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Blood component therapy in patients having massive obstetric hemorrhage in a tertiary care center in Puducherry

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Abstract:

INTRODUCTION: A proper transfusion protocol must be followed for every patient with massive obstetric hemorrhage (MOH), as each patient may need a different pattern of transfusion support. In this background, it is prudent to understand the current prevalent practices and devise preparatory strategies for managing blood requirements during such scenarios. This study helps us know the pattern and type of blood components given to patients with MOHs.

METHODOLOGY: This prospective cross-sectional study was conducted on patients with a MOH admitted to a single center at a tertiary care teaching hospital in Puducherry between January 2020 and October 2021. During the hospital stay, patient parameters such as diagnosis, obstetric history, blood loss, transfusion of blood products, transfusion reaction, blood group, length of hospital stay, laboratory parameters, and patient vitals and comorbidities were recorded in a predesigned pro forma and tabulated into Excel sheet and analyzed using SPSS software version 19.0.

RESULTS: Fifty-four patients with MOH were included in our study. The median blood loss was 2.15 L, with a range of 2 L. The mean difference between the baseline and posthemorrhage hemoglobin is 1.7 g/dl. No correlation was observed between the number of packed red blood cell (PRBC) transfused and baseline hemoglobin or between random donor platelets (RDP) transfusion and baseline platelet count. The median number of hospital stays was 10 days, ranging from 7 to 14.5 days. Eleven (20.38%) patients had a hysterectomy done to control bleeding. The remaining 43 patients were managed successfully by other measures such as medical management, compressive surgical suturing, and arterial ligation. Forty-eight (88.9%) patients survived, and 6 (11.1%) patients expired.

CONCLUSION: The percentage of RDP and cryoprecipitate transfused to the patients was less than PRBC and fresh frozen plasma (FFP). The FFP-to-PRBC ratio was 2. Regular transfusion audits must be conducted to assess the flaws and improve current strategies.

Keywords:

Blood component therapy, blood loss, massive obstetric hemorrhage, postpartum hemorrhage

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Introduction

Maternal mortality is recognized as a significant global health problem. In developing countries, the leading cause is obstetric hemorrhage. The WHO estimates that maternal deaths are directly related to obstetric hemorrhage and account for 24% or an estimated 1,27,000 maternal deaths annually.[1] Hemorrhages accounted for 27.1% of maternal deaths worldwide. Postpartum hemorrhage remains one of the primary causes of obstetric hemorrhage, with an incidence of 2%–4% in vaginal delivery and 6% in cesarean section.[2] The maternal mortality rate in our country was 113 in 2016–2018.[3] Even in developed countries with advanced systems of providing medical care, delayed or improperly executed transfusion contributes to morbidity and mortality associated with obstetric hemorrhage. Obstetric hemorrhage

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can occur at any time in pregnancy, antepartum or postpartum hemorrhage (PPH).

Estimates for PPH incidence vary in literature but range from 3% to 5%, with <1% of obstetric patients being transfused, often in emergencies. The overall global incidence of PPH is estimated to be 6%–11%, and severe PPH 1%–3%, with substantial variations across regions.[4] In comprehensive emergency obstetric care, blood transfusion is one of the essential components which reduces mortality and morbidity. The transfusion rate in obstetrics is 0.9%–2.3% based on population-wide data from developed countries.[2,5] High-risk deliveries should be conducted in tertiary centers and highly equipped facilities to reduce mortality and morbidity. One of the essential needs during delivery and hemorrhage is transfusion support. Sometimes massive transfusion protocol is needed to resuscitate patients until the bleeding is controlled.[6,7] The rationale use of blood products is essential as there is global insufficiency of blood. It is costly, and the risk of adverse effects of transfusion always remains. Hemodynamic values do not help diagnose massive obstetric hemorrhage (MOH) as the physiological changes associated with pregnancy, such as relative hemodilution and high cardiac output, mask the clinical presentation of hypovolemia that leads to delay in recognition of blood loss, and initiation of treatment.[8] Obstetric hemorrhage is further complicated by anemia in pregnancy, gravida, previous obstetric history, and pregnancy complications. Various medical, surgical, and radiological interventions are available to control PPH. Many trials are done, such as the World Maternal Antifibrinolytic Trial, on an extensive basis to validate and form new protocols to manage and have safe delivery during pregnancy.[9]

In this background, it is prudent to understand the current prevalent practices to devise preparatory strategies for managing blood requirements during such scenarios. Since very few studies have been done regarding transfusion support in patients with MOH patients in India, and especially in this part of the country, this study was designed with an aim to describe the determinants and usage patterns of blood components in patients with MOHs in a tertiary care center in southwestern India.

Methodology

Study design

This prospective cross-sectional study was conducted on patients with a MOH who were admitted to the department of obstetrics at the tertiary care teaching hospital in Puducherry between January 2020 and October 2021.

Study participants

All patients with MOH of any cause during the study period were included in our study. MOH was defined as "blood loss >1500 ml or a decrease in hemoglobin >4 g/dl or 10% decrease in hematocrit or which threatens the hemodynamic stability of the patient and which requires a blood transfusion."[10] Patients with known bleeding disorders and clotting factor deficiency were excluded from our study.

Study procedure

Consecutive patients with MOH admitted to the hospital were selected. During the hospital stay, patient parameters such as diagnosis, obstetric history, blood loss, transfusion of blood products, transfusion reaction, blood group, length of hospital stay, laboratory parameters, and patient vitals and comorbidities were recorded in a predesigned pro forma and tabulated into an Excel sheet. All patients were followed till discharge/death.

Statistical analysis

Descriptive statistics for continuous variables such as age, weight, and laboratory parameters were presented either with a mean with standard deviation (SD) or a median with an interquartile range depending on the data distribution. The categorical variables, such as diagnosis and type of transfusion were expressed as the frequency with proportions. The normality of the data was tested using the Kolmogorov–Smirnov test. The comparison of the rise in hemoglobin and transfusion triggers was performed using a correlation between the number of units transfused and the rise in hemoglobin. The exposures, such as diagnosis and morbidities with outcomes, were performed using the Chi-square test/Fisher exact test. All statistical analyses were carried out at a 95% confidence interval, and a $P < 0.05$ was considered statistically significant.

Statement of ethics

Ethical clearance was obtained from the Institutional Ethical Committee under project no: JIP/IEC/2019/433.

Results

Totally 54 patients were included in the study. There was no missing data. The biophysical characteristics of the patients included are summarized in Table 1. The minimum age was 18 years, and the maximum was 37 years, with a mean of 27.2 and a SD of 4.6.

The various causes of hemorrhage in relation to the parity of the patients are summarized in Table 2.

Baseline laboratory parameters

The median baseline hemoglobin was 9.8 g/dl (range 7.8–10.97 g/dl). The minimum platelet count was

35,000/μL, and the maximum was 5,70,000/μL. The mean platelet count at admission was 1,82,944/μL (SD 98,779/μL). The mean hemoglobin at admission was 9.2 with SD (2.43), and posthemorrhage was 7.5 (SD 2.23). The mean difference between the baseline and post-haemorrhage Hb was 1.7 g/dl.

Table 1: Biophysical features of the included patients

Biophysical characteristics of the study participants	*n*
Age (years)	
≤25	19
26-29	16
≥30	19
Gravida	
Primi	20
G2	19
G3	10
≥G4	5
Comorbidity (surgical)	
Previous LSCS	18
Other surgeries	4
Nil	32
Comorbidity (medical)	
Hypertension	6
Diabetes mellitus	6
Hypothyroidism	7
Anemia	2
Acute fatty liver	2
Seizure disorder	1
Rheumatic heart disease	1
Blood group	
A (RhD positive+negative)	12+1
B (RhD positive+negative)	18+1
O (RhD positive+negative)	19+1
AB RhD positive	1
Obstetric history	
Normal pregnancy	27
Placental abnormalities	10
Abruption	6
Hypertensive disorders	4
Ectopic pregnancies	3
Miscarriages	4

LSCS=Lower segment cesarean section

Table 2: Causes of hemorrhage in relation to parity

	Primi	G2	G3	≥G4	Total
Atonicity	8	9	3	0	20
Structural placental abnormalities	0	1	2	1	4
Traumatic	2	0	2	1	5
Ruptured ectopic	2	1	0	1	4
Miscarriages	0	2	0	1	3
Secondary PPH	1	0	0	0	1
Scar rupture	0	2	1	0	3
Placental abruption	2	0	0	1	3
Atonicity+traumatic	3	2	0	0	5
Atonicity+abruption	2	2	2	0	6
Total	20	19	10	5	54

PPH=Postpartum hemorrhage

Blood loss

The median blood loss was 2.15 litres (L) [range 1.5L-3.5L]. The primary cause of obstetric hemorrhage was atonicity, i.e., 20 (37%). Only one case (2%) had secondary PPH due to placental tissue retention. Five (9%) patients had atonicity and traumatic PPH. Six (11%) patients had abruption and atonicity. Four patients had ruptured ectopic. Three patients had scar rupture.

Nineteen patients in the age group of ≤25 years and ≥30 years had a MOH. Patients more than 30 years had more than 3.5 L blood loss. The association between age and amount of blood loss was not statistically significant, with a $P = 0.29$ by Fisher's exact test. The amount of blood loss in relation to parity is shown in Figure 1.

Transfusion therapy

A massive transfusion protocol was activated in 11 patients. Total number of components transfused, including packed red blood cell (PRBC), fresh frozen plasma (FFP), random donor platelets (RDP), and cryoprecipitate, was 925. The average blood loss deficit is 1235 ml with SD (688.9) in all cases. The median number of blood products transfused to patients with MOH is given in Table 3. Twenty-three (42.6%) patients had ≤3 PRBC transfusions. Twenty-five (46.3%) patients had > three units but <7. The number of units of PRBC transfused in relation to estimated blood loss is shown in Table 4. Six (11.1%) patients received seven or more PRBC units of transfusion. Four patients referred from outside the hospital were transfused with whole blood in their referral center. The ratio of FFP to PRBC was 2.1 in our study. The median ratio of FFP to PRBC is 1. The ratio of FFP to PRBC transfusion had a moderate correlation with a spearman correlation coefficient value of 0.4 and a $P = 0.01$. FFP, RDP, and cryoprecipitate transfusion were given to 94.4%, 68.5%, and 46.3%, respectively, of MOH patients.

There was no correlation (rho-0.1) between the number of PRBC transfused and baseline hemoglobin. No

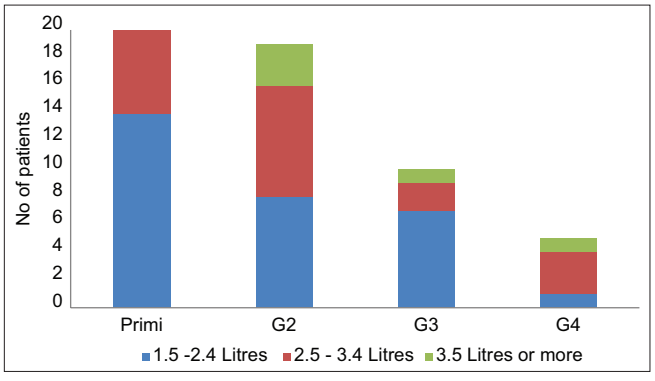

Figure 1: Amount of blood loss in relation to parity

correlation (rho-0.03) between RDP transfusion and baseline platelet count was observed. The average blood loss deficit in the expired patient was 2666 ml with SD (303.7), whereas in survived patients, it was 1334 ml with SD (385.9).

Six transfusion reactions (11.1%) were noted. Four were febrile nonhemolytic transfusion reactions, and two were allergic. Thirty-two patients were suspected of having disseminated intravascular coagulation (DIC), and four were in overt DIC.

The relation of PRBC transfusion with regard to blood loss and the patient's age is given in Tables 4 and 5, respectively. The difference in PRBC transfusion between groups with regard to blood loss was different, and the difference was significant with a $P = 0.03$ by Fisher's exact test.

Four patients went into DIC. Of the 54 patients, 48 survived. The details of the outcomes of the patients and those who succumbed are summarized in Tables 6 and 7, respectively.

The procedure done to control hemorrhage is shown in Table 6. Medical management was sufficient in blood loss of fewer than 2.5 L, whereas surgical procedures such as arterial ligation, followed by surgical suturing and hysterectomy, were required in blood loss of more than 2.5 L. The procedure to control hemorrhage was different in groups and was statistically significant with a $P = 0.01$.

The median hospital stay was 10 days with an interquartile range (25–75) of 7–14.5 days. Obstetric hemorrhage in relation to hospital stay was not statistically significant, with a $P = 0.7$. Thirty-three patients had a hospital stay of ≤10 days. Only four patients had a hospital stay of >20 days. The average number of blood units utilized increased as the length of hospital stay increased and was statistically significant, as shown in Table 8.

Table 3: Summary of blood products transfused per patient

Blood products	The median number of units (range)
PRBC	4 (1-14)
FFP	4 (4-20)
RDP	4 (0-17)
Cryoprecipitate	0 (0-33)

PRBC=Packed red blood cells, FFP=Fresh frozen plasma, RDP=Random donor platelets

Table 4: The number of units of packed red blood cells in relation to the amount of blood loss

PRBC	1.5-2.4 L	2.5-3.4 L	≥3.5 L	Total
≤3	18	4	1	23
4-6	10	11	4	25
>6	2	4	0	6

PRBC=Packed red blood cells

Table 5: The number of units of packed red blood cells in relation to age

PRBC	≤25 years, *n* (%)	26-29 years, *n* (%)	≥30 years, *n* (%)	Total
≤3	7 (30.4)	9 (39.1)	7 (30.4)	23
4-6	9 (36)	6 (24)	10 (40)	25
>6	3 (50)	1 (16.7)	2 (33.3)	6

PRBC=Packed red blood cells

Table 6: Outcomes of patients with massive obstetric hemorrhage

Outcomes	*n* (%)
Hysterectomy	11
Sepsis	5
AKI	4
MODS	3
CNS hemorrhage	1

AKI=Acute kidney injury, MODS=Multiorgan dysfunction syndrome, CNS=Central nervous system

Discussion

The median number of PRBC transfused was 4 (1–14). As there is no substitute for blood, PRBC transfusion becomes vital during this crucial hemorrhage period. All high-risk pregnancies should be referred to centers with expertise in the management and availability of blood and blood products. Twenty-three (42.6%) were transfused ≤3 units PRBC, 25 (46.3%) patients with 4–6 units, and six patients with more than six units of PRBC. The coefficient was – 0.02 and P - 0.86, which was not statistically significant. A retrospective analysis of transfusion management for obstetric hemorrhage in a Japanese obstetric center by Matsunaga *et al*. shows a negative correlation between the volume of red cell transfusion and the hemoglobin concentration before transfusion in 187 obstetric patients.[11]

The median FFP transfusion was 4 (4–20). FFP is an integral part of Massive transfusion protocol (MTP). In massive hemorrhage, patients will have dilutional coagulopathy due to infusion of crystalloids, so transfusion of FFP is mandatory. FFP contains all the stable clotting factors of 1 IU/ml. Obstetric hemorrhage has more chance of acquired coagulopathy by dilutional or consumption coagulopathy. Due to hemorrhage, clotting factors, fibrinogen, and platelets may be rapidly consumed. Consumption coagulopathy is seen in DIC and other complications of massive hemorrhage. Our study did not include any patients with factor deficiency. Another study by Fazal and Poornima on transfusion practice in obstetric hemorrhage in a tertiary care center shows that the median FFP/PRBC ratio for each patient was 1.42.[12]

Table 7: Details of patients who succumbed/expired

Blood loss (L)	Number of PRBCs transfused	Blood deficit	Cause of PPH	Length of hospital stay	Complications
1.5	3	750	Traumatic	7	Sepsis, AKI
1.5	8	0	Traumatic	4	Cardiac shock
3	14	0	Uterine rupture	7	DIC
2	3	1250	Abruption	42	Sepsis, MODS
1.8	5	550	Abruption	18	Allergic reaction
1.7	4	700	Abruption+atonicity	12	AKI, MODS

DIC=Disseminated intravascular coagulation, AKI=Acute kidney injury, MODS=Multiorgan dysfunction syndrome, PPH=Postpartum hemorrhage, PRBC=Packed red blood cells

Table 8: Length of hospital stay in relation to the number of packed red blood cell units transfused

Length of hospital stay	PRBCs utilized, mean (SD)	ANOVA
≤10 days	3.8 (2.4)	F=5.845 (P<0.01)
11-20 days	4.1 (2.2)	
≥20 days	8.5 (5.3)	

SD=Standard deviation, PRBC=Packed red blood cells

In our study, the median FFP/PRBC ratio was 1. Platelets also form an essential integral of hemostasis. The correction of anemia is essential before the transfusion of platelets. A decrease in hematocrit due to anemia disrupts the laminar flow of platelets. Generally, platelets are away from the central luminal flow and are toward the periphery of the vessels, so it helps in vessel hemostatic maintenance. In hemorrhage due to bleeding, anemia develops, which causes the platelets to come to the center leading to decreased hemostasis.[13] Platelet transfusion is given to correct loss during hemorrhage and in conditions like DIC, where platelets are consumed. The median transfusion of platelets was 4 (0–17) in our study. None of our patients had primary platelet disorder. Cryoprecipitate was transfused to a few patients suspected of having DIC or with more chances of developing DIC. The median transfusion of cryoprecipitate was 0 (0–33). Fibrinogen is an essential indicator in obstetrics during massive hemorrhage. Fibrinogen is rich in cryoprecipitate. Fibrinogen is a marker of hemorrhage severity, and early fibrinogen supplementation improves the clinical outcome and reduces mortality in severe obstetric hemorrhages.[14] Fibrinogen concentrates are the first choice in managing hypofibrinogenemia in obstetric hemorrhage. Due to the unavailability of fibrinogen concentrates in our center, the next best option was cryoprecipitate transfusion.

None of our patients was Bombay blood group. Bombay blood group is scarce, and managing a Bombay blood group patient with MOH is very difficult. Most pregnant patients with the Bombay blood group with a high risk of bleeding are successfully managed with autologous transfusion. Autologous blood is collected at 32 weeks to be used during delivery when needed. Pytel *et al*. share their experience managing 13 pregnant patients with rare blood groups.[15] Intraoperative cell salvage is done in most surgeries where expected blood loss is >2 L, such as oncological, orthopedics, and other surgeries. It is not tried in obstetrics due to the risk of amniotic fluid embolism and maternal–fetal alloimmunization. The Giancarlo Maria review on intraoperative cell salvage in obstetrics tells us about the feasibility of using cell salvage in the obstetrics population.[16]

These patients should be managed from the first trimester with regular follow-up, correction of anemia, patient blood management, assessment for PPH, early recognition, and control of bleeding. Ideally, patient blood management should be followed in all high-risk cases. PBM evolves on three pillars to maintain adequate hemoglobin levels, control bleeding, and improve hemostasis. Obstetrics is a good field of choice to implement PBM because any pregnant lady can develop PPH. Any pregnant lady with no comorbidities with no predisposing factors can develop PPH. All obstetricians should be educated on PBM and encouraged to implement it in all cases. It helps in improving the outcomes and reduces mortality and morbidity. Subrek *et al*. speak on expert opinion and literature review on patient blood management in pregnancy and childbirth.[17]

A study by Patricia *et al*. shows that young females <20 years are more prone to pregnancy complications such as poor fetal growth, including PPH.[18] A study on pregnancy outcomes in elderly primigravida showed that 3% of their study population had antepartum hemorrhage, and 3% had a PPH.[19]

In our blood center, there is 100% component preparation. We do not use whole blood. Four patients who were referred from other hospitals were transfused with whole blood. The mean use of whole blood in these patients is 3. With the advancement in component preparation and fractionation, targeted treatment has become possible. Whole blood becomes a lifesaving option in the resource-poor setting until the patient is referred to a higher center for further management. Whole blood is still preferred in resource-poor, military, and trauma settings. Fresh whole blood can also be used in obstetric emergencies like massive PPH. Low titer O whole blood is preferred in these settings and MTP. There is no fixed titer for low titer O whole blood. It varies from institute to institute and depends

on institutional policy. Generally, a low titer means anti-A and anti-B <256.[20] The low titer is preferred because there will be less chance of hemolysis since the plasma of O patients has both anti-A and anti-B. Another theoretical advantage of whole blood is the confirmed ratio of PRBC, FFP, and platelets, reduced donor exposure, decreased chance of TTI, decreased transfusion reaction, and low production cost. A study on whole blood for PPH: early experience at two institutions by Morris *et al.* was done. Another pilot study by Munoz *et al.* shows that whole blood transfusion reduces overall component transfusions in 34 cohort patients in placenta accreta spectrum cases.[4]

Massive transfusion protocol was activated in 11 (20%) of our patients. A study done by Ochiai *et al*. on massive blood transfusion protocol for PPH in a university hospital in Japan shows that 24 (0.7%) of their deliveries needed MTP.[21] In our study, there was more activation of MTP. This could be because our institute is a tertiary care center that handles most high-risk and referred cases. In MTP, components must be given in the ratio of 1:1:1 or 2:1:1. In another retrospective study in PPH treated with a massive transfusion protocol at a tertiary obstetric center, 0.26% of patients had MTP activation.[22]

The strength of the study was that it was a prospective study, and we followed all the patients up to discharge/death. None of the patients was denied any blood product due to the lack of inventory, so transfusion bias due to the unavailability of bloodstock is ruled out.

Conclusion

Although many improvements and development have occurred in obstetrics, obstetrics hemorrhage is one of the leading causes of mortality and morbidity. Transfusion support is one of the essential components of management during hemorrhage. The percentage of RDP and cryoprecipitate transfused to the patients was less than PRBC and FFP. The FFP-to-PRBC ratio was 2. Most of our cases had atonicity. Atonicity was one of the strong factors for hemorrhage. Surgical procedures like arterial ligation are the definitive treatment in a few cases. The mean length of hospital stay is longer for patients with increased transfusion but could directly be due to the severity of the condition. Eleven percent of our patients who required massive transfusion expired, which is high, explaining the seriousness of MOH, which needs a multidisciplinary approach.

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Conflicts of interest
There are no conflicts of interest.

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