were more with the patients who received exchange transfusion where 5 patients out of 12 developed complications had received exchange transfusion, while 3 patients out of the 12 who received simple transfusion and 4 out of 12 were not transfused, developed postoperative complications.

A retrospective observational study reported by Griffin and Buchanan in 1993 examined outcomes in SCD children undergoing 66 surgical procedures without preoperative transfusion[10]. There was only one episode of acute chest syndrome (ACS) and no pain crises after 46 minor procedures. The authors concluded that any potential benefit from transfusion would therefore be low and the risks of transfusion were not justified for minor procedures.

The retrospective study of 1.079 procedures by Koshy *et al.* also examined the effects of transfusion[12]. They found that perioperative transfusion was associated with a lower rate of SCD-related complications in hemoglobin SS patients undergoing low-risk procedures, with crude rates of 4.8% with transfusion and 12.9% without transfusion. The discrepancy between this outcome and that reported by Griffins *et al.*[10] may be attributable to differing populations. In 1995 Vichinsky *et al.* published the results of a prospective randomized trial that examined target goals for transfusion for 604 surgical procedures[9]. This study compared an aggressive transfusion regimen, designed to decrease the hemoglobin S concentration to less than 30%, with a conservative regimen, designed to increase the hemoglobin concentration to 10 g/dl. Aggressive transfusion techniques included exchange transfusion or serial transfusions, whereas the conservative technique involved simple perioperative transfusion. The incidence of perioperative SCD-specific complications, approximately 15%, was similar in both groups. The incidence of transfusion-related complications was higher in the aggressive transfusion group (14%) than the conservative transfusion group (7%). This study clearly demonstrated that a conservative transfusion regimen had fewer complications than, but similar efficacy to, an aggressive regimen. As the study did not have a nontransfusion arm, however, the value of prophylactic transfusion was not examined.

We concluded from this retrospective study that blood transfusion is a critical and, in many circumstances, life-saving part of evolving strategies for the treatment of patients with SCD. Because of the complications associated with transfusions, and to a lesser extent the cost, many areas of controversy remain regarding some indications for transfusions. Simple conservative transfusions may be required for major surgeries. Exchange transfusions carry more complications and are not proved to be more effective than conservative approach. Preoperative evaluation of patients by a hematologist is recommended. Our results have to be substantiated by a prospective study conducted on a larger group of patients.

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