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Risk Factors for Blood Transfusion in Women with Placenta Previa Undergoing Cesarean Delivery: A Retrospective Case-Control Study

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ABSTRACT

Background: Hemorrhage is a leading cause of maternal death. Placenta previa increases risk of massive bleeding, requires massive blood transfusion, and increases incidence of hysterectomy.

Objective: To identify risk factors for blood transfusion in Thai women with placenta previa undergoing cesarean section.

Methods: This was a retrospective case-control study of patients who had placenta previa and underwent cesarean section during January 2002 to December 2011. A total of 885 singleton pregnancies with placenta previa who delivered by cesarean section after 24 weeks' gestation were analyzed. Patients with placenta adherence were not included.

Results: Of 885 patients studied, 166 patients (18.8%) received blood transfusion. Independent risk factors (odds ratio (OR); 95% confidence interval (CI) for transfusion were preoperative anemia (OR 2.8; 1.8-4.37), history of uterine curettage (OR 1.82; 1.08-3.05), previous cesarean section (OR 2.61; 1.52-4.48), complete placenta previa (OR 3.03; 1.96-4.68), general anesthesia (OR 3.8; 2.53-5.72), and after-hours surgery (OR 1.6; 1.06-2.42). **Conclusion:** Incidence of blood transfusion in women with placenta previa was 18.8%. Risk factors for blood transfusion were preoperative anemia, history of uterine curettage and/or cesarean section, complete placenta previa, general anesthesia, and after-hours surgery. Identification of these risk factors may alert practitioners to undertake preoperative precautions to avoid massive bleeding.

Keywords: Blood transfusion, cesarean section, placenta previa, risk factors

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INTRODUCTION

emorrhage is a leading cause of maternal death, particularly in developing countries.¹ Placenta previa is one of the leading causes of obstetric hemorrhage.² Although the exact causes of placenta previa remain unknown, associated risk factors include advanced maternal age, multiparity, previous cesarean section, abortion, smoking, and cocaine use during pregnancy.³

Pregnancy complicated with placenta previa increases risk of massive blood loss, blood transfusion and hysterectomy.⁴⁻⁶ Placenta previa also increases neonatal complications such as prematurity, birth asphyxia, intensive care admission and death.⁷ Rate of transfusion during and/ or after delivery increases from 1% in uncomplicated cesarean section cases to 27.7% in cesarean section cases involving placenta previa.⁸

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The aim of this study was to identify risk factors for blood transfusion in Thai women with placenta previa undergoing cesarean section. Identification of the risk factors for blood transfusion associated with cesarean section complicated by placenta previa may help to establish and/or improve standardized management protocols for these patients.

MATERIALS AND METHODS

After receiving study protocol approval from the Siriraj Institutional Review Board (SIRB), we conducted a retrospective chart review of cases that sought obstetric care at Siriraj Hospital during January 2002 to December 2011. Inclusion criteria included: singleton pregnancy with placenta previa and delivery by cesarean section at 24 weeks' gestation or more. Exclusion criteria included: placenta adherence, gestational age <24 weeks, and incomplete medical information.

Data were obtained from hospital database patient records. Diagnostic information in our hospital database is coded using the International Classification of Diseases (ICD-10). Information regarding therapeutic measures, such as operative procedures and blood transfusion, is coded using ICD-9-CM (clinical modification). Patients that received blood transfusion intraoperatively and/ or up to 7 days postoperatively were designated as the blood transfusion group. Decision for blood transfusion was made by attending anesthesiologist or obstetrician, based on patient's health status, amount of blood loss, and effect of blood loss on vital signs.

Characteristics of placenta previa were recorded. Diagnosis of placenta previa was based on transabdominal or transvaginal sonography prior to delivery and/or subsequent recognition during cesarean section. Four types of placenta previa have been described, based on the relationship between placenta and internal orifice of the uterus or internal os, as follows: 1. complete placenta previa (placenta totally covering cervical os); 2. partial placenta previa (placenta partially covering cervical os); 3. marginal placenta previa (lower edge of placenta reaches internal os, but does not cover it); and, 4. low-lying placenta (placenta positioned in lower uterine segment, but lower edge does not reach internal os).

Baseline maternal characteristics, age, body mass index (BMI), gestational age at delivery, preoperative hematocrit, associated morbidity, obstetric history and grading of placenta previa were recorded. Recorded maternal outcome factors included amount of intraoperative blood loss, blood transfusion or not, choice of anesthesia, type of surgical procedure, and length of hospital stay. Recorded neonatal outcome factors included birth weight, preterm birth (<37 weeks), Apgar score, intensive care admission and neonatal death.

Potential risk factors for blood transfusion were selected according to previous studies, as follows: maternal age, parity, history of cervical dilatation and curettage, previous cesarean section, anemia (hemoglobin <11 mg/dl), antepartum hemorrhage (hemorrhage that occurred from 22 weeks' gestation to cesarean section), type of placenta previa (complete or in complete, to include partialis, marginalis, and low-lying), placenta position, choice of anesthesia, time of surgery (normal hours; 9 am to 4 pm, Monday through Friday or after-hours; outside normal service hours and public holidays), and urgency of surgery.^{6,9,10}

Statistical analysis

Data analysis was performed using SPSS version 17 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics are presented as mean \pm standard deviation (SD), median (25th to 75th percentile) or number (%). The χ^2 , Fisher's exact test, and t-tests were used to analyze comparative data. Univariate predictors of blood transfusion were analyzed by chi-square test and presented as odds ratio (OR) and 95% confidence interval (CI). Multivariable analysis by multiple logistic regressions was applied, with results displayed as adjusted OR and 95% CI. A p-value <0.05 was considered statistically significant.

RESULTS

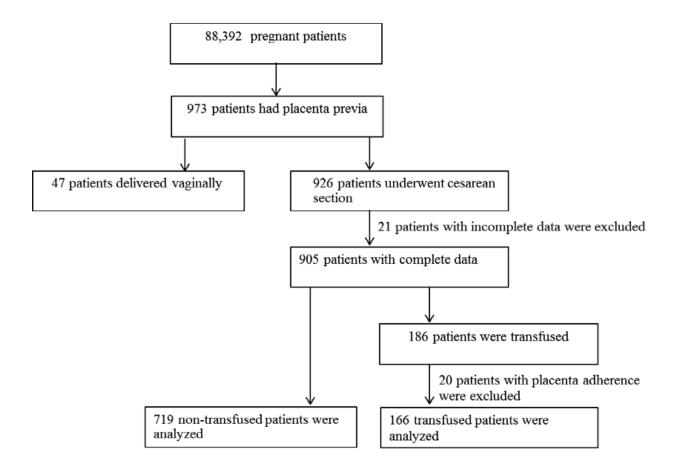
Out of 88,392 patients who delivered at our hospital during the 10-year study period, 973 (1.1%) were diagnosed with placenta previa. Out of the 973 placenta previa patients, 926 (95%) underwent caesarean delivery and 47 patients (5%) delivered vaginally. Of the 926 patients who delivered by caesarean section, 186 (18.8%) were transfused. However, 20 transfusion patients who had placenta adherence were excluded from analysis. Finally, 166 transfused and 719 nontransfused patients were evaluated, as shown in the flow chart diagram below.

Maternal characteristics are shown in Table 1. Transfused women had significantly higher multiparity (p<0.001), more frequent history of abortion (p= 0.018), and placenta previa totalis (p<0.001). Transfused patients also had lower gestational age at delivery and a lower preoperative hematocrit (p<0.001). There were no significant differences in age, BMI, or associated medical comorbidities.

Surgical procedure and maternal and neonatal outcomes are summarized in Table 2. Patients with transfusion had a higher rate of general anesthesia (p<0.001) and surgical complications (p<0.001), a higher amount of blood loss (p<0.001), and longer hospital stays (p=0.025). Of

166 transfused patients, 110(66.3%), 27(16.3%), and 29 (17.4%) patients received intraoperative, postoperative and both intra and postoperative blood transfusion, respectively. In patients with intraoperative transfusion, 76 (69%) had severe hemorrhage, with 17 (15.5%) reported as being hemodynamically unstable. Dropping hematocrit was the reason for postoperative transfusion in 96.3% of patients. Transfused patients received 2.12 ± 1.56 (mean \pm SD) units of packed red cells. Mean hematocrit was $25.2 \pm 4.2\%$ pre-transfusion (74 data) and $28 \pm 4\%$ post-transfusion (160 data). Of transfused patients, 122 (76.3%) had hematocrit levels $\leq 30\%$. Fresh frozen plasma and platelets were given to 7.8% and 3.6% of transfused patients, respectively. Newborns of mothers that received transfusion during delivery compared to newborns of mothers that did not receive transfusion had significantly lower birth weight and Apgar score and a higher rate of preterm birth, intensive care admission, and death.

Risk factors for blood transfusion are shown in Table 3. Variables found to be statistically significant in univariate analysis were further



	Total	No transfusion	Transfusion	p-value
	(N=885)	(N=719)	(N=166)	
Age (year)	32.07 ± 5.20	32.14 ± 5.07	31.77 ± 5.69	0.41
Gestational age (week)	36.49 ± 2.83	36.83 ± 2.50	34.99 ± 3.59	< 0.001
BMI (kg/m ²)	27.07 ± 3.62	27.14 ± 3.59	26.74 ± 3.73	0.20
Preop-hematocrit (%)	35.09 ± 4.04	35.60 ± 3.79	32.86 ± 4.35	< 0.001
Preop-problems				
Diabetes	27 (3.1%)	21 (2.9%)	6 (3.6%)	0.64
Chronic hypertension	8 (0.9%)	6 (0.8%)	2 (1.2%)	0.57
Obstetric history				
Gravidity				
1	368 (41.6%)	318 (44.2%)	50 (30.1%)	< 0.001
2	293 (33.1%)	241 (33.5%)	52 (31.3%)	
≥3	224 (25.3%)	160 (22.3%)	64 (38.6%)	
Abortion				
0	666 (75.3%)	548 (76.2%)	118 (71.1%)	0.018
1	161 (18.2%)	132 (18.4%)	29 (17.5%)	
≥2	58 (6.6%)	39 (5.4%)	19 (11.4%)	
Placenta grading				
Total	476 (53.8%)	348 (48.4%)	128 (77.1%)	< 0.001
Partial	54 (6.1%)	46 (6.4%)	8 (4.8%)	
Marginal	122 (13.8%)	108 (15.0%)	14 (8.4%)	
Low lying	233 (26.3%)	217 (30.2%)	16 (9.6%)	

TABLE 1. Baseline maternal characteristics.

Values are presented as mean \pm S.D.; frequencies (%)

analyzed using multiple logistic regressions. Independent variables associated with blood transfusion were preoperative anemia (odds ratio (OR): 2.8; 95% confidence interval (CI): 1.8-4.37), history of uterine curettage (OR: 1.82; 95%CI: 1.08-3.05), previous cesarean section (OR: 2.61; 95%CI: 1.52-4.48), complete placenta previa (OR: 3.03; 95%CI: 1.96-4.68), general anesthesia (OR: 3.8; 95%CI: 2.53-5.72) and after-hours surgery (OR: 1.6; 95%CI: 1.06-2.42).

DISCUSSION

The incidence of placenta previa continues to increase as a result of a variety of contributing factors. Moreover, the Asian race has the highest prevalence of placenta previa. The incidence of placenta previa in our study was 1.1%, which is consistent with previous reports.^{9,11-13} Compared to our result of 18.8% transfusions in patients with placenta previa, Boyle, et al.¹² reported a transfusion incidence of 28.9%. However, 16.3% of their patients had complex procedures, such as hysterectomy and/or arterial ligation, as compared to only 3.5% of our patients.

Previously reported risk factors for blood transfusion in patients with placenta previa include advanced maternal age and obstetric history, such as multiparity, previous cesarean section, dilatation and curettage, and location and type of placenta.^{6,9,10,14} We found maternal age >34 years not to be an independent risk factor for blood transfusion, which contrasted with the results of Oya, et al.⁹ Though blood transfusion was not specified, Ohkuchi, et al,¹⁵ (analyzing data from 10,053 cases) reported that maternal age ≥35 years was an independent risk factor for over-average blood loss during parturition.

Our study identified an association between previous cesarean section in patients with placenta

	Total	Non-transfusion gr	Transfusion gr	p-value
	(N=885)	(N=719)	(N=166)	
Choice of anesthesia				
General anesthesia	292 (33.0%)	183 (25.5%)	109 (65.7%)	< 0.001
Regional anesthesia				
Spinal	585 (66.1%)	528 (73.4%)	57 (34.3%)	
Epidural	8 (0.9%)	8 (1.1%)	0 (0 %)	
Surgery				
CS alone	862 (97.4%)	718 (99.9%)	144 (86.7%)	< 0.001
CS with hysterectomy	18 (2.0%)	0 (0%)	18 (10.9%)	
CS with arterial balloon	1 (0.1%)	1 (0.1%)	0 (0%)	
alone or with ligation				
CS with arterial ligation alo	one $4(0.5\%)$	0 (0%)	4 (2.4%)	
Blood loss (ml)	701.07 ± 579.25	532.27 ± 240.45	1432.23 ± 940.20	< 0.001
Maternal hospital stay (day)	6.87 ± 6.48 (2,72)	$6.59 \pm 6.05 \ (2,72)$	8.08 ± 7.98 (2,51)	0.025
Birth weight (g)	2826.07 ± 608.40	2897.69 ± 557.79	2515.84 ± 714.16	< 0.001
Birth weight <2,500 g	221 (25.0%)	149 (20.7%)	72 (43.4%)	< 0.001
Apgar score				
1 minute	7.82 ± 2.22	8.20 ± 1.81	6.18 ± 2.98	< 0.001
5 minutes	9.43 ± 1.57	9.63 ± 1.25	8.59 ± 2.35	< 0.001
Apgar 5 minutes ≤7	50 (5.6%)	20 (2.8%)	30 (18.1%)	< 0.001
NICU admission	124 (14.0%)	62 (8.6%)	62 (37.3%)	< 0.001
Preterm birth <37 weeks	308 (34.8%)	219 (30.5%)	89 (53.6%)	< 0.001
Fetal or neonatal death	17 (1.9%)	9 (1.3%)	8 (4.8%)	< 0.001

TABLE 2. Procedures	, maternal	and neonatal	outcomes.
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CS, Cesarean section; NICU, Neonatal Intensive Care Unit, Values are presented as mean ± S.D. (min, max); frequencies (%)

previa and risk of blood transfusion, which corresponded with results reported by Hasegawa, et al,¹⁰ who found that previous cesarean section was often associated with massive bleeding (>2,500 ml) and consecutive transfusion. By contrast, Oya, et al,⁹ found that history of two or more dilatation and curettage procedures, not cesarean sections, was associated with perioperative need for transfusion. We also observed a correlation between dilatation and curettage history and blood transfusion, but the number of patients was too small for analysis. Interestingly, we found multiparity to be associated with increased risk of transfusion, but the correlation was found to be statistically significant only in univariate analysis, but not in multivariable analysis.

Ultrasound examination provides useful information in patients with placenta previa, such as identifying the presence of sponge-like cervical wall (five or more hypo echogenic areas >5 mm in diameter), which is a risk factor for massive bleeding during cesarean section in cases of placenta previa.¹⁰ We found that complete placenta previa was an independent risk factor for blood transfusion. In contrast to our findings, Jang, et al,⁶ reported that anterior placental location was associated with significant blood loss (>1,000 ml), but not with massive transfusion (10 units red cells during or after surgery) and hysterectomy. In our patients, the average amount of red cell transfusion was much less at 2.12 ± 1.56 units per patient.

Placenta previa has frequently been mentioned as an important cause of antepartum bleeding, which may lead to maternal anemia^{2,11} and emergency surgery. We did not find any kind of correlation which supports that causal relationship in this study. However, anemia was found to be an independent risk factor for blood transfusion, which

	Non-transfusion gr (N=719)	Transfusion gr (N=166)	Crude OR (95%CI)	Adjusted OR (95%CI)	p-value
Age (year)					
<35	491 (68.3%)	103 (62.0%)	1	1	0.27
≥35	228 (31.7%)	63 (38.0%)	1.32 (0.93-1.87)	1.26 (0.83-1.92)	
Anemia					
No	631 (87.8%)	106 (63.9%)	1	1	< 0.001
Yes	88 (12.2%)	60 (36.1%)	4.06 (2.76-5.98)	2.80 (1.80-4.37)	
Parity					
0	399 (55.5%)	61 (36.7%)	1	1	
1	253 (35.2%)	70 (42.2%)	1.81 (1.24-2.64)	0.67 (0.40-1.13)	0.14
≥2	67 (9.3%)	35 (21.1%)	3.42 (2.09-5.58)	1.42 (0.79-2.55)	0.25
Dilatation and curetta	ge				
No	630 (87.6%)	135 (81.3%)	1	1	
Yes	89 (12.4%)	31 (18.7%)	1.63 (1.04-2.55)	1.82 (1.08-3.05)	0.02
Previous CS					
No	603 (83.9%)	115 (69.3%)	1	1	
Yes	116 (16.1%)	51 (30.7%)	2.31 (1.57-3.39)	2.61 (1.52-4.48)	0.001
Antepartum hemorrha	age				
No	408 (56.7%)	51 (30.7%)	1	1	
Yes	311 (43.3%)	115 (69.3%)	2.96 (2.06-4.25)	1.40 (0.85-2.30)	0.19
Placenta previa type					
Incomplete ^a	371 (51.6%)	38 (22.9%)	1	1	
Complete ^b	348 (48.4%)	128 (77.1%)	3.59 (2.43-5.31)	3.03 (1.96-4.68)	< 0.001
Placenta position					
Posterior	511 (71.1%)	99 (59.6%)	1	1	
Anterior	208 (28.9%)	67 (40.4%)	1.66 (1.17-2.36)	1.40 (0.92-2.13)	0.12
Anesthesia					
Regional	536 (74.5%)	57 (34.3%)	1	1	
General	183 (25.5%)	109 (65.7%)	5.60 (3.90-8.04)	3.80 (2.53-5.72)	< 0.001
Cesarean section					
Elective	382 (53.1%)	45 (27.1%)	1	1	
Emergency	337 (46.9%)	121 (72.9%)	3.05 (2.10-4.42)	1.26 (0.74-2.14)	0.40
Time of surgery					
Normal hours	474 (65.9%)	75 (45.2%)	1	1	
After-hours	245 (34.1%)	91 (54.8%)	2.35 (1.67-3.31)	1.60 (1.06-2.42)	0.03

TABLE 3. Risk factors associated with blood transfusion.

CS, Cesarean section, ^aLow-lying, marginal, partial; ^bTotal, Values are presented as frequencies (%)

is in contrast to the results of Oya, et al.⁹ Similar to Oya, et al,⁹ findings, antepartum hemorrhage and urgency of surgery were not associated with transfusion. Frederiksen, et al,¹⁶ also found that urgency of surgery did not affect risk of hemorrhage in women with placenta previa. We observed that after-hours surgery was an independent risk factor for blood transfusion. Although we have defined normal and after-hours for this study, it should be noted that normal working hours vary by facility and institution and that our finding may contradict the findings of other related reports.

In most cases, spinal anesthesia was performed on patients with lower-grade placenta previa undergoing less complex operations. Our spinal anesthesia rate of 64.6% is comparable with Boyle, et al,¹² who reported a rate of 60% in a similar population. However, Boyle, et al.¹² found no correlation between anesthesia and transfusion, which is in contrast to our findings. Hong, et al,¹⁷ reported that patients with placenta previa totalis undergoing cesarean section under general anesthesia required significantly more transfusions than patients with epidural anesthesia. This finding is consistent with the observations of Frederiksen, et al,¹⁶ that found that general anesthesia increased the need for blood transfusion in women with placenta previa.

We found the rate of preterm birth to be significantly higher in the transfusion group. Preterm maternal hemorrhage has been reported to lead to increased incidence of preterm delivery and subsequent unfavorable neonatal outcomes, such as asphyxia, need for intensive care, and death.^{7,11,18,19} Although there is a large body of evidence that red cell transfusion deteriorates surgical patient outcome,²⁰ we are unclear about the reasons for the worse outcome in our transfused patients, both mother and newborn.

Our study had some inherent limitations, despite its large sample size. Due to the retrospective nature of the study, there was often insufficient information relating to transfusion-related outcome, accurate amount of blood loss, and pre-transfusion hemoglobin/hematocrit levels. Additionally, we were often not able to correlate the decision for transfusion to clearly defined criteria or to a particular doctor. However, the vast majority of parameters presented in this study (Tables 1-3) represent either factual case data or a reproducible measurement. It is for this reason that we do not ascribe any significant influence of bias. Also, our results may not be applicable to or consistent with facilities that have standardized transfusion practice. Prospective controlled trials are needed that have clearly defined transfusion "go/no go" criteria.

In summary, preoperative anemia, history of uterine curettage, previous caesarean section, complete placenta previa, general anesthesia, and after-hours surgery are risk factors for blood transfusion in Thai women with placenta previa undergoing caesarean section. In patients with these preoperative risk factors, a multidisciplinary approach is recommended to avoid excessive bleeding and the resulting need for blood transfusion.

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Conflict of Interest Declaration

The authors hereby declare no personal or professional conflicts of interest regarding any aspect of this study.

What is already known on this topic?

Pregnancy complicated with placenta previa increases risk of massive blood loss, blood transfusion, and hysterectomy. Placenta previa also increases neonatal complications, such as prematurity, birth asphyxia, intensive care admission, and death. Risk factors previously reported for blood transfusion included advanced maternal age, obstetric history such as multiparity, previous cesarean section, dilatation and curettage, and placenta at anterior position.

What this study adds?

In this study, the incidence of placenta previa and blood transfusion were 1.1% and 18.8%, respectively. Additional risk factors for blood transfusion included anemia (hemoglobin <11 mg/dl), antepartum hemorrhage (hemorrhage that occurred from 22 weeks' gestation to cesarean section), and placenta previa totalis.

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