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Original Research Paper

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MASSIVE OBSTETRIC HEMORRHAGE: ETIOLOGY, PATIENT CHARACTERISTICS, MANAGEMENT AND ITS OUTCOME IN TERTIARY CARE CENTRE

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ABSTRACT

Background: Obstetric hemorrhage is one of the most common causes of maternal deaths causing 25% with estimated 1,27,000 deaths annually in developed and developing countries (WHO). Massive Transfusion Protocol (MTP) is the recommended therapeutic transfusion strategy for the clinical management of Massive Obstetric Hemorrhage.

Methods : An observational study, on 75 women, during 18 months duration with MOH causing hemoglobin deficit of > 4 g/dl was done. Amount of Blood loss estimated visually and co-related with laboratory parameterchanges. Patient characteristics and etiologies were studied. Maternal outcome studied in terms of interventions and complications.

Results: MOH was more common in multigravida (72%) almost equal occurence in antepartum (44%) and postpartum (45%) period. Most common causes were Abruption(24%), Atonic PPH(28%).Majority had estimated blood loss of 1500-2000ml (78.67%). Median number of PRBC transfused is 5and FFP is 4. Ratio established is PRBC:FFP 1.17:1. Most common complication was DIC (35%), Acute Kidney injury (21%) and Bladder injury(14%). Mortality observed in 12% study population.

KEYWORDS : Massive Obstetric Hemorrhage, Blood transfusion, Maternal Outcome.

INTRODUCTION

In India, an estimated 67000 maternal deaths occur each year with obstetric hemorrhage as second leading cause (21.56%) [1]. Definitions of Massive obstetric hemorrhage are : RCOG (2016) Severe PPH ≥ 2000 ml ,NHS England Maternity Dashboard Metrics (2017) ≥1500 ml, Scottish CASMM : ≥ 5 units or treatment for coagulopathy [2] UKOSS : >8 units of blood within 24 hours of delivery, BCSH (2006) Blood loss of ≥ 150 ml per minute, loss of 50% blood volume in 3 hours, loss of 100 % blood volume in 24 hours. Massive obstetric hemorrhage or hemorrhage requiring massive transfusion has no universal definition world wide. It is considered as loss of 50% blood volume within 3 hours, decrease in haemoglobin of ≥4gm/dl ,acute loss requiring transfusion of ≥4 units of blood within 1 hour,transfusion of ≥ 10 units of RBC units within 24 hours.

For our study purpose, it is defined as hemoglobin deficit >4g/dl. MOH can be classified into – Antepartum, Intrapartum, Postpartum. Most common causes attributed to MOH are uterine atony, placenta previa and abnormal invasive placenta. Uterine atony is most common cause accounting for 80-90% causes complicating 1 in 20 pregnancies [3] Placenta previa accounts for 0.5% of total deliveries while AIP(adherent invasive placenta) has an incidence of approximately 0.2-3 per 1,000 deliveries. Depending on the depth of attachment it is termed: *placenta accreta* (placenta attached to the myometrium); *placentaincreta* (placenta invades the myometrium); or *placenta percreta* (placenta invades through the myometrium) [4] AIP often leads to severe PPH requiring blood transfusions and sometimes also the need for hysterectomy. Other causes of MOH are : H. mole, Ectopic pregnancy, Placental abruption, Coagulopathies, Rupture uterus, Lacerations in vagina, Uterine atony, Retained placenta.

Serial measurement of hemoglobin, hematocrit, coagulation profile (platelet count, PT, aPTT, INR) point of care monitors (TEG, ROTEM, FIBTEM) is essential for early intervention in MOH. Adjuncts like cryoprecipitate, fibrinogen concentrate, and recombinant factor VII is recommended in uncontrolled hemorrhage with use of more than 10 unit packed cells is anticipated. Early use of blood products is essential in MOH to avoid dilutional coagulopathy.

OBJECTIVE

a) To assess the underlying obstetric risk factors associated with massive obstetric hemorrhage (MOH).
b) To study demographic factors, diagnostic workup, indications of transfusion in different categories.
c) To describe the blood product transfusion pattern in MOH.
c) To study correlation between the volume of RBC Transfusion, Fresh Frozen Plasma, Platelets, Cryoprecipitate, Factor VII and Fibrinogen.
d) To study outcome in different categories.

METHODOLOGY

It is a prospective, cross sectional study conducted at a tertiary care center GMC Nagpur (March 2018- September 2019) on 75 women undergoing obstetric hemorrhage with hemoglobin deficit of 4 g/dl in the span of 3 hours in our indoor setting & referred from outside with proper communication.Data was collected for women undergoing massive obstetric hemorrhage. Maternal demographics , obstetric profile like gravida, gestational age, past obstetric history, present medical history, antenatal diagnostic procedures and fetal condition, complications were noted. Amount of blood loss estimated via visual (Fig 1) and direct methods(Fig 2,3),Continuous variables were presented as Mean SD. Mean hemoglobin was compared during ANC and after event by performing paired t-test, mean % drop in hemoglobin, mean blood product ratio between mortality and survivor by performing independent t test, number of blood products transfused, need for conservative surgical procedures were observed. Statistical software STATA version 14.0 was used for data analysis. Lastly maternal outcome was studied in terms of mortality,ICU stay, who developed complications like AKI , septicemia, who required obstetric hysterectomy to control intractable hemorrhage.

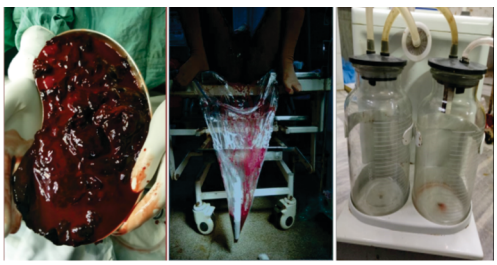


Figure 1 : Methods of Assessment of of Estimation of Blood Loss.

Inclusion criteria:

a. Booked and unbooked antenatal and post natal cases admitted to labour ward with obstetric hemorrhage.

Exclusion criteria:

a) Cases with pre existing coagulopathy.
b) Patients on anticoagulants.
c) Cases of sickle cell disease and hemolytic anemia.

Investigations done :

Complete Blood Count,Urine Routine, Sickling/Hb electrophoresis, Coagulation Profile (Bleeding Time, Clotting Time, PT, aPTTK, INR),Liver Function Tests, Renal function Tests, Ultrasonography, D-Dimer if required,Fibrinogen if required

OBSERVATIONS

In this study, 75 cases were identified according to the criteria. Following results were seen.

Table no 1 : Distribution according to demographic and obstetric factors.

Characteristic group	Group	Frequency	Percentage
Age	20-25	35	46.6%
	25-30	27	36%
	30-35	9	12%
	35-40	4	5.3%
Booking Status	Booked	6	8%
	Unbooked	69	92%
Outside Post natal cases	Yes	11	14.67%
	No	64	85.33%
Gravida	Primigravida	21	28%
	Multigravida	54	72%
Gestational Age (weeks)	<28	9	12%
	28-32	7	9.3%
	32-36	13	17.3%
	36-42	36	48%

Table shows maximum number of patients come under 20-25 years of age (46.6%). Unbooked cases comprises 92%, Out of which 11(16 %) cases were delivered outside and 84.05% were referred antenatal cases. MOH was more commonly found in multigravida (72%) with maximum number of patients (48%) in third trimester.

Table no 2 : Distribution according to risk factors

Risk Factors	No of cases	Percentage
Atonic PPH	21	28%
Abruption	18	24%
Placenta accreta	5	6.67%
Placenta previa	11	14.67%
Rupture Uterus	6	8%
HELLP Syndrome	4	5.33%
Traumatic	9	12%
Ectopic Pregnancy	6	8%
H.mole	1	1.33%
Incomplete abortion	1	1.33%

Table above shows distribution of risk factors.Atonic PPH(28%), Abruption (24%), Placenta Previa (14.67%),Traumatic (12%), Ectopic (8%), Rupture Uterus (8%), Placenta accreta (6.67%), HELLP induced Coagulopathy (4%). Least common was H.mole and incomplete abortion. Out of total cases of atonic PPH 3.9% were in association with traumatic PPH (mixed) and 1.3% each was associated with HELLP and Mullerian anomaly.

Table no 3 Distribution according to Estimated Blood Loss

	No of Cases	Percent
1500-2000 ml	59	78.67%
2000-2500 ml	10	13.33%
>2500ml	6	8%

Above table shows Estimated blood loss of 1500-2000 ml were 59(78.67%), 2000-2500 ml were 10(13.33 %), >2500 ml were 6 (8%).

Table no 4 Distribution according to % Hemoglobin drop

	No of cases	Percent
40-45%	37	49.33%
45.1-50%	27	36%
50.1-55%	6	8%
55.1-60%	5	6.67%

Above table show 37 cases (49.33%) has % hemoglobin drop in range of 40-45%. 27(36%) cases within 45.1-50%. Least common were 5(6.67%) within 55.1-60% drop.

Table no 5 Distribution according to Hemoglobin in ANC

	During ANC	After Event	P Value
Mean	9.84	5.3	<0.0001, HS
SD	1.03	0.95	
Mean Deficit	4.53 ± 0.55		
% Deficit	46.14%		

Above table shows mean deficit of Hemoglobin in this study is 4.53 with mean deficit of 46.14 % within 3 hours of MOH.

Table no 6 Distribution of Laboratory Investigations

	Mean	SD	Median	Range
Platelet	171853.3	72579.83	160000	39000-422000
INR	1.46	0.49	1.3	1-4
PT	18.25	5.8	17.6	10-41
APTT	36	10.34	34.5	12- >60

Above table shows that study population had varied platelet count in range of 39000-422000 with lowest value in association with placenta previa (39000/mm^3). Mean INR in this study was 1.46 with range in between 1-4. 7 cases (9.33%) were in DIC. Mean value of PT was 18.25 sec and aPTT was 36 sec. 11/75 cases had prolonged PT, aPTT.

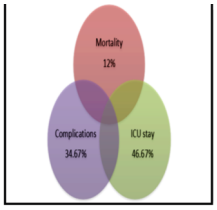
Table no 7 Number of blood Products Transfusion

	Mean	SD	Median	Range
BT	4.88	1.13	5	4-9
Ratio	1.17	0.46	1	0.44-4
FFP	4.53	1.61	4	2-12
Platelet	1.52	2.03	0	0-8
Cryoprecipitate	0.16	1.02	0	0-8

Above table shows mean number of PRBC transfusion is 4.88, FFP is 4.53, platelet is 1.52. Maximum number of cases received 5 PRBC and 4 FFP. Ratio established in this study with PRBC:FFP is 1.17:1.

Figure2: (a) Distribution of maternal outcome (b) causes of mortality (c) complications

(a)



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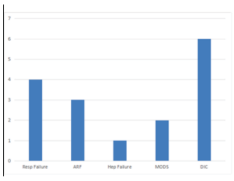
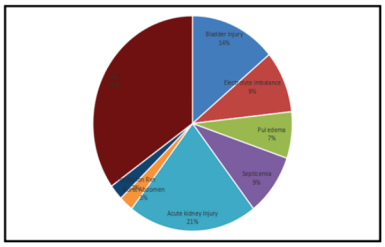
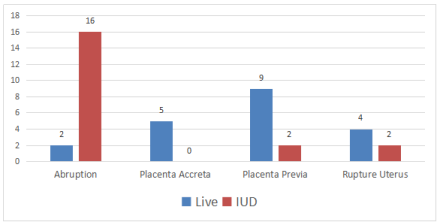




(c)

Figure 3 : Distribution of Fetal Outcome



Overall 46.67% of cases required ICU stay, 34.6%had complications and 12% was the mortality rate in the study. Most common complication being Acute Kidney injury (21%), Bladder injury(14%), electrolyte imbalance(9%), septicemia (9%), pulmonary edema (7%).Bladder injury most commonly associated with obstetric Hysterectomy(83.33%). Only a single case was in relation with rupture uterus. Few patients had more than one complications. Abruption has associated poor fetal outcome (88.89%).

DISCUSSION :

Massive Obstetric hemorrhage is often complicated by an acquired coagulopathy,due to dilution and/or consumption of clotting factors, mainly fibrinogen and platelets.It requires early recognition,rapid stabilization of the patient,massive transfusion protocol activation, immediate control of bleeding (includes medical, mechanical, surgical, hemostatic interventions).This study not only analyse the association between the PRBC: FFP ratio and the outcome of MOH in different pathologies. Results suggest a possible benefit of higher number of PRBC transfusion in MOH.

In this study, It was analysed 46.6% cases were between 20-25 years of age. Most of them were unbooked antenatal cases. MOH were more common among multigravida (72%) with almost half of the study population between 36-42 weeks of gestation. Causes for MOH were 44% antepartum, while 45.3% were postpartum, ectopic 8% and 1.33% H.mole and Abortion each. Abruption(24%) was most common amongst antenatal cases, other causes include Placenta Previa (14.67%), Rupture Uterus (8%), Placenta accreta (6.67%), HELLP induced Coagulopathy (5.33%), Atonic PPH (28%) in postpartum cases. Estimated blood loss of 1500-2000 ml were 78.67%, 2000-2500 ml were 13.33 % >2500 ml were 8%. 80.9% of Atonic PPH has EBL of 1500-2000 ml, traumatic (75%), abruption (72.22%). While 83.33% of Uterine rupture has EBL of 2000-2500 ml, placenta previa (63.63%). Coagulopathy (50%) has EBL >2500ml. Mean deficit of Hemoglobin in this study is 4.53 with mean deficit of 46.14 % within 3 hours of MOH. Median number of PRBC transfused were 5 units and FFP were 4 units.66.67% were cesarean section while 21.33%were vaginal in comparison toa retrospective study on blood transfusion pattern in patients with obstetric hemorrhage at Government Medical College, Trivandrum analyzed the obstetric indications and risk factors for transfusion where Significant risk factors for MOH, were placenta previa abruption, uterine atony, uterine inversion and rupture uterus. Most common cause for MOH is atonic PPH (28%), with median blood loss of 2000 ml,(range of 1500-4000 ml).[5]Another cohort study(2004-2006) including all 98 hospitals with a maternity unit in Netherlands where 327 women requiring massive transfusion for obstetric were identifiedThe median blood loss was 4500 mL and the median number of PRBCs transfused was 11 units.[6] Among women receiving massive transfusion, the most common cause of hemorrhage was uterine atony. ICU admission (69%) and 0.9% mortality compared to our study where 46.67% of cases required ICU stay and 12% was the mortality rate. In this study, fall in platelet count appeared noticeably lower in abruption cases compared to other causes which indicate that the coagulopathy of MOH differs significantly depending on its cause, and thus more targeted transfusion strategy is needed depending on aetiology, instead of the one universal strategy as recommended by RCOG Guidelines (2009)

In this study, DIC was found in 26.9% .3 out of 7 cases were attributed to abruption followed by 2 cases of atonic PPH, 1 case of HELLP syndrome and traumatic each. Compare to Israeli study, in one third of 87 women with DIC, the coagulopathy was attributed to uterine atony or genital tract lacerations.[7] Similar observations were reported from a Canadian study conducted at Nova Scotia tertiary maternity hospital (1980-2009) where Antecedent causes for DIC included abruption (37%), postpartum hemorrhage or hypovolemia (29%), preeclampsia/HELLP (14%), acute fatty liver (8%), sepsis (6%), and amniotic fluid embolism (6%).There were six direct maternal deaths and 3 out of 6 were due to DIC with a case fatality rate of 6.25%.[8]. Another similar study done of 25 obstetric patients with a diagnosis of DIC in Songklanagarind University Hospital from January 1993 to December 2005 included major association with abruption[9].In this study, blood products ratio established with PRBC:FFP is 1.17:1 overall. Whereas American College of Obstetrician and Gynecologists (ACOG)recommends early and aggressive transfusion at an RBC:FFP in ratio of 1:1. following an MTP may potentially facilitate the resolution of coagulopathies, hypothermia, and acidosis.[10]The Royal College of Obstetricians and Gynaecologists (RCOG) The "Green-top Guideline: Blood Transfusion in Obstetrics" recommends 12-15 ml/kg of FFP for every 6 units of RBCs.[11]Matsunaga et al.(2012) investigated 196 cases of massive obstetric bleeding necessitating aggressive coagulation factor supplementation. The study determined that when the transfusion therapy was performed to meet specific haemostatic targets, the calculated FFP/RBC ratio was 1.3 when converted from whole blood.[12]

In this study, PRBC:FFP is found higher in MOH with no mortality 1.21:1 compared to mortality cases. Similarly Bonnet et al. analysed the FFP/RBC ratio in 38 cases of maternal death caused by massive obstetric bleeding with FFP/RBC rose above 1 at 12 h following haemorrhage onset. FFP:RBC ratio in 4 out of 5 patient groups was less than 1; median FFP:RBC ratio was 0.6.[13] Another similar study where Snyder et al. suggested a temporal relationship between the FFP:RBC ratio and mortality in massively obstetric hemorrhage patients. They demonstrated that a higher FFP:RBC ratio was associated with a lower mortality risk when the FFP:RBC ratio was considered a fixed value at 24 hours. It is also considered that the actual FFP:RBC ratio may be less important than the timing of the FFP transfusion. Earlier administration of FFP has better outcome.

Another relevant fact is that less than half of the patients received platelets, only two cases were supplemented with cryoprecipitate and none received hemostatic agents whereas In Western countries, obstetric hemorrhage is managed with medications that has coagulation factors like fibrinogen concentrates and factor VIIa. These coagulation factors cannot be administered as a treatment in our center and FFP is the only option for supplementation of coagulation factors.

CONCULSION:

Being a leading cause of maternal mortality and morbidity, a multidisciplinary protocol for obstetric hemorrhage management (including laboratory assessment, transfusion support, and use of adjuvant therapies) is recommended to improve rapid diagnosis and targeted therapy of MOH induced Coagulopathy. Insufficient evidence exists regarding MTP in the setting of MOH. Although conducting an RCT would be an ideal method to obtain such evidence, withholding of an MTP from patients with severe obstetric bleeding would be clinically dangerous and, as a result, is ethically impossible. Hence, to retrospectively examine large-scale observational studies is best option.This study shows the importance of population-wide studies with regards to comparing rates of transfusion and outcomes for women with MOH. In conclusion, for massive obstetric hemorrhage where appropriate supplementation of coagulation factors is essential, the transfusion of PRBC : FFP = 1.17:1 is desirable

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