

Original Article

Analysis of risk factors for pernicious placenta praevia

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Abstract: Objective: To study the risk factors of placenta praevia and its influence on maternal and perinatal outcomes. Methods: a retrospective analysis of 260 cases of patients with pernicious placenta praevia (PPP) in Qilu Hospital of Shandong University and Shandong Rizhao People's Hospital from January 2012 to December 2015 was processed. Among them, 118 cases of patients with placenta attached to the uterine cesarean scar were assigned as PPP group, while the remaining 142 patients were assigned as ordinary placenta praevia (OPP) group. We selected 120 healthy pregnant women in the same period in our hospital as control group. The clinical data and perinatal outcomes of the three groups were compared. Results: the pregnancy complications and neonatal outcomes of PPP group were worse than that in OPP group and the control group ($P < 0.05$). Multivariate logistic analysis showed age (≥ 35 years old, OR: 2.263, 95.0% CI: 1.346-4.749), parity (2 times, OR: 1.826, 95.0% CI: 1.162-3.013; ≥ 3 times, OR: 4.692, 95.0% CI: 1.737-5.845), abortion (1 time, OR: 1.427, 95.0% CI: 0.723-2.136; ≥ 2 times, OR: 3.648, 95.0% CI: 1.827-5.656), previous cesarean section (≥ 2 times, OR: 2.783, 95.0% CI: 1.562-4.918) were risk factors for PPP. Conclusion: single factor analysis showed that the number of cesarean section, abortion, pregnancy number and age were the independent risk factors for R. Reasonable assessment of treatment options, timely termination of pregnancy, as well as adequate preoperative evaluation of patients for reducing complications and uterine resection ratio are necessary to effectively improve the pregnancy outcomes.

Keywords: Pernicious placenta praevia, diagnosis and treatment strategies, risk factors, pregnancy outcome

Introduction

Placenta praevia is a serious complication in late pregnancy, and also the most common cause of obstetric hemorrhage that seriously threatens the lives of mothers and infants. What is more, recent study reports that the incidence of placenta praevia is as high as 1.28% [1], and the incidence is increasing with each passing year. Moreover pernicious placenta praevia (PPP), one more severe type of placenta praevia, is defined as that the placenta is attached to the original uterine scar sites, which results in a crisis situation for patients [2].

Many studies showed that the incidence of PPP complicated with placenta implantation and refractory postpartum hemorrhage is increased with the increasing number of cesarean section, and the incidence of concurrent placenta implantation is as high as 50% [3]. For

PPP patients with cesarean section, due to endometrial damage, poor wound healing and other factors [4], the villi and the placenta are easier to invade the muscle layer and even the serous layer, which results in placenta implantation that will further lead to incomplete separation of placenta during delivering; the rupture of placental marginal sinus can result in severe bleeding during the operation, then lead to severe complications such as disseminated intravascular coagulation, hysterectomy, infection and even death. The main reasons of maternal mortality are severe blood loss (more than 2000 ml) and other complications such as ureter, bladder and bowel injury etc..

According to WHO survey, the rate of cesarean section in China is as high as 46.2% at present [5], which is significantly higher than other countries. The cesarean section and placenta related pathological pregnancy has brought us a severe challenge. So, studying risk factors of

PPP then adopting effective prevention and treatment are the keys to improve the maternal and perinatal status of PPP patients currently [6]. The previous studies cannot accurately reflect the incidence of placenta praevia and risk factors as well as its influence on pregnancy outcome [7, 8].

We analyzed the clinical data of 260 cases of placenta praevia in our hospital retrospectively, to study the risk factors of PPP and its effect on perinatal outcomes. The related factors of perinatal complications in patients with PPP were also studied to provide basis for clinical diagnosis and treatment of PPP, and the specific reports are as follows.

Materials and methods

General status

We retrospectively studied the clinical data of 260 patients diagnosed as placenta praevia from January 2012 to December 2015 in Qilu Hospital of Shandong University and Shandong Rizhao People's Hospital Inclusion criteria [9]: All the patients were diagnosed in accordance with Obstetrics and Gynecology (Eighth Edition) diagnostic criteria. Exclusion criteria: ① Patients with cardiovascular or cerebral-vascular disease, organic diseases of liver, kidney and lung and other important organs; ② Patients with malignant tumor or mental disease; ③ Patients with malformation fetus diagnosed; ④ Prior treatment for bleeding, preterm labor or other complications. According to the prenatal imaging study or intra-operative diagnosis of placenta, the patients were divided into two groups: PPP group (118 cases) and OPP group (142 cases), in addition, we selected 120 cases of healthy pregnant women in our hospital during the same period as control group.

Methods

Diagnostic method: Ultrasonic diagnosis of PPP: ① Low echo band of space between posterior placenta and the myometrium becomes thin (<2 mm) or disappears, placenta blood flows into myometrium; ② Continuous interruption of uterine clip film and increased blood flow signals; ③ The strong echo band between the uterine serous layer and the bladder is discontinuous, with rich blood flow. A definite diagnosis of PPP could be made by the combination of ultrasonic diagnosis and the history of cesarean section.

Research method: To ensure the authenticity and integrity of information, we repeatedly checked the contents of records that collected from our hospital, and the main research contents include: ① Pregnancy related data: age, pregnancy, birth, abortion times, cesarean section, previous cesarean section information, history of preterm birth, past history, family history, pregnancy complications; ② Unhealthy habits, such as smoking, drinking, etc.; ③ Related complications: placenta implantation, Disseminated intravascular coagulation (DIC), hysterectomy, maternal outcome (recovery, complications, death), hemorrhagic shock, cases of blood transfusion and the amount of postpartum hemorrhage, postpartum blood transfusion, etc.; ④ Neonatal condition: mean gestational age, body weight, Apgar score, perinatal death, etc..

Diagnostic criteria [10]: Placenta implantation: an abnormal placental pathological condition caused by placental villi invasion or penetration of the uterus, it is divided into adhesion, implantation and penetration. The results are confirmed during the cesarean section delivery or post operative pathology report.

Postpartum hemorrhage: Blood loss more than 500 ml after virginal delivery within 24 hours, or more than 1000 ml in cesarean section.

Gestational diabetes mellitus: Occurred or the discovered at the first time after pregnancy.

Placental abruption: Placenta that in the normal position partially or completely separated from uterine wall before fetal disengagement. Premature birth: delivered between 28 weeks and 37 weeks.

Neonatal asphyxia: Apgar score within 1 minute after delivery <7 points; 0-3 for severe asphyxia, 4-7 for mild asphyxia.

Statistical analysis

SPSS18.0 was performed for statistical analysis, and measurement data was presented by mean \pm standard deviation ($\bar{x}\pm s$), comparison among the three groups was examined with one-way ANOVA, comparison between two groups was examined with t-test, enumeration data was presented by percentage (n%). Comparison of sample rate was done by Pearson χ^2 test. Univariate analysis was performed to

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Table 1. Comparison of three groups of pregnant women about general information ($\bar{x} \pm s$)

Group	Age (year)	Parity	Gravidity	Times of abortion	Pregnancy (week)	Times of cesarean section
PPP group (118 cases)	31.72±4.83 ^a	1.51±0.76 ^{a,b}	4.18±1.46 ^{a,b}	1.83±1.27 ^{a,b}	35.73±2.45 ^a	1.53±0.42 ^{a,b}
OPP group (142 cases)	30.89±4.87	1.18±0.54	3.32±1.29	1.24±1.06	36.14±2.56	1.24±0.35
Control group (120 cases)	29.05±4.46	0.78±0.61	2.84±1.16	0.94±0.88	38.41±2.68	0.86±0.63
P	0.000	0.000	0.00	0.000	0.000	0.000
F	10.001	39.227	32.146	20.984	38.453	59.579

Note: a: PPP group vs. control group, $P < 0.01$; b: PPP group vs. OPP group, $P < 0.05$.

Table 2. Comparison of the history of pregnancy complications between three groups of pregnant women [n (%)]

Variables	PPP group (118 cases)	OPP group (142 cases)	Control group (120 cases)	P	χ^2
Family history of placenta	4 (3.89)	3 (2.12)	0 (0.00)	0.132	2.267
History of placenta	8 (6.78)	9 (6.34)	1 (0.83)	0.818	0.042
History of premature birth	9 (7.63)	11 (7.75)	2 (1.67)	0.902	0.015
Gestational Hypertension	5 (4.24)	6 (4.23)	4 (3.33)	0.478	0.504
Gestational diabetes	7 (5.93)	9 (6.34)	6 (5.00)	0.307	1.043
Placental abruption	1 (0.85)	2 (0.14)	0 (0.00)	0.756	0.097
Long-term smoking history	3 (2.54)	4 (2.82)	2 (1.67)	0.586	0.296

Note: a: PPP group vs. control group, $P < 0.01$; b: PPP group vs. OPP group, $P < 0.05$.

examine the risk factors for PPP, which were further analyzed by Logistic regression analysis, and calculated the OR value and 95% CI. $P < 0.05$ was considered with statistical difference, while $P < 0.01$ was considered with significant difference.

Result

General status

Parity, times of pregnancy, times of abortion and cesarean section of PPP group were significantly higher than those of OPP group and control group ($P < 0.05$). The pregnancy weeks of PPP group were significantly shorter than that of the control group ($P < 0.01$), while the age of PPP group was significantly higher than that of the control group ($P < 0.01$); And there are no significant difference between OPP group and control group in age ($P > 0.05$), while the pregnancy weeks of OPP group were significantly shorter than that of control group ($P > 0.05$). See **Table 1** for details.

Three groups of pregnant women and the history of pregnancy complications

There were no significant differences in the family history of placenta praevia, placenta

praevia history, premature birth, gestational hypertension, gestational diabetes, placental abruption and long-term smoking history and other aspects among the three groups ($P > 0.05$). Please see **Table 2** for details.

Logistic regression analysis of risk factors for PPP

After correction, regression analysis of influencing factors showed that age (≥ 35 years, OR: 2.263, 95.0% CI 1.346-4.749), parity (2 times, OR: 1.826, 95.0% CI 1.162-3.013; ≥ 3 times, OR: 4.692, 95.0% CI 1.737-5.845), abortion (1 time, OR: 1.427, 95.0% CI 0.723-2.136; ≥ 2 times, OR: 3.648, 95.0% CI 1.827-5.656), number of previous cesarean section (≥ 2 times, OR: 2.783, 95.0% CI 1.562-4.918) are the risk factors of PPP (**Table 3**).

Pregnancy complications and outcomes of three groups of pregnant women

Patients with PPP had significantly higher rates in placenta implantation, hemorrhagic shock, DIC, cases of blood transfusion as well as uterus resection than those patients in OPP group and control group ($P < 0.01$), see **Table 4** for more details. What is more, the amount of bleeding, postpartum hemorrhage and post-

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Table 3. Logistic analysis of risk factors of PPP

		β	SE	Walds	OR (95.0% CI)
Age (years)	≤ 23				1.0
	23~34	-0.061	0.364	0.02	0.976 (0.418-1.693)
	≥ 35	0.806	0.417	3.895	2.263 (1.346-4.749)
Parity (times)	1				1.0
	2	0.527	0.284	4.173	1.826 (1.162-3.013)
	≥ 3	1.639	0.592	8.035	4.692 (1.737-5.845)
Abortion (times)	0				1.0
	1	0.362	0.313	2.026	1.427 (0.723-2.136)
	≥ 2	1.225	0.482	10.374	3.648 (1.827-5.656)
Number of previous cesarean section (times)	1				1.0
	≥ 2	1.112	0.367	9.835	2.783 (1.562-4.918)

Table 4. Comparison of numbers of patients with the pregnancy complications between the three groups

Variables	PPP group (118 cases)	OPP group (142 cases)	Control group (120 cases)	P	χ^2
Placenta implantation	51 (43.22) ^{a,b}	8 (5.63)	0 (0.00)	0.000	142.37
DIC	7 (5.93) ^{a,b}	0 (0.00)	0 (0.00)	0.000	15.834
Cases of blood transfusion	61 (51.69) ^{a,b}	9 (6.34)	1 (0.83)	0.000	172.825
Hysterectomy	10 (8.47) ^{a,b}	0 (0.00)	0 (0.00)	0.000	22.803
Mortality	0 (0.00)	0 (0.00)	0 (0.00)	1.000	0.000
Hemorrhagic shock	12 (10.17) ^{a,b}	0 (0.00)	0 (0.00)	0.000	27.513

Note: a: PPP group vs. control group, $P < 0.01$; b: PPP group vs. OPP group, $P < 0.01$.

partum blood transfusion volume also increased significantly than OPP group and control group ($P < 0.01$) (**Figure 1**).

Perinatal outcome of three groups of pregnant women

The rates of newborns with Apgar score within 1 min < 7 and Apgar score within 5 min < 7 in PPP group were significantly higher than those in the control group ($P < 0.05$). The incidence of premature birth, transferring to Neonatal intensive care unit (NICU) in PPP group were significantly higher than that in control group ($P < 0.01$) and OPP group ($P < 0.05$). The average body weight and mean gestational weeks in PPP group were significantly lower than those in the control group ($P < 0.01$), but there were no statistical difference between OPP group and control group ($P > 0.05$). There was no perinatal mortality occurred in all three groups ($P > 0.05$). See **Table 5** for more details.

Discussion

PPP complicated with placenta implantation may lead to placental adhesion to the surface of the muscular layer, then further result in massive hemorrhage, which will seriously threaten the lives of mother and infant. And epidemiological survey shows [11], with high rate of cesarean section in China and the implementation of two-child policy, the incidence of PPP is increasing year by year. However the studies on the incidence of PPP are controversial.

One study showed that the incidence of placenta praevia patients complicated with placenta implantation was up to more than 50% [12]. Moreover, the other one [13, 14] reported that proportion of PPP patients with complete placenta praevia was significantly more than OPP, and it may be related to the previous cesarean section and other factors (such as multiple pregnancies and abortion, etc.), leading to that

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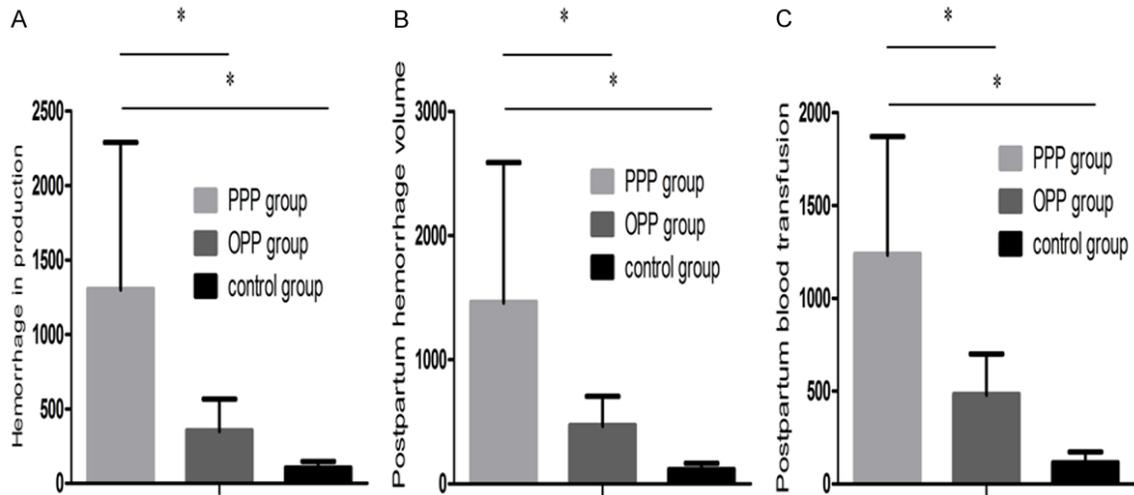


Figure 1. Comparison of three groups of pregnant women about hemorrhagic and blood transfusion volume. A: Hemorrhage in production, B: Postpartum hemorrhage volume, C: Postpartum blood transfusion volume, PPP group versus OPP group, and PPP group versus control group, * $P < 0.01$.

Table 5. Comparison of perinatal outcomes in three groups of pregnant women

Variables	PPP group (118 cases)	OPP group (142 cases)	Control group (120 cases)	P	F/ χ^2
Preterm infant	77 (65.25) ^{a,b}	71 (50.00)	5 (4.17)	0.000	101.245
Neonatal weight (kg)	2.67±0.58 ^a	2.71±0.59	3.82±0.61	0.000	81.823
Mean gestational age (week)	35.73±2.45 ^a	36.14±2.56	38.41±2.68	0.000	85.084
Transferred to NICU	68 (57.63) ^{a,b}	58 (40.85)	0 (0.00)	0.000	95.191
Apgar score within 1 min <7	23 (19.49) ^a	21 (14.79)	0 (0.00)	0.000	24.359
Apgar score within 5 min <7	17 (14.41) ^a	10 (7.04)	0 (0.00)	0.000	18.710
Perinatal mortality	0 (0.00)	0 (0.00)	0 (0.00)	1.000	0.000

Note: a: PPP group vs. control group, $P < 0.05$; b: PPP group vs. OPP group, $P < 0.05$.

the placenta continues to extend, sometimes even extends to the uterine cervix which could cause major bleeding during the process of childbirth [14]. At present, there is also study on the risk factors of placenta praevia, it suggested that the main factors could be considered as age, times of abortion, cesarean section history, repeated curettage and smoking [15]. For the pregnant women who had history of cesarean section, during the healing of incision, the normal muscles of uterine wall were gradually replaced by collagen, resulting in the lack of blood circulation of the placenta, and further caused the placenta hyperplasia hypertrophy. It is generally believed that the number of cesarean section is closely related to the occurrence of the disease. A British study on 399674 pregnant women has showed that the incidence of PPP in vaginal delivery population

was 4.4‰ [16], while the incidence in cesarean section population was 8.7‰. And results of a meta-analysis also showed that the risk of placenta praevia of pregnant women with history of cesarean section was 1.51 times to that of pregnant women without history of cesarean section [17]. In addition, multiple pregnancies may be also the risk factor for the disease. Hossain et al. found that the incidence of placenta praevia in pregnant women with multiple-pregnancy history was about three times of the general population [18]. The reason might be that multiple pregnancies may result in endometrial damage to the placenta, and affect the placenta planting of the next pregnancy.

Our study showed that placenta praevia could also cause serious complications of pregnant women and fetus. Severe postpartum hemor-

rhage, placenta accreta, premature birth, hemorrhagic shock and DIC are the common complications of placenta praevia. Postpartum hemorrhage is a serious complication in the delivery period, which is the leading cause of maternal death in our country [19]. The implantation of placenta on the uterine scar can lead to the loss in contraction function of normal muscle tissues and rupture of blood sinus. In addition, the placenta leaflets were cut in operation and eventually lead to maternal bleeding, or the poor uterine contraction after stripping cannot close the blood sinus, which also can lead to refractory postpartum hemorrhage. High risk factors of PPP complicated with placenta accrete is not known, however, puerperal infection, fertility, repeated curettage and cesarean section might be the reasons of endometrial damage. The decidua dysplasia and invasion of the trophoblast cells were the causes. The pathogenesis may also be related to the imbalance between the ability of the human placenta and the erosion of the placental villi. Uterine damage is mainly caused by placenta peeling and bleeding during pregnancy; uterine bleeding and bleeding after cesarean section can lead to the increasing incidence of hemorrhagic shock, DIC, hysterectomy, the puerperal infection and other complications [20]. Therefore, to find the bleeding site and control the bleeding volume is one of the determinant factors to keep the uterus and save the life of the patients. Our study proved that placenta accreta, bleeding shock, DIC, hemorrhage volume, the number of blood transfusion and postpartum blood transfusion as well as uterus resection rate were significantly higher in PPP patient than those of the OPP group and control group, which is consistent with the domestic and foreign reports. Due to the potential risk of prenatal hemorrhage, placenta praevia can also affect the outcomes of perinatal infants, such increase the incidence of iatrogenic preterm labor, high risk of low birth weight, asphyxia and so on; placenta praevia patients often suffer from acute hemorrhage, leading to maternal anemia, low blood volume and lack of maternal blood oxygen content. As a result, the gas interchange disturbance and placenta dissecting from uterine wall could reduce the contact area between the villi and the placental blood sinus, then affects blood exchange between maternal and fetus, causing fetal growth retardation, which would

greatly increase the risk of neonatal asphyxia, NICU, death and so on. There was no neonatal death in all three groups, which might be relevant to the in-time termination of pregnancy.

In conclusion, the single factor analysis showed that the number of cesarean section, abortion, pregnancy times and age are the independent risk factors of PPP. Placenta praevia complicated with placenta accreta will do great harm to the maternal and fetus. Patients with placenta praevia should be regularly examined, and their comprehensive situation and change of condition should be carefully assessed; a reasonable therapeutic regimen should be evaluated to select timely termination of pregnancy; adequate preoperative evaluation of patients for reducing complications and uterus resection ratio are necessary to effectively improve the pregnancy outcome.

Disclosure of conflict of interest

None.

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