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Factors Associated with Morbidity and Mortality in Anesthesia During Intra-Abdominal Surgery in Sickle Cell Patients in a Low-Income Country: The Case of Centre Hospitalier Monkole

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ABSTRACT

***Objective**: This study investigated the factors associated with morbidity and mortality in sickle cell patients anesthetized for intra-abdominal surgery in Monkole.*

***Methods**: Prospective study conducted in sickle cell patients anesthetized for intra-abdominal surgery (excluding cesarean section) from 01/01/2011 to 12/31/2020 and recruited exhaustively and consecutively. The variables studied were pre, per and postoperative until discharge from hospital. Data were analyzed with SPSS 24.0 for $p < 0.05$.*

***Results**: Of 258 anesthetized sickle cell patients, 74 were for intra-abdominal surgery, including 59.5% of women with an average age of 16.4 years. The majority (95%) were transfused several time, 18% were under hydrea and none under exchange transfusion. Jaundice was present in 49%, heart murmur in 22%, 96% were ASA III. Anesthetic duration was ≥ 2 hours in 59.5%. Simple transfusion was done in 63.5% of cases. Intraoperative incidents accounted for 4% (bronchospasm, hypercapnia and allergy). Postoperative complications (anemia, parietal infection, convulsions, pancreatitis, pneumonia) accounted for 20% and 3 deaths were recorded (sepsis: 2 and pulmonary embolism: 1). Splenic surgery [ORa: 4.35 (1.51-7.20 95% CI) p=0.018]; the presence of jaundice [ORa: 3.18 (1.04-7.80 95% CI) p=0.024] and duration of anesthesia ≥ 2 hours [ORa: 9.09 (1.27-12.87 95% CI p=0.033] were the determinants of intraoperative transfusion. Heart murmur [ORa: 10.50 (2.77-13.76 95% CI) p=0.001] and hemoglobin < 6g/dl [ORa: 3.08 (2.82-17.59 95% CI) p =0.008] were associated with postoperative complications.*

***Conclusion**: Morbi-mortality seems linked to the severity of the surgery and the pathology and not to the anesthesia act.*

Keywords
Anesthesia, Sickle cell, Intraabdominal surgery, Monkole, Low-income country.

Introduction

Anesthesia in sickle cell patients is considered an anesthesia with a high risk of perioperative complications because of the multi-organ damage associated with sickle cell disease. Indeed, sickle cell disease (SCD) is an autosomal recessive inherited disease characterised by the presence of an abnormal hemoglobin called Hb S. This hemoglobin S is responsible for a deformation of the structure and a modification of the rheological properties of the red blood cell, which are responsible for the clinical manifestations of this hemoglobinopathy [1-3].

Clinical manifestations of sickle cell disease can be acute or chronic, some of which require surgical management and anesthesia, particularly for intra-abdominal surgery concerning: splenic, vesicular, gynaecological, obstetrical indications. Anesthesia in SCD patients is specific and requires the avoidance of hypoxia, acidosis, dehydration and hypothermia; factors that favor falciformation and therefore the occurrence of perioperative complications such as acute chest syndrome, painful crisis, stroke, etc. [4].

Reduction of hemoglobin S below 30% is proposed without strong evidence in reducing postoperative morbidity and mortality, and it is rarely accessible in low-income countries. For some surgical indications, exchange blood transfusion may be required to achieve this goal and the preferred transfusion standard is the use of reconstituted, single-donor, leukoreduced, phenotyped packed red cells [5-7]. Extended phenotyping is expensive for patients in low-income countries and yet unavailable.

However, sickle cell disease is widespread in the World Health Organization (WHO) African region, where prevalence rates of the βS gene range from 2% to 30% in at least 40 countries [8]. In sub-Saharan Africa, where more than 250,000 newborns are diagnosed each year, it represents a prevalence of 1 to 2% of births in some countries [9]. In the Democratic Republic of Congo (DRC), the prevalence of the heterozygous form varies between 25-30% in the general population, while that of the homozygous form varies between 0.96% and 1.4% [10,11].

Historically, surgery in sickle cell patients has been associated with relatively increased risks of perioperative mortality, vaso-occlusive crisis, acute chest syndrome, postoperative infections and congestive heart failure [1,12-16]. Judicious perioperative assessment and management are essential to mitigate these risks. Elsewhere, there is a risk of red cell alloimmunization and transfusion reactions following perioperative transfusion [1].

In a systematic review of the literature on perioperative care of children with sickle cell disease spanning the period 1965 to 2019, Schyrr et al. found that the majority of surgeries were intra-abdominal: 28.57%, cardiovascular: 26.32%, orthopaedic: 12.03% etc [17].

In a randomised multicentre study, Vichinsky et al. [18] compared the rate of perioperative complications in 551 patients between patients who received an aggressive transfusion regimen designed to reduce hemoglobin S to less than 30% (group 1) and patients who received a conservative regimen designed to increase hemoglobin to 10 g/dl (group 2). It was found that the frequency of serious complications was similar in both groups (31% in group 1 and 35% in group 2), and that acute chest syndrome was observed in 10% in both groups resulting in 2 deaths in group 1.

Non-specific complications may also be observed such as fever, infections, bleeding, thrombosis, embolism and death. There is no consensus as to whether sickle cell patients are at greater risk of developing these complications compared to the general population [14,18].

Koshy et al. conducted a retrospective review of 1079 surgical procedures covering a decade [14]. This study found that cholecystectomy, splenectomy, dilatation/curettage, caesarean section, hysterectomy, tonsillectomy, adenoidectomy, myringotomy and orthopaedic surgery were the most frequent procedures. Typical sickle cell complication rates were 0% for tonsillectomy and adenoidectomy, 2.9% for hip surgery, 3.9% for myringotomy, 7.8% for non-obstetric intra-abdominal surgery, 16.9% for caesarean section and hysterectomy, and 18.6% for dilatation/curettage.

In Niger, Daddy et al. [19] evaluated the perioperative management of sickle cell patients at the National Hospital in Niamey. Of the 14 homozygous sickle cell patients, one complication observed in the postoperative period was a non-febrile seizure.

Perioperative transfusion, particularly transfusion exchange, is commonly used for preoperative preparation to prevent possible complications that may occur perioperatively. Although the optimal hemoglobin level to be achieved is not determined, there is an advantage of increased oxygen delivery to the tissues over increased viscosity when the hemoglobin level is maintained at more or less 10g/dl [20].

In the DRC, in an observational, cross-sectional study conducted at the Centre Hospitalier Monkole from January 1st, 2011 to August 31st, 2015, Mbombo et al. [21] observed 79 sickle cell patients who needed to undergo a surgical procedure. They found that the indication was mostly for intra-abdominal surgery (≥23%), after superficial surgery. Preoperative lowering of hemoglobin S (<40%) would decrease the incidence of these complications by reducing the risk of hemoglobin S polymerisation [22]. However, neither hemoglobin S measurement nor transfusion exchange are easily performed in the Democratic Republic of Congo, but sickle cell patients are still anesthetised in this country without enough knowledge or possible complications. Moreover, no study has investigated the factors associated with perioperative complications during anesthesia for intra-abdominal surgery in our setting where resources are limited for optimal management of these patients. Thus, this study was conducted to determine

the factors associated with morbidity and mortality in anesthesia for sickle cell patients undergoing intra-abdominal surgery.

Methods

Type, Setting and Period of the Study

This is a prospective analytical study conducted among sickle cell patients who underwent anesthesia for intra-abdominal surgery during the period from January 1st, 2011 to December 31st, 2020, i.e. over ten years. It was conducted at the Centre Hospitalier Monkole (CHM) which is a second level hospital located in the urban-rural municipality of Mont Ngafula where it acts as the General Referral Hospital for the health zone of Mont Ngafula I. The CHM organises all medical and medico-technical services and is a reference centre for the management of sickle cell disease.

Study Population and Sampling

The studied population consisted of all sickle cell patients who underwent anesthesia for intra-abdominal surgery during the study period. Patients were recruited exhaustively and consecutively.

The sample size n was calculated by the formula: 1.962 x (P)(1-P)/d2. 1.96= Z-value for the 95% confidence limits, P estimated prevalence, d ½ of the desired confidence interval (0.025 for +/-5%) n = 85 patients.

Included in this study were all patients with sickle cell disease confirmed by hemoglobin electrophoresis who underwent anesthesia for intra-abdominal surgery. Patients anesthetised for caesarean section or for selective splenic embolization were excluded.

Data Collection

We designed a database in electronic form in an Excel file. Patient data were recorded regularly from the anesthesia consultation, through the intraoperative period, to discharge from hospital.

Conduct of anesthesia in sickle cell patients at the CHM

There is a consultation between the surgeon, the anesthetist and the sickle cell referent. The surgical indication is often suggested by the sickle cell referent and confirmed by the surgeon. The anesthetic consultation is compulsory and the patient is operated on as far as possible away from sickle cell crises and when in "steady state". The compulsory pre-operative examinations are the haemogram and the blood grouping. Other investigations are carried out on a case by case basis and as far as possible because of financial difficulties. Pre-operative transfusion exchange was not performed whatever the type of surgery, but only the simple transfusion aiming at an Hb level between 7 and 9g/dl. For all major surgeries, particularly intra-abdominal, a reservation of phenotyped blood products was made as far as possible with Hb AA blood. Hb S was not measured preoperatively and transfusion exchange was not performed to reduce it to less than 30%.

The Study Variables Included:

- **Socio-demographic variables:** Age calculate on the latest birthday and grouped into three: one to 5 years, 6 to 17 years and 18 years and over; gender; residence in relation to the health zone (that covered by the CHM and not).
- **Clinical variables:** History of transfusion, surgery and anesthesia, hydroxyurea intake, indication for surgery (grouped into three: splenic pathology, vesicular pathology and other), degree of emergency, alcohol intoxication, cardiac auscultation, pulmonary auscultation, presence of fever, presence of jaundice, Mallampati and Cormack scores, ASA class (American Society of Anesthesiologists).
- **Paraclinical variables:** Hemoglobin (Hb) level, considering a level below 6g/dl as severe anemia, platelet count, white blood cell count, activated partial thromboplastin time, prothrombin level, creatinine level, transaminases, cardiac ultrasound performed.
- **Intraoperative variables:** Surgical procedure (grouped into three: splenectomy, cholecystectomy and others), use of premedication, technique and anesthetics, duration of procedures, qualifications of providers, intraoperative complications and transfusion as well as time of surgery (daytime: 8:00 am to 5:00 pm and nighttime: 5:00 pm to 8:00 am and public holidays).
- **Postoperative variables:** Postoperative complications, postoperative analgesia, patient outcomes and causes of death. Complications are considered to be any adverse event that may or may not be life-threatening and/or functional.

Statistical Analysis

Data were entered using Excel 2013, double-checked, coded and exported to SPSS 24.0 for analysis. Chi-square or Fisher's exact test was used to compare proportions. Logistic regression was used to search for associated factors. The strength of association between a factor and an adverse event was measured by calculating the Odd ratios and their 95% confidence intervals. The p-value was set at less than 5%.

Ethical and Regulatory Aspects

The protocol was submitted to and approved by the Ethics Committee of the School of Public Health of the University of Kinshasa under the number ESP/CE/150B/2021. Informed consent was obtained, The Monkole hospital management had given its agreement. We have no conflict of interest in this work.

Results

During this period, a total of 8,643 patients were operated on at the CHM, 258 of whom were sickle cell patients, i.e. 2.9%. One hundred, thirty-five sickle cell patients underwent intra-abdominal surgery. Of these 135 patients, 61 were excluded because they benefited from caesarean section or splenic arterioembolization. Thus, our study retained 74 patients.

Socio-Demographic Characteristics of Patients

Table 1 presents the socio-demographic characteristics of the patients.

Of the 74 patients selected, there were 44 women (59.5%) and 30 men (40.5%), giving a sex ratio of 0.7 (M/F). The mean age of the

patients was 16.4 years (with a standard deviation of 11.1) and the extremes were 4 and 60 years. The majority of patients were between 6 and 17 years of age (55.4%). In 75.7% of cases, the patients came from the health zone not covered by the CHM and 24.3% from the zone covered by the CHM.

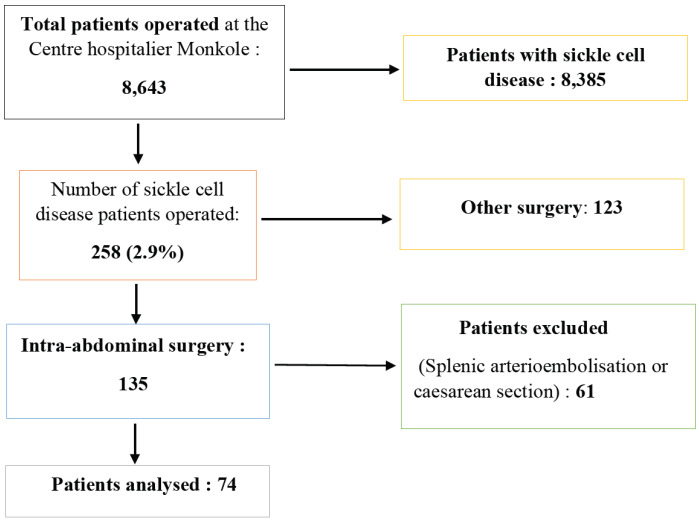

Figure 1: Patients flow chart.

Table 1: Socio-demographic characteristics of the patients.

Variables	Frequency n=74	%
Age (years)		
1 - 5	8	10.8
6 - 17	41	55.4
≥ 18	25	33.8
Gender		
Male	30	40.5
Female	44	59.5
Residence		
Health zone	18	24.3
Outside health zone	56	75.7

Clinical Characteristics of Patients

Table 2 presents the clinical characteristics of the patients.

The indications for surgery were dominated by splenic pathology (hypersplenism, splenomegaly, splenic abscess, splenic abscess rupture, splenic infarction) with 40 cases or 54.1%, gallbladder pathologies: 27 cases (36.5%) included vesicular lithiasis with or without cholecystitis. The other indications (7 cases or 9.5%) recorded were: uterine myomas, acute intestinal obstruction, acute peritonitis, acute appendicitis, ectopic pregnancy, hemorrhagic ovarian cyst. The majority (79.3%) of the surgeries were without infectious risk, most (71.6%) of the patients had no surgical or anesthetic history; 94.6% of the patients were polytransfused, 17.6% were on hydroxyurea and no patient was on a transfusion exchange programme. Patients were classified as ASA III in 94.59%, ASA II in 4.1% and ASA IV in 1.35% of cases. Cardiac auscultation was abnormal in 21.6% of patients and pulmonary auscultation was abnormal in 9.5%. Jaundice was present in 48.6% and fever in 6.8%. Mallampati score was I in 90.5% and II in 9.5% of cases, Cormack grade was I in 91.8%.

Table 2: Clinical characteristics of the patients.

Variables	Frequency n=74	%
Indications		
Splenic diseases	40	54.1
Gallbladder diseases	27	36.5
Other diseases	7	9.5
Surgery without infectious risk	59	79.3
History		
Never transfused	4	5.4
Polytransfused	70	94.6
Transfusion exchange	0	0
Surgical history	21	28.4
Anesthetic history	21	28.4
Alcohol intoxication	8	10.8
Use of hydroxyurea	**13**	**17.6**
Presence of fever	5	6.8
Presence of jaundice	36	48.6
Presence of heart murmur	16	21.6
Abnormal pulmonary auscultation	7	9.5
Mallampati score		
I	67	90.5
II	7	9.5
Cormack grade		
Not concerned	3	4.1
I	68	91.8
II	3	4.1
ASA class		
II	3	4.1
III	70	94.59
IV	1	1.35

Legend: ASA: American Society of Anesthesiologists.

Paraclinical Characteristics of Patients

Table 3 presents the paraclinical characteristics of the patients.

The mean Hb level was 7.5g/dl (range 3.2 and 11.5g/dl). In 17.6% of the cases the Hb level was <6g/dl, in 67.6% it was 7g/dl and above and in 14.7% it was between 6 and 6.9g/dl. In 64.9% the white blood cell count was >12,000/mm^3 and ≤12,000/mm^3 in 35.1%. The platelet count was between 150,000-450,000/mm3 in half of the cases, above 450,000/mm3 in 25.7% and below 150,000/mm^3 in 24.3%.

The prothrombin level was measured in 57 patients (77%) and pathological in 27 patients (36.48%). The activated partial thromboplastin time was performed in 57 patients (77%) and was pathological in 13 patients (17.56%). Creatinemia was performed in 46 patients (62.2%) and was pathological in 2 patients (2.7%). Transaminases were performed in 58 patients (78.4%) and were pathological in 11 patients (14.9%). Cardiac ultrasound was performed in 11 patients and was pathological in 3 patients (4%).

Table 3: Paraclinical characteristics of patients.

Blood count data				
Variables	**Frequency (n=74)**	**%**		
Hb level (g/dl)				
< 6	13	17.6		
6-6,9	11	14.9		
≥ 7	50	67.6		
White blood cell count (/mm³)				
≤ 12,000	26	35.1		
> 12,000	48	64.9		
Platelet count (/mm³)				
< 150,000	18	24.3		
150,000- 450 ,000	37	50.0		
> 450,000	19	25.7		
Coagulation, biochemistry and cardiax ultrasound data				
Variables	**Frequency n= 74**	**%**	**Normal Frequency (%)**	**Pathological Frequency(%)**
PT				
Realized	57	77	30 (40.5)	27 (36.48)
Not realized	17	23		
APTT				
Realized	57	77	44 (59.45)	13 (17.56)
Not realized	17	23		
Creatinine level				
Realized	46	62.2	44 (59.45)	2 (2.7)
Not realized	28	37.8		
Transaminases				
Realized	58	78.4	44 (59.45)	14 (18.9)
Not realized	16	21.6		
Cardiac ultrasound				
Performed	11	14.9	8 (10.8)	3 (4)
Not performed	63	85.1		

Legend: PT: Prothrombin level, APTT: Activated partial thromboplastin time.

Intraoperative Patient Characteristics

Table 4 presents the intraoperative characteristics of the patients. The majority of patients received general anesthesia (97.3%) with orotracheal intubation and were extubated (96%) on a table at the end of the operation. Induction was performed with propofol for all patients (72) operated under general anesthesia, representing 97.3% of cases. Anesthesia was maintained with halogen (sevoflurane in 32 patients (43.2%) or isoflurane in 35patients (47.3%) or propofol in 5 patients (6.7%) in association with curares (pancuronium or atracurium in 32 patients (43.2%), suxamethonium in 34 patients (45.9%) and morphinics (fentanyl in 28 patients (37.8%) or sufentanil in 44 (59.45%). One patient was operated under laryngeal mask. Two patients (2.7%) received locoregional anesthesia. Post-operative pain was managed with multimodal analgesia (ketoprofen or ibuprofen for a maximum of three days, paracetamol and tramadol) and this analgesia included morphine in 37 patients, i.e. 50% of cases.

The procedures were performed by a senior surgeon in 94.6% of cases for an average duration of one hour and twenty minutes. The anesthetist was senior in all cases. The duration of anesthesia was more than two hours in 44 patients (59.5%) with an average time of 2 hours 25 minutes.

Splenectomy represented 54.1% of the surgical procedures performed on the patients and cholecystectomy in 36.5%. The other procedures concerned 7 patients (9.5%) and consisted of appendicectomy, interannexal hysterectomy, evisceration cure, emptying enterotomy, salpingectomy and ovarian cystectomy. The majority (91.9%) of the operations were scheduled and therefore performed during the day (87.8%). Six patients (8.1% of cases) underwent emergency surgery and 12.2% of the procedures were performed at night.

Table 4: Intraoperative characteristics of patients.

Variables	Frequency n=74	%
Use of premedication	**14**	**18.9**
Anesthetic technique		
GA with intubation*	72	97.3
LRA	2	2.7
Induction narcotic		
Propofol	72	97.3
Maintenance narcotic		
Propofol	5	6.7
Isoflurane	35	47.3
Sevoflurane	32	43.2
Curare		
Non	8	10.8
Suxamethonium	34	45.9
Pancuronium/Atracurium	32	43.2
Morphinic		
Fentanyl	28	37.8
Sufentanil	44	59.45
Extubation		
On table	71	96
Not involved	3	4
Use of morphine for postoperative pain	**37**	**50**
No morphine	37	50
Surgical procedures		
Splenectomy	40	54.1
Cholecystectomy	27	36.5
Other acts	7	9.5
Senior surgeon	70	94.6
Junior surgeon	4	5.4
Senior anesthetist	**74**	**100**
Duration of anesthesia		
< 2 hours	30	40.5
≥ 2 hours	44	59.5
Duration of surgery		
< 2 hours	38	51.4
≥ 2 hours	36	48.6
Degree of urgency		
Scheduled	68	91.9
Emergency	6	8.1
Time of surgery		
Daytime	65	87.8
Night	9	12.2

*Legend: GA: General Anesthesia, LRA: Loregional Anesthesia, * One patient was operated under laryngeal mask.*

Intra and Postoperative Complications and Need of Blood Transfusion

Table 5 presents the intra- and postoperative complications and need of blood transfusion. Forty-seven patients or 63.5% were transfused intraoperatively. Anesthetic and surgical incidents accounted for 4.1% (one bronchospasm, one hypercapnia, two probable allergic reactions) and 6.8% (two cases of haemorrhage and three cases of injury to the digestive tract) of cases. Post-operative complications were observed in 15 patients, i.e. 20.3% of cases, and 3 deaths were recorded (two cases of sepsis with multivisceral failure and one highly probable case of pulmonary embolism). These postoperative complications were: anemia requiring transfusion (4), transient desaturation (3), parietal infection (1), convulsions (1), pancreatitis (1), hyperviscosity (1), pneumonia (1), vomiting (1), decompensation of heart valve disease (1) and tuberculosis discovered incidentally during the investigation of the fever (1). No cases of acute chest syndrome was recorded.

Table 5: The intra- and postoperative complications and blood transfusion.

Variables	Frequency n=74	%
Intraoperative transfusion		
No	27	36.5
Yes	47	63.5
Intraoperative anesthetic incidents		
Yes	3	4.1
No	71	95.9
Intraoperative surgical incidents		
Yes	5	6.8
No	69	93.2
Postoperatives complications		
No	56	75.7
Yes	15	20.3
Deaths	3	4.1

Factors Associated with Postoperatives Complications and Intraoperative Transfusion

The factors associated with complications are summarized in table 6. Univariate analysis reveals that age between 6 and 17 years ($p = 0.011$), spleen surgery ($p = 0.035$), presence of jaundice ($p = 0.015$), duration of surgery ($p = 0.049$) and duration of anesthesia ($p = 0.004$) greater than or equal to 2 hours were associated with intraoperative transfusion. But with a multivariate analysis, only splenic surgery ($p = 0.018$), presence of jaundice ($p = 0.024$) and duration of anesthesia greater than or equal to 2 hours ($p = 0.033$) remained as factors associated with intraoperative transfusion.

In univariate analysis, abnormal cardiac auscultation on anesthetic assessment ($p < 0.001$) and hemoglobin level <6 g/dl ($p = 0.04$) were associated with the occurrence of postoperative complications and in multivariate analysis, these two parameters (respectively $p = 0.001$ and $p = 0.008$) persisted as factors associated with the occurrence of postoperative complications.

Discussion

This study was conducted to determine the factors associated with complications during anesthesia in course of intra-abdominal surgery in sickle cell patients in the context of a low income country. We found that anesthesia in sickle cell patients affected 2.9% of patients. We registered 74 patients instead of the expected 85 because of cost limiting access to surgery for poor patients. Splenectomy and cholecystectomy were the main procedures and were performed under general anesthesia with tracheal intubation for a duration of ≥2 hours in 59% of these cases. Simple transfusion was performed in 63.5% of cases intraoperatively and no transfusion exchange was performed. Anesthetic and surgical incidents accounted for 4.1% (one bronchospasm, one hypercapnia, two probable allergic reactions) and 6.8% (two cases of haemorrhage and three cases of injury to the digestive tract) of cases respectively. Postoperative complications (anemia requiring transfusion, transient desaturation, parietal infection, convulsions, pancreatitis, hyperviscosity, pneumonia, vomiting, valvular decompensation and incidental tuberculosis) were observed in 15 patients, i.e. 20.3% of the cases, and 3 deaths were recorded (two cases of sepsis with multivisceral failure and one highly probable case of pulmonary embolism). No case of acute chest syndrome or stroke were recorded. Spleen surgery, presence of jaundice and duration of anesthesia greater than or equal to 2 hours were associated with need intraoperative transfusion. Heart murmur and hemoglobin <6 g/dl were associated with the occurrence of postoperative complications. In a low income country, with limited knowledge of the HbS level, no transfusion exchange process and with interventions performed by laparotomy sometimes above and below the umbilical, one would expect more adverse events. The explanation could be found in the good preparation of the patients, the availability of basic drugs and materials for anesthetic safety and the fairly optimised organisation.

However, our sample size is not large as in the study reported by Brumm et al. [23] who had 1,702 patients in 925 hospitals.

The mean age of our population was 16.4 years, unlike the study by Brumm et al. [23] who found a mean age of 33.03 years, but the study only included patients aged 18 years and over. Nevertheless the female sex predominated in both studies, 59.5% for us and 64.3% for Brumm et al, without explanation. Perhaps this difference does not exist in patients not admitted for surgery.

In our series, 5.4% of the patients had no previous transfusion history compared to 24% in Vichinsky et al. [18]. The majority of patients in both studies had a previous history of polytransfusion, 94.6% in the present study and 69.5% in Vichinsky et al. [18]. Correct follow-up and possibly hydroxyurea use in the Vichinsky series could explain its relatively low rate of prior transfusion. This polytransfusion is a consequence of the shortened lifespan of sickled red blood cells. It should be noted that in our context, patients are polytransfused because of the late diagnosis of the disease and ignorance.

In our study, the indications for surgery were splenic pathology in 54.1% of cases and vesicular pathology in 36.5%. Vichinsky et al. [18] found a predominance of vesicular disease (36.5%) in

Table 6: Factors associated with intraoperative transfusion and postoperative complications.

Facteurs associated with intraoperative transfusion				
Variables	**Univariate analysis**		**Multivariate analysis**	
	P	**OR (IC95%)**	**p**	**ORa (IC95%)**
Age (years)				
≥ 18		1		1
6-17	**0.011**	3.95 (1.36-11.43)	0.873	1.89 (0.19-3.93)
< 6	0.367	2.12 (0.41-10.89)	0.094	0.11 (0.09-1.44)
Indications				
Other		1		1
Spleen	**0.035**	6.29 (1.14-34.57)	**0.018**	4.35 (1.51-7.20)
Bladder	**0.919**	0.92 (0.17-4.93)	0.200	0.25 (0.03-2.07)
Jaundice				
No		1		1
Yes	**0.015**	3.50 (1.27-9.62)	**0.024**	3.18 (1.04-7.80)
Duration of anesthesia				
< 2 hours		1		1
≥ 2 hours	**0.004**	4.45 (1.62-12.20)	**0.033**	9.09 (1.27-12.87)
Duration of surgery				
< 2 hours		1		1
≥ 2 hours	**0.049**	2.70 (1.01-7.25)	0.371	3.26 (0.26-43.27)
Factors associated with postoperatives complications				
Variables	**Univariate analysis**		**Multivariate analysis**	
	P	**OR (IC95%)**	**p**	**ORa (IC95%)**
Cardiac auscultation				
Normal		1		1
Pathological	**<0.001**	10.42 (2.96-36.63)	**0.001**	10.5 (2.77-13.76)
Hemoglobin level				
≥ 7 g/dl		1		1
6-6,9 g/dl	0.084	3.28 (0.85-12.65)	0.106	1.79 (0.75-9.11)
<6 g/dl	**0.040**	4.38 (1.07-17.87)	**0.008**	3.8 (2.82-17.59)

his series. The young age in our series explains the predominance of splenic pathology, especially in patients under 10 years old. None of the patients in our series had received a preoperative transfusion exchange, whereas in the study by Vichinsky et al., half had received an transfusion exchange. This technique is not yet commonly used in our setting because of financial difficulties. However, Vichinsky observed 33% of complications compared to 20% in our series.

In our study, 94.59% of patients were classified as ASA III and 4.1% as ASA II compared to Vichinsky et al. [18] who had 51% of patients classified as ASA III against 47.5% classified as ASA II. The difference is justified by the fact that the sample size for Vichinsky et al. was large, i.e. 551 patients compared with 74 patients in the present study. In addition, the predominance of splenic pathology with repetitive and severe anemia also explains why many of our patients were classified as ASAIII. Unfortunately, not all patients with abnormal cardiac auscultation benefited from cardiac ultrasound. Thus it was not possible to diagnose possible heart disease, although sickle cell patients are often exposed to it. Moreover, this pathological cardiac auscultation was associated with postoperative complications. Thus, out of 11 patients who had a cardiac ultrasound, three were pathological.

The mean hemoglobin level was 7.5g/dl in our series compared to Vichinsky et al. [18] who had a mean hemoglobin of 7.9g/dl. In the study by Vichinsky et al. [24] 53.5% of patients were transfused preoperatively to achieve a Hb level of 10g/dl. It should also be noted that in our series, some children (13 patients i.e. 16%) with hypersplenism could not raise their Hb level to more than 6g/dl. They were anesthetised with very low levels of around 3.2g/dl and received blood transfusion intraoperatively, once the splenic vascular pedicle had been clamped.

In our study 12.2% of the patients had elevated liver transaminases and 2.1% of the patients had elevated creatinine as noted by others [18]. However, many patients in our series did not undergo a paraclinical assessment because of financial difficulties. Indeed, sickle cell disease in our country seems to affect more poor people. This situation is aggravated by the fact that there is no health coverage and therefore patients have to take care of themselves, which is difficult or even impossible for some. These financial difficulties explain that for complementary examinations, the demand was very selective for all patients.

General anesthesia was performed in 97.3% of cases with propofol as the induction hypnotic, results similar to those of Daddy et al. [19] in Niamey. The maintenance hypnotic in our study was essentially

divided between sevoflurane at 43.2% and isoflurane at 47.3%, unlike Daddy et al. who used halothane. This difference is due to the availability of the products, in fact in the hospital where we carried out the study, halothane is very rarely used and even less so in sickle cell disease because of its cardiac and hepatic side effects.

Multimodal analgesia in our series required the use of morphine in 50% of cases, unlike Daddy et al. [19] who did not use morphine but with less than 50% of intra-abdominal surgery known to be painful. Indeed, correct treatment of postoperative pain is an important element of anesthetic management of sickle cell patients to avoid complications [4].

The majority of cases had anesthesia duration of more than 2 hours with an average duration of 2 hours 25 minutes in our series which seems to be similar to the series of Vichinsky et al. [18] who had an average duration of 2 hours 30 minutes.

Our study recorded a high intraoperative transfusion rate of 63.5% due to the main indication being hypersplenism and splenic sequestration responsible for the anemia. Other authors had a lower rate of 44.7% [23] and 40% [19].

Postoperative complications were observed in 20.3% of cases in our series and three deaths were recorded (4.1%). Daddy et al. [19] in their study had recorded complications in 6.6% of cases in the form of non-febrile seizure. Brumm et al. [23] observed 35% of cases of sickle cell crisis. However, Vichinsky et al. [18] observed 33% of cases with at least one complication, of which 7.5% of complications were minor, marked by fever in most cases. In the latter study, 0.3% of cases resulted in death. These were two patients with a common history of acute chest syndrome, a serious incident which fortunately we did not encounter in our series. Authors have reported no difference in the occurrence of complications after cholecystectomy in sickle cell and non-sickle cell patients [24,25]. The first death in our series concerned a patient operated on for postoperative peritonitis with evisceration. He died on the third postoperative day in a state of multivisceral failure. Schyrr [17] in a review of the literature with recommendations for clinical practice made in 2020 reported, on 5 prospective studies, a rate of complications ranging from 0 to 45% and a mortality of 0 to 1.7% after cholecystectomy. The second death was related to a patient classified as ASA IV due to sepsis complicated by encephalopathy, operated for peritonitis due to ruptured splenic abscess. He had suffered an intraoperative cardiac arrest which recovered after resuscitation. But a second irreversible cardiac arrest occurred immediately postoperatively. The third death concerned a patient operated on for laparoscopic cholecystectomy, who suffered an abrupt cardiac arrest 6 hours after the operation, which was attributed to a probable pulmonary embolism.

A high ASA class is an independent predictor of postoperative morbidity and mortality [26], and all our patients were of high ASA class (III).

Anesthetic incidents accounted for 6.8% of cases in our series. These were mainly hypercapnia, bronchospasm and probable allergic reaction to curare. Vichinsky et al. [18] recorded 19.5% of intraoperative incidents.

However, Firth P [1] in 2004 found that morbidity and mortality during anesthesia in sickle cell patients, which were 50% higher than in non-sickle cell patients, decreased with improved anesthetic care of the patients.

Spleen surgery [ORa: 4.35 95% CI (1.51-7.20) p=0.018] was associated with intraoperative transfusion because hypersplenism and large splenomegaly, which were the indications for surgery, are major factors in worsening anemia in sickle cell patients. The presence of jaundice [ORa: 3.18 95% CI (1.04-7.80) p=0.024] was also associated with intraoperative transfusion as jaundice is a stigma of hemolysis and therefore a shortening of the lifespan of red blood cells. Duration of anesthesia greater than or equal to 2 hours [ORa: 9.09 95% CI (1.27-12.87) p=0.033] was also associated with intraoperative transfusion either by increased blood loss due to prolonged surgery or by blood loss requiring hemostasis procedures that increased the duration of surgery.

Pathological cardiac auscultation at the pre-anesthetic assessment and a hemoglobin level below 6g/dl were associated with the occurrence of post-operative complications. No anesthetic factors were identified. Vichinsky et al. [18] found that a history of pulmonary disease and high-risk surgery were independent predictors of acute chest syndrome. Older age and the number of hospitalizations in the year before surgery were significant independent predictors of the occurrence of painful attacks. Anemia appeared in our study probably because of the indications which were in themselves factors of anemia (splenomegaly, hypersplenism).

Prophylactic transfusions would decrease the frequency of most complications in patients with sickle cell disease [20], they are frequently used as part of the perioperative management, but no study to date has proven this benefit [18,27]. Furthermore, the level of evidence for some of these recommendations is not very high [20]. Transfusion remains a procedure that must be performed with great caution in view of the significant risks associated with red blood cell transfusions, notably alloimmunization and exposure to infectious diseases [28]. Therefore, transfusion in our series was only curative to correct severe or intolerable anemia.

The weaknesses of our study is the small sample size, the monocentric nature and the absence of complete paraclinical results. Nonetheless, its strengths are that it is the first to address the subject in our country, that it is prospective and conducted in a sickle cell referral centre, with an anesthesia rate close to the prevalence of sickle cell disease in the country. The patients came from both the health zone served by the hospital and from areas not served (moreover, there are more) and therefore it is a true reflection of the sickle cell patients in our area.

Conclusion

Anesthesia for sickle cell patients concerns about 2.9% of the patients operated on in this series. The patients were fairly young, undergoing general anesthesia for splenic or vesicular pathology, ASA III, often transfused intraoperatively, with the associated factors of splenic surgery, the presence of jaundice preoperatively and the duration of anesthesia exceeding two hours.

Postoperative complications were related to pathological cardiac auscultation and a hemoglobin level below 6g/dl. There appeared to be no contribution of anesthesia to the occurrence of these complications. Future studies are planned for other types of surgery, notably orthopaedic and obstetric.

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