PERINATAL JOURNAL

Original Article

Perinatal Journal 2021;29(3):210–216

Conditions that increase the risk of cesarean-related blood transfusions: a single-center cohort study

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Abstract

Objective: This study aimed to define the conditions that increase the possibility of receiving a blood transfusion in patients who had a cesarean section.

Methods: This study was conducted between January 2016 – May 2020 in a university hospital located in Konya, Turkey. Pregnant women undergoing cesarean section were included. Of 4303 eligible patients, 188 women were the transfused group and 4115 women were the non-transfused group. Logistic regression analysis was performed for potential confounding factors.

Results: A total of 4303 eligible patients were evaluated in this study. There were 4115 patients (95.6%) in the non-transfused group. The transfused group consisted of 188 patients (4.4%). The probability of transfusion was higher in pregnant women with placenta previa, placenta accreta spectrum, thrombocytopenia, preoperative anemia, macrosomia above 4500 g, and multiple gestations [adjusted OR values (95% CI); 10.58 (range 4.75–23.57), 7.75 (range 3.22–18.61), 7.85 (range 3.46–17.79), 5.71 (range 4.21–7.74), 4.22 (range 1.21-14.67) and 2.10 (range 1.18-3.72), respectively]. There was no increase in the possibility of transfusion in 4000–4500 gram macrosomia, uterine fibroids, preeclampsia, premature rupture of membranes, previous cesarean sections and gestational diabetes mellitus.

Conclusion: Placenta previa, placenta accreta spectrum, thrombocytopenia, preoperative anemia, macrosomia above 4500 g and multiple gestations increase the possibility of transfusion. Perioperative blood preparation is vital in such patients. Prevention of anemia during pregnancy is critical in reducing transfusions.

Keywords: Blood transfusion, cesarean section, peripartum hemorrhage, postpartum hemorrhage.

Özet: Sezaryen ile ilişkili kan nakli riskini artıran durumlar: tek merkezli kohort çalışması

Amaç: Bu çalışma, sezaryen doğum yapan hastalarda kan nakli olma olasılığını artıran durumları tanımlamayı amaçlamaktadır.

Yöntem: Çalışma, Konya'da bulunan bir üniversite hastanesinde Ocak 2016 ve Mayıs 2020 tarihleri arasında gerçekleştirildi. Çalışmaya sezaryen doğum yapan gebeler dahil edildi. Uygun 4303 hastanın 188'i nakil grubunda iken 4115'i nakil olmayan grupta idi. Potansiyel karıştırıcı faktörler için lojistik regresyon analizi yapıldı.

Bulgular: Bu çalışmada toplam 4303 uygun hasta değerlendirildi. Nakil olmayan grupta 4115 (%95.6) hasta yer aldı. Nakil grubu ise 188 (%4.4) hastadan oluşmaktaydı. Nakil olasılığı; plasenta previa, plasenta akreta spektrumu, trombositopeni, preoperatif anemi, 4500 gramın üzerinde makrozomi ve çoğul gebeliği olan gebelerde daha yüksekti [düzeltilmiş OR değerleri (%95 CI) sırasıyla 10.58 (aralık: 4.75–23.57), 7.75 (aralık: 3.22–18.61), 7.85 (aralık: 3.46–17.79), 5.71 (aralık: 4.21–7.74), 4.22 (aralık: 1.21-14.67) ve 2.10 (aralık: 1.18-3.72)]. Makrozomi seviyesi 4000–4500 gram arasında olan, uterin fibroid, preeklampsi, erken membran rüptürü, daha önce sezaryen geçmişi ve gestasyonel diabetes mellitus olan hastalarda nakil olasılığında artış olmadı.

Sonuç: Plasenta previa, plasenta akreta spektrum, trombositopeni, preoperatif anemi, 4500 gramın üzerinde makrozomi ve çoğul gebelikler, nakil olasılığını artırmaktadır. Bu tür hastalarda perioperatif kan hazırlığı hayati öneme sahiptir. Nakil olasılığını azaltmak için gebelik esnasında aneminin önlenmesi çok önemlidir.

Anahtar sözcükler: Kan nakli, sezaryen, peripartum hemoraji, postpartum hemoraji.

Introduction

Obstetric hemorrhage is still one of the most important causes of morbidity and mortality in women of reproductive age.[1] Cesarean section alone is considered an important reason for this.[2] Cesarean rates are increasing all over the world.[3] In peripartum hemorrhage, the condition of the mother can deteriorate rapidly, and many complications, including maternal death, may occur if blood products are not available at the time of need. Some studies have shown that conditions such as placen-

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e-mail: muratisikalan@gmail.com / **Received:** October 24, 2021; **Accepted:** November 6, 2021

How to cite this article: Işıkalan MM, Özkaya EB, Özkaya B, Şengül N, Ferlibaş E, Acar A. Conditions that increase the risk of cesarean-related blood transfusions: a single-center cohort study. Perinatal Journal 2021;29(3):210–216. doi:10.2399/prn.21.0293006

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tal anomalies and preoperative maternal anemia increase the possibility of blood transfusion in cesarean operations.[4–7] There is inconsistent information in the literature as to whether conditions such as the number of previous cesarean sections, multiple pregnancies, macrosomia and uterine fibroids increase the possibility of transfusion. However, there are a limited number of studies evaluating blood transfusion risk in cesarean operations.

There is still no consensus on which patients should be prepared for a blood transfusion. Preoperative blood transfusion preparation is done for all patients scheduled for cesarean surgery in many centers.[8,9] However, there are still some difficulties in obtaining blood and blood products in many parts of the world. On the other hand, when the increasing cesarean rates are taken into account, unnecessary blood preparation will lead to both a decrease in blood stocks and an increase in costs.

The aim in this study was to evaluate the conditions that increase the possibility of receiving a blood transfusion in patients who had a cesarean section in a tertiary center. The evaluation of factors that are not known preoperatively were excluded from the scope of this study (adhesion, atony, T-shaped incision, etc.).

Methods

This study was conducted in the province of Konya, Turkey at a University hospital, where the complicated cases out of 5000 births per year were collected. The study was approved by the University Ethics Committee (Decision no: 2020/2808) and conducted according to Helsinki Declaration and good clinical practice. All births between January 2016 and May 2020 were analyzed in the electronic database. All patients who gave birth before 24 weeks, those who gave birth vaginally and those whose data was incomplete were excluded. In addition, 3 patients pregnant with twins one of which was a normal vaginal delivery and the other by cesarean section were excluded from the study.

Gestational age was calculated based on the last menstrual date and confirmed by an early stage ultrasound at less than 12 weeks. Information such as age, body mass index (BMI), gestational week, obstetric history, preoperative and postoperative hemoglobin values and whether or not they received perioperative blood transfusion were recorded for all patients with complete blood count done at most seven days before the operation. Patients who decided to have a cesarean section at least eight hours in advance were defined as 'elective cesarean'. All other cesareans were defined as "emergency cesarean". If more than one complete blood test was performed preoperative, the values closest to the time of delivery were recorded. Anemia was defined as a hemoglobin value below 11 g/dL.[10,11] Thrombocytopenia was defined as a platelet value below 100 k/μL. Only pregnant women with uterine fibroids larger than 5 cm were included for the uterine fibroids criterion. The diagnosis of preeclampsia was made according to the criteria in the latest American College of Obstetricians and Gynecologists (ACOG) bulletin.[12]

Pregnant women with new-onset hypertension and proteinuria after 20 weeks of gestation were defined as preeclampsia. In addition, pregnant women with new-onset hypertension and end-organ damage, even without proteinuria, were also included in this group. Gestational diabetes mellitus (GDM) was diagnosed according to the criteria of the American Diabetes Association.[13] Accordingly, the diagnosis was made with one-step 75-g OGTT or two-step 100-g OGTT tests between 24–28 weeks.

Placenta previa, placenta accreta spectrum (PAS) and polyhydramnios were diagnosed with Samsung H70 (Hampshire, UK) or Voluson E8 (GE Healthcare, Chicago, IL, USA) ultrasound devices. Placenta previa was defined as the placenta covering the entire internal os. The diagnosis of PAS was based on ultrasound showing multiple placental lacunaes, disruption of the bladder line, loss of the clear zone, myometrial thinning, abnormal vascularity and placental bulge. These diagnoses were confirmed either perioperatively or pathologically.[14] Polyhydramnios was defined as the measurement of the single deepest pocket ≥8 cm.

Control hemoglobin values were measured approximately 24 hours after the cesarean section in the clinic where the study was conducted. The blood transfusion decision was made according to the patient's vital signs, perioperative estimated bleeding amount and intraoperative hemoglobin levels, or postoperative hemoglobin level below 7 g/dL. Transfusion indications were set by an anesthesiologist during the operation or by obstetricians during the postoperative period. Women who received a blood transfusion during the cesarean section or up to 24 hours postoperatively were defined as the 'transfused group'. All other patients were defined as the 'non-transfused group'.

Statistical analysis

All data were analyzed by the Statistical Package for the Social Sciences, SPSS version 23 (SPSS Inc.,

Chicago, IL, USA). The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. The chi-square test was used for the analysis of categorical data and the Student's t-test or the Mann-Whitney U test was used for continuous variables. Adjusted odds ratios and 95% confidence intervals were calculated with the logistic regression for potential confounding factors. A p-value of 0.05 was considered statistically significant.

The G* Power 3.1 program (Düsseldorf, Germany) was used for post hoc power analysis. The α error probability, effect size and power of the study were 0.05, 0.5, and 0.99, respectively.

Results

A total of 4303 eligible patients were evaluated in this study. There were 4115 patients (95.6%) in the non-transfused group. The transfused group consisted of 188 patients (4.4%) (**Fig. 1**). The amount of transfused blood ranged from 1–6 bags. The highest frequency of blood transfused was 2 (60.6%) (**Fig. 2**).

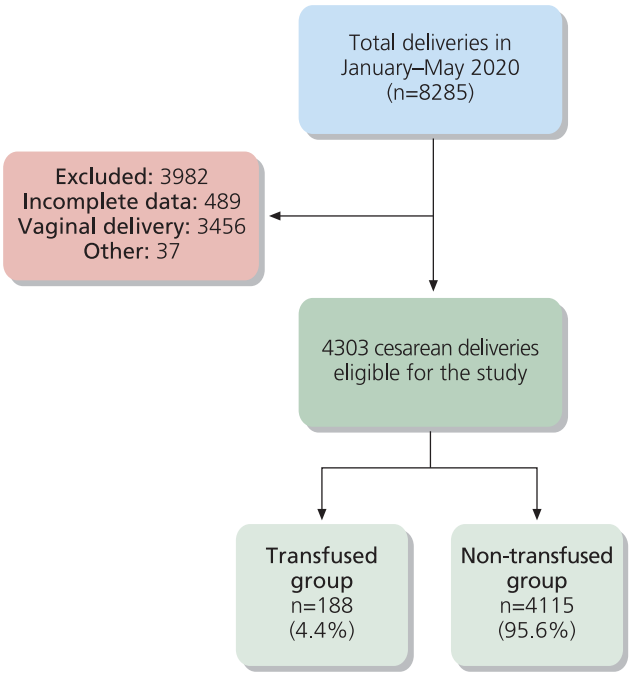

Fig. 1. Subject selection.

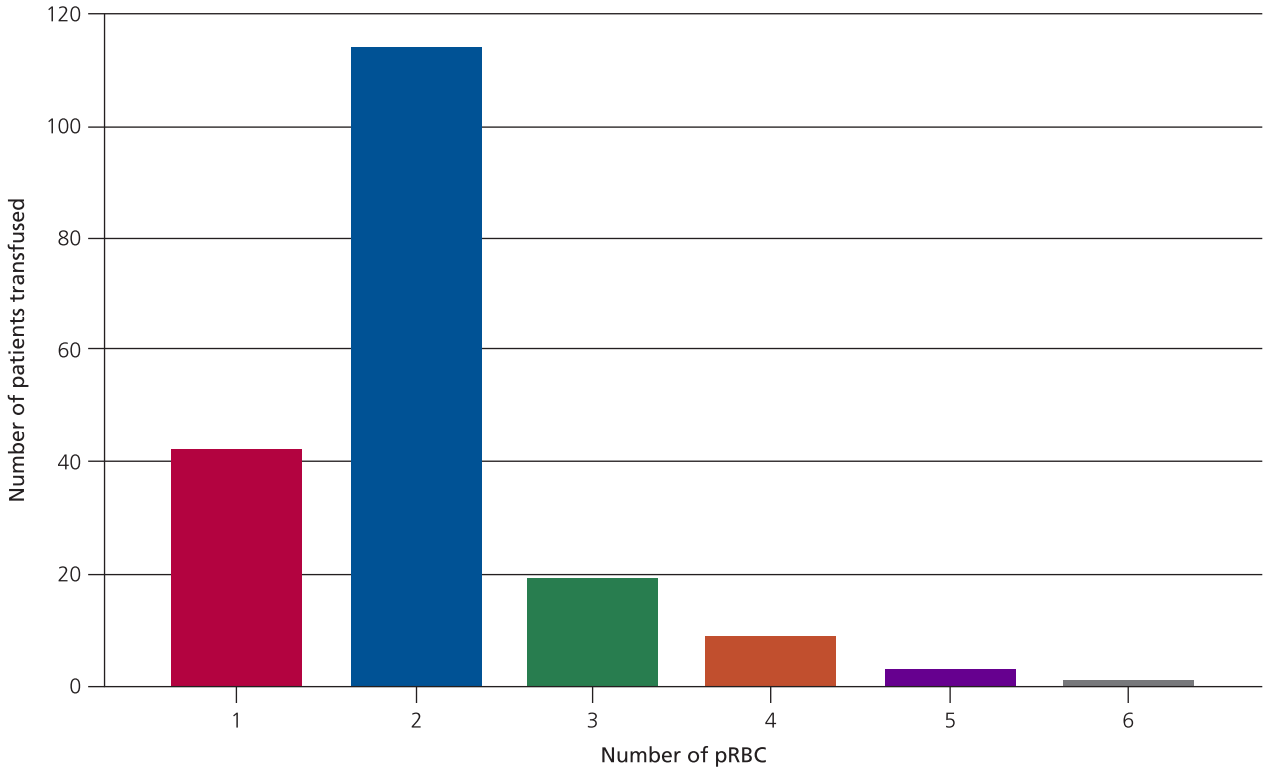

Fig. 2. Distribution of transfused blood packs (**pRBC:** packed red blood cell).

The transfused group had a lower average age (29.0±6.0 vs 27.9±6.0, p=0.007). In addition, multiple gestation rates were higher in the transfused group (3.7% vs 7.4%, p=0.010). Preoperative hemoglobin and hematocrit values were lower in the transfused group (p-values <0.001 and <0.001, respectively). The groups were homogeneously distributed in terms of BMI, gravida, parity, number of previous cesarean sections and indications (**Table 1**).

There was no significant difference between the two groups in terms of GDM, preeclampsia, PROM, emergency cesarean, general anesthesia and birth weight. In the transfused group, the rates of placenta previa, PAS, ablatio placenta and babies over 4500 g were higher (p-values <0.001, <0.001, <0.001, and 0.043, respectively). Pregnant women in the transfused group gave birth in an earlier week of gestation (median value was 38.0 vs 37.6, p<0.001) (**Table 2**).

In the logistic regression analysis, the possibility of transfusion was found to be higher in placenta previa, PAS, thrombocytopenia, preoperative anemia, macrosomia over 4500 grams and multiple gestations [adjusted OR values (95% CI); 10.58 (range 4.75–23.57), 7.75 (range 3.22–18.61), 7.85 (range 3.46–17.79), 5.71 (range 4.21–7.74), 4.22 (range 1.21–14.67) and 2.10 (range 1.18–3.72), respectively]. There was no increase in the possibility of transfusion in macrosomia over 4000 grams, uterine fibroids, preeclampsia, PROM, previous cesarean sections and GDM (**Table 3**).

Discussion

This study clearly determines some of the conditions that increase the possibility to receive a blood transfusion. Preoperative anemia, placenta previa, PAS, thrombocytopenia, macrosomia more than 4500 gram and multiple gestations are indications in which we identified patients with a high risk of receiving a blood transfusion.

Cesarean-related transfusion rates vary greatly from 0.53% to 20% in different studies.[6,7,9,15] The reason for this may be factors such as the socioeconomic status of the countries where the study was conducted, anemia rates or the different orientations of physicians regarding transfusion. Transfusion attitude has been

Table 1. Baseline characteristics of the groups.

	No pRBC transfusion n=4115	pRBC transfusion n=188	p-value
Age (year)	29.0±6.0	27.9±6.0	**0.007**
BMI (kg/m²)	26.2±4.0	26.3±4.1	0.677
Gravidity	2.0 (2.0, 4.0)	2.0 (1.0, 3.7)	0.392
Parity	1 (0.0, 2.0)	1 (0.0, 2.0)	0.950
Nulliparous	1295 (31.5)	63 (33.5)	0.556
Multiple gestation	153 (3.7)	14 (7.4)	**0.010**
Number of previous cesarean sections			
Primary	2043 (49.6)	103 (54.8)	0.187
Two	1198 (29.1)	43 (22.9)	
Three	594 (14.4)	32 (17.0)	
Four or more	280 (6.8)	10 (5.3)	
Preoperative hemoglobin (g/dL)	12.4±1.2	11.1±1.5	**<0.001**
Preoperative hematocrit (%)	37.1±4.2	33.1±5.2	**<0.001**
Preoperative anemia	574 (13.9)	91 (48.4)	**<0.001**
Thrombocytopenia	24 (0.6)	8 (4.3)	**<0.001**
Indication for cesarean section			
Previous cesarean	2072 (50.4)	85 (45.2)	0.062
Previous myomectomy	3 (0.1)	1 (0.5)	
Maternal-fetal indication	1982 (48.2)	96 (51.1)	
CDMR	37 (0.9)	4 (2.1)	
Other	21 (0.5)	2 (1.1)	

BMI: body mass index; **CDMR:** cesarean delivery on maternal request; **pRBC:** packed red blood cell; **PROM:** premature rupture of membranes. Data are presented as mean ± standard deviation, median (25%, 75% interquartile range) or n (%). Significant values are shown in bold.

Table 2. Comparison of the groups in terms of obstetric outcomes.

	No transfusion n=4115	Transfusion n=188	p-value
GDM	174 (4.2)	6 (3.2)	0.627*
Polyhydramnios	179 (4.3)	7 (3.7)	0.680
Preeclampsia	378 (9.2)	18 (9.6)	0.857*
PROM	248 (6.0)	13 (6.9)	0.618*
Placenta previa	21 (0.5)	9 (4.8)	**<0.001***
PAS	21 (0.5)	7 (3.7)	**<0.001***
Ablatio placenta	8 (0.2)	4 (2.1)	**<0.001***
Gestational age at birth (week)	38.0 (24.0–41.6)	37.6 (28.3–40.6)	**<0.001†**
Emergency cesarean	1301 (31.6)	60 (31.9)	0.931*
General anesthesia	747 (18.2)	44 (23.4)	0.069*
Birth weight (g)	3140.0 (300, 5010)	3055.0 (350, 4720)	0.062†
>4000 g macrosomia	175 (4.4)	10 (5.7)	0.406
≥4500 g macrosomia‡	16 (0.4)	3 (1.7)	**0.043***

GDM: gestational diabetes mellitus; **PAS:** placenta accreta spectrum; **PROM:** premature rupture of membranes. Data are presented as mean ± standard deviation, median (min–max) or n (%). P-values were obtained by *Chi-square test and the †Mann-Whitney U. Significant values are shown in bold. ‡Multiple pregnancies excluded from the calculation.

shown to vary widely among clinicians.[16] In the present study, transfusion rates were determined as 4.4%. Preoperative anemia is one of the most important factors that increase the risk of blood transfusion and shows how important it is to combat anemia during pregnancy. In the present study, the possibility of blood transfusion increased 5.7 times in pregnant women with preoperative anemia. The Royal College of Obstetricians and Gynecologists (UK) and the French College of Gynecologists and Obstetricians recommend that the hemoglobin level in pregnant women should be 8 g/dl and above.[17] Treating preoperative anemia is one of the most important measures to reduce transfusion during cesarean operations.

It is known that platelet counts below 100 k/μL (70 k/μL according to some studies) before surgical procedures increase the risk of hemorrhage.[18,19] As expected, in the present study, the possibility of transfusion was found to be 7.8 times higher in patients with thrombocytopenia.

Table 3. Odds ratios for blood transfusion.

	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
Placenta previa	9.80 (4.42–21.70)	**<0.001**	10.58 (4.75–23.57)	**<0.001**
PAS	7.54 (3.16–17.96)	**<0.001**	7.75 (3.22–18.61)	**<0.001**
Thrombocytopenia	7.57 (3.35–17.09)	**<0.001**	7.85 (3.46–17.79)	**<0.001**
Preoperative anemia	5.78 (4.29–7.80)	**<0.001**	5.71 (4.21–7.74)	**<0.001**
>4500 g macrosomia*	4.32 (1.24–14.99)	**0.021**	4.22 (1.21–14.67)	**0.023**
Multiple gestation	2.08 (1.18–3.67)	**0.011**	2.10 (1.18–3.72)	**0.011**
>4000 g macrosomia*	1.320 (0.68–2.54)	0.408	1.380 (0.71–2.66)	0.338
Uterine fibroids	1.37 (0.49–3.81)	0.540	1.67 (0.59–4.69)	0.330
Preeclampsia	1.04 (0.63–1.72)	0.857	1.11 (0.67–1.83)	0.666
PROM	1.15 (0.65–2.04)	0.618	1.13 (0.63–2.02)	0.670
GDM	0.75 (0.23–2.39)	0.628	0.874 (0.27–2.80)	0.874
Polyhydramnios	0.85 (0.39–1.83)	0.680	0.896 (0.41–1.93)	0.780
Number of cesareans†				
2	0.71 (0.49–1.02)	0.067	0.76 (0.53–1.10)	0.155
3	1.06 (0.71–1.60)	0.750	1.02 (0.63–1.64)	0.922
≥4	0.70 (0.36–1.37)	0.307	0.71 (0.35–1.45)	0.358

*Multiple pregnancies are excluded from the calculation for the birth weight odds ratio. †Primary cesarean section is the reference group. Adjusted for: Age, nulliparity, body mass index, emergency cesarean, general anesthesia, gestational age. **GDM:** gestational diabetes mellitus; **PAS:** placenta accreta spectrum; **PROM:** premature rupture of membranes.

Multiple pregnancies are thought to be a risk factor for postpartum hemorrhage, as this is one cause for enlargement of the entire uterus.[4,5] In the present study, it was determined that the possibility of transfusion is higher in multiple pregnancies (adjusted OR=2.10; 95% CI 1.18–3.72). Since the size of the placental bed is larger in multiple pregnancies, it will not be surprising to have more bleeding even if there is no atony. However, Akinlusi et al. stated in their study that multiple gestations do not increase the possibility of receiving a blood transfusion in cesarean operations (crude OR=1.25; 95% CI 1.25–4622.06).[9] Polyhydramnios, another reason for increased uterine volume, is also a risk factor for atony. However, in the present study, an increase in the possibility of blood transfusion was not detected in pregnant women with polyhydramnios.

Another reason why uterine volume increases is macrosomia, defined as birth weight over 4000 or 4500 g, regardless of gestational age.[20] In a study, an increase in the risk of postpartum hemorrhage was found in pregnant women carrying macrosomic fetuses (OR 3.18; 95% CI 2.47–4.10),[21] so the risk of transfusion was found to be higher in cesarean deliveries of babies over 4500 grams. However, there was no increase in transfusion risk in pregnant women carrying macrosomic babies of 4000–4500 g.

There are inconsistent studies in the literature regarding the impact of increase in the number of previous cesarean sections on blood transfusion. In a study conducted by Rouse et al. in 2006, it was found that as the number of cesarean sections increased, the risk of transfusion increased.[6] In a study by Abdelazim et al., the risk of blood transfusion was found to be 4.7 times higher in pregnant women with a third cesarean section compared to pregnant women with a second cesarean section.[2] In some studies, it has been found that the increase in the number of previous cesarean sections does not increase the risk of postpartum bleeding.[15,22] In the present study, there was no evidence that the number of cesarean sections had increased the risk of transfusion. In countries with a high number of previous cesarean sections, the experience of obstetricians and the clinic's transfusion habits may be effective in these differences.

In a multicentric study, it was determined that uterine fibroids increased the risk of cesarean delivery and postpartum hemorrhage in pregnant women.[23] In some studies, an increase in the possibility of blood transfusion was found in uterine fibroids above 5 cm, where the size and location of the fibroids are determinants.[24] In the present study, there was no increase in the possibility of receiving blood transfusion when cesareans were performed on pregnant women with uterine fibroids of 5 cm or more. It is difficult to determine the risk of bleeding in pregnant women with fibroids due to many confounder factors such as the location, number of fibroids, and the distance to the incision site.

In a study in which cesarean and normal vaginal deliveries were evaluated together, the risk of peripartum blood transfusion was found to be higher in the presence of hypertension (OR=2.41; 95% CI 2.29–2.53).[25] In the current study, the transfusion rate was not increased in patients with preeclampsia. The reason for this may be that only women who gave birth by cesarean section were evaluated in the current study.

Although the fasting glucose levels of the patients who received transfusions were found to be high, there are not enough studies on this subject.[25] In our current study, it was determined that GDM did not increase the risk of blood transfusion.

The strength of this study is that it evaluated the patients who received a cesarean-related transfusion in a sufficient number of cases in terms of the many confounder factors (polyhydramnios, PROM, myoma uteri, macrosomia, etc.) in a tertiary center.

This study also has limitations. The limitations of the study are that it is single-centered, retrospective, and the patients who underwent transfusion are not sub-grouped and analyzed according to the amount transfused. It is also known that the experience of the surgeon plays a role in bleeding. Therefore, the possible confounder effect of surgeries performed by different teams can be considered among the limitations.[26]

Conclusion

In conclusion, the risk of blood transfusion in cesarean operations varies greatly between different countries. Pregnant women with placenta previa, PAS, thrombocytopenia, preoperative anemia, >4500 g of macrosomia and multiple gestations should be prepared for blood transfusion before a cesarean operation. Tackling anemia during pregnancy will decrease cesarean-related transfusion rates.

Funding: This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Compliance with Ethical Standards: The authors stated that the standards regarding research and publication ethics,

the Personal Data Protection Law and the copyright regulations applicable to intellectual and artistic works are complied with and there is no conflict of interest.

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