Prophylactic red blood cell exchange may be beneficial in the management of sickle cell disease in pregnancy

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BACKGROUND: Sickle cell disease (SCD) is associated with chronic hemolysis and painful episodes. Pregnancy accelerates sickle cell complications, including prepartum and postpartum vasoocclusive crisis, pulmonary complications, and preeclampsia or eclampsia. Fetal complications include preterm birth and its associated risks, intrauterine growth restriction, and a high rate of perinatal mortality. The purpose of this study was to evaluate pregnancy outcomes in patients with SCD who underwent planned preventive red blood cell exchange (RBCX).

STUDY DESIGN AND METHODS: We retrospectively evaluated the complications of SCD in 37 pregnant patients. Patients with SCD who had undergone prophylactic RBCX were compared with a control group who had not undergone RBCX during pregnancy.

RESULTS: Forty-three exchange procedures were performed in 24 patients. The control group comprised 13 patients with a mean age of 27.4 ± 3.3 years who had not undergone RBCX during pregnancy. Four of the five patients who developed a vasoocclusive crisis died. There was a significant difference in maternal mortality between the study and control groups ($p = 0.011$). There was also a significant difference in the incidence of vasoocclusive crisis between the study and control groups. One fetal death occurred in the 20th gestational week in a patient in the control group, although there were no postpartum complications in either the babies or the mothers in the control group.

CONCLUSION: This study has demonstrated that prophylactic RBCX during pregnancy is a feasible and safe procedure for prevention of complications. Given the decrease in the risks of transfusion, RBCX warrants further study.

Sickle cell diseases (SCDs) are a group of inherited single-gene autosomal recessive disorders caused by the sickle cell gene, which affects hemoglobin (Hb) structure.[1] SCD includes sickle cell anemia with the *SS* genotype, some heterozygous conditions of the *S* gene, and other clinically abnormal Hbs such as beta thalassemia, HbC, HbD, and HbE among others. The primary manifestations of SCD are chronic hemolytic anemia and episodes of severe pain crises due to vasoocclusion.[1-3] Repeated vasoocclusive crises can affect multiple organ systems, and individuals with SCD have increased risks of stroke, renal dysfunction, pulmonary hypertension, retinal disease, and avascular necrosis.[2-5] Pregnant females with SCD experience these medical risks, as well as vascular effects to the gravid uterus and placenta, which creates an additional risk for the mother and fetus. In females with SCD, the underlying anemia and multiorgan dysfunction can complicate pregnancy by affecting the cardiovascular, renal, hematologic, and respiratory systems.[6-10] Improvements in medical care

ABBREVIATIONS: RBCX = red blood cell exchange; SCD(s) = sickle cell disease(s).

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and treatment for individuals with SCD, coupled with advancements in neonatal care, have contributed to a decline in morbidity and mortality both for mother and fetus; however, the physiologic changes in pregnancy still carry important clinical risks for some patients with SCD.[8,9]

Previous studies have reported that females with SCD had a higher prevalence of preeclampsia, lung disease, and heart disease during the antenatal, intrapartum, or postpartum periods compared with women without hemoglobinopathies. In addition, the odds of fetal death, preterm birth, low birthweight, and cesarean delivery were higher for females with SCD compared with those with no reported hemoglobinopathies after adjusting for maternal age, education, parity, plurality, insurance status at delivery, prenatal care utilization, smoking, and infant sex.[6-9] The maternal mortality rate was 1.6 per 1000 deliveries in patients, compared to 0.1 per 1000 in women without SCD. Pregnant women with SCD had a higher risk for preeclampsia, eclampsia, venous thromboembolism, cardiomyopathy, intrauterine fetal demise, and intrauterine growth restriction.[11] The odds of fetal death among deliveries to women with SCD were 2.2 times greater than those without SCD. The odds of preterm delivery, low birthweight, and having babies small for gestational age were 1.5-fold greater[12] among women with SCD.

Patients with SCD who survive childhood and who become pregnant are likely to suffer aggravated morbidity and mortality. Low- and middle-income countries generally report increased maternal and perinatal morbidity and mortality in association with SCD.[9-14] In Turkey, maternal and fetal morbidity and mortality remain a major problem in pregnant patients with SCD. This retrospective study investigates the pregnancy outcomes of SCD patients who underwent prophylactic red blood cell exchange (RBCX) procedures from January 2000 to March 2013, and results were compared with a control group.

PATIENTS AND METHODS

Study design

This was a single-center, retrospective, and cross-sectional study. A total of 37 pregnant patients, diagnosed with SCD were involved in the study between 2000 and 2013. While 24 patients received RBCX and were classified in the study group, 13 patients did not receive RBCX procedure and constituted the control group. Our hypothesis was that prophylactic RBCX decreases the incidence of maternal and fetal complications during pregnancy in patients with SCD.

Informed consent was obtained from all subjects. After approval was obtained from our institutional review board, data were extracted from a validated hospital information management system regularly checked by the record inspection group of the related department.

Clinical and laboratory data

The clinical diagnosis of painful crisis was based on the following criteria: widespread pain typically involving the limbs, vertebrae, or ribs that could be attributed to vascular occlusion and/or ischemic tissue damage, as well as the relief of symptomatic pain after the administration of an analgesic medication. The term "steady state" was defined as being pain-free and having experienced no acute clinical events in the 30 days before the sampling. Stroke or transient ischemic attack was defined according to criteria from the American Neurological Association.[15] Hepatic necrosis was defined by the results of basic biochemical testing. Acute chest syndrome was defined by clinical and radiologic signs.[16]

A complete blood count was performed using an automated cell counter (Cell-Dyn 3700, Abbott Laboratories, Abbott Park, IL). Homozygous SCD and sickle cell β-thalassemia were defined using Hb electrophoresis performed with high-performance liquid chromatography (HPLC; Bio-Rad Laboratories, Inc., Irvine, CA). Sickle cell β^0-thalassemia is defined by the absence of normal β chains and, therefore, no HbA on Hb electrophoresis because almost all the Hb consists of HbS. The diagnosis of sickle-cell β^+ thalassemia was straightforward: If HbA is detected as 5% to 30% of the total Hb in Hb electrophoresis in patients who have homozygous HbS disease, whereas blood transfusion from normal individuals is absent. HbCC patients were defined by using HPLC and alkali gel electrophoresis.[17] Complete blood count and HbS levels were measured before and after procedures. We monitored HbS concentrations every 3 months during pregnancy. Quality control measurements were performed by the Bio-Rad External Quality Assurance Service (Bio-Rad Laboratories Pty Ltd, NSW, Australia).

The obstetric database

The database was established in 2004 and prospectively updated. It contains information regarding maternal age, marital status, parity, antenatal diagnoses, and maternal complications. The condition of the fetus is also monitored during and after delivery and detailed data regarding the modes of delivery; APGAR scores at 1, 5, and 10 minutes; sex, fetal distress, and birthweight were recorded. Both the mother and the neonate in every case were followed up by hematology and obstetrics departments for possible complications until discharge from the hospital.

Data were extracted from previously authorized and validated Hospital Data Management Systems (Version 1.5, Datasel Information Systems, Ankara, Turkey; Nucleus

Hospital Information Management System, Version 9.2.40, Monad Software and Counseling, Ankara, Turkey). These systems consist of items specific for SCD. The accuracy of data was checked by a group attending for supervision of data records.

RBCX

Two different continuous-flow apheresis systems (Cobe Spectra Version 7.0 and Spectra Optia Version 7, Terumo BCT, Lakewood, CO) were used to exchange 60% to 70% of the patients' red blood cells (RBCs) with cross-matched donor RBCs of the same blood type to reduce the HbS level to less than 30%. The RBCs were also matched for Rh (C, c D, e) and Kell (K) blood group antigens to minimize alloimmunization. As the patients who will undergo exchange transfusion need to have negative direct and indirect antiglobulin tests (IATs), these tests were performed before RBCX procedure in all patients. Leukofiltered RBC suspensions preserved for 1 to 7 days with CPD with a hematocrit (Hct) level of approximately 70% were used. The target Hct levels were determined according to the steady-state Hct levels of patients who were regularly examined as outpatients. The need for RBC transfusion was averaged according to the target Hct level.[18] Patients who had a complicated pain episode, characterized by clinical deterioration, a Hb level of less than 7g/dL, leukocytosis in the absence of infection, and an underlying pulmonary or cardiac disease, required hypertransfusion with a target Hct of 27% to 28% after the exchange.

The inlet pump flow rate and centrifugation speed were automatically adjusted according to variables preset by patient data (weight, height, sex, and Hct level) during RBCX. In these procedures, cells were exposed to a maximum centrifugation speed of $930 \times g$ based on the apheresis system guide (Cobe Spectra Apheresis System Essentials Guide, Terumo BCT). In some patients, the inlet pump flow rate was adjusted manually. The total blood volume was calculated according to body weight (70-75 mL/kg) and the RBC volume calculation was based on Hct values. The citrate anticoagulant rate was selected during RBCX via a standardized citrate infusion protocol.[19] The procedure was computer-guided: patient characteristics (height, weight, preapheresis Hct, mean Hct of RBC units, volume of the replacement fluids, and targeted final Hct) were entered by the apheresis operator before starting the procedure.

Timing of delivery

The patients who had a normally growing fetus were allowed elective birth through induction of labor, or by elective cesarean section if indicated, after 38 weeks of gestation. Because the risks of abruption, preeclampsia, peripartum cardiomyopathy, and acute sickle cell crisis are unpredictable, planned delivery time of baby was arranged to 32 to 38 weeks of gestation for prevention of late pregnancy complications and associated adverse perinatal events. The delivery was postponed if the amniotic fluid lecithin-to-sphingomyelin ratio was immature. Lecithin-to-sphingomyelin ratio was determined prospectively using transvaginally and transabdominally collected amniotic fluid from patients with SCD between 32 and 34 weeks of gestation. If lecithin-to-sphingomyelin ratio was 2.0 or more, the delivery was planned.[20] Women who had hip replacements or restriction of hip movement due to avascular necrosis underwent cesarean section.

Cord blood pH measurement

Blood samples from the umbilical artery were collected in heparinized 1-mL syringes, capped, and transported on ice to the laboratory for analysis within 10 minutes of delivery on an automatic pH analyzer (Model 2369, Roche, Indianapolis, IN).

Statistical analysis

Statistical analysis was performed using a statistical package (SPSS, Version 17.0, SPSS, Inc., Chicago, IL). All numerical data are expressed as mean values ± SD or as proportions. Pre–post measures data were analyzed using the Wilcoxon test. The categorical variables between the groups were analyzed using the Fisher exact test. p values of less than 0.05 were considered to indicate significance.

RESULTS

RBCX group

A total of 37 patients were included in this study. Forty-three RBCX procedures were performed in 24 patients and 90.6% of the procedures were performed in an outpatient setting. Twenty-two patients had homozygous HbS disease, one patient had sickle-cell $\beta^{+/0}$ thalassemia (4.1%), and one homozygous HbCC (4.1%) disease. Ninety-five percent of the patients were Eti-Turks, which may reflect genetic homogeneity. Four patients who were in vasoocclusive crisis were treated with automated RBCX procedure in the first trimester. Fifteen patients received prophylactic RBCX treatment in the second trimester, and all patients received prophylactic treatment in the third trimester. Nine of 24 patients received RBCX procedure only in the third trimester (Table 1).

All technical data for the procedures are presented in Table 2. The fraction of patients' remaining cells was 26 ± 2%. HbS values decreased to less than 30% and the Hct levels increased, allowing for perfusion of the

TABLE 1. Distribution of RBCX procedure according to trimester of the patients

	Trimester		
PN*	First	Second	Third
1			X
2	X†	X	X
3		X	X
4		X	X
5		X	X
6			X
7			X
8			X
9	X†	X	X
10		X	X
11		X	X
12	X†	X	X
13	X†	X	X
14		X	X
15		X	X
16		X	X
17		X	X
18			X
19		X	X
20		X	X
21			X
22			X†
23			X
24			X

* Patient number.
† Vasoocclusive crisis occurred.

placenta, as determined by Doppler ultrasonography. Hypertransfusion was required in four patients with a painful crisis in the first trimester. No crises occurred among SCD patients who underwent prophylactic RBCX procedures.

Each apheresis procedure took 2 to 3 hours. No technical problems related to cell separators were noted. Four adverse events were recorded during 43 RBCX sessions (9.3%), which included one episode of anxiety, one allergic reaction, and two episodes of paresthesia caused by hypocalcemia during apheresis that required oral calcium supplementation. None of these events justified discontinuing the session. Difficulties with venous access were recorded eight times (18.6%).

The 24 patients in the RBCX group experienced a total of 43 RBCXs with a total of 168 RBC units transfused. Before the RBCXs began, there was one patient (4.1%) who had RBC alloantibodies, but there were four patients (16.6%) whose IAT became positive after exchange transfusions. We could not perform RBC antibody identification test for three patients, but we detected anti-D alloantibodies in one patient. We also noticed that no transfusion-transmitted infections (hepatitis B virus, hepatitis C virus, or human immunodeficiency virus) had developed.

Outcomes of delivery in the study group are presented in Table 3. Cesarean sections were planned by obstetricians for patients whose amniotic fluid L/S ratio was 2.0 or more. Twenty-two patients were delivered by cesarean section and 29.2% of patients with SCD had a second gravida.

One patient developed postpartum HELLP (hemolysis-elevated liver enzymes-low platelets) syndrome. Excessive vaginal bleeding occurred in two patients and RBC transfusion was required. A preterm baby with gestational age of 28 weeks was followed up in the neonatal intensive care unit for 31 days until he weighed 1300 g. Maternal and fetal complications are shown in Table 4.

Control group

The control group comprised 13 cases with mean age of 27.4 ± 3.3 years. Four of five patients who experienced vasoocclusive crisis died (three in the 12th gestational week and one in the 16th gestational week; Table 5). There was a significant difference between groups in terms of maternal loss ($p = 0.011$; Table 6). The 22-year-old patient who had progressive pain with hemolysis and acute renal failure was referred from another center when she was at 12th week of pregnancy. She had developed progressive pain with hemolysis and acute renal failure. She was treated with intravenous (IV) fluids, analgesics, and 2 units of RBCs, but died 2 days later in the intensive care unit. The second patient was 31 years old. She was gravida 2 in her third trimester of pregnancy and presented with a vasoocclusive crisis. We initially treated her with IV fluids and analgesics, but 24 hours later, she developed acute cyanosis, a nonproductive cough, dyspnea, and pleuritic chest pain and was diagnosed with acute chest syndrome. She was treated with broad-spectrum antibiotics, blood transfusions, supplemental oxygen therapy via nasal prongs, and bronchodilators, but she died of respiratory failure 6 hours later. The other two pregnant SCD patients, both from 23 to 27 years of age, were admitted to the emergency department with a vasoocclusive crisis. Neither could be effectively managed and died within several hours. A surviving patient at 36 weeks of gestation presented with generalized pain and vasoocclusive crisis and she was managed successfully with simple transfusion and fluids. A 33-year-old pregnant sickle cell anemia patient in the control group, with positive IAT, had intrauterine fetal loss on 20th gestational week and medical abortion procedure was performed. One patient had to use an antihypertensive drug, analgesics, and antibiotic drugs during pregnancy. The remaining six cases achieved the term without any maternal and fetal complications (Tables 5 and 6). All patients who reached the term were delivered by cesarean section with no postpartum complications in babies and mothers. Nevertheless, in terms of developing maternal complications during pregnancy, we observed higher rates in the control group and these results were significant ($p = 0.042$; Table 6).

TABLE 2. Variables associated with automatic RBCX in pregnant SCD patients

Technical details	Mean ± SD	Minimum	Maximum
Blood volume processed (mL)	5029.3 ± 543.8	3693	6477
Total ACD-A used (mL)	321.9 ± 34.7	230	434
Inlet flow rate (mL/min)	46.8 ± 3.9	40	55
Total blood volume (mL)	3685.4 ± 376.9	2965	4537
Hct (%)			
Before procedure	24.2 ± 3.5	15.0	31.0
After procedure	27.5 ± 1.1	26.0	31.0
Hb (%)			
Before procedure	74.5 ± 13.3	40.8	99.0
After procedure	24.6 ± 10.1	8.3	69.5
Number of RBC units used	6.2 ± 0.6	5.0	7.0
Replacement volume (mL)	1893.9 ± 231.8	1276	2482

TABLE 3. Outcomes of delivery in SCD patients who underwent RBCX procedure

Delivery outcomes	Mean ± SD	Minimum	Maximum
Age (years)	27.5 ± 4.0	21	37
Gestational week	35.5 ± 2.7	28	38
Gravida	1.3 ± 0.4	1	2
Weight of the baby (kg)	2604.3 ± 728.7	800	3630
APGAR score			
1 min	8.1 ± 0.9	6	9
5 min	9.7 ± 0.8	7	10
10 min	9.7 ± 0.8	7	10
Cord blood pH	7.3 ± 0.1	7.0	7.4

TABLE 4. Maternal and fetal complications in SCD patients who underwent RBCX procedure

	Number	Percent
Mode of delivery		
Normal vaginal delivery	2	8.4
Cesarean section	22	91.6
Gravida		
1	17	70.8
2	7	29.2
Maternal complications		
HELLP syndrome after delivery. The patient was followed up in the ICU and was discharged from the surgical ICU.	1	4.1
Vaginal bleeding. Two units of RBCs transfused.	1	4.1
Vaginal bleeding after cesarean section. One unit of RBCs transfused.	1	4.1
None	21	87.7
Neonatal complications		
Preterm birth. Stayed at the ICU for 31 days. Discharged after stabilizing and weighing 1300 g.	1	4.1
None	23	95.9

HELLP = hemolysis-elevated liver enzymes-low platelets; ICU = intensive care unit.

DISCUSSION

SCD is an inherited hemoglobinopathy that affects multiple systems with increased incidence of maternal and fetal complications in pregnant women.[6,8] These include an increased rate of urinary tract infections, as well as major complications such as septicemia, toxemia, and thrombophlebitis arising close to the expected time of delivery.[6,8-14,21] In Turkey, hemoglobinopathies are the most common genetic disease and prevalence studies in the Cukurova region of southern Turkey have reported a 10% incidence of sickle cell trait. Hence, SCD is an important public health problem in our country and region.[22,23] SCDs have heterogeneous phenotype and shown to different clinical abbreviation among the communities. Despite improvements in medical management, SCD remains associated with severe morbidity and decreased survival. With the added burden of pregnancy, follow-up of these patients is difficult. We have followed two pregnant sickle cell patients and they died before the RBCX procedure from vasoocclusive crisis. We become aware of another two SCD patients who died from vasoocclusive crisis during pregnancy in a Regional Authoritative Meeting for evaluation of maternal death arranged by Ministry of Health, Adana Division of Mother and Child Health.

RBCX is an underutilized therapy for both prevention and management of SCD complications. Exchange transfusions improve the control of blood volume and viscosity, while decreasing the risk of transfusion-related hemochromatosis.[24] Subjects with SCD who are treated with long-term transfusion programs seem to be susceptible to iron-induced toxicity, including cardiac abnormalities and death.[24] RBCX may be a safe, simple, and efficient method for reducing iron accumulation during long-term transfusion therapy. RBCX has been shown to reduce iron overload in patients with SCD who are treated with a long-term transfusion regimen.[24] We measured plasma ferritin level in neither group but there were no symptoms of iron overload.

Exchange transfusion is indicated as a prophylactic measure to prevent the recurrence of cerebrovascular accidents and before extensive surgery.[24-27] Studies on prophylactic transfusions in SCD patients do not reach the same conclusions: while some indicate that they do not alter the outcome of pregnancy or only decrease the number of vasoocclusive events[28-30] others indicate that

TABLE 5. Complications in control group

Complication	Number	Percent
Vasoocclusive crisis	5*	38.40
Hypertension	1	7.69
Intrauterine loss	1	7.69
None	6	46.15
Total	13	100

* Four were lost.

they might favorably affect overall maternal and fetal health.[31] A pragmatic approach may be to avoid routine prophylactic transfusions for an uncomplicated pregnancy, but to consider this option for women who develop severe SCD complications[29,32,33] or who are known to be at high risk for vasoocclusive events.

A multicenter study of pregnant patients with SCD in the United Kingdom investigated the effects of prophylactic blood transfusion on maternal and fetal outcomes and recommended exchange transfusions in all females with homozygous SCD beginning at 28 weeks of gestation to reduce the risk of maternal complications in the third trimester and puerperium. However, earlier prophylactic blood transfusion programs can be beneficial in females with poor obstetric and hematologic histories.[28]

Some studies have shown that the use of prophylactic RBCX in pregnancy can be effective and well tolerated by the mother to be as well as the fetuses.[31,34,35] In particular, this procedure may lead to maternal benefits, such as a reduced number and duration of hospital admissions, a reduction in the number of simple top-up transfusions, and less need for other supportive therapy.[31,35] Neonatal advantages are also described, since it has been proven that the number of preterm deliveries, the prevalence of low-birthweight fetuses, and the perinatal death rate are significantly lower in children of routinely transfused SCD patients.[31]

Our study patients had end organ failures before pregnancy and they were admitted to hospital several times due to causes like painful vasoocclusive crises (n = 24), recurrent infections (n = 20), acute chest syndrome (n = 5), leg ulcers (n = 6), hepatic necrosis (n = 1), neurologic events (n = 2), and bone necrosis (n = 2) so they had undergone RBCX procedures. Our previous clinic experience also shows that automated RBCX is an effective and safe procedure in patients with SCD.[24,36-38] Considering the aforementioned issues, we established a policy to perform RBCX for management of SCD patients during pregnancy. We performed 39 prophylactic RBCX procedures in 24 pregnant SCD patients in the second and third trimesters. Four patients who experienced vasoocclusive crisis in the first trimester and one patient who experienced vasoocclusive crisis in the third trimester received RBCX for treatment. While four out of five patients who experienced vasoocclusive crisis and who did not receive RBCX were lost in the control group, in the study group, four patients who experienced vasoocclusive crisis in the first trimester recovered from crisis as they underwent therapeutic RBCX procedure. These four patients in the study group did not experience vasoocclusive crisis during the second and the third trimesters of pregnancy as they had undergone prophylactic RBCX procedure. It should be stated that none of the patients who underwent RBCX procedure in the second and third trimesters experienced vasoocclusive crisis, whereas four out of five patients in the control group who experienced vasoocclusive crises died as they could not undergo RBCX procedure.

Maternal mortality, as well as the incidence of cesarean section, preterm labor, and pregnancy morbidity, is higher among females with SCD. More than 50% of obstetric patients with SCD will have a pain crisis during pregnancy, and the management of these can be challenging.[39] In our study, there were no crises during pregnancy among the SCD patients who underwent prophylactic RBCX procedures. Koshy and colleagues[29] showed that prophylactic transfusion significantly reduced the incidence of painful crisis of SCD and substantially reduced the cumulative incidence of other complications in pregnant women during gravidity. We performed RBCX procedures in four patients with an indication for vasoocclusive crisis during pregnancy. These patients completed their pregnancies without any other problems. There was no fetal, neonatal, or maternal morbidity. These results establish the RBCX procedure as a flexible and useful means of managing gravid patients with sickle hemoglobinopathies.

Our study has some limitations. First is the small number of patients in control group. Second is the missing data in control group as records of another institution had to be used for analysis. For example, we could not access amniotic fluid L/S ratio, direct or IAT results, cord blood pH, and APGAR score records in some of the patients in the control group. For this reason we could not compare these variables statistically between the two groups. Nevertheless, we may conclude that RBCX procedure during pregnancy is favorable because while four patients in control group were lost, there were no deaths in the study group and also, while there was one intrauterine loss in the control group, no intrauterine losses occurred in the study group. However, it should be stated that peripartum and neonatal complications did not occur in patients in the control group who achieved term. In terms of fetal complications during the pregnancy and even after the delivery, there was no significance between study and control groups in terms of fetal complications. However, we observed significantly higher maternal complication rates in the control group. One patient in the control group who developed vasoocclusive crisis could be successfully managed without RBCX procedure through

TABLE 6. The categorical variables compared between RBCX and control groups*

	Total	Study	Control	p value
Maternal complications				
No	28 (75.7)	21 (87.5)	7 (53.8)	0.042†
Yes	9 (24.3)	3 (12.5)	6 (46.2)	
Fetal complications				
No	35 (94.6)	23 (95.8)	12 (92.3)	1.000
Yes	2 (5.4)	1 (4.2)	1 (7.7)	
Maternal loss				
No	33 (89.2)	24 (100.0)	9 (69.2)	0.011†
Yes	4 (10.8)	0 (0.0)	4 (30.8)	

* Data are reported as number (%).
† p values of less than 0.05 were considered to indicate significance.

other treatment modalities including simple transfusion, hydration therapy, antibiotic, and analgesic drugs.

Four complications were experienced in a total of 43 RBCX procedures. A minimal or mild allergic reaction was observed and treated using medications; no fever was observed. We attempted to avoid procedure-related complications by using leukoreduced cell suspensions and by achieving a postapheresis Hct value that was identical to the steady-state value. No technical problems related to cell separators were noted, so we may conclude that RBCX is a safe procedure in pregnant women due to low, tolerable, and manageable procedure-related complication rates.

The timing of delivery in pregnant SCD has not been assessed in randomized controlled trials. Observational studies show increased perinatal mortality particularly during late pregnancy, and there is also an increased risk of complications such as preeclampsia, abruption, and acute sickle pain. Most women will go into spontaneous labor, and vaginal delivery is the recommended mode of delivery.[13,21,32] Nevertheless, the rate of cesarean section was high in our study group (22 patients, 91.6%) and the control group (five patients, 62.5%). There were no surgical and medical complications during or after cesarean section.

Pregnant females with SCD have an increased risk of maternal and perinatal mortality and morbidity, which can be reduced by effective multidisciplinary care throughout pregnancy. Preconceptual optimization of SCD is advised, including screening for chronic disease complications and medication review. Regular antenatal review is essential and ultrasound monitoring of fetal growth, at least four times per week, beginning at 24 weeks, is recommended.[14,40-42] Blood should be transfused for pregnant females with acute anemia, acute stroke, or acute chest syndrome, but the role of prophylactic blood transfusion is not clear and further trials are necessary.

Olujohungbe and coworkers[43] reported alloimmunization rates as 8% to 72% in multiple transfused patients with SCD. This ratio was found as 16.6% in our study and this result was comparable with the literature. Although our study has put forward the fact that prophylactic RBCX is a safe and reliable method in pregnant women with SCD, we recommend close monitorization of these patients for alloimmunization.

Pregnant patients with SCD require close surveillance by multidisciplinary teams, which should include hematologists, obstetricians, anesthetists, and pediatricians who are experienced in the management of this disorder. Our team manages adult sickle cell patients and has great experience as we have been performing RBCX procedure for more than 10 years to treat severe cases of SCD.[24,36-38]

In conclusion, our study demonstrates that prophylactic RBCX during pregnancy is a feasible and safe procedure for prevention of HbS-associated complications in patients with SCD. Although these results were favorable, further randomized multicenter studies are required to compare prophylactic RBCX and other treatment modalities in gravid sickle cell patients.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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