Risk factors for postpartum hemorrhage after elective cesarean deliveries for twin pregnancies

Xiaojie Wan[1], Wei Zhao[1], Li Zhao[1], Nan Li[2], Hong Wen[1]

[1]Women's Hospital School of Medicine Zhejiang University, Hangzhou, China
[2]National and Local Joint Engineering Research Center of Ecological Treatment Technology for Urban Water Pollution, Zhejiang Provincial Key Laboratory for Water Environment and Marine Biological Resources Protection, College of Life and Environmental Sciences, Wenzhou University, China

ABSTRACT

Objectives: To identify the high-risk factors associated with postpartum hemorrhage (PPH) after an elective cesarean delivery of twins.

Material and methods: This retrospective cohort study included all women with twin gestations who chose to have an elective cesarean delivery after 28 weeks of gestation at at the Women's Hospital, School of Medicine, Zhejiang University between September 2014 and April 2019. Women with an intrauterine fetal demise of one or both twins were excluded. PPH was defined as an estimated blood loss of ≥ 1,000 mL within 24 h of birth. A total of 532 women were analyzed and classified into the PPH group (n = 70) and the no-PPH group (n = 462). Univariate and multivariate logistic regression analyses were performed to assess the independent risk factors.

Results: Among the 532 women pregnant with twins, PPH occurred in 13.2% women (n = 70). There were statistically significant differences in preeclampsia (p = 0.005), premature rupture of membrane (PROM, p < 0.001), placenta previa (p < 0.001), anemia [hemoglobin (Hb) < 100 g/L; p = 0.003], and antenatal magnesium sulfate ($MgSO_4$) use (p < 0.001) between the two groups. However, the following were the independent risk factors for PPH after an elective cesarean delivery for a twin pregnancy: preeclampsia [odds ratio (OR): 2.91; 95% confidence interval (CI): 1.33–6.36], PROM (OR: 8.57; 95% CI: 2.54–28.89), placenta previa (OR: 9.46; 95% CI: 3.59–24.89), antenatal $MgSO_4$ use (OR: 7.64; 95% CI; 3.18–18.41), and anemia (Hb < 100 g/L; OR: 2.68; 95% CI: 1.42–5.06).

Conclusions: Preeclampsia, PROM, placenta previa,and antenatal $MgSO_4$ use were the risk factors for PPH after an elective cesarean delivery for twin pregnancies. Risk factor identification and prevention should be a priority.

Keywords: elective cesarean delivery; postpartum hemorrhage; risk factors; twin pregnancies

Ginekologia Polska

INTRODUCTION

In recent years, the incidence of twin pregnancies has significantly increased because of the advancements in and application of assisted reproductive technologies [1]. Twin pregnancies are associated with a higher risk of perinatal morbidity and mortality [2]. Compared with singleton pregnancies, women with twin pregnancies are at a four-fold higher risk for severe maternal complications, such as postpartum hemorrhage (PPH) [3]. PPH, which is the leading cause of maternal mortality worldwide, is among the common complications associated with a twin pregnancy [3]. PPH is defined as a cumulative blood loss of ≥ 1,000 mL or blood loss accompanied by signs and symptoms of hypovolemia within 24 h of birth regardless of the route of delivery [3]. Uterine atony is the most common cause of PPH and accounts for approximately 80% of cases [4]. Compared to singleton pregnancies, twin pregnancies have many more complications because the myometrial contractility of the uterus is damaged by the uterine contraction fatigue caused by hyperexpansion, resulting in a higher rate of PPH [5].

Although several attempts have been made to develop predictive models for PPH on singleton gestations [6, 7], we herein aimed to study predictive models for PPH in twin gestations. For twin gestations, few studies have analyzed

the risk factors for PPH after vaginal and cesarean deliveries and a comparison between the two delivery types [8–10]. We need much clinical data to build predictive models of PPH in twin pregnancies. Recently, the global prevalence of cesarean delivery for twin pregnancies has increased significantly [11, 12]. This study was primarily aimed at evaluating high-risk factors for PPH after an elective cesarean delivery for a twin pregnancy by analyzing the clinical data, providing a clinical basis for the prevention and treatment of PPH, and providing data for building predictive models of PPH in twin pregnancies.

MATERIAL AND METHODS

This retrospective study was carried out at the Women's Hospital, School of Medicine, Zhejiang University from September 2014 to April 2019. Approval was received from the Institutional Ethics Committee before starting the study. The following were the inclusion criteria for the study: (1) both intrauterine twins survived; (2) the gestational period was ≥ 28 weeks; (3) the twins were delivered by elective cesarean delivery at the best time to perform the operation to suit the patient and the maternity team; and (4) patients had complete medical records available for review.

A total of 532 pregnant women were enrolled in the study. We obtained the baseline characteristics of the patients from their medical records, including maternal age, parity, body mass index, medical and surgical histories, pregnancy complications, and medication history. For patients who experienced PPH, the records were further reviewed to identify all documented medical and surgical interventions that were performed.

Intraoperative blood loss was estimated by adding the blood and gauze into the suction bottle and excluding the approximate amniotic fluid volume. During the cesarean section, 20-U oxytocin was injected into the uterus immediately after delivery of the placenta When uterine atony was identified, the obstetrician promoted uterine contraction using drugs, such as 100 μg of carbetocin IV, 250 μg of hemabate IM, and 1 mg of carboprost PO. If the drugs failed to promote uterine contractions, obstetricians used uterine cavity tamponade, external compression with uterine sutures, selective devascularization by ligation, or even hysterectomy.

Obstetric records were reviewed for the following aspects: maternal age, parity, uterine height (≥ 40 cm), *in vitro* fertilization and embryo transfer (IVF-ET), body mass index (BMI ≥ 30), pregnancy diseases (gestational diabetes mellitus, intrahepatic cholestasis during pregnancy, pregnancy hypertension, and preeclampsia), chronic hypertension, placental factors (placenta accreta and placenta previa), scarred uterus, myoma of the uterus, premature rupture of membrane (PROM), chorionicity, neonatal sex, preoperative

laboratory evaluations (hemoglobin and platelet levels), gestational week (≥ 37 weeks), maximal vertical pocket (MVP) of amniotic fluid (MVP ≥ 9 cm), combined neonatal birth weight (≥ 5000 g), anesthesia methods, and the use of antenatal magnesium sulfate.

In our study, 22 pregnant women with severe preeclampsia were treated with magnesium sulfate ($MgSO_4$) in order to prevent eclampsia within 24 h before cesarean delivery. Its usage was 4 g $MgSO_4$ loading dose added to 5% glucose 100 mL rapid intravenous drip within 30 minutes, and then 1–2 g/h $MgSO_4$ intravenous drip maintained for 6–12 h per day.

All statistical procedures were performed using SPSS 19.0. Cases and controls were compared using the t-test for continuous variables and the chi-squared or Fisher's exact test for categorical variables. Logistic regression analysis was subsequently used to identify the risk factors for PPH after an elective cesarean delivery for a twin pregnancy. Differences with $p < 0.05$ were considered significant.

RESULTS

Herein, PPH occurred in 70/532 (13.2%) women. The average volume of bleeding was 1,314.9 mL ± 419.8 mL. Overall, 45 patients were treated with blood transfusion. Moreover, among 43 women whose bleeding could not be stopped using uterine contraction drugs, 41 women were treated with uterine cavity tamponade, one woman underwent complete hysterectomy, and one woman was treated with ascending uterine artery ligation. All women had a good prognosis without maternal death. There were no significant differences in maternal age, parity, gestational weeks, uterine height, BMI, MVP, or twins' weights between the two groups ($p < 0.05$; Tab. 1).

Table 2 shows the characteristics of the twin pregnancies after elective cesarean delivery. There were significant differences between groups in obstetric characteristics, such as preeclampsia ($p = 0.005$), PROM ($p < 0.001$), placenta previa ($p < 0.001$), anemia [hemoglobin (Hb) < 100 g/L; $p = 0.003$], and antenatal $MgSO_4$ use ($p < 0.001$).

Multivariate logistic regression analysis was used to analyze the risk factors for PPH after an elective cesarean delivery for a twin pregnancy. The results (Tab. 3) showed that preeclampsia [odds ratio (OR): 2.91; 95% confidence interval (CI): 1.33–6.36), PROM (OR: 8.57; 95% CI: 2.54–28.89), antenatal $MgSO_4$ use (OR: 7.64; 95% CI: 3.18–18.41), placenta previa (OR: 9.46; 95% CI: 3.59–24.89), and anemia (Hb < 100 g/L; OR: 2.68; 95% CI: 1.42–5.06) were the independent risk factors for PPH after an elective cesarean delivery for a twin pregnancy.

DISCUSSION

In this retrospective cohort study, the PPH rate after an elective cesarean delivery for a twin pregnancy was

Table 1. Analysis of continuous variables by the incidence of postpartum hemorrhage

	No-PPH group	PPH group	p value
Number of patients	462	70	
Maternal age [years]	31.1 ± 4.0	30.9 ± 4.2	0.85
Parity	0.2 ± 0.4	0.3 ± 0.5	0.76
Gestational weeks at delivery	35.9 ± 1.3	35.7 ± 1.7	0.73
Uterine height [cm]	39.8 ± 3.2	39.9 ± 3.9	0.87
BMI [kg/m^2]	28.3 ± 10.4	27.9 ± 2.5	0.70
Twins' weights [g]	5013 ± 685	5021 ± 813	0.75
MVP [cm]	10.2 ± 2.2	10.8 ± 3.2	0.31

Data are presented as median (interquartile range) or mean ± standard deviation
BMI — body mass index; MVP — the maximal vertical pocket; PPH — postpartum hemorrhage

13.2%, which corroborates a previous report [5]. A study has compared different high-risk factors for PPH between singleton pregnancies and twin pregnancies, including premature delivery, hypertension, the use of intrapartum magnesium sulfate, the administration of general anesthesia, admission hematocrit levels being < 30%, and admission platelet levels being < 100,000/mL [6, 8]. The study has also studied placenta previa and placental abruption as high-risk factors for PPH in singleton pregnancies and gestational weeks ≥ 41 as a high-risk factor for PPH in twin pregnancies [6, 8].

In the present study, preeclampsia was shown to be an independent risk factor for PPH after an elective cesarean delivery for a twin pregnancy; however, the reason behind this finding remains undetermined. As suggested by Minakami et al. [13], PPH-inducing preeclampsia may be caused by a gradual decrease in the activity of antithrombin III or platelets during the second trimester of a twin pregnancy. However, in our study, only one case of PPH complicated by preeclampsia was accompanied by thrombocytopenia, and the activity of antithrombin III was not tested for this patient. The incidence of preeclampsia has been reported to be 2–3 times higher in twin pregnancies than in singleton pregnancies [14]. In previous studies, preeclampsia was reported as an independent risk factor for developing severe PPH and was associated with an increased probability of requiring transfusion after the delivery of twins [9, 15]. It was also suggested that early diagnosis of preeclampsia in women during a twin pregnancy can help prevent or reduce the occurrence of PPH and improve their prognosis.

Our findings suggested that PROM was an independent risk factor for PPH after an elective cesarean delivery for a twin pregnancy. Because of the high pressure of the uterine cavity in a twin pregnancy, the probability of PROM is 7–88% [9, 10]. After PROM, the role of the membranes as a barrier disappears, and therefore, pathogens are more likely to invade the uterine cavity, leading to chorioamnionitis, which is another high-risk factor for PPH [10] Notably,

PROM and chorioamnionitis are causal factors, which may also be a high-risk factor for PPH. However, all six patients who experienced PROM experienced PPH in our study, and only three patients had a pathologically confirmed diagnosis of chorioamnionitis. Therefore, we need a larger sample size to confirm that PROM is an independent risk factor for PPH after an elective cesarean delivery.

Our study also showed that placenta previa was an independent risk factor for PPH after an elective cesarean delivery for a twin pregnancy. Placenta previa is a severe complication of pregnancy and is the most common cause of PPH [16]. The causes of placenta previa-induced PPH are the low placenta position, large dissection surface, poor contraction of the lower uterine segment, and open blood sinuses. Our study showed that placenta accreta did not increase the risk of PPH after an elective cesarean delivery for a twin pregnancy, which was different with some studies [17, 18]. The difference was not significant due to the small number of placenta accreta cases in the study.

Intrapartum MgSO$_4$ administration to women with hypertensive disorders during pregnancy is associated with an increased probability of PPH and uterine atony [19]. Our results showed that the use of antenatal magnesium sulfate was an independent risk factor for PPH after an elective cesarean delivery for a twin pregnancy. MgSO$_4$ use has been proposed for preeclampsia prevention because it can decrease acetylcholine (Ach) in the neuromuscular junction, interfere with actin–myosin, block NMDA receptors, and depress selected catecholamines, resulting in myometrial relaxation, decreased uterine contractility, arterial vasodilation, and lower systolic blood pressure [20]. However, a meta-analysis revealed no difference in the risk of postpartum uterine atony or the risk of PPH with or without the use of intrapartum magnesium sulfate [21]. A large number of samples are still needed to confirm whether magnesium sulfate has an effect on uterine contractions and PPH. For women with twin pregnancies who can choose elective

Table 2. Characteristics of elective cesarean delivery for twin pregnancies

		No-PPH group	PPH group	p value
Number of patients		462	70	
Maternal age [years]	≥ 35	90	12	0.67
Parity	≥ 3	99	17	0.59
IVF		259	44	0.29
BMI ≥ 30		113	16	0.77
Pregnancy complications	Gestational diabetes mellitus	71	9	0.58
	Gestational hypertension	14	6	0.1
	Preeclampsia	25	10	**0.005**
	Intrahepatic cholestasis during pregnancy	28	6	0.42
Chronic hypertension		3	0	1
Placental factors	Placenta accreta	1	2	0.06
	Placenta previa	8	10	**< 0.001**
Uterine height (> 40 cm)		254	36	0.58
Scarred uterus		41	8	0.49
Uterine fibroids		14	3	0.85
Premature rupture of membrane		5	6	**< 0.001**
Chorionicity	Dichorionic twins	370	53	0.079
	Monochorionic twins	89	17	–
	Monoamniotic twins	3	0	–
Preoperative laboratory evaluation				
	Hemoglobin < 100 g/L	46	16	**0.003**
	Platelet < 100 × 10^9/L	6	3	0.07
Fetal weight (≥ 5000 g)		247	40	0.57
MVP (≥ 9 cm)		320	49	0.90
Neonatal gender	Two boys	150	29	0.21
	A boy and a girl	149	24	–
	Two girls	163	18	–
Gestational week at delivery (≥ 37 weeks)		186	30	0.08
Anesthesia	Epidural anesthesia	435	56	0.07
	Combined spinal–epidural anesthesia	26	4	–
	General anesthesia	1	2	–
Antenatal MgSO$_4$ use		11	11	**< 0.001**

BMI — body mass index; IVF-ET — *in vitro* fertilization and embryo transfer; MgSO$_4$ — magnesium sulfate; MVP — maximal vertical pocket; PPH — postpartum hemorrhage
P values in bold indicate significant differences (p < 0.05)

cesarean section, the safest time to perform the operation is after the half-life of magnesium sulfate.

Women with a multiple pregnancy are at greater risk of developing anemia. Our research found that maternal anemia (Hb < 100 g/L) was an independent risk factor for PPH after an elective cesarean delivery for a twin pregnancy. A retrospective cohort study reported that maternal anemia (Hb < 100 g/L) was associated with antepartum hemorrhage [22]. In addition, a systematic review and meta-analysis showed that maternal anemia and prenatal anemia (Hb < 90 g/L) increased the PPH risk [23]. Therefore, it is very important to treat anemia during pregnancy to prevent PPH.

CONCLUSIONS

A twin pregnancy and an elective cesarean delivery are high-risk factors for PPH [9], resulting in a high rate of PPH in pregnant women who undergo elective cesarean deliveries for twin pregnancies. Our analysis showed that pre-eclampsia, placenta previa, PROM, antenatal MgSO$_4$ use, and anemia (Hb < 100 g/L) were high-risk factors for PPH after

Table 3. Results of multivariable logistic regression model to predict risk factors for postpartum hemorrhage after elective cesarean delivery for a twin pregnancy

Characteristic	OR	95% CI
Preeclampsia	2.91	1.33–6.36
Premature rupture of membrane	8.57	2.54–28.89
Antenatal MgSO$_4$ use	7.64	3.18–18.41
Placenta previa	9.46	3.59–24.89
Anemia (Hb < 100 g/L)	2.68	1.42–5.06

CI — confidence interval; Hb — hemoglobin; MgSO$_4$ — magnesium sulfate; OR — odds ratio

an elective cesarean delivery for a twin pregnancy. We hope to further expand the sample size to develop and validate a model that can predict PPH in twin pregnancies. Through the model, preventive measures can be taken as early as possible to reduce maternal morbidity and mortality while reasonably controlling medical expenditures.

Article information and declarations

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