

# An Analysis of Large Volume Blood and Blood Product Transfusion in Critically Ill Obstetric Patients: A Retrospective Study

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## ABSTRACT

**Objectives:** (1) To study the clinical profile of patients requiring massive blood transfusion ( $\geq 4$  units). (2) To study the pattern of component requirement in these patients. (3) To study the maternal and fetal outcome.

**Materials and methods:** *Design:* It is a retrospective database analysis over 2.5 years from January 2014 to June 2017. *Setting:* Rural tertiary care center in Anand, Gujarat, India. *Population/sample:* Cases with severe obstetric hemorrhage requiring acute transfusion  $\geq 4$  units were included. Samples size is 69. Data were obtained from the medical record department. Parameters analyzed were demographic and obstetric profile, transfusion and laboratory data, adverse maternal and neonatal outcome, data pertaining to intensive care unit (ICU), critical surgical intervention, and complications. Statistical analysis was done using Stata 14.

**Results:** Of total 2619 institutional deliveries and 185 postpartum women referred from outside in the study period, 69 patients required large volume blood transfusion (2.4%). 95% were referred from the government and private setups. Postpartum hemorrhage (PPH) was the leading cause of hemorrhage with high case fatality index and maximum blood product consumption.  $p$  value = 0.0033 (nonparametric test). 76.8% required ICU admission and 40.5% required ventilatory support. 23% underwent peripartum hysterectomy. Maternal mortality occurred in 10% patients.

**Conclusion:** Major blood loss in obstetric practice is the leading cause of maternal morbidity and mortality. Improper transfusion practices contribute to a lot of avoidable complications. Rapid recognition of anticipated and unanticipated hemorrhage, early aggressive hemostatic resuscitation, and multidisciplinary intervention can ensure optimal fetomaternal outcome.

**Keywords:** Massive blood transfusion, Maternal mortality, Postpartum hemorrhage, Severe obstetric hemorrhage.

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## INTRODUCTION

Severe obstetric hemorrhage is a major cause of maternal morbidity and mortality worldwide. The availability of blood and safe transfusion practices is a dream in many countries. Massive blood loss is arbitrarily defined as loss of one blood volume in 24 hours.<sup>1</sup> Major obstetric blood loss is defined as a blood loss more than 2000 mL or the rate of blood loss is more than 150 mL per minute or 50% blood volume loss within 3 hours.<sup>2,3</sup> The major causes of hemorrhage include placenta previa, accreta, atony, genital tract lacerations, uterine rupture, inversion, and hematological abnormalities.<sup>4</sup> Major obstetric hemorrhage usually results in a decrease in hemoglobin  $>4$  g% or acute transfusion requirement of more than 4 units.<sup>2,3</sup>

Patients treated for massive hemorrhage with only packed red cells or crystalloids face a risk of dilutional coagulopathy. This can be prevented with early infusion of fresh frozen plasma and cryoprecipitate.<sup>5</sup> It has been found that early tissue hypoperfusion can cause upregulation of thrombomodulin that can lead to the activation of protein C pathway and in turn enhance fibrinolysis.<sup>6</sup> Supportive measures such as central venous pressure monitoring and avoidance of hypothermia are crucial. Importance is now being stressed upon cultivating the knowledge of transfusion practices among obstetricians to avoid unnecessary complications.

## MATERIALS AND METHODS

It is a retrospective observational database analysis conducted in the Department of Obstetrics and Gynaecology in Pramukhswami

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Swami Medical College over a period of two-and-half years from January 2015 to June 2017. Data were collected from the labor room registers and medical record department after the ethic committee approval. Approval for the study was given by the Institutional Ethics Committee.

Records of all obstetrics patients with bleeding from the uterovaginal canal requiring acute blood transfusion  $\geq 4$  units were studied. All patients were hospitalized in the acute phase. Detailed history was taken from each patient and a thorough clinical and obstetric examination was done. Simultaneous resuscitation was commenced wherever required after obtaining the blood samples for laboratory investigations. Data pertaining to ICU care, critical surgical

intervention, and complications were obtained. Critically ill patients were managed in collaboration with intensivist. Other parameters analyzed were demographic and obstetric profile, transfusion and laboratory data, adverse maternal and neonatal outcome.

Statistical analysis was done using Stata 14. Data are expressed as numbers or percentages, mean (standard deviation), or median as appropriate. Descriptive statistics was used for the assessment of data. As the number of observations in each category is less, nonparametric test (Kruskal–Wallis rank test) was used to find the association between etiology of hemorrhage and mean blood product consumption. *p* value <0.05 was considered statistically significant.

## RESULTS

The total number of deliveries during the study period was 2619. 185 patients were postpartum, delivered outside, and referred to our institution. 69 patients required large volume blood and blood product transfusion which amounts to 2.4%

Table 1 shows the demographic features. 81% of patients belonged to the age group between 21 years and 30 years. Majority were 2nd and 3rd gravidas. Most of the patients belonged to low socioeconomic status. Only 4.3% were prebooked patients while majority were referred patients mostly from the private setups. 49.2% underwent spontaneous vaginal deliveries while cesarean

**Table 1:** Distribution of patients according to demographic data and obstetric profile

	N	(%)
Age		
<20	5	7.2
21–30	56	81.1
31–40	8	11.5
>40	0	0
Gravida		
1	17	24.6
2	18	26
3	18	26
≥4	16	23.1
Socioeconomic status		
Low	42	60.8
Middle	27	39.1
High	0	0
Booking status		
Booked	3	4.3
Unbooked	Pvt 46	66.6
	Govt 20	28.9
	Total 66	95.6
Type of admission		
Antepartum	42	60.8
Postpartum	27	39.1
Mode of termination of pregnancy		
D&E	1	1.4
Spontaneous vaginal delivery	34	49.2
Instrumental delivery	2	2.8
Cesarean delivery	25	36.2
Hysterotomy	1	1.4
Laparotomy (rupture uterus)	6	8.6

section was performed in 36.2% patients. Indications for cesarean included major degree placenta previa, abruption, and fetal distress among others.

With reference to Table 2, among the etiologies causing severe obstetric hemorrhage, PPH was the leading factor followed by antepartum hemorrhage, rupture uterus, and inversion. 9 patients have been grouped into others category which included patients with blood coagulation abnormalities, thrombocytopenia, and hemolysis elevated liver enzyme and low platelet count (HELLP) syndrome.

The mean blood indices during hemorrhagic episodes and postresuscitation are shown in Table 3. The number of patients who had very low hemoglobin below 5 g/dL was 27 (39%). Patients with activated partial thromboplastin time (APTT) more than 120 and INR >5 were 10 (14%). 16 patients (23%) had platelet count less than 50,000/cubic mm. Postresuscitation hematological and coagulation profile were found to improve and within normal range.

Table 4 shows the distribution of blood products that were consumed. The number of patients requiring massive transfusion ≥10 units was 7. The average blood product transfusion within first 4 hours of resuscitation was 9.3.

We tried to find an association between the etiology of hemorrhage and average blood product consumption. It was found that PPH was responsible for maximum blood transfusion. Using the Kruskal–Wallis rank test, *p* value was found to be 0.0033 which was significant (Table 2).

Table 5 shows the complications that occurred in the study population. 52% had deranged coagulation out of which majority had abruption. 76.8% patients required ICU admission and the average ICU stay was 4.1 days. The mean hospital stay was 10.6 days. 40.5% patients required ventilatory support. 15.9% patients underwent exploratory laparotomy for rupture uterus, PPH, and rectus sheath hematoma. One patient was taken for hysterotomy for 25 weeks in view of severe antepartum hemorrhage with type 4 placenta previa. Peripartum hysterectomy was done for 23.1% patients. 21.7% patients were taken for cervicovaginal exploration under general anesthesia for traumatic PPH. Mortality occurred in 10.1% women among the study population, mostly in patients presenting with PPH. Preterm delivery occurred in 42% while the live birth rate was 56.5%.

## DISCUSSION

In 2009, the total maternal deaths globally were 2,443,000. Obstetric hemorrhage contributed to 27% of these deaths. 99% deaths occurred in low-resource countries.<sup>4</sup> According to WHO 2008, 127,000 maternal deaths occur annually around the world due to obstetric hemorrhage and it is the leading cause of maternal mortality.<sup>7</sup> In 2015, 830 women died per day globally and the primary causes were hemorrhage and infection.<sup>8</sup> The maternal mortality ratio (MMR) in 2015 worldwide was 216/1,00,000 live births.<sup>9</sup> In India, the MMR in 2015 was 174/1,00,000 live births.<sup>10</sup> According to the sample registration scheme (SRS), in India, during survey of causes of deaths (2001–2003), PPH accounted for 38% of maternal deaths.<sup>11</sup>

Major blood loss in obstetric practice is a challenge to obstetricians, hematologists, and blood banks. Although routine antenatal care is stressed upon and is considered as a corner stone to reduce maternal morbidity and mortality, however, the occurrence of hemorrhage cannot be predicted. Postpartum hemorrhage is still the major cause of maternal morbidity and mortality. Postpartum hemorrhage can be primary (within

**Table 2:** Etiological factors responsible for massive transfusion and mean blood product consumption

Etiology	N	(%)	Mortality	Case fatality index	Blood product consumption		
					Mean	SD	Median
Incomplete abortion	1	1.4	0	—	NA	NA	NA
PPH	23	33.3	5	21.7	22.69565	18.85696	16
Abruption	16	23.1	0	—	10.75	4.626013	8
Placenta previa	7	10.1	0	—	11.42857	4.466809	11
Rupture uterus	6	8.6	1	16.6	7.333333	1.175119	7.5
Inversion	5	7.2	0	—	9.4	2.50998	8
Rectus sheath hematoma	2	2.8	0	—	NA	NA	NA
Others	9	13.9	1	11.11	20.16667	27.83664	11

Nonparametric test (Kruskal–Wallis rank test) used. *p* value = 0.0033  
NA, not applicable

**Table 3:** Laboratory indices: during event and posttransfusion

	During event			Posttransfusion		
	Mean	SD	Median	Mean	SD	Median
Hb	5.692754	1.652869	5.696377	9.269697	0.9193162	9.3
TC	19621.74	19809.1	17000	14063.64	8592.027	12000
Platelet	141562.3	114821.4	129000	147772.7	80180.82	130000
INR	1.775294	1.35328	1.215	1.009231	0.3234497	0.94
APTT	47.23706	32.04891	33.5	31.76923	11.92132	30
Serum creatinine	1.28942	1.349857	0.9	0.9280303	0.7701008	0.8

**Table 4:** Blood component consumption

Units	Components			
	Red blood cells (N)	FFP (N)	Platelet (N)	Cryoprecipitate (N)
1–2	5	6	6	0
3–4	40	37	16	3
4–9	20	12	10	7
≥10	4	7	5	3

N, number of patients requiring the said units  
Hb, hemoglobin

24 hours) or secondary (24 hours–6 weeks). Major PPH is broadly categorized as moderate (1,000–2,000 mL) or severe (more than 2,000 mL) blood loss.<sup>12</sup> Postpartum hemorrhage is responsible for 8% of maternal death in the developed countries and 19.7% of death in developing countries.<sup>4</sup> Postpartum hemorrhage formed the largest group requiring massive transfusion in our study. The average blood product consumption was also highest in this group. This was also proved statistically. The case fatality index was also the highest. In our scenario, case fatality index was taken as number of fatalities due to a particular condition divided by the number of total cases due to that condition in our study population. Many studies have reported that placenta accreta has become an important cause of intractable hemorrhage. This is consequent to the increasing number of cesarean sections.<sup>13</sup> Placenta previa and accreta formed 10% of our study population. Three patients had previous 3 cesareans. Abruptio constituted an important (23%) of the study group. A high ICU admission rate was noted, which proves the severe and critical nature of these patients. 52 patients were transfused with blood on desperate basis, where group-specific bloods were dispatched before completion of the cross-match procedure which was confirmed later.

**Table 5:** Distribution of patients according to medical, surgical, and perinatal outcome

	N	(%)
Medical outcome		
Deranged RFT	26	37.6
Deranged LFT	16	23.1
Deranged coagulation profile	36	52.1
ICU admission	53	76.8
Mean hospital stay	10.68166 (mean)	8.794749 (SD), 9 (median)
Mean ICU stay	4.144928 (mean)	6.737899 (SD), 2 (median)
Patients requiring ventilatory support	28	40.5
Transfusion-related complications	2	2.8
Mortality	7	10.1
Surgical outcome		
Cervicovaginal exploration under GA	15	21.7
Hysterotomy	1	1.4
Exploratory laparotomy	11	15.9
Peripartum hysterectomy	16	23.1
Perinatal outcome		
Abortion	1	1.4
Preterm deliveries	29	42
Full-term deliveries	38	55
Intrauterine fetal demise	28	40
Neonatal intensive care admissions	6	8.6
Live births	39	56.5



Traditionally, resuscitation has been centered on the administration of crystalloids and packed red cells. However, excessive crystalloid resuscitation can cause third spacing and may worsen hemodynamic and renal perfusion.<sup>14</sup>

Recent data show early coagulopathy changes prior to hemodilution and before consumption of clotting factors occur.<sup>15</sup> Charbit et al. reported that early changes in the coagulation profile occur during the early period of blood loss.<sup>16</sup> The concept has therefore now changed to administration of blood products early into the hemorrhagic episode. Studies have shown improved survival using higher ratio of fresh frozen plasma (FFP) to red blood cells (RBC) transfusion as compared to conventional approach.<sup>17-19</sup> Massive transfusion protocols (MTPs) have been designed to interrupt the lethal triad of acidosis, hypothermia, and coagulopathy. Massive transfusion protocols have a predefined ratio of RBC, FFP/cryoprecipitate, and platelet which are transfused in ratio of 1:1:1 or 2:1:1.<sup>20</sup> In our setup, we have used the combination of blood products from commencement of resuscitation with favorable results. Antifibrinolytic agents such as tranexemic acid have been found to be useful in bleeding episodes. Mortality has also been found to be reduced with the early administration of tranexemic acid in bleeding patients.<sup>21-23</sup> We have also found favorable results with tranexemic acid, especially in surgical site bleeding complications.

Though MTPs have been introduced in our institute, it is still in its nascent stage and we could not determine in how many patients MTP was activated and how many patients received blood components on physician's discretion. As it is a retrospective study, we could not ascertain the determinants involved in physician's decision-making for ordering the volume of blood product or the subjective assessment of blood loss. The study was conducted in a single setup. To arrive at the outcome data of sufficient statistical power, a large population-based multicenter analysis needs to be conducted.

## CONCLUSION

Obstetric hemorrhage and its sequelae can be largely avoided through skilled birth attendance. Recognition of early warning signs of anticipated and unanticipated hemorrhage is the key to its successful management. Massive transfusion protocol is a widely accepted method. This protocol needs to be adopted liberally by the developed and developing nations. Standardized guidelines and protocols for implementing this method in a hassle-free manner is the need of the hour. This is possible through active cooperation and collaboration between gynecologists and blood bank. There is ample potential for research in this direction. Our study aims to highlight the immediate necessity of implementation of this protocol worldwide to help reduce maternal morbidity and mortality.

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## CONTRIBUTION TO AUTHORSHIP

Dr Rumi and Dr Shilpa were instrumental in conceiving the study topic. The planning and detailing of the study were done by Dr Shilpa, Dr Nitin, and Dr Rumi. Data collection responsibilities were shared by Dr Rumi and Dr Vishal. Dr Vishal and Dr Smruti contributed toward the analysis of the study. The study was carried out stepwise by Dr Rumi, Dr Smruti, and Dr Nitin. Regarding manuscript writing, introduction, and review of literature were compiled by Dr Rumi and Dr Shilpa. Dr Rumi and Dr Vishal carried out data analysis and statistical analysis. Critical review and final drafting were done by Dr Nitin and Dr Smruti. Proof reading was done by Dr Nitin.

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