

Life-threatening postpartum hemorrhage (≥ 5000 mL): a single center experience

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ABSTRACT

Objectives: To investigate the etiology, interventions and outcome of life-threatening postpartum hemorrhage (PPH) (≥ 5000 mL).

Material and methods: Retrospective analysis was performed on the clinical data of 42 patients with life-threatening PPH in Peking University Third Hospital from January 2010 to December 2019. According to the causes of PPH, 35 patients were divided into the placenta accrete spectrum (PAS) group and seven patients into the uterine atony group.

Results: Compared with the uterine atony group, the gravidity, parity, times of cesarean section, abortion and intrauterine operation of the PAS group were significantly higher, but the gestational age of delivery and the birth weight of newborn were significantly lower (33.35 ± 3.94 weeks vs 37.31 ± 1.93 weeks; 2228.29 ± 840.49 g vs 2809.00 ± 500.99 g; $p < 0.05$). For all the patients, the transfusion volume of packed red blood cell (PRBCs), fresh frozen plasma (FFP) and platelets were respectively 23.49 ± 8.42 U, 2345.24 ± 826.16 mL and 0.81 ± 1.19 U, the ratio was basically conformed to the recommended massive transfusion protocol (MTP) (1:1:1). The catheter placement time in the PAS group was significantly longer (7.88 ± 6.05 days vs 3.86 ± 0.90 days, $p < 0.05$). There were no significant differences in complications and maternal outcomes. No maternal deaths.

Conclusions: Placenta accrete spectrum (PAS) is the most important cause of life-threatening PPH. For these patients, MTP is effective, multidisciplinary cooperation and management lead to a good prognosis.

Key words: life-threatening postpartum hemorrhage; interventions; prognosis

Ginekologia Polska

INTRODUCTION

Postpartum hemorrhage (PPH) is the most common complication of obstetric delivery, massive postpartum bleeding is the leading cause of maternal death [1–3], most patients with PPH can be controlled by aggressive conservative treatment, a small number of patients may require surgery, interventional therapy or even hysterectomy to stop bleeding effectively [4]. Countries around the world have formulated relevant guidelines for PPH, including a package plan for identification of high-risk factors, estimation of blood loss, monitoring, treatment and prognosis [5–11]. The amount of PPH is closely related to the outcome of patients. In the average non-pregnant adult, circulating blood represents a total of 7% of body

weight, or approximately 5 liters. Severe PPH is considered when the bleeding rate is > 150 mL/min, or when the bleeding volume exceeds 50% of the blood volume within three hours, or when the bleeding volume exceeds systemic blood volume within 24 hours [12]. A large amount of PPH almost loses systemic blood volume (≥ 5000 mL), and the pathophysiology of the human body will undergo important changes. Whether such life-threatening PPH will cause damage to various organ systems, and how to monitor and manage it in clinical practice is a challenge for obstetricians. Against this background, the aim of this study was to examine the etiology and risk factors of life-threatening PPH (≥ 5000 mL), evaluate the curative effectiveness of interventions and prognosis.

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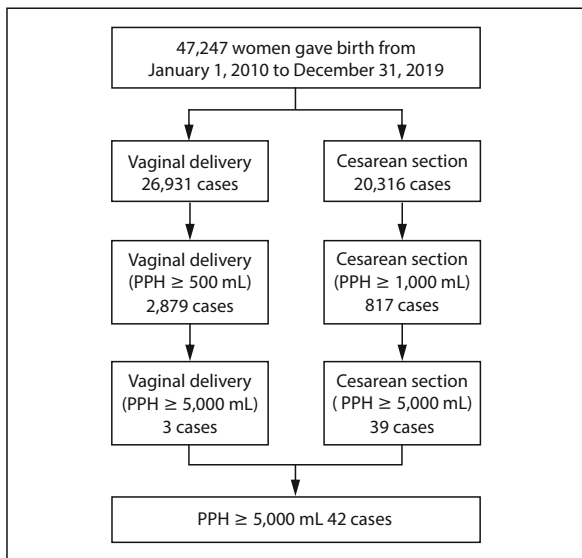


Figure 1. Profile of the study participants; PPH — postpartum hemorrhage

MATERIAL AND METHODS

Study design

Postpartum hemorrhage (PPH) in China is defined as an estimated blood loss of ≥ 500 mL after vaginal delivery or ≥ 1000 mL after cesarean delivery during or within 24 hours of delivery. Life-threatening PPH is considered when the bleeding volume exceeds systemic blood volume (≥ 5000 mL) within 24 hours, patients meeting the above criteria were selected as subjects. The case inclusion process is shown in Flowchart (Fig. 1).

Population

This was a retrospective observational study of 42 cases of life-threatening PPH with a blood loss greater than 5000 mL during or within 24 hours of delivery at Peking University Third Hospital from January 2010 to December 2019. The cases were divided into two groups by cause of hemorrhage: the placenta accrete spectrum (PAS) group (35 cases) and the uterine atony group (7 cases).

Quantitative blood loss

Blood loss was estimated by a combination of direct measurement and gravimetric method [13]. Create a list of dry weights for delivery items that may become blood soaked with directions on how to calculate blood loss. Quantitative methods for estimating vaginal blood loss include direct collection of blood into plastic bags and gravimetric methods wherein pads are weighed before and after use, the difference in the weight being used to determine the amount of blood lost. During cesarean section, begin the process of quantification of blood loss when the amniotic

membranes are ruptured or after the infant is born. After the born of infant and before the delivery of the placenta, replace suction canister. At the end of the surgery, weigh all blood-soaked materials and clots, add the volume of quantified blood calculated by weight with the volume of quantified blood in the suction canister and remove the volume of irrigation fluid to determine total quantification of blood loss. Calculate the amount of blood loss according to the blood volume = blood weight \div 1.05.

Protocol of reducing the blood loss

For uterine atony patients, a sequence of mechanical and pharmacological measures was performed to stop bleeding. If pharmacological measures fail to control the hemorrhage, the surgical interventions including uterine balloon tamponade, selective arterial occlusion or embolization by interventional radiology, uterine compression sutures, stepwise uterine devascularization and internal iliac artery ligation and other more conservative therapies were initiated.

For PAS patients, we have been exploring and making efforts on the protocol of reducing life-threatening PPH. From preoperative evaluation to surgical operation to postoperative treatment, a series of measures were taken to reduce PPH and serious complications. Preoperative diagnosis was performed in combination with ultrasound and/or magnetic resonance imaging (MRI). Since 2016, our center has started to use the "Placenta accreta scoring system" designed by Chong et al. [14] of the third hospital of Peking university to predict the type of placenta accreta, intraoperative blood loss, and hysterectomy rate. According to different scoring levels, a customized follow-up and treatment options for patients can be made including the time of termination of pregnancy, preoperative preparation, selection of surgical methods, and organization of experienced teams containing obstetrics, pediatrics, urology, vascular surgery, anesthesiology and laboratory doctors. During the operation, according to different scoring levels, cystoscopy, stent placement, femoral artery isolation, and preparations to place an abdominal aorta balloon and hysterectomy can be performed. Vessel interruption and perfoliate compression suture (VIP-CS) operation was performed in our center, it was proved to be a simple, efficient and safe hemostasis method to control bleeding for PAS. The obstetric management team was responsible for the initial judgment, fully communicate with the anesthesia team to ensure timely and effective fluid resuscitation, blood transfusion and correction of disseminated intravascular coagulation (DIC). After surgery, the patient was transferred to intensive care unit for further observation and treatment.

Protocol of Blood Products Transfusion

Transfusion of packed red blood cells (PRBCs) was started when 1500 mL of blood (30% of blood volume) was

Table 1. Patient baseline characteristics

Variables	Total (n = 42)	PAS (n = 35)	Uterine atony (n = 7)	p value
Age [years]	33.60 \pm 4.07	33.14 \pm 3.69	35.86 \pm 5.37	0.108
BMI [kg/m ²]	22.94 \pm 2.96	22.97 \pm 3.01	22.77 \pm 2.90	0.876
Gravidity	3.50 \pm 1.55	3.91 \pm 1.34	1.43 \pm 0.54	0.000
Parity	1.95 \pm 0.66	2.09 \pm 0.61	1.29 \pm 0.49	0.002
Plurality	6	3 (8.58%)	3 (42.86%)	0.076
Times of cesarean section	1.10 \pm 0.76	1.29 \pm 0.67	0.14 \pm 0.38	0.000
Times of abortion and intrauterine operation	1.24 \pm 1.08	1.46 \pm 1.04	0.14 \pm 0.38	0.000
Gestational age of delivery [weeks]	34.00 \pm 3.95	33.35 \pm 3.94	37.31 \pm 1.93	0.014
Mode of delivery				
Cesarean section	39	34 (97.14%)	5 (71.43%)	1.000
Elective	30	26 (76.47%)	4 (80.00%)	
Emergency	9	8 (23.53%)	1 (20.00%)	
Spontaneous vaginal delivery	3	1 (2.86%)	2 (28.57%)	0.108
Birth weight [g]	2349.27 \pm 813.01	2228.29 \pm 840.49	2809.00 \pm 500.99	0.043

BMI — body mass index; PAS — placenta accrete spectrum

lost, for PAS patients, preoperative evaluation intraoperative bleeding will be more, with the start of operation red blood cells were infused. The targeted hemoglobin level was 9 gm/dL. We performed massive transfusion protocol (MTP) [10], the ratio of PRBCs: fresh frozen plasma (FFP): platelets are optimally 1:1:1 to imitate replacement of whole blood.

Data collection

We reviewed maternal characteristics included age, gravidity, parity, body mass index (BMI), times of cesarean section, times of abortion and intrauterine operation, fetal characteristics included plurality, gestational age and birth weight and obstetrical factors included spontaneous vaginal delivery, cesarean delivery with elective or emergency, blood loss, blood products transfusion, intervention measures, postoperative complications and prognosis.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 19.0, New York, USA). Independent samples t-test was used for comparisons between the two groups. The Chi-square test was performed to ascertain differences in qualitative variables. $p < 0.05$ was considered statistically significant.

Ethical approval

This study was approved by the Medical Ethics Committee of Peking University Third Hospital, Beijing, China (IRB00006761-M2017377).

RESULTS

A total of 47,247 women gave birth in our center during the study period, of which 42 (0.89‰) women with a blood loss greater than 5,000 mL during or within 24 hours of delivery, bleeding was controlled in all cases, and all the patients were survived. PAS is the most important cause of life-threatening postpartum hemorrhage (35/42, 83.33%).

The baseline characteristics for patients with life-threatening PPH are summarized in Table 1. The gravidity, parity, times of cesarean section, times of abortion and intrauterine operation in the PAS group were significantly higher than those in the uterine atony group. The gestational age of delivery and the birth weight of newborn were significantly lower than those in the uterine atony group ($p < 0.05$). There were no significant differences between the two groups in age, plurality, length of hospital stays and the mode of delivery.

Obstetric interventions with life-threatening PPH are summarized in Table 2. All patients with life-threatening PPH were operated by physicians with senior technical titles. The transfusion volume of PRBCs, FFP and platelets were respectively 23.49 \pm 8.42 U, 2345.24 \pm 826.16 mL and 0.81 \pm 1.19 U, the ratio was basically conformed to the recommended MTP (1:1:1). The amount of blood loss, operation time, PRBCs transfusion, FFP transfusion and fibrinogen transfusion in the PAS group were higher than those in the uterine atony group, and the RBCs transfusion was significantly higher than that in the uterine atony group (25.04 \pm 8.92U vs 18.90 \pm 6.37U; $p < 0.05$). There was no significant differ-

Variables	Total n = 42	PAS (n = 35)	Uterine atony (n = 7)	p value
Amount of Blood loss [mL]	6835.05 ± 2032.43	6968.43 ± 2118.31	6168.14 ± 1475.40	0.348
Operation time [minutes]	268.43 ± 105.23	274.94 ± 104.68	235.85 ± 109.94	0.376
Red blood cells [units]	23.49 ± 8.42	25.04 ± 8.92	18.90 ± 6.37	0.047
Fresh frozen plasma [mL]	2345.24 ± 826.16	2402.86 ± 851.81	2057.14 ± 660.447	0.318
Platelet [units]	0.81 ± 1.19	0.82 ± 1.31	0.90 ± 0.88	0.849
Fibrinogen [g]	6.42 ± 3.62	6.76 ± 3.55	5.50 ± 3.45	0.426
Uterine tamponade	5 (11.90)	3 (8.57)	2 (28.57)	0.394
Surgical suture	34 (80.95)	26 (74.29)	6 (85.71)	0.871
Vascular ligation	28 (66.67)	23 (65.71)	5 (71.43)	1.000
Embolization	1 (2.38)	0	1 (14.29)	0.167
Abdominal aortic balloon occlusion	9 (21.43)	9 (25.71)	0 (0)	0.314

PAS — placenta accrete spectrum

Variables	Total (n = 42)	PAS (n = 35)	Uterine atony (n = 7)	p value
DIC	8 (19.05)	5 (14.29)	3 (42.86)	0.219
Pelvic organ injury	6 (14.29)	5 (14.29)	1 (14.29)	1.000
Heart failure	2 (4.76)	2 (5.71)	1 (14.29)	1.000
Secondary surgery	5 (11.90)	3 (8.57)	2 (28.57)	0.394
Acute kidney injury	1 (2.38)	1 (2.86)	0	1.000
Pulmonary edema	1 (2.38)	1 (2.86)	0	1.000
Thrombosis	4 (9.52)	4 (11.43)	0	1.000
Gastrointestinal recovery time [day]	3.02 ± 1.39	2.85 ± 0.89	3.86 ± 2.73	0.372
Catheter placement time [day]	7.20 ± 5.72	7.88 ± 6.05	3.86 ± 0.90	0.001
Length of hospital stay [day]	14.74 ± 7.72	14.54 ± 8.23	15.71 ± 4.61	0.719
Hysterectomy	34 (80.95)	30 (85.71)	4 (57.14)	0.219
ICU admission rate	40 (95.24)	34 (97.14)	6 (85.71)	0.746
Length of stay in ICU [hour]	53.80 ± 43.48	52.50 ± 43.91	60.14 ± 44.06	0.677

DIC — disseminated intravascular coagulation; ICU — intensive care unit; PAS — placenta accrete spectrum

ence in uterine tamponade, surgical suture, vascular ligation and abdominal aortic balloon occlusion for hemostasis between the two groups.

Intra- and post-operative complications and maternal outcomes with life-threatening PPH are summarized in Table 3. There were no significant differences in DIC, pelvic organ injury, heart failure, secondary surgery, acute kidney injury, pulmonary edema, thrombosis, gastrointestinal function recovery time, length of hospital stays, intensive care unit (ICU) admission rate and length of stay in ICU between the two groups. The catheter placement time in the PAS group was significantly longer than that in the uterine atony group (7.88 ± 6.05 days vs 3.86 ± 0.90 days, $p < 0.05$). The rate of hysterectomy in the PAS group was higher than that in

the uterine atony group, but there were not any significant differences. No maternal deaths.

DISCUSSION

Postpartum hemorrhage (PPH) occurs in approximately 5% of all live births and, even though it is largely a preventable and most often a treatable condition, remains a leading cause of maternal morbidity and mortality [2–3]. The guidelines of various countries mainly define PPH according to the amount of blood loss, the amount of PRBCs transfusion or the drop of hemoglobin, most of which take 500 mL as the minimum standard. Different literatures have different definitions for severe PPH: the amount of blood loss > 1,500 mL, or > 2,000 mL, or > 2,500 mL within

24 hours of delivery; transfusion of 4 or 5 units of PRBCs or a decrease in hemoglobin levels ≥ 4 g/dL [5–11]. NATA consensus statement defining severe PPH as ongoing blood loss of more than 1,000 mL within 24 h or blood loss accompanied by signs/symptoms of hypovolaemia, and massive life-threatening PPH as ongoing blood loss of more than 2,500 mL or hypovolemic shock, whatever the mode of delivery [11]. Severe PPH is considered when the bleeding rate is > 150 mL/min, or when the bleeding volume exceeds 50% of the blood volume within three hours, or when the bleeding volume exceeds systemic blood volume within 24 hours [12]. The incidence of MOH (Massive hemorrhage which defined as the loss of more than 2500 mL of blood) is approximately 6‰ deliveries [15]. As a regional referral center, the proportion of critical patients in our hospital is as high as 80%, the incidence of PPH in our center is higher than reported in the literature. In the past 10 years, there were 42 patients with postpartum hemorrhage ≥ 5000 mL in our center, with an incidence of 0.89‰.

In this study, it was found that PAS was the primary reason for life-threatening PPH (35/42, 83.33%). For the PAS patients, placental villi erode the myometrium, local myometrium is missing, the placenta cannot be completely dissected, and the attached uterus cannot contract. Meanwhile, the implanted part lacks myometrium, and local uterine blood sinuses cannot be closed, which often leads to life-threatening postpartum hemorrhage. Due to the high rate of the first cesarean section and the liberalization of the second-child policy in China, the incidence of PAS has increased significantly. According to literature, the incidence of PAS has increased from 0.08% in the 1980s to 0.3% recent years [16]. As a regional referral center, our hospital receives patients with PAS from all over the country, and the incidence rate of PAS is 3.84% in the past two years. Recent epidemiological studies have also found that a prior cesarean section and a history of previous intrauterine surgical procedures are the two most important risk factors for PAS suggesting that a failure of decidualization in the area of a previous uterine scar can have an impact on both implantation and placentation [17]. One multicenter study of more than 30,000 patients who had cesarean deliveries without labor found that the risk of placenta accreta increased with the number of cesarean deliveries was 0.24%, 0.31%, 0.57%, 2.13%, 2.3% and 6.74% for women experiencing their first through sixth cesarean deliveries, respectively [18]. Consistently with the literature reports, the gravidity, parity, times of cesarean section, times of abortion and intrauterine operation in PAS group were significantly higher than those in patients with uterine atony group.

Medical and surgical attempts to control bleeding must not be delayed by prolonged volume resuscitation in the face of ongoing blood loss. When uterine compression su-

tures, selective arterial ligation and other more conservative therapies have failed, hysterectomy is considered the definitive treatment. In China patients and their families have a strong desire to preserve the uterus, believing that the uterus not only bears the function of gestating life, but also the organ that produces menstruation. The removal of the uterus will cause young patients to lose fertility function, and the double trauma of body and mind may affect the prognosis and long-term quality of life. Therefore, it is difficult to decide about direct hysterectomy before surgery. As a result, timing a hysterectomy can be difficult. In our study, 34 cases (34/42, 80.95%) were performed hysterectomy, in the PAS group 30 cases (30/35, 85.71%) were performed hysterectomy, in the uterine atony group 4 cases (4/7, 57.14%) were performed hysterectomy. Early recourse to hysterectomy is recommended, especially where bleeding is associated with PAS [19].

Replenishing the lost blood volume must take place simultaneously with control of the bleeding. In our center, a multidisciplinary team with anesthesia, intensive care, surgical and hematology departments was quickly built under such circumstance. Anesthetists play an important role in the management of patients with life-threatening PPH. A senior anesthetist should be consulted early to help assess, initiate and continue prompt resuscitation of these patients, using their expertise in fluid and transfusion therapy as well as their experience in managing critically ill patients. In this study, the transfusion volume of PRBCs, FFP and platelets were respectively 23.49 ± 8.42 U, 2345.24 ± 826.16 mL and 0.81 ± 1.19 U, the ratio was basically conformed to the recommended MTP (1:1:1) [10]. This rational is to maintain thrombin generation and fibrinogen by the replacement of coagulation factors as early as possible [20, 21]. This infusion ratio is also controversial. Formulaic protocols, such as 1:1 or 6:4 PRBCs: FFP, based on data derived from traumatic bleeding, have been advocated for the management of major hemorrhage. However, there is no evidence that this improves outcomes in PPH. Recent guidelines from the International Society of Thrombosis and Haemostasis on the management of coagulopathy associated with PPH recommend against a 1:1:1 RBC: FFP: PLT ratio and suggest that if eight units of RBC and FFP have been infused and tests of haemostasis remain unavailable, fibrinogen supplementation (cryoprecipitate or fibrinogen concentrate) and platelet transfusion should be considered [22]. Jones RM suggested that if antenatal thrombocytopenia or consumptive coagulopathy were not present, platelets were only required for PPH > 5000 mL [23]. The empirical use of fixed-ratio blood product administration will lead to over transfusion of blood products but waiting for laboratory-based coagulation testing results may cause treatment delays and adverse outcomes, particularly in the setting of rapid and continuous bleeding.

Peripartum transfusion increased the incidence of stroke, a rapid increase in hemoglobin and hematocrit induced enhanced blood viscosity, possibly increasing the risk of thrombosis and hypertensive encephalopathy [24, 25]. Although the patients in our study had received a large number of blood product transfusions, with reasonable volume management of the intraoperative anesthesiology department and the postoperative ICU, only four cases occurred thrombosis, two of these cases were femoral artery thrombosis after abdominal aortic balloon placement.

Complications of life-threatening PPH mainly include DIC, pelvic organ injury, heart failure, pulmonary edema, renal function injury, thrombus, intestinal obstruction, hysterectomy and other organ failure, even leading to maternal death. In recent years, due to the progress of multidisciplinary cooperation, obstetric technology and nursing level, although the incidence of postpartum hemorrhage has not decreased, the case fatality rate due to severe postpartum hemorrhage has decreased year by year. Surgical complications may be aggravated by placental pathology distorting lower uterine segment and pelvic anatomy and increased blood supply to pelvic organs during pregnancy. In this study, due to the high proportion of patients with PAS, most of these patients had ureteral catheters or stents preoperatively, and 11.90% (5/42) of them had urinary system injuries, including four cases of bladder injuries and one case of ureteral injuries. Therefore, the overall catheter placement time was significantly longer in PAS group than that of patients in the uterine atony group. Modified conventional procedures and preoperative placement of ureter stents reduced the risk of urinary tract injury from 33% to 6% [19].

Generalizability of these findings is also uncertain, given that, as a tertiary referral center, our hospital may receive more life-threatening cases of PPH compared with others. Increasing cesarean delivery rates globally may lead to a higher incidence of PAS and therefore life-threatening PPH. Massive transfusion protocol (MTP), a multidisciplinary approach and early hysterectomy are the very core of managements.

CONCLUSIONS

Placenta accrete spectrum (PAS) is the most important cause of life-threatening PPH. For these patients, MTP is effective, multidisciplinary cooperation and management lead to a good prognosis.

Authors' contributions

XYG designed the study, collected the data, interpreted the results, and drafted the manuscript. YYZ supervised the study, interpreted the results. YZ conceived of the study, supervised the study, interpreted the results.

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Conflict of interests

The authors have no conflicts of interest.

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