Original Article

Clinical Analysis of Postpartum Hemorrhage Requiring Massive Transfusions at a Tertiary Center

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Abstract

Background: The reports on massive transfusions (MTs) in obstetrics have recently been an increasing trend. We aimed to define the clinical features, risk factors, main causes, and outcomes of MTs due to severe postpartum hemorrhage (PPH) and the frequency trends over the past 10 years.

Methods: We retrospectively analyzed the data of 3552 PPH patients who were at ≥28 weeks of gestation in the Obstetric Department of Peking University First Hospital from January 2006 to February 2015. The clinical records of patients receiving MT with ≥5 units (approximately 1000 ml) of red blood cells within 24 h of giving birth were included. The Pearson's Chi-square and Fisher's exact tests were used to compare the frequency distributions among the categorical variables of the clinical features.

Results: One-hundred six women were identified with MT over the 10-year period. The MT percentage was stable between the first 5-year group (2006–2010) and the second 5-year group (2011–2015) (2.5‰ vs. 2.7‰, $\chi^2 = 154.85$, $P = 0.25$). Although uterine atony remained the main cause of MT, there was a rising trend for placental abnormalities (especially placenta accreta) in the second 5-year group compared with the first 5-year group (34% vs. 23%, $\chi^2 = 188.26$, $P = 0.03$). Twenty-four (23%) women underwent hysterectomy, and among all the causes of PPH, placenta accreta had the highest hysterectomy rate of 70% (17/24). No maternal death was observed.

Conclusions: There was a rising trend for placental abnormalities underlying the stable incidence of MT in the PPH cases. Placenta accreta accounted for the highest risk of hysterectomy. It is reasonable to have appropriate blood transfusion backup for high-risk patients, especially those with placenta accreta.

Key words: Blood Transfusion; Placenta Accreta; Postpartum Hemorrhage; Prognosis

Introduction

Postpartum hemorrhage (PPH) remains a common cause of maternal morbidity and mortality worldwide. Massive transfusion (MT) is a relatively new obstetric conception, and it signifies major obstetric hemorrhage that requires extensive coordination of the obstetric, anesthesia, and blood bank teams. The workload encountered in these cases can be extreme and should arouse sufficient attention.[1] However, little is known about the incidence, management, and clinical outcomes of MT in obstetrics.[1] Although there is no agreed definition for MT worldwide, researchers have applied a transfusion of ≥10 units of red blood cell (RBC) within 24 h, 50% blood volume loss within 3 h, or a transfusion of ≥4 RBC units within 1 h as criteria for MT.[2,3] In Scotland, the incidence of MT, defined as >2500 ml blood loss or ≥5 units of RBC within 24 h of giving birth, has risen over the years, with its incidence being reported as 3.7/1000 maternities in the 2003–2005 triennium and 5.9/1000 maternities in the 2009–2012 triennium.[4] Moreover, the study from New York State between 1998 and 2007 had a similar result.[3] Has the same rising trend of MT appeared in China? What are the main causes of such cases compared with other countries? To answer these questions, we designed a retrospective study of MT due to severe PPH, in order to define the clinical

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features, risk factors, main causes, prognosis, and the trends of frequency over the past 10 years.

Methods

We retrospectively collected PPH case data from patients who were at ≥28 weeks of gestation in the Obstetric Department of Peking University First Hospital from January 2006 to February 2015. Women were eligible for inclusion in the study if they had received ≥5 units (approximately 1000 ml) of RBC transfusion within 24 h of giving birth according to the Scotland criteria which were accepted by most researchers.[3] Patients with <28 weeks of gestation were excluded from the study. All patients were selected and followed up by medical records. Clinical features, including maternal age, previous gestational history, mode of delivery, primary cause of hemorrhage, number of red cell concentrate units transfused, and outcomes, were evaluated. The research protocol was approved by the Ethics Committee of Peking University First Hospital before the study began.

Patients were divided into the first 5-year group (2006–2010) and the second 5-year group (2011–2015) according to the time of birth. We compared and analyzed main causes and outcomes of MT between these two groups.

Statistical analysis

Continuous variables were calculated as the median and range, and discrete data were calculated as frequencies and percentages. The Pearson's Chi-square or Fisher's exact tests were used to compare frequency distributions between categorical variables of clinical features. Two-sided $P < 0.05$ was considered statistically significant. SPSS version 11.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

Results

A total of 3552 PPH cases were collected, of which 106 women with blood transfusions of ≥5 units were identified to fulfill the study inclusion criteria. During the study, there were an estimated 40,231 deliveries in the Peking University First Hospital (16,149 in first 5-year and 24,082 in second 5-year), thus making the estimated incidence of MT associated with PPH 26/10,000 births (41/16,149 in first 5-year and 65/24,082 in second 5-year). No significant difference for MT incidence was observed between the first and second 5-year groups (2.5‰ vs. 2.7‰, $\chi^2 = 154.85$, $P = 0.25$).

The demographic and baseline clinical features of the patients in the first and second 5-year groups were determined [Table 1]. The median estimated blood loss within 24 h after delivery was 2944 and 2732 ml for two groups, respectively. The amounts of blood transfusion were 15.4 and 11.5 units, respectively, which was parallel with the blood loss in 24 h in the first and second 5-year groups. Although there was no significant difference in maternal age, gravidity, parity, previous history of PPH or cesarean delivery, antenatal anemia, and severe preeclampsia between the first and second 5-year groups, the percentage of medical induction of labor and cesarean rates rose in the second 5-year group compared with the first 5-year group [Table 1]. The induction rate in the second 5-year group was higher than that of the first 5-year group (46% vs. 24%, $\chi^2 = 191.88$, $P = 0.03$).

The predominant cause of MT was uterine atony (mostly due to multiple gestation, uterine leiomyomas, and chorioamnionitis) throughout the 10-year period, which accounted for 55% of the MTs, followed by placental abnormalities (placenta previa, placenta accreta, and placental abruption) at 29%, laceration (uterine rupture) at 11%, and coagulation dysfunction (amniotic embolism) at 5%. However, there was a significant rising trend of placental abnormalities (especially placenta accreta) in the second 5-year group compared with the first 5-year group (34% vs. 23%, $\chi^2 = 188.26$, $P = 0.03$). Detailed data are shown in Table 2.

Hemostasis was achieved with medical therapy alone in 15% (16/106) of the MT cases. The most common uterotonic agent administered was syntocinon (95%), followed by prostaglandin F2a (59%) and misoprostol (56%). B-Lynch sutures and hydrostatic balloons arrested bleeding in 32% (34/106) and 3% (3/106) of the cases, respectively. Hysterectomy was required to arrest bleeding in 23% (24/106) of the women. In addition, among the hysterectomy cases, 17 cases were found to have placenta accreta, which indicated that placenta accrete associated with high hysterectomy rates compared with other PPH causes [Table 3].

The minimum hematocrit level recorded during the resuscitation period was 15%. Three patients had bladder injury due to severe placenta accreta, and five patients had acute renal failure. Only three cases of electrolyte disturbance and one pulmonary edema case due to massive liquid transfusion were observed. Sixteen patients were transferred to the intensive care unit for close monitoring; however, none of them required postoperational mechanical ventilation. The postoperational average hospital stay was 11.5 days. There was no maternal death, and none of the patients developed end-organ dysfunction (such as respiratory/ventilator failure, chronic renal failure, or Sheehan's syndrome). However, one patient with amniotic fluid embolism was kept in a vegetative state immediately following resuscitation.

Discussion

Recent research studies have revealed that the estimated percentage of MT (defined as transfusion of ≥10 units of RBC within 24 h) was 24 per 10,000 maternities (95% confidence interval (*CI*): 19–26) per year.[2,3] Our study revealed that the frequency of massive blood transfusion in our department was close to those studies.

Table 1: Basic clinical features of patients in the first (2006–2010) and second (2011–2015) 5-year periods

Clinical characters	Total (N = 106)	First 5-year (n = 41)	Second 5-year (n = 65)	χ^2	P
Blood loss over 24 h (ml), median (range)	2814 (1000–10,000)	2944 (1000–8400)	2733 (1100–10,000)	72.34	0.78
RCC transfused per case (unit), median (range)	13.0 (5.0–40.0)	15.4 (5.0–40.0)	11.5 (6.0–40.0)	65.27	0.84
Maternal age (years), median (range)	31.3 (25.0–43.0)	31.2 (25.0–43.0)	31.4 (26.0–40.0)	42.38	0.91
Gravidity (times), median (range)	2 (1–7)	2 (1–7)	2 (1–5)	50.16	0.89
Parity (times), median (range)	1 (0–3)	1 (0–3)	1 (0–2)	70.55	0.79
Previous CS, *n*	27	9	18	81.43	0.66
Previous PPH, *n*	2	1	1	0.00	1.00
Antenatal anemia, *n*	8	4	4	0.00	1.00
Severe preeclampsia, *n*	10	5	5	0.00	1.00
Medical induction of labor, *n* (%)	40 (38)	10 (24)	30 (46)	191.88	0.03
Cesarean delivery, *n* (%)	69 (65)	25 (61)	44 (68)	192.07	0.03

MT: Massive transfusion; PPH: Postpartum hemorrhage; CS: Cesarean section.

Table 2: Compositional variation of primary PPH causes in the first (2006–2010) and second (2011–2015) 5-year periods, *n* (%)

Causes	Total (N = 106)	First 5-year (n = 41)	Second 5-year (n = 65)	χ^2	P
Uterine atony	58 (55)	27 (61)	31 (50)	90.42	0.09
Placenta abnormality	31 (29)	10 (23)	21 (34)	188.26	0.03
Laceration	12 (11)	5 (11)	7 (11)	6.13	0.98
Coagulation dysfunction	5 (5)	2 (5)	3 (5)	5.01	0.96

PPH: Postpartum hemorrhage.

Further, we noticed a rising trend of medical induction of labor and cesarean delivery in the MT cases, which indicated that artificial intervention might be associated with adverse outcomes. Medical induction can independently increase the risk of MT due to uterine atony. Therefore, it is crucial to restrict the indication of medical induction to prevent unnecessarily induced labor. The potential reasons might include associated factors, such as advanced maternal age, multiple births, obesity, increased obstetric intervention, and a higher rate of former cesarean section in our department, which is a tertiary center for high-risk pregnancy.

According to the literature, the most common causes for MT were uterine atony, abnormal placentation, trauma, and coagulation dysfunction.[5,6] Among patients who received MT in our study, uterine atony was the most common cause throughout the 10-year period (55%). Although the etiology composition was significantly diverse, there was no significant difference for uterine atony between the first 5-year group (2006–2010) and the second 5-year group (2011–2015). This might be related to the regular obstetric emergency training and comprehensive management of our department, which results in the timely treatment of PPH caused by uterine atony and a subsequent decrease in MTs (from 61% during 2006–2010 to 50% during 2010–2015). However, the percentage of abnormal placentation rose from 23% during 2006–2010 to 34% during 2011–2015, especially for placenta accreta. Since placenta accreta was associated with cesarean section and other forms of uterine cavity operation, it was believed that the rising trend of placenta accreta might be related to the high cesarean rate in China over the past several decades (approximately 35.0%–46.5%).[7] We also hypothesized that the problem might be increasingly severe because the Chinese Government only has allowed two kids per couple instead of one since 2015. It is important to make accurate identifications during the antenatal care period as to provide precise PPH risk evaluations and blood transfusion estimations for such patients before cesarean section. The preparation work should include blood cross-matching, blood bank notification, and communication with anesthetists to be well prepared for emergency planning and massive blood transfusion.[8]

The treatment for PPH is multifactorial and involves timely identification and supportive resuscitation, along with the use of pharmacological, mechanical, and surgical methods to arrest bleeding. Massive blood transfusion used to be associated with severe morbidity; however, modern facilities have significantly improved this outcome.[9,10] A previous analysis of the Nationwide Inpatient Sample suggested a cause-specific peripartum hysterectomy frequency of 3.6/10,000 deliveries in the United States between 1994 and 2007.[6] In our study, 24 of the 40,231 pregnancies required hysterectomy, for an estimated 5.9/10,000 cases. As a tertiary center of obstetrics, the intrauterine transferring system of high-risk pregnancy might account for the hysterectomy rate bias.

Compared with all other PPH causes, placenta accreta had the highest hysterectomy rate. In our study, 17 of the 24 (70%) hysterectomy cases had placenta accrete, reflecting a difficulty in controlling bleeding among the group included in this study. A literature review suggested that abnormal placentation underlies up to 50% of all peripartum hysterectomies, which indicates that placenta accreta likely introduces a greater risk for massive blood transfusion compared with other indications for peripartum hysterectomy.[6] One population-based case-control study in the UK showed that previous and ongoing cesarean

Table 3: Clinical characteristics and prognoses of the hysterectomy patients

Patient number	Age (years)	Delivery mode	Amount of PPH within 24 h (ml)	Amount of red cell transfusion (unit)	Main cause of PPH	Surgical complication
1	33	CS	8000	35	Placenta accreta	–
2	31	CS	5000	22	Placenta previa with accreta	–
3	31	CS	10,000	35	Placenta adhesion	–
4	32	CS	8300	40	Placenta previa	Bladder injury
5	43	Vaginal	6800	33	AFE	Vegetative state
6	37	CS	7740	22	Placenta accreta	ARF
7	29	CS	4040	14	Placenta accreta	Electrolyte disturbance
8	26	CS	5005	14	Placenta accreta	ARF
9	29	CS	5145	14	Uterine atony	-
10	29	CS	3555	12	Placenta accreta	Bladder injury
11	30	CS	8000	40	Placenta accreta	ARF
12	32	CS	5677	22	Placenta accreta	–
13	32	Vaginal	5255	28	AFE	–
14	34	CS	3258	11	Placenta accreta	Electrolyte disturbance
15	37	CS	6240	32	Placenta accreta	Bladder injury
16	33	CS	4500	26	Placenta adhesion	ARF
17	32	CS	5207	24	Placenta accreta	–
18	37	CS	5050	24	Placenta accreta	Pulmonary edema
19	34	CS	3070	11	Placenta accreta	–
20	31	Forcep	7866	26	Uterine rupture	Electrolyte disturbance ARF
21	33	Vaginal	4640	20	AFE	–
22	31	CS	2835	10	Placenta accreta	–
23	22	CS	2061	8	Placenta accreta	–
24	33	CS	2326	6	Placenta previa	–

AFE: Amniotic fluid embolism; ARF: Acute renal failure; CS: Cesarean section; PPH: Postpartum hemorrhage.

deliveries are risk factors for peripartum hysterectomy (odds ratio 3.52, 95% *CI*: 2.35–5.26 and odds ratio 7.13, 95% *CI*: 3.71–13.7, respectively) and that the odds increased with the number of previous cesarean deliveries.[11] The early recognition of placenta accreta by experienced ultrasound or magnetic resonance imaging experts and prophylactic antenatal planning for women who are at a high risk of PPH are keys to improving outcomes and preventing these women from requiring MT.[12,13]

One key strength of our study was that we adopted an MT definition during PPH based on the quantity of RBC transfused, which is an objective and easily ascertained indicator, rather than more subjective and imprecise methods of quantification (i.e., estimation of blood loss). Because the MT definition has not been widely accepted in the Chinese mainland, we believe that our estimate of the MT incidence during PPH is a robust one. However, MT might be affected by multiple factors, and the primary cause of PPH might be difficult to identify. Therefore, the compositional analysis of the primary MT causes might be somewhat biased. Our study failed to detect independent correlative factors for MTs through multivariate analysis because of the small sample of MT cases included. Further, the resuscitation protocol and the proportion of compositional blood transfusions were not assessed in this study. However, they are important and merit further investigation. Therefore, a future large population study is needed to evaluate the appropriate transfusion protocol and prophylactic blood transfusion backup and to facilitate PPH implementation in obstetric units.[14,15]

Although uterine atony remained the main cause of MT, there was a rising trend for placental abnormalities underlying the stable incidence of MT in the observed PPH cases, and placenta accreta accounted for the highest risk of hysterectomy. Medical induction might be a risk factor for obstetric MT.

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Conflicts of interest

There are no conflicts of interest.

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