



Research Paper

Analysis of risk factors related to severe postpartum hemorrhage of twin pregnancies delivered by cesarean section

Fufen Yin^{a,1}, Ruixue Li^{b,1}, Junshu Xie^a, Xiaohong Zhang^{a,*}^a Department of Obstetrics and Gynecology, Peking University People's Hospital, Beijing, China^b Department of Obstetrics and Gynecology, Liupanshui Maternal and Child Health Care Hospital, Guizhou, China

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ABSTRACT

Objective: To investigate the risk factors of severe postpartum hemorrhage (PPH) in cesarean section of twin pregnancy, and to provide clinical basis for pregnancy management and perioperative obstetric management of twin pregnancy.

Methods: The clinical data of 631 twin pregnancies with gestational age ≥ 28 weeks delivered by cesarean section at Peking University People's Hospital (PKUPH) from January 2004 to January 2017 were retrospectively analyzed. Methods of conception, the combined weight of twins, serum albumin level before cesarean section, operation time and other factors on the amount of blood loss during cesarean section were analyzed.

Results: The proportion of severe PPH was significantly higher in in vitro fertilization-embryo transfer (IVF-ET) group, the combined weight of twins > 6000 g group, serum albumin before cesarean section < 30 g/dl group than in the natural pregnancy group, 4000–6000g group, < 4000 g group and serum albumin ≥ 30 g/dl group respectively ($P < 0.05$). The proportion of severe PPH in the elective surgery group of twin pregnancy was higher than that in the emergency surgery group, but the difference was not statistically significant ($P > 0.05$). Moreover, according to the surgical indications, the emergency surgery group was divided into premature rupture of membranes (PROM), labor, fetal distress and others groups, no significant difference were detected among these groups ($P > 0.05$).

Conclusion: IVF-ET, the combined weight of twins, serum albumin before operation were significantly correlated with severe PPH of twin pregnancies delivered by cesarean section, revealing that it is necessary to strengthen pregnancy management of twin pregnancy.

1. Introduction

With the increase of older maternal age and the progress of assisted reproductive technology (ART), the number and proportion of twin pregnancy continues to increase.^{1,2} Although for some patients, vaginal delivery is possible for twin pregnancy, cesarean section has become the main choice for delivery due to the elderly parturient women and precious fetuses.^{3,4} Postpartum hemorrhage (PPH) is defined as blood loss ≥ 500 mL after vaginal delivery or ≥ 1000 mL after cesarean section within 24 h.⁵ Severe PPH refers to the blood loss ≥ 1000 ml after delivery

of the fetus within 24 h.⁶ PPH is the leading cause of maternal mortality worldwide, causing almost 25% of all pregnancy-related deaths. All pregnant women had the possibility of suffering PPH, but more likely to occur in those patients with one or more risk factors.⁷ PPH can be a life-threatening emergency and the consequences will be serious for severe PPH if it was not controlled in time.⁸ Published studies have identified that twin pregnancy and cesarean delivery were both high risk factors for PPH.^{7,9} Growth discordance, gestational age at ≥ 41 weeks and hypertensive disorders have been proved to be associated with PPH in women with twin pregnancies undergoing cesarean section.^{10,11}

* Corresponding author. Department of Obstetrics and Gynecology, Peking University People's Hospital, Xizhenmen South Street, Xicheng District, Beijing, China.
E-mail address: zhangxh202109@126.com (X. Zhang).



¹ Contributed equally.

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However, no study has comprehensively explored the risk factors of severe PPH in cesarean delivery of twin pregnancy.

The objective of this study was to explore the risk factors of severe PPH of twin pregnancies delivered by cesarean section, so as to provide clinical basis for pregnancy management of twin pregnancy and obstetric treatment during perioperative period.

2. Materials and methods

The present study was performed in the Department of Obstetrics and Gynecology, Peking University People's Hospital (PKUPH; Beijing, China). A total of 631 cases of twin pregnancies delivered by cesarean section in PKUPH from January 2004 to January 2017 were selected as the research object. Inclusion criteria were twin pregnancy, gestational age of termination ≥ 28 weeks, no abnormality in intrauterine fetal structure screening, and live birth (except one stillbirth, abortive or reduced fetus). To explore the related risk factors of severe PPH, method of conception, the combined weight of twins, timing of operation and other factors were retrospectively analyzed in 631 cases. Serum albumin content before cesarean section was analyzed in 468 cases to explore its correlation with severe PPH. Clinically, < 4000 g is similar to normal single fetal weight, $4000\text{--}6000$ g is the weight of most twins, when twins BW > 6000 g, risk of PPH increased significantly. So, in this paper, 631 twin pregnancy cases with cesarean section were divided into < 4000 g, $4000\text{--}6000$ g and > 6000 g groups to explore correlation between the combined weight of twins and severe PPH. The amount of blood loss in all cases in this study was estimated on the basis of prophylactic use of oxytocin after delivery of the second twin fetus, and active use of uterine tamponade, uterine compression suture, pelvic vascular ligation and other surgical procedures for postpartum hemorrhage if there was a tendency to continue bleeding. All the methods used to estimate the amount of blood loss were volume method + weighing method, that is, blood loss of cesarean section = (total amount of liquid attracted by negative pressure bottle - amniotic volume) + blood after placenta + postoperative vaginal blood accumulation + blood seepage of intraoperative gauze and dressing. In our research, PPH and severe PPH of twin pregnancies delivered by cesarean section was defined as blood loss ≥ 1000 mL after cesarean section within 24 h.

SPSS software (version 13.0; SPSS Inc., Chicago, IL, USA) was used to perform the statistical analysis. Unary linear regression was used to determine whether there was correlation between the two variables. T test is adopted for comparison of the mean values of two samples of measurement data (independent sample T test is adopted according to whether the data is subject to normal distribution). χ^2 test and Fisher's exact test were used for the counting data.

3. Results

3.1. Postpartum hemorrhage of twin pregnancy

From January 2004 to January 2017, 29,038 cases were delivered in PKUPH, and the rate of twin pregnancy was 2.43%. Severe PPH occurred in 69 cases of twin pregnancy (10.94%). PPH in twin pregnancy averaged 540 ± 546 ml, cesarean delivery 558 ± 554 ml, and vaginal delivery 368.38 ± 424.57 ml. Among the 631 cases of twin pregnancy with cesarean section, 30 cases were treated with intrauterine packing for hemostasis, 19 cases with B-Lynch suture for hemostasis, 153 cases with uterine artery ligation, 6 cases with arterial embolization and 2 cases with hysterectomy. Seven patients were admitted to ICU due to bleeding. No maternal deaths occurred. Comparison of general conditions between the two groups (severe PPH vs non severe PPH), the basic data including age, body mass index (BMI), complicated with hypertension or diabetes mellitus, uterine myoma and the previous cesarean section have been made. Among these factors, the results showed that complicated with hypertension proved to be associated with PPH in women with twin pregnancies undergoing cesarean section (Table 1).

Table 1

Comparison of general conditions between the two groups n(%).

	≥ 1000 ml n = 76	< 1000 ml n = 583	χ^2	P
Age			0.041	0.840
<35	52 (78.79)	439 (77.70)		
≥ 35	14 (21.21)	126 (22.30)		
Pre-pregnancy BMI			3.321	0.068
<28	42 (87.50)	549 (94.17)		
≥ 28	6 (12.50)	34 (5.83)		
BMI at cesarean section			3.183	0.074
<28	20 (26.32)	204 (36.49)		
≥ 28	56 (73.68)	351 (63.51)		
Complicated with hypertension			4.448	0.035
Yes	18 (26.87)	93 (16.49)		
No	49 (73.13)	471 (83.51)		
Complicated with diabetes mellitus			0.21	0.646
Yes	8 (11.94)	79 (13.98)		
No	59 (88.06)	486 (86.02)		
Previous CS			0.494	0.482
Yes	3 (4.62)	17 (3.00)		
No	62 (95.38)	549 (97.00)		
Complicated with Uterine Myoma				0.205
Yes	2 (3.00)	6 (1.06)		
No	65 (97.00)	558 (98.94)		

3.2. Effect of ART on blood loss of severe PPH in twin pregnancies

According to the conception method, 631 twin pregnancy cases of cesarean section were divided into IVF-ET assisted pregnancy group and natural pregnancy group. The rate of severe PPH in IVF-ET assisted pregnancy group was significantly higher than that in natural pregnancy group (14.25% vs 6.79%, $P < 0.05$) (Table 2).

3.3. Correlation between the combined weight of twins and severe PPH in twin pregnancies

Among the 631 cases, 72 cases (11.4%) with the combined weight of

Table 2

Risk factors of severe postpartum hemorrhage in twin pregnancy of cesarean section.

Risk factors	N	Non-severe PPH	Severe PPH	P
		n (%)	n (%)	
Conception method				0.002
IVF-ET	351	301 (85.75)	50 (14.25)	
Natural pregnancy	280	271 (93.21)	19 (6.79)	
Combined weight of twins				0.000
< 4000 g	72	66 (91.67)	6 (8.33)	
$4000\text{--}6000$ g	499	452 (90.58)	47 (9.42)	
> 6000 g	60	44 (73.33)	16 (26.67)	
Preoperative serum albumin level				0.000
Albumin < 30 g/dl	98	73 (74.49)	25 (25.51)	
Albumin ≥ 30 g/dl	370	333 (90.00)	37 (10.00)	
Timing of cesarean section				0.063
Elective surgery	410	359 (87.56)	51 (12.44)	
Emergency surgery	221	203 (91.86)	18 (8.14)	

twins < 4000g, 499 cases (79.1%) with the combined weight of twins between 4000g and 6000g and 60 cases (9.5%) with the combined weight of twins > 6000g. There was a positive correlation between the combined weight of twins and blood loss through linear regression study ($P < 0.05$) (Table 2).

3.4. Correlation between serum albumin levels before cesarean section and severe PPH in twin pregnancies

A total of 468 cases with clinical data of serum albumin levels before cesarean section were selected from the 631 cases, including 45 cases of severe preeclampsia, 19 cases of preeclampsia, 28 cases of gestational hypertension, 13 cases of chronic hypertension complicated with preeclampsia and 3 cases of gestational proteinuria. According to the serum albumin content, the cases were divided into five groups: <25g, 25–30g, 30–35g, 35–40g and ≥ 40 g. We compared the mean blood loss of each group and the difference among the groups, and found that there was significant difference in blood loss between the three groups with serum albumin ≥ 30 g and the two groups with serum albumin < 30g ($P < 0.05$). The 468 cases were furtherly divided into < 30g and ≥ 30 g groups, statistical analysis found the rate of severe PPH was significantly higher in serum albumin < 30g group than that in the ≥ 30 g group ($P < 0.05$) (Tables 2 and 3).

3.5. Correlation between timing of operation and severe PPH in twin pregnancies

According to the timing of operation, 631 cases of twin pregnancy with cesarean section were divided into the elective surgery group and emergency surgery group. No statistical significance was found in the number and rate of severe postpartum bleeding between the two groups ($P > 0.05$) (Table 2). In addition, 221 cases of emergency surgery were divided into groups according to surgical indications, and there was no significant difference among the groups ($P > 0.05$) (Table 4)

4. Discussion

The incidence of twin pregnancies has risen markedly in the past 20 years due to the use of ART.^{12,13} As China is facing the liberalization of the three-child policy, the number of elderly parturient women increases, and the proportion of pregnancy using ART increases.¹⁴ Advanced age, assisted reproduction and twin pregnancy have become a new triad.¹⁵ Twin pregnancy was a high-risk pregnancy, and the main causes of maternal mortality associated with twin pregnancy reported in previous literatures were preeclampsia and eclampsia, placental abruption, cesarean delivery and PPH.^{12,16–18} This paper summarized the situation of severe PPH in twin pregnancies of cesarean section, analyzed the risk factors of severe PPH, and aimed to prevent the occurrence of severe hemorrhage. A secondary analysis of a cross-sectional World Health Organization Multicountry Survey, which compared the clinical data of 4,756 twin deliveries with 308,111 singleton deliveries from 29 countries, revealing that potentially life-threatening conditions, maternal near miss, severe maternal outcomes, and maternal deaths were 2.14

Table 3
Comparison of blood loss among serum albumin groups.

	n	Bleeding/ml	P
Serum albumin level			0.000*
< 25 g/dl	25	1090 ± 1278.67	
25–30 g/dl	73	875.52 ± 934.87	
30–35 g/dl	140	531.86 ± 356.14	
35–40 g/dl	136	480.22 ± 309.07	
≥ 40 g/dl	94	581.65 ± 588.77	

*The mean blood loss of each group was compared, significant difference in blood loss was found between the three groups with serum albumin ≥ 30 g and the two groups with serum albumin < 30g

Table 4

Comparison of blood loss among groups of different surgical indications.

	n	Bleeding/ml	P
Surgical indications			0.997
PROM	100	509.10 + 458.83	
Labor	87	498.62 + 501.98	
Fetal distress	31	518.23 + 722.56	
Others	3	533.33 + 404.15	

PROM: premature rupture of membrane.

(1.99–2.30), 3.03 (2.39–3.85), 3.19 (2.58–3.94), and 3.97 (2.47–6.38) times higher, respectively, among twin pregnancies.¹² PPH was more frequently associated with severe maternal outcomes among twin pregnancies.^{5,12}

Data analysis in our hospital showed that among the 631 twin pregnancy cases of cesarean section, 30 cases were treated with intrauterine packing for hemostasis, 19 cases with B-Lynch suture for hemostasis, 153 cases with uterine artery ligation, 6 cases with arterial embolization, 2 cases with hysterectomy and seven patients were admitted to ICU due to bleeding. Though no maternal deaths occurred, twin pregnancy was still a threat to maternal safety. Special hemostatic methods, such as uterine packing or B-Lynch suture, were often required for twin pregnant women undergoing cesarean section, which increased the risk of postoperative ICU admission.

Previous studies have shown that pregnancy-induced hypertension followed by prolonged labor was an identifiable risk factor for PPH.^{19,20} The results in this paper revealed that complicated with hypertension was associated with PPH in women with twin pregnancies undergoing cesarean section. As for twin pregnancies complicated with hypertension, PPH needs to be prevented in advance.

The use of ART has increased in many countries in the past years and the trend continued to increase.^{1,21,22} The risk of PPH in assisted reproduction singleton pregnancy was significantly higher than that in natural pregnancy.^{23–25} A history of ART increased the likelihood of needing a peripartum hysterectomy to control hemorrhage and in women having a peripartum hysterectomy, 13.4% of the risk is attributable to mode of conception.²³ The incidence of peripartum hysterectomy due to bleeding was 1.2/1000 in natural pregnancy and 9.7/1000 in assisted reproductive technology pregnancy.²³ For ART twin pregnancy, the risk of peripartum hysterectomy due to bleeding increased by 3 times.²³ In this study, the rate of severe PPH in ART twin pregnancies (50/351, 14.25%) was significantly higher than that in the natural pregnancy group (19/280, 6.79%). These results suggested that twin pregnancies with ART had a higher risk of bleeding. The reasons may be related to the medical history of pelvic adhesions, intrauterine adhesions, endometriosis, laparoscopy and multiple hysteroscopic operations due to infertility in the ART pregnancy group.

Due to excessive uterine fiber extension, uterine contraction weakness caused by excessive uterine expansion.^{26,27} Studies have proved that pregnancies with macrosomia having a birth weight (BW) > 4000g, there was an increased risk of PPH. Fetal weight gain in twin pregnancy was related to maternal nutrition and maternal weight gain.²⁸ China's "Pre-pregnancy and Pregnancy Health Care Guidelines" for nutrition and body weight increase during pregnancy recommendations were as follows, proper nutrition before and during pregnancy, control of the rate of gestational weight gain (GWG), record body weight and BMI before the first birth visit. Studies showed that the incidence of very preterm delivery (VPTD), pre-eclampsia, perinatal mortality were associated with GWG ratio, and a GWG ratio of 0.55–0.56 kg/wk appeared optimal in terms of twin pregnancy outcomes.²⁹

Our study in this paper showed that there was a positive correlation between twin body weight and blood loss through linear regression study Postpartum bleeding increased significantly in patients with combined weight of twins >6000g. Fetal weight should be dynamically monitored by ultrasound during pregnancy. If it was estimated that the combined

weight of twins >6000g, adequate preparation such as adequate blood sources and experienced surgeons should be made to prevent PPH. In addition, strong uterine contraction agents should be given in time during the operation, and hemostasis methods such as uterine packing or B-Lynch suture should be adopted in time if necessary.

Albumin is a blood component that reflects the nutritional status of the body, maintains the blood colloid osmotic pressure and ensures the normal metabolism and transport of substances in the body.^{30,31} As the growth and development of the fetus requires active intake of protein from the mother, twin pregnancy itself was an important cause of hypoproteinemia in the late trimester because of the large amount of protein required for fetal growth and development.^{32–34} Previous data showed that twins with hypoproteinemia had an increased risk of adverse pregnancy outcomes and increased incidence of complications such as postpartum bleeding and puerperal infection.³⁵ The increased risk of postpartum hemorrhage for these patients may be due to tissue edema secondary to hypoproteinemia and preeclampsia hypoproteinemia in the third trimester.^{36–38}

Data analysis in this paper showed the rate of severe PPH was significantly higher in serum albumin < 30g group than that in the ≥30g group, revealing that preoperative hypoproteinemia in twin pregnancies with caesarean section increased the risk of severe PPH. In the late trimester of twin pregnancy, attention should be paid to the correction of hypoproteinemia, the intake of high-quality protein should be appropriately increased, the level of serum albumin should be monitored, and the occurrence of preeclampsia should be vigilant. For twin pregnancies complicated with hypoproteinemia, more attention should be paid to the prevention and control of PPH during delivery.

There were some limitations in the current research. First, twin pregnant women delivered vaginally were not included in this study. Second, owing to the limited sample size and missing data, some clinical factors were not included in the analysis. In addition, the research was retrospective study and, prospective validation was needed to verify the most reliable risk factors related to severe postpartum hemorrhage of twin pregnancies delivered by caesarean section.

5. Conclusion

This is the first study to comprehensively explore the risk factors of severe PPH in cesarean delivery of twin pregnancy in Chinese population. Maternal hypertensive disease, IVF-ET, excessive combined twin weight and preoperative hypoproteinemia increased the risk of severe PPH in cesarean delivery twins. It is necessary to strengthen prenatal health care for twin pregnancies, dynamically monitor fetal weight, manage the growth rate of pregnancy weight and correct late pregnancy hypoproteinemia. Twin pregnancy delivery should be prepared to prevent severe PPH.

Author contributions

YFF: Wrote the manuscript; LRX: Directed and performed the analyses; XJS: Edited the manuscript; XYL: Collected the clinical data; ZXH: Originated the study and checked the manuscript.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Peking University People's Hospital Ethics Committee.

Consent to participate

Not applicable. This is a clinical retrospective study and these are standard hospital operations for all authors.

Consent for publication

All authors consent for publication.

Declaration of competing interest

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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