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Research Article

Analysis of Factors Affecting Postpartum Hemorrhage in Twin Pregnancy

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Abstract

Objective: To explore the factors affecting postpartum hemorrhage in twin pregnancy.

Methods: The clinical data of 839 twin pregnancy patients who delivered at the Second Hospital of Shandong University from May 2010 to July 2020 were retrospectively analyzed. According to the amount of postpartum hemorrhage, patients were divided into postpartum hemorrhage group (PPH group) and non-PPH group. The basic population information and clinical data during pregnancy were compared between the two groups.

Results: A total of 839 women with twin pregnancy were included in this study, and hemorrhage occurred in 11% (n=96). The Binary logistic regression model predicts the risk of factor of postpartum hemorrhage in twin pregnancy: gestation week of delivery, placenta previa, polyhydramnios, acute delivery, anemia, placental adhesions and DIC (disseminated intravascular coagulation).

Conclusions: There are many factors that affect postpartum hemorrhage in twin pregnancy. Choosing the right gestational week for delivery, strengthening pregnancy management, and improving pregnancy complications can reduce the risk of postpartum hemorrhage in twin pregnancy.

Keywords: Postpartum hemorrhage; Pregnancy; Pregnancy; Twin; Retrospective studies; Risk factor

Abbreviations

PPH: Postpartum Hemorrhage; DIC: Disseminated Intravascular Coagulation; BMI: Body Mass Index

Introduction

Postpartum hemorrhage (PPH) is classically defined as a blood loss of >500mL after vaginal birth or that of >1000mL after cesarean delivery, with no adjustment for multiple pregnancies [1]. According to the World Health Organization, PPH is the leading cause of maternal mortality in developing countries (close to 30%) and the second leading cause of maternal mortality in developed countries (approximately 13%) [2]. PPH is responsible for approximately 68000 annual deaths in pregnant women, which means that one pregnant woman dies every 8 min due to PPH [3]. The 2014 National Maternal and Child Health Inspection Report described the main causes of maternal mortality in China. Although maternal mortality due to obstetric hemorrhage (more than 80% of PPH) has been declining for more than a decade, it is still the most common cause of maternal mortality [4]. Studies have reported uterine weakness, birth canal injury, placental factor, and coagulation dysfunction as the four major causes of PPH. Of these, uterine weakness is the most common cause of PPH that accounts for approximately 70%-80% of PPH [4,5]. Twin pregnancy leads to uterine smooth muscle overextension, which affects the uterine contraction after delivery and increases uterine weakness. Additionally, the circulating blood volume and uterine blood flow in women pregnant with twins increase to ensure adequate blood supply to the uterus, placenta, and fetal tissues. Thus, twin pregnancy is a significant risk factor for PPH [1,5-8]. With the wide application of assisted reproductive technology and the increase in maternal age, the twin pregnancy rate is increasing every year [9-11]. Factors affecting PPH in singleton pregnancy have been investigated in numerous studies [2,4]. However, the risk factors for PPH in twin pregnancy remain unknown. The present study attempts to explore the risk factors for PPH in twin pregnancy through a retrospective analysis of the clinical data of patients with twin pregnancy.

Materials and Methods

Study population

The present retrospective study analyzed the data of 839 patients after obtaining institutional ethical clearance. All the patients had twin pregnancy with >26 weeks of gestation, and they delivered at the Second Hospital of Shandong University between May 2010 and July 2020.

Diagnostic criteria and statistical indicators

The World Health Organization's definition of PPH, that is, the bleeding volume of vaginal delivery exceeding 500mL or that of cesarean section delivery exceeding 1000mL, without adjusting for the bleeding volume of multiple pregnancy, was considered [1,3]. The diagnostic criteria of pregnancy complications were adopted from Gynecology and Obstetrics, edited by Xie Xing et al., 9th edition of Human Health Publishing House [4].

According to the estimated bleeding volume, the patients were divided into the PPH group (n=96) and the control group (non-PPH

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group; n=743). The basic information of the population included age, body mass index (BMI), number of pregnancies, number of miscarriages, and whether to having a live birth. Clinical data during pregnancy included pregnancy method, gestational week of delivery, delivery method, total fetal birth weight, and complications during pregnancy.

Statistical analysis

Statistical analysis was performed using the SPSS 22.0 software. The measurement data are expressed as percentiles, whereas the count data are expressed as percentages (%). The Kruskal–Wallis test was used to compare the means between the groups, and Chi-square test was used to compare the rates between the groups. Finally, the binary logistic regression model was used to predict the risk factors for PPH in twin pregnancy. A P value of <0.05 was considered statistically significant.

Results

The present study was conducted in 839 patients, of which 96 patients exhibited PPH mainly due to uterine weakness, accounting for 71.88% of the PPH cases (Table 1).

All the patients with PPH were treated with oxytocin; 31.25% patients were treated with carboprost suppositories, 70.83% patients were treated with carboprost tromethamine injection, and 28.12% patients were treated with arterial ligation and suture (Table 2).

The average age of the patients was 30 years (range: 27, 33), and the average BMI was 30.07kg/m^2 (range: 27.73, 32.7221). No significant difference was observed in the demographic factors between the two groups (P >0.05). The PPH group exhibited fewer patients (33.3%) with a history of miscarriage than the non-PPH group (47%), and this difference was statistically significant (P <0.05). The number of primipara patients in the PPH group (45.8%) was higher than that in the non-PPH group (33.6%), and this difference was statistically significant (P <0.05) (Table 3) [12].

In this study, 21.1% of the patients received treatment with the assisted reproductive technology, and no significant difference in this parameter was observed between the PPH and non-PPH groups (20.5% and 26.0%, respectively; P >0.05). Most patients (93.7%) underwent elective cesarean section to deliver, and no significant difference in this parameter was observed between the PPH and non-PPH groups (93.9% and 91.7%, respectively; P >0.05). The gestational week of delivery was greater in the PPH group than in the non-PPH group, and the difference was statistically significant (37 (36, 37) and 36 (35, 37), respectively; P <0.05). The total weight of two newborns was higher in the PPH group than in the non-PPH group (5167.5 (4645, 5775)g and 5090 (4540, 5570)g, respectively; P = 0.076). The number of patients who required blood transfusion was significantly higher in the PPH group than in the non-PPH group (36.5% and 4.4%, respectively; P <0.05). The analysis of complications during pregnancy indicated that gestational diabetes mellitus, premature membrane rupture, placenta previa, polyhydramnios, anemia, and placental adhesions may be the risk factors for PPH, whereas patients with a scarred uterus are at a relatively low risk of having PPH (Table 4).

After adjusting for confounding factors, the logistic regression model exhibited that the number of miscarriages and a scarred uterus were the protective factors for PPH. Moreover, the patients with a history of miscarriage exhibited a reduced risk of PPH during twin pregnancy (odds ratio (OR) = 0.524; 95% confidence interval (CI): 0.322-0.853), similar to patients with a scarred uterus (OR = 0.352; 95% CI = 0.159-0.781). The risk factors for PPH identified were: gestational age (OR = 1.237; 95% CI: 1.084-1.412), placenta previa (OR = 4.586; 95% CI: 1.686-12.473), polyhydramnios (OR = 7.168; 95% CI: 1.963-26.167), acute labor (OR = 15.165; 95% CI: 3.352-68.606), anemia (OR = 4.918; 95% CI: 2.794-8.657), placental adhesions (OR = 3.367; 95% CI: 1.277-8.876), and disseminated intravascular coagulation (DIC) (OR = 20.951; 95% CI: 1.481-296.373) (Table 5).

Table 1: Statistics of the cause of bleeding.

Bleeding Cause	Cases (%)
Uterine Inertia	69 (71.88)
Tissue Lesion	4 (4.17)
Placenta Factor	6 v(6.25)
Mixed Factors	9 (9.37)
Unknown Reason	8 (8.33)
Total	96 (100)

Table 2: Statistics of the method of hemostasis.

Hemostasis Method	PPH (%)	No PPH (%)	Total (%)
Oxytocin	96 (100)	743 (100)	839 (100)
Carboprost Suppositories	30 (31.25)	220 (29.61)	250 (29.80)
Carprost Tromethamine Injection	68 (70.83)	328 (44.15)	396 (47.20)
Misoprostol	3 (3.13)	7 (0.94)	10 (1.19)
Arterial Ligation	16 (16.67)	22 (2.96)	38 (4.52)
Evacuation of Uterus	0 (0)	2 (0.27)	2 (0.24)
Partial Suture	2 (2.08)	0 (0)	2 (0.24)
B-lynch Suture	7 (7.29)	0 (0)	7 (0.83)
Quadrilateral Suture	2 (2.08)	1 (0.13)	3 (0.36)
Total	96 (100)	743 (100)	839 (100)

Table 3: Statistics of the basic information of the population.

Parameter	No PPH	PPH	Total	P Value
Age	30 (27, 33)	30 (28, 32)	30 (27, 33)	0.559
BMI	30.01 (27.73, 32.74)	30.51 (27.84, 32.56)	30.07 (27.73, 32.7221)	0.392
G(%)				0.017
G0	33.5 (249/743)	45.8 (44/96)	34.9 (293/839)	
G1	66.5 (494/743)	54.2 (52/96)	65.1 (546/839)	
A(%)				0.012
A0	53.0 (394/743)	66.7 (64/96)	54.6 (458/839)	
A1	47.0 (349/743)	33.3 (32/96)	45.4 (381/839)	
Birth History (%)				0.017
Primipara	33.5 (249/743)	45.8 (44/96)	34.9 (293/839)	
Maternal	66.5 (494/743)	54.2 (52/96)	65.1 (546/839)	

*Note: G: ≤1 = 0 > 1 = 1; A: ≤0 = 0; > 0 = 1 (Chi-square test).

Discussion

Twin pregnancies increase the risk of unhealthy pregnancy

Table 4: Clinical features of the population.

Parameter	No PPH (n=743)	PPH (n=96)	Total (N=839)	P Value
Pregnancy Method (%)				0.207
IVF	152 (20.5)	25 (26.0)	177 (21.1)	
Natural Pregnancy	591 (79.5)	71 (74.0)	662 (78.9)	
Gestational age	36 (35, 37)	37 (36, 37)	37 (35, 37)	0.008
Delivery Method (%)				0.388
Spontaneous Deliver	45 (6.1)	8 (8.3)	53 (6.3)	
Cesarean Section	698 (93.9)	88 (91.7)	786 (93.7)	
Total Fetal Birth Weight	5090 (4540, 5570)	5167.5 (4645, 5727.5)	5100 (4550, 5600)	0.076
Bleeding Volume	300 (250, 400)	800 (400, 1000)	300 (250, 400)	<0.05
Whether Blood Transfusion (%)				<0.05
No Blood Transfusion	710 (95.6)	61 (63.5)	771 (91.9)	
Blood Transfusion	33 (4.4)	35 (36.5)	68 (8.1)	
Complication (%)				
Placental Abruption	9 (1.2)	1 (1.0)	10 (1.2)	1
GDM	69 (9.3)	4 (4.2)	73 (8.7)	0.094
Hypertension in Pregnancy	166 (22.3)	24 (25.0)	190 (22.6)	0.558
Chronic Hypertension	5 (0.7)	1 (1)	6 (0.7)	0.519
Premature Rupture of Membranes	157 (21.1)	14 (14.6)	171 (20.4)	0.134
Scarred Uterus	139 (18.7)	8 (8.3)	147 (17.5)	0.012
Placenta Previa	17 (2.3)	8 (8.3)	25 (3.0)	0.003
Placental Placenta	3 (0.4)	0 (0)	3 (0.4)	1
Uterine Fibroids	20 (2.7)	3 (3.1)	23 (2.7)	1
Polyhydramnios	7 (0.9)	5 (5.2)	12 (1.4)	0.004
Oligohydramnios	8 (1.1)	0 (0)	8 (1.0)	0.607
Heart Disease	22 (3.0)	4 (4.2)	26 (3.1)	0.742
Elderly Primipara	13 (1.7)	4 (4.2)	17 (2.0)	0.231
Emergency Delivery	8 (1.1)	4 (4.2)	12 (1.4)	0.052
Thyroid Disease	24 (3.2)	4 (4.2)	28 (3.3)	0.858
Choroiditis	2 (0.3)	0 (0)	2 (0.2)	1
Anemia	373 (50.2)	79 (82.3)	452 (53.9)	0
Hepatitis B	30 (4.0)	5 (5.2)	35 (4.2)	0.788
DIC	1 (0.1)	2 (2.1)	3 (0.4)	0.036
Placental Adherence	21 (2.8)	7 (7.3)	28 (3.3)	0.047
Others	129 (17.4)	17 (17.7)	146 (17.4)	0.933

and PPH [1]. The widespread use of ovulation-stimulating drugs, increase in maternal age, and emergence and promotion of assisted reproductive technology have resulted in an increase in the rate of twin pregnancy [9-11,13,14]. Studies have exhibited that the incidence of PPH in twin pregnancy is significantly higher than that in singleton pregnancy [13,15-17].

The increased risk of PPH is due to the loss of normal contraction and retraction of uterine muscle fibers due to excessive extension, excessive expansion of the uterus to postpartum uterine fatigue, increased placental attachment area, and difficulty in normal closing of blood sinusoids [18,19]. PPH may lead to severe complications such as shock, renal failure, respiratory failure, DIC, pituitary infarction, hysterectomy, and death. Serious secondary anterior pituitary hypofunction sequelae may be observed if the shock is severe and prolonged, despite revival. In the absence of timely and appropriate medical treatment, a woman may die from PPH in an average of 2h [5,17,20]. Therefore, the identification of the risk factors for PPH in twin pregnancy is vital for optimal treatment.

The present study exhibited that prior pregnancy (including childbirth and miscarriage) reduces the risk of PPH. This finding is consistent with those of Lisonkova et al. and may be attributed to changes in the hormones or other aspects of the uterus caused by

Table 5: Results of multivariable logistic regression model to predict postpartum hemorrhage after a forward selection algorithm.

Parameter	OR (95% CI)	P Value
Number of Abortions	0.524 (0.322-0.853)	0.009
Gestational Week of Delivery	1.237 (1.084-1.412)	0.002
Scarred Uterus	0.352 (0.159-0.781)	0.01
Placenta Previa	4.586 (1.686-12.473)	0.003
Polyhydramnios	7.168 (1.963-26.167)	0.003
Emergency Delivery	15.165(3.352-68.606)	<0.05
Anemia	4.918 (2.794-8.657)	<0.05
Placental Adherence	3.367 (1.277-8.876)	0.014
DIC	20.951 (1.481-296.373)	0.024

the previous pregnancy [12]. Studies have reported that women with twin pregnancies achieved through in vitro fertilization are more prone to PPH [1,9,21-23]. This finding is in contrast with those of the present study, which revealed a nonsignificant difference in the incidence of PPH between assisted reproduction-based and natural twin pregnancies (P >0.05). Studies have reported that cesarean section increases the risk of PPH [2,6,12,16,17]. Conversely, some studies have reported that PPH risk in women with twin pregnancy is higher in vaginal trial delivery than in cesarean section [24,25]. In the present study, most patients chose elective cesarean section to deliver, and no significant difference in PPH was observed between these patients and those who opted for vaginal delivery (P >0.05). This finding is consistent with those of Nwankwo et al. and Yang et al. [11,22]. This result may be related to low number cases of vaginal delivery in the present study, and further research is required to confirm this finding. Studies by Seow et al. and Shunji et al. exhibited that the incidence of PPH increases with an increase in gestational age [6,26]. The present study indicated that the estimated bleeding volume increases with an increase in gestational age, reaching a peak at approximately 34 weeks. The estimated bleeding volume was relatively smaller at approximately 36 weeks, after which the upward trend reappeared. This may be related to a gradual decrease in the activity of antithrombin-III and the number of platelets in the last month of twin pregnancy [7]. In the present study, the average estimated bleeding volume at 39-40 weeks was low, which may be due to the low delivery volume in this gestational week. The uterus stops growing at 39 weeks in twin pregnancy, and the placental weight stabilizes after 37 weeks. Therefore, we suggest that the decision of delivery at approximately 36 weeks in case of twin pregnancy will reduce the risks of PPH and other complications [26].

The present study exhibited that a scarred uterus is a protective factor for PPH. This finding is in contrast to those of Lisonkova et al. and Rissanen et al [12,16]. Further studies with a larger sample size are required to confirm the findings of the present study. The present study considered placenta previa, polyhydramnios, acute labor, anemia, placental adhesions, and DIC as complications related to increased risk of PPH [6,22,27]. This may be related to factors such as excessive uterine inflation, weak contraction, soft birth canal laceration, and coagulation dysfunction [23,28].

Clinical Implications

Through this study, we have discovered the risk factors and the protective factors of postpartum hemorrhage in twin pregnancy. Provided a scientific basis for clinical diagnosis and treatment. The risk of complications associated with twin pregnancy could be reduced with timely diagnosis and treatment. Selection of the right time and method of delivery may reduce the incidence of PPH.

Research Implications

The amount of bleeding volume of PPH depends only on the clinical estimation and measurement, which may underestimate the actual amount of blood loss by 30%-50%. Difficulty accurately estimating the amount of bleeding and misdiagnosis of PPH have been identified as the factors restricting an accurate reporting of PPH, and the present study suffers from these limitations [4,16].

Strengths and Limitations

This study is based on a large sample of China, collected clinical data of twin pregnancy patients in the past ten years, and thoroughly analyzed the relationship between various pregnancy complications and postpartum hemorrhage.

In this study, the blood routine examinations of the patients before and after delivery were not perfect. The use of estimated bleeding volume to study postpartum hemorrhage has certain limitations.

Conclusion

The present study exhibited that prior pregnancy (including childbirth and miscarriage) and the scarred uterus in twin pregnancy are protective factors for PPH, whereas the gestational week, placenta previa, polyhydramnios, acute labor, anemia, placental adhesions, and DIC are risk factors for PPH. The risk of complications associated with twin pregnancy could be reduced with timely diagnosis and treatment. Selection of the right time and method of delivery may reduce the incidence of PPH.

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