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Risk factors of severe postpartum hemorrhage in pregnant women with placenta previa or low-lying placenta: a retrospective cohort study

Huiying Hu[1†], Liying Wang[1†], Jinsong Gao[1*], Ziyi Chen[1], Xiaoxu Chen[1], Pingping Tang[1] and Yifeng Zhong[1]

Abstract

Background The severe postpartum hemorrhage (SPPH) leads to dangerous maternal conditions, and its rate is still increasing and the trend in related risk factors is changing. Placenta-related problems remain the high-risk factor for SPPH. The object is to investigate the prevalence and the risk factors of the severe postpartum hemorrhage in pregnant women with placenta previa or low-lying placenta.

Method A retrospective analysis of pregnant women with placenta previa or low-lying placenta after 28 weeks gestation from May 2018 to May 2023 in the Peking Union Medical College Hospital was conducted. The primary outcome was severe postpartum hemorrhage defined as blood loss ≥ 1000 mL within 24 h of childbirth, or with signs or symptoms of low blood volume requiring transfusion of ≥ 4U of red blood cells. Univariate and multivariate logistic regression were used to identify potential risk factors of severe postpartum hemorrhage and receiver operating curve to evaluate the prediction performance.

Results Of the 14,964 women, 201 met the inclusive criteria. SPPH rate was 1.3% overall and 18.9% in women with placenta previa or low-lying placenta. Weight (aOR = 0.93, 95%CI 0.87–0.99), increta or percreta placenta (aOR = 7.93, 95%CI 2.53–24.77) were the risk factors. The area under the ROC curve was 0.69(95%CI 0.59–0.80) for increta or percreta placenta alone, and 0.72(95%CI 0.62–0.82) for the combination of times of cesarean sections and anterior placenta.

Conclusions Placenta accreta spectrum was the key independent risk factor of SPPH in women with placenta previa or low-lying placenta. Antenatal risk assessment of SPPH in these population is highly desirable and optimal intervention could be planned.

Keywords Placenta previa, Low-lying placenta, Severe postpartum hemorrhage, Risk factors

†Huiying Hu and Liying Wang contributed equally to this work.

*Correspondence:
Jinsong Gao
gaojingsong@pumch.cn

[1]Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, National Clinical Research Center for Obstetric and Gynecologic Diseases, No. 1 Shuaifuyuan, Dongcheng District, Beijing, China

Background

Postpartum hemorrhage (PPH) is the leading cause of maternal morbidity and mortality globally [1, 2]. Compared to normal postpartum hemorrhage, severe postpartum hemorrhage (SPPH) lead to both severe maternal and infant complications and death [3, 4]. Once severe postpartum hemorrhage is predicted accurately, prompt management may significantly improve the outcomes.

Despite all efforts, the severe postpartum hemorrhage rate is still increasing and the trend in related risk factors is changing [5]. Placenta previa remains the high-risk factor for SPPH. Several studies [6–9]have investigated the prediction model for PPH in pregnancies with placenta previa or low-lying placenta. However, all studies are at high risk of bias due to the limited sample size [5]. And the definition of SPPH varied from 1000 to 2000 ml blood loss or from 4 to 8U red blood cells transfusion. Thus, there is still a lack of reliable prediction method for the SPPH. The aim of this study is to identify the risk factors for severe postpartum hemorrhage defined by the Chinese guideline [10] in women with placenta previa or low-lying placenta and enable planned intervention to decrease SPPH.

Methods

The retrospective study was performed in women gave birth in the Peking Union Medical College Hospital from May 2018 to May 2023. The inclusive criteria were: maternal age of above 18 years, giving birth after 28 weeks of gestational, with placenta previa or low-lying placenta. Placenta previa is defined as when placenta adjacent to, reached or covered the cervical os according to the last obstetrical ultrasound assessment. It includes placenta previa (placenta completely or partially covering the cervix os) and low-lying placenta (placental edge measuring < 2 cm from the cervical os) [11].

The outcome was severe postpartum hemorrhage defined as blood loss ≥ 1000 mL within 24 h of childbirth, or with signs or symptoms of low blood volume requiring transfusion of ≥ 4U of red blood cells, regardless of the mode of delivery [10]. Placenta accreta spectrum was suspected by the ultrasound or the magnetic resonance imaging, and diagnosed by the failure of placenta detachment during delivery. PAS was classified into accreta, increta, or percreta according to increasing depth of perceived invasion within the myometrium [12].

Based on previous relevant studies and medical files, the data of the maternal characteristics, obstetric-related factors, maternal and neonatal outcomes were collected.

The maternal characteristics were: age, weight (refers to the pre-pregnancy weight), height, gravidity, parity.

The obstetric-related factors were: weight gain during pregnancy, method of conception, fetus number, hematology before delivery (hemoglobin, hematocrit, platelet count, weight blood cell), pregnant complications (hypertensive disorders of pregnancy, gestational diabetes mellitus), times of abortions, mode of abortion, gestational week of delivery, times of previous cesarean sections, type of placenta previa, main position of placenta, type of placenta accreta spectrum.

The maternal and neonatal outcomes were: mode of delivery, uterine artery embolization or ligation, hysterectomy, length of hospital stay, maternal admission to the intensive care unit, premature birth, neonatal asphyxia, neonatal admission to the intensive care unit.

Ethical approval for the study was obtained from the ethics committee of Peking Union Medical College Hospital (reference number, I-22PJ720). Written informed consent was waived due to the non-interventional retrospective nature of the study and impossibility of obtaining patient consent retrospectively.

Medians, interquartile ranges, and Mann–Whitney U test were used for data description and comparision for continuous variables; numbers, percentages and $\chi 2$ or Fisher's exact test for categorical variables. The risk factors were preliminarily analyzed by univariable analysis to explore the relationship. And the multivariate logistic regression was conducted to eliminate the potential confounders and identify the independent risk factors. Statistical software package SPSS 27.0 was used for data analyses.

Results

Study population

A total of 14,964 women gave birth in Peking Union Medical College Hospital from May 2018 to May 2023. There are 201 (1.34%) women had placenta previa or low-lying placenta and the incidence of SPPH (18.9%, 38/201) is much higher than the general population (1.3%). The characteristics and the relevant factors are summarized in Table 1. The median (IQR) maternal age was 35.5 (32.0–38.0) years, median height was 162.0 (160.0-165.0) centimeters, median weight was 59.0(54.8–62.0) kilograms, median gravidity was 2.0 (1.0–3.0) times, median hemoglobin was 119.0(111.0-127.0) g/L, median platelet count was 194.0(164.5–228.0) $*10^9$ g/L; 120 (59.7%) were nulliparous, 82 (40.8%) were preterm birth, 137(68.2%) were with placenta previa and 64(31.8%) with low-lying placenta, 51 (25.4%) were with placenta accreta spectrum and of whom 33(16.4%) with increta or percreta placenta and 18(9.0%) with accreta placenta.

The incidence of SPPH was 42.5% in women with previous cesarean sections in the context of the placenta previa or low-lying placenta, 33.9% in women with anterior-placenta, 54.5% in women with increta or percreta placenta, 73.3% in women with anterior-placenta and previous cesarean sections.

Table 1 Characteristics of the women with placenta previa

	non-SPPH (*n* = 163)	**SPPH (*n* = 38)**	***p*-value**
Height(cm)	162(160–165)	161.8(158-164.3)	0.067
Weight(kg)	59(55-62.5)	58(51.5–60)	0.046
BMI(kg/m^2)	21.9(20.5–23.9)	22.3(20.1–23.5)	0.594
Weight gain during pregnancy(kg)	11.4(8–14)	11.7(9–14)	0.541
Maternal age			
<35yares	80(49.1)	13(34.2)	0.098
≥ 35years	83(50.9)	25(65.8)	
Gravidity	2(1–3)	3(2–4)	0.010
Parity			
0	105(64.4)	15(39.5)	0.005
≥ 1	58(35.6)	23(60.5)	
Gestational weeks at delivery			
28–36 + 6 weeks	55(33.7)	27(71.1)	<0.001
≥ 37 weeks	108(66.3)	11(28.9)	
Fetus number			
1	155(95.1)	34(89.5)	0.349
2	8(4.9)	4(10.5)	
Method of conception			
Natural	113(69.3)	25(65.8)	0.672
In vitro fertilization	50(30.7)	13(34.2)	
Regular prenatal visit			
Yes	153(93.9)	36(94.7)	1.000
No	10(6.1)	2(5.3)	
Fetal position			
Head presentation	141(86.5)	29(76.3)	0.117
Non-head presentation	22(13.5)	9(23.7)	
Hematology before delivery			
Hemoglobin(g/L)	119(112–127)	122(109.5-126.8)	0.778
platelet count (*10^9/L)	197(167–232)	185(158.8-201.3)	0.126
Hematocrit(%)	35.1(33–37)	35.1(34–37)	0.764
white blood cell (*10^{12}/L)	8.2(7-9.4)	8(6.9–8.6)	0.210
Pregnant complications			
Hypertensive disorders of pregnancy	3(1.8)	1(2.6)	0.571
Gestational diabetes mellitus	33(20.2)	7(18.4)	0.800
Times of abortions	0(0–1)	1(0–2)	0.028
Type of abortion			
Surgical abortion	55(33.7)	18(47.4)	0.116
Medial abortion	14(8.6)	3(7.9)	1.000
Natural abortion	32(19.6)	13(34.2)	0.052
Times of previous cesarean sections			
0 time	140(85.9)	21(55.3)	<0.001
1 time	18(11.0)	10(26.3)	
≥ 2 times	5(3.1)	7(18.4)	
Main position of placenta			
Anterior-placenta	41(25.2)	21(55.3)	<0.001
Non-anterior placenta	122(74.8)	17(44.7)	
Type of placenta previa			
Low-lying placenta	57(35)	7(18.4)	0.049
Placenta previa	106(65)	31(81.6)	
Increta or percreta placenta	15(9.2)	18(47.4)	<0.001
Accreta placenta	13(8.0)	5(13.2)	0.489

Table 2 Risk factors for severe postpartum hemorrhage: univariate and multivariate analysis

variables	OR(95%CI)	aOR(95%CI)*
Height	0.93(0.86-1.00)	0.98(0.94–1.01)
Weight	0.95(0.90–0.99)	0.93(0.87–0.99)
Gravidity	1.30(1.05–1.60)	0.50(0.21–1.22)
Parity	2.78(1.34–5.73)	2.49(0.70–8.85)
Gestational weeks	0.21(0.10–0.45)	0.42(0.16–1.12)
Times of abortions	1.35(1.02–1.78)	2.37(0.88–6.40)
Times of previous cesarean sections	3.23(1.85–5.62)	2.58(0.83–8.05)
Hemoglobin	0.99(0.96–1.02)	1.01(0.97–1.05)
Platelet count	1.00(0.99-1.00)	1.00(0.99-1.00)
Increta placenta	1.75(0.58–5.24)	2.73(0.67–11.22)
Increta or percreta placenta	8.88(3.88–20.35)	7.93(2.53–24.77)
Anterior placenta	3.68(1.77–7.63)	1.63(0.59–4.50)
Placenta previa	2.38(0.99–5.75)	1.39(0.45–4.29)

aOR, adjusted odds ratio; OR, odds ratio

* Multivariate logistic regression model with multiple imputation including variables listed in the column

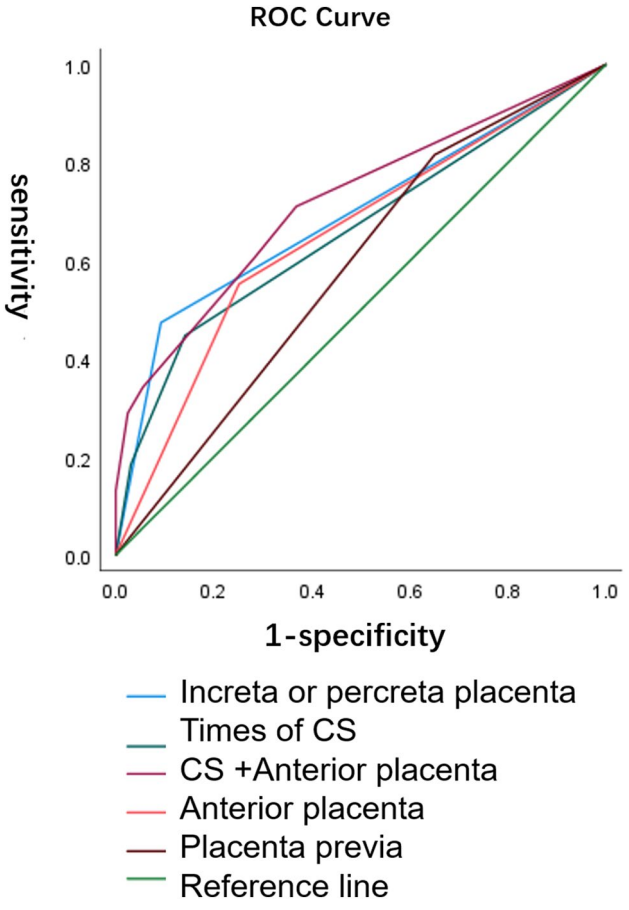

Fig. 1 ROC for times of previous cesarean sections, type of placenta previa, main position of placenta, increta or percreta placenta, combination of times of cesarean sections and anterior placenta

Table 3 Maternal outcomes

	non-SPPH (*n* = 163)	SPPH (*n* = 38)	*p*-value
Mode of delivery			
Vaginal delivery	9(5.5)	1(2.6)	0.746
Cesarean section	154(94.5)	37(97.4)	
Uterine artery embolization or ligation	1(0.6)	3(7.9)	0.022
Hysterectomy	0(0)	2(5.3)	0.035
Length of hospital stay (day)	5(4–7)	8(5-9.3)	0.013
Admission to ICU	2(1.2)	12(31.6)	<0.001

Table 4 Neonatal outcomes

	non-SPPH (*n* = 171)	SPPH (*n* = 42)	*p*-value
Birth weight(gram)	2860(2570–3150)	2575(2263.8-2912.5)	0.012
Premature birth	62(36.3)	31(73.8)	<0.001
1 min Apgar score	10(10–10)	10(9.8–10)	0.411
5 min Apgar score	10(10–10)	10(10–10)	0.386
Neonatal asphyxia	2(1.2)	2(4.8)	0.175
Admission to NICU	49(28.7)	21(50)	0.008

Risk factors of SPPH

In the univariate analysis, factors associated with a higher risk of SPPH were: weight, gravidity, parity, gestational week of delivery, times of abortion, times of previous cesarean sections, type of placenta previa, main position of placenta, increta or percreta placenta. In the multivariate analysis, the independent risk factors were increta or percreta placenta (aOR=7.93, 95%CI 2.53–24.77) and weight (aOR=0.93, 95%CI 0.87–0.99) (See Table 2).

Receiver operating characteristic curves (ROC)

The ROC curves of different factors to predict SPPH were presented in Fig. 1. The area under the ROC curve was 0.66(95%CI 0.55–0.77) for the times of previous cesarean sections, 0.58(95%CI 0.49–0.68) for type of placenta previa, 0.65(95%CI 0.55–0.75) for main position of placenta, 0.69(95%CI 0.59–0.80) for increta or percreta placenta, and 0.72(95%CI 0.62–0.82) for combination of times of cesarean sections and anterior placenta .

Maternal and neonatal outcomes

Maternal and neonatal outcomes were showed in Tables 3 and 4. Women with SPPH had higher rates of uterine artery embolization or ligation, hysterectomy, length of hospital stay and maternal admission to the intensive care unit; their babies had higher rates of premature birth, neonatal asphyxia and neonatal admission to the intensive care unit.

Discussion

The temporal most rapid increasing risk factors for SPPH are the placenta-related problems [5, 13]. Our study focused on the high-risk population, namely with

placenta previa or low-lying placenta, and investigated the risk factors for SPPH based on this context. Antenatal prediction of SPPH in these population is highly desirable because outcomes are optimized when pregnancies are transferred and deliveries occur at high level maternal care facility.

The rate and definition of SPPH varied according to different nation guidelines. Given the varied individual tolerance, the definition of blood loss ≥ 1000 mL within 24 h of childbirth, or with signs or symptoms of low blood volume requiring transfusion of ≥ 4U of red blood cells are more reliable in Chinese population. The rate of SPPH of our study is 18.9%, which is in accordance with the Asian data in the previous meta-analysis [14].

Women with placenta previa or low-lying placenta are at high risk of adverse outcomes, including PPH [15]. Compared with low-lying placenta, placenta previa have a higher risk of PPH [16, 17]. In terms of SPPH, whether low-lying placenta and placenta previa were statistically significant for SPPH is not consistent [6–9, 18]. Our study indicated that the severity of placenta previa is not the risk factor for SPPH.

The location of the placenta was studied and the anterior placenta was the risk factor for both SPPH [9] and placenta accreta spectrum [19, 20] in women with placenta previa. Our study demonstrated that the anterior placenta was risk factor in univariate analysis but not independent in multivariate analysis, which may imply that the anterior placenta may cause SPPH through placenta accreta spectrum.

The placenta accreta spectrum underwent the largest increasing change for PPH due to the increasing cesarean delivery rate in China and across the world [5, 13, 21, 22]. Consistent to previous studies [6–9], our study showed that placenta accreta spectrum was the key independent risk factor for SPPH in women with placenta previa. The risk factors for placenta accreta spectrum in our population were presented in Table S1. and further illustrate that the times of cesarean section and anterior placenta may cause SPPH by increasing the rate of placenta accreta spectrum.

However, the prenatal diagnosis of placenta accreta spectrum and placental implantation degree is complex [23, 24] and the definite diagnosis was made after delivery. And 50-66.7% of the prenatal diagnosis in China are missed [12]. Thus, we analyzed the more available major confounders, the times of cesarean section and anterior placenta, and the AUC of the combined factors was 0.72(95%CI 0.62–0.82) and it was also with moderate performance.

Weight was another independent risk factor and the definition of SPPH considered individual tolerance in our study. It indicated that pregnant women with lower body weight have lower capacity and are more prone to severe postpartum hemorrhage and blood transfusion.

Lower pre-pregnancy weight indicated that patients have poor tolerance to bleeding, making them more susceptible to hemorrhagic shock and in need of blood transfusion. Increta or percreta placenta was the key risk factor for SPPH in pregnancies with placenta previa or low-lying placenta. The times of cesarean section and anterior placenta may cause SPPH through the increasing risk of increta or percreta placenta. These risk factors may be useful to predict the high-risk population. Caution should be exercised for placental accreta spectrum and severe postpartum hemorrhage on the basis of a history of cesarean section combined with low-lying or previa placenta, since clinical detection rate of placental accreta spectrum during pregnancy is unsatisfactory. Timely referral to a qualified hospital for delivery is necessary, and more thorough screening and optimal treatment strategy could be planned to decrease the rate of the SPPH and the maternal-fetal mortality.

The main limitation of our study was that it was a retrospective study in a single center with limited patient number. And our hospital, as a tertiary hospital, received a large number of critically ill obstetric patients transferred from other hospitals in northern China. Potential recall bias might occur when the maternal characteristics (such as pre-pregnancy weight) were collected after referral. It might limit the generalizability of the findings. Secondly, some detailed imaging data were lacking for further analysis. Future large-scale cohort researches and multi-center prospective studies should be performed.

Abbreviations

PPH	postpartum hemorrhage
SPPH	severe postpartum hemorrhage
CS	cesarean section
aOR	Adjusted odds ratio
CI	Confidence interval
ROC	Receiver operating characteristic curve

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-024-06876-3.

Supplementary Material 1

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Not applicable.

Author contributions

Jinsong Gao, Huiying Hu, Liying Wang designed the study, participated in the operation, and drafted the manuscript. Liying Wang, Ziyi Chen, Xiaoxu Chen, Pingping Tang, Yifeng Zhong collected the clinical data and performed the statistical analysis. All authors read and approved the final manuscript.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Ethical approval for the study was obtained from the ethics committee of Peking Union Medical College Hospital (reference number, I-22PJ720). Written informed consent was waived due to the retrospective study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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