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Risk Factors for Peripartum Blood Transfusion in Women with Placenta Previa: A Retrospective Analysis

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Abstract

Background: The incidence of placenta previa has been increasing. It is of a great importance to determine the clinical risk factors for peripartum blood transfusion in women with placenta previa in an effort to anticipate cases of severe hemorrhage.

Methods: A total of 129 consecutive cases of placenta previa (64 cases of complete placenta previa and 65 cases of marginal placenta previa), including 43 cases requiring blood transfusion, were retrospectively analyzed. Maternal and neonatal clinical data were examined with univariate and multivariate logistic regression analyses for potential risk factors for peripartum blood transfusion.

Results: The independent risk factors for blood transfusion were maternal age greater than 34 years (adjusted odds ratio [OR]=3.7; 95% confidence interval [CI]=1.5–7.5, $p<0.05$), history of having undergone dilatation and curettage more than once (adjusted OR=4.8; 95% CI=1.1–26.2, $p<0.05$), and complete placenta previa (adjusted OR=2.6, 95% CI=1.2–5.9, $p<0.05$). Body mass index, gravidity, parity, previous cesarean section, antepartum hemorrhage, use of tocolytic agents, gestational age at delivery, preoperative anemia, emergent surgery, birth weight, and Apgar score were not associated with the incidence of blood transfusion.

Conclusion: Risk factors for blood transfusion in women with placenta previa are advanced maternal age, repeat dilatation and curettage, and complete placenta previa. Women with placenta previa who are at risk for blood transfusion should be carefully managed with sufficient preparation for blood transfusion.

(J Nippon Med Sch 2008; 75: 146–151)

Key words: placenta previa, cesarean section, risk factors, blood loss

Introduction

Placenta previa has recently been estimated to be present in 0.28% to 2.0% of all deliveries, and its incidence has been increasing with the rate of cesarean section[1]. Placenta previa is thought to be related to endometrial atrophy, a defect caused by previous scarring or inflammation in the endometrium, resulting in abnormally low implantation of the placenta at the internal uterine os with an abundant blood supply.

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The rates of blood transfusion and cesarean hysterectomy are increased with placenta previa because of the often massive peripartum hemorrhage[2]. The volume of hemorrhage during surgery in cases of placenta previa is significantly higher than in cases of normal placental presentation, and the rate of blood transfusion is also significantly increased from 2.3% to 15%[3]. Placenta previa accreta is one of the most important risk factors for severe hemorrhage, which can be fatal. In the present study, we evaluated the incidence of and associated risk factors for peripartum blood transfusion in women with placenta previa.

Materials and Methods

A retrospective analysis was performed through the review of the medical charts of women with placenta previa who had given birth at Nippon Medical School Tama Nagayama Hospital from August 1993 through June 2007. Placenta previa was diagnosed with serial transvaginal ultrasonographic scans and confirmed within 1 week of delivery. Twin gestations were excluded. Both complete and marginal placenta previas were included. Complete placenta previa was defined as complete coverage by the placenta of the internal os, and marginal placenta previa was defined as the edge of the placenta reaching the internal os but not covering it[4]. Informed consent was obtained from each patient, and Institutional Review Board approval was granted.

The subjects were divided into two groups: patients who had received blood transfusion within 24 hours of surgery were designated as the blood transfusion group, and those who did receive blood transfusion were designated as the non-blood transfusion group. Blood transfusion was considered if the estimated volume of hemorrhage reached 30% to 40% of the blood volume (1,500–2,000 mL). The decision for transfusion was made by the attending obstetrician or anesthesiologist with consideration of the patient's health status, the duration of hemorrhage, and the effects of hemorrhage on vital signs. Maternal demographic data and neonatal outcomes were reviewed. In both groups, the following factors were examined: maternal age at the time of delivery, body mass index (BMI), gravidity, parity, previous cesarean section, history of dilatation and curettage (D&C), preoperative hemoglobin and hematocrit, type of placenta previa (complete or marginal), antepartum hemorrhage, use of tocolytic agents on the day of surgery, gestational age at delivery, mode of cesarean section (emergency or elective), total volume of blood loss, birth weight, and Apgar score at 5 minutes. Antepartum hemorrhage was defined as hemorrhage that occurred from 22 weeks' gestation to cesarean section. Tocolytic agents included prophylaxis with magnesium sulfate or ritodrine. The total volume of blood loss was defined as the total volume of hemorrhage during the 24 hours of cesarean delivery.

To examine the characteristics of both groups, such variables as maternal age at the time of delivery, BMI, gravidity, parity, preoperative laboratory data, gestational age at the time of delivery, blood loss, birth weight, and Apgar score were analyzed with Student's *t*-test.

For univariate and multivariate analyses, each variable was subdivided into 2 or 3 categories. Maternal age at delivery was divided into 3 categories: age <25 years, 25 to 34 years (reference), and >34 years. BMI was divided into 2 categories: <25 (reference) and ≥25. Gravidity was divided into 3 categories: 0 (reference), 1, and, ≥2. Parity was divided into 3 categories: 0 (reference), 1, and ≥2. A history of previous cesarean section was divided into 2 categories: a history of previous cesarean section (reference) and no history of previous cesarean section. A history of D&C was divided into 3 categories: no D&C (reference), 1 D&C, and ≥2 D&Cs. Gestational age at delivery was divided into 3 categories: <34 weeks, 34 to 36 weeks (reference), and >36 weeks. Antepartum hemorrhage was divided into 2 categories: those without hemorrhage (reference) and those with hemorrhage. Use of tocolytic agents on the day of surgery was divided into 2 categories: no treatment with tocolytic agents (reference) and treatment with tocolytic agents. The type of placenta previa was divided into 2 categories: complete placenta previa and marginal

Table 1 Characteristics of subjects

Variables	Total n=129	Blood transfusion group n=43	Non-blood transfusion group n=86	p value
Maternal age at delivery (y)	32.1 +/− 5.0	34.2 +/− 5.3	31.1 +/− 4.5	<0.001
BMI	23.6 +/− 2.6	23.9 +/− 2.3	23.3 +/− 2.7	0.3
Gravidity	1.14 +/− 1.28	1.51 +/− 1.53	0.95 +/− 1.09	0.018
Parity	0.71 +/− 0.84	0.84 +/− 0.97	0.65 +/− 0.75	0.224
Pre-operative laboratory data				
Hemoglobin (mg/dL)	10.8 +/− 1.0	10.8 +/− 1.1	10.8 +/− 0.9	0.978
Hematocrit (%)	32.4 +/− 4.2	32.4 +/− 5.2	32.5 +/− 3.6	0.955
Gestational age at delivery (w)	35.9 +/− 2.9	35.3 +/− 3.8	36.1 +/− 2.3	0.097
Blood loss (mL)	1,525 +/− 1,676	2,520 +/− 2,537	1,027 +/− 504	<0.001
Birth weight (g)	2,430 +/− 565	2,448 +/− 663	2,420 +/− 508	0.807
Apgar score	8.3 +/− 1.8	8.4 +/− 1.9	8.3 +/− 1.7	0.762

Data are expressed as mean +/ − standard deviation.

placenta previa (reference). The mode of cesarean section was divided into 2 categories: emergency and elective cesarean section (reference).

The magnitude of the univariate associations between potential risk factors and blood transfusion was quantified with the use of odds ratios (ORs). Logistic regression analysis was used to calculate ORs with 95% confidence intervals (CIs).

For multivariate analysis, the independent variables initially included were as follows: maternal age at the time of delivery, gravidity, parity, previous cesarean section, history of D&C, type of placenta previa, and mode of cesarean delivery. For the final model, all independent variables were selected with a stepwise procedure (JMP, version 4; SAS Institute, Tokyo, Japan). A probability value of <0.05 was considered to indicate statistical significance.

Results

From August 1993 through June 2007, 130 women with placenta previa gave birth at Nippon Medical School Tama Nagayama Hospital. One case of twin gestation was excluded. Consequently, 129 cases were included in the study. All deliveries were by cesarean section. The study subjects were divided into 2 groups: a blood transfusion group (n=43) and a non-blood transfusion group (n=86). The volume of blood transfused in the blood transfusion group was 1,335 ± 1,569 mL (mean ± SD). In the blood transfusion group, 7 patients with placenta previa accreta were included; these patients underwent cesarean hysterectomy under general anesthesia. The other 122 patients underwent routine cesarean section under regional anesthesia.

The characteristics of the 2 groups are shown in **Table 1**. The 2 groups differed significantly in terms of maternal age at the time of delivery, gravidity, and the total volume of blood loss but not in terms of BMI, parity, preoperative hemoglobin or hematocrit, gestational age at the time of delivery, neonatal birth weight, or Apgar score at 5 minutes.

Table 2 shows the univariate association analysis of each clinical factor with blood transfusion. Maternal age greater than 34 years, a history of 2 or more D&Cs, and complete placenta previa were risk factors for peripartum blood transfusion in patients with placenta previa.

A multivariate logistic regression model was developed with maternal age, gravidity, parity, previous cesarean sections, history of D&C, type of placenta previa, and mode of cesarean delivery. The independent variables of the final model selected by the stepwise procedure were as follows: maternal age (3 categories), history of D&C (3 categories), and type of placenta previa (2 categories). **Table 3** shows the results of multivariate logistic regression analysis. The risk factors for blood transfusion confirmed by multivariate logistic regression analysis were maternal age greater than 34 years (adjusted OR=3.7, 95% CI=1.5–7.5, $p<0.05$), history of

Table 2 Univariate association with blood transfusion

Variables	Total n=129	Blood transfusion group n=43	Non-blood transfusion group n=86	Crude OR	95% CI	p value
Maternal age at delivery (y)						
<25	8 (6.2%)	2 (25%)	6 (75%)	1.1	0.2 − 5.0	0.952
25 − 34	79 (61.2%)	19 (24.1%)	60 (75.9%)	1		Reference
>34	42 (32.6%)	22 (52.4%)	20 (47.6%)	3.4	1.6 − 7.8	0.002
BMI						
<25	98 (76%)	32 (32.7%)	66 (67.3%)	1		Reference
>24	31 (24%)	11 (35.5%)	20 (64.5%)	1.1	0.5 − 2.6	0.771
Gravidity						
0	49 (38%)	14 (28.6%)	35 (71.4%)	1		Reference
1	45 (34.9%)	12 (26.7%)	33 (73.3%)	0.9	0.4 − 2.3	0.837
>1	35 (27.1%)	17 (48.6%)	18 (51.4%)	2.4	1.0 − 5.9	0.064
Parity						
0	63 (48.8%)	21 (33.3%)	42 (66.7%)	1		Reference
1	47 (36.4%)	12 (25.5%)	35 (74.5%)	0.7	0.3 − 1.6	0.378
>1	19 (14.7%)	10 (52.6%)	9 (47.4%)	2.2	0.8 − 6.4	0.133
Previous cesarean section						
Yes	16 (12.4%)	7 (43.7%)	9 (56.3%)	1.7	0.6 − 4.8	0.349
No	113 (87.6%)	36 (31.9%)	77 (68.1%)	1		Reference
History of D&C						
0	93 (72.1%)	27 (29%)	66 (71%)	1		Reference
1	27 (20.9%)	10 (37%)	17 (63%)	1.4	0.6 − 3.5	0.429
>1	9 (7%)	6 (66.7%)	3 (33.3%)	4.8	1.2 − 24.5	0.033
Type of placenta previa						
Complete	64 (49.6%)	27 (42.2%)	37 (57.8%)	2.2	1.1 − 4.8	0.036
Marginal	65 (50.4%)	16 (24.6%)	49 (75.4%)	1		Reference
Antepartum hemorrhage						
Yes	66 (51.2%)	19 (28.8%)	47 (71.2%)	0.9	0.4 − 1.9	0.684
No	63 (48.8%)	24 (38.1%)	39 (61.9%)	1		Reference
Tocolytic agent						
Yes	55 (42.6%)	19 (34.5%)	36 (65.4%)	1.1	0.5 − 2.3	0.801
No	74 (57.4%)	24 (32.4%)	50 (67.6%)	1		Reference
Gestational age at delivery (w)						
<34	18 (14%)	7 (38.9%)	11 (61.1%)	1.2	0.4 − 3.6	0.745
34 − 36	52 (40.3%)	18 (34.6%)	34 (65.4%)	1		Reference
>36	59 (45.7%)	18 (30.5%)	41 (69.5%)	0.8	0.4 − 1.8	0.645
Mode of cesarean section						
Emergency	50 (38.8%)	17 (34%)	33 (66%)	1.1	0.5 − 2.2	0.217
Elective	79 (61.2%)	26 (32.9%)	53 (67.1%)	1		Reference

OR=odds ratio; CI=confidence interval

2 or more D&Cs (adjusted OR=4.8, 95% CI=1.1–26.2, $p<0.05$), and complete placenta previa (adjusted OR=2.6, 95% CI=1.2–5.9, $p<0.05$).

Discussion

The risk factors for excessive blood loss during cesarean section have previously been reported as a function of various maternal diseases[5,6]. The risk factors previously reported for blood transfusion associated with cesarean section for various indications, including placenta previa, are a lack of prenatal care, grand multiparity, previous cesarean section, general anesthesia, severe preoperative hematocrit less than 25%, and placenta previa[5,6]. Furthermore, although blood transfusion was not specified, risk factors for excessive blood loss during cesarean section have been reported to include

Table 3 Risk factors for blood transfusion in patient with placenta previa: Results of multivariate logistic regression analysis (n=129)

Variables	Adjusted OR	95%CI	p value
Maternal age at delivery (y)			
>34	3.7	1.5 − 7.5	0.004
History of D&C			
>1	4.8	1.1 − 26.2	0.048
Type of placenta previa			
Complete	2.6	1.2 − 5.9	0.023

OR=odds ratio; CI=confidence interval

maternal age greater than 34 years, leiomyoma, low-lying placenta, placenta previa, placental abruption, elevated BMI, and low and high birth weights[7,8].

With respect to hemorrhage and placenta previa, several studies involving ultrasonographic examination of the placenta have generated useful information about the prediction of bleeding. The central part of a placenta overlapping the internal os, a sponge-like echo in the uterine wall adjacent to the placenta[9], and a thick placental edge[10] are reported risk factors for severe hemorrhage. Tuvolic[11] has suggested that compared with incomplete placenta previa, complete placenta previa is related to a higher requirement for antepartum and postpartum blood transfusions and a higher frequency of postpartum hemorrhage and hysterectomy. In agreement with these previous reports, our results show that complete placenta previa is an independent risk factor for blood transfusion in women with placenta previa. The elevated risk of placenta previa accreta is an important risk factor for severe hemorrhage in women with a complete placenta previa. However, even in placenta previa without accreta, abundant vascularization to a broad area of the lower segment of the uterine with weak myometrial contractions after removal of the placenta may significantly increase the risk of hemorrhage.

Our study also found that maternal age greater than 34 years and a history of 2 or more D&Cs are independent risk factors for blood transfusion during cesarean section for placenta previa. Although these factors have not been identified in previous studies as risk factors for blood transfusion in women with placenta previa, maternal age and D&C have previously been reported to affect the implantation of the placenta and are known risk factors for placenta accreta[12,13]. Of the 7 women older than 34 years with placenta previa acrreta in the present study, 2 had undergone 2 or more D&Cs. In contrast, repeat cesarean section is also a well-known risk factor for placenta accreta[12], but in the present study a history of cesarean section was not significantly associated with blood transfusion.

Frederiksen et al.[14] have reported that neither elective surgery nor emergent surgery affects the risk of hemorrhage during surgery in women with placenta previa. In agreement with this previous report, our results show that emergent cesarean section is not an independent risk factor for blood transfusion in women with placenta previa. In addition, our study shows that antepartum hemorrhage is not an independent risk factor. Therefore, neither antepartum hemorrhage nor emergent surgery necessarily predict gross hemorrhage during cesarean section. Even if no hemorrhage occurs during gestation, the volume of hemorrhage during cesarean section should not be underestimated. Frederiksen et al.[14] have also reported that general anesthesia increases blood loss during cesarean section in women with placenta previa. In the present study, because general anesthesia was used only in cases of placenta previa accreta and regional anesthesia was used in other cases, the affect of anesthesia on blood transfusion was not analyzed.

Several studies have suggested the beneficial use of tocolytic agents, such as ritodrine[15] and

magnesium sulfate[16], for prolonging pregnancy in women with symptomatic placenta previa. Towers[17] have reported that third-trimester preterm tocolysis for several indications, including placenta previa, does not increase the risk of blood transfusion. In agreement with this previous report, our results suggest that the use of tocolytic agents just before cesarean section does not affect the risk of blood transfusion. Tocolytic agents can thus be used when antepartum hemorrhage occurs owing to uterine contractions in women with placenta previa without the attendant risk of blood transfusion during cesarean section.

In summary, independent risk factors for peripartum blood transfusion in women with placenta previa are advanced maternal age, repeat D&C, and complete placenta previa. Women at risk should be carefully managed with sufficient preparation for blood transfusion.

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(Received, November 12, 2007)
(Accepted, March 17, 2008)