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Determinants of mortality after massive transfusion - A prospective study

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Abstract:

INTRODUCTION: Massive hemorrhage calls for massive transfusions (MTs) to maintain adequate hemostasis. Massive transfusion protocols (MTPs) are the appropriate treatment strategy for such patients replacing conventional use of crystalloids. These help in standardizing and optimizing the delivery of blood components in a well-balanced ratio.

AIM AND OBJECTIVES: The aim of the study is to propose an ideal ratio of blood components for MTP after assessing relationship between ratios of blood components transfused and mortality.

METHODOLOGY: MT was defined as receiving >4 packed red blood cell (PRBC) units within 1 h with the anticipation of continued need for blood products. All MT patients above 13 years of age regardless of cause of bleed were included in the study from December 2015 to October 2017 accounting for a total of 61 patients. Subgroup categorization of study population was done, and physician-driven ratios of the blood components were calculated for each case. The ratios were grouped as high (>1), equal (=1), and low (<1) ratios of fresh frozen plasma (FFP):PRBC and platelet: PRBC, and the relationship of these ratios to the clinical outcome in terms of mortality was examined.

RESULTS AND DISCUSSION: Sixty-one patients underwent MT of which the overall hospital mortality rate was 8.1% with 100% mortality among patients with penetrating trauma followed by 25% with gastrointestinal bleed. Emergency admission was an independent risk factor for mortality. Hypotension before the initiation of MT was detrimental for survival. Efficient communication existed between the treating physicians and transfusion. Majority of survivors received equal ratios of FFP: PRBC and platelet: PRBC, and all nonsurvivors received low ratios of FFP: PRBC. Analysis was statistically indicating better survival with 1:1:1 ratio of PRBC: FFP: platelet.

CONCLUSION: The need of the hour is to establish an institutional MTP and ensure compliance with the same. A prospective randomized controlled trial needs to be done to overcome the limitations and confounders of the present study and establish a universal protocol.

Keywords:

Massive hemorrhage, massive transfusion, massive transfusion protocol, ratio of blood components

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Introduction

Massive hemorrhage is a common complication in a large number of clinical settings, and management of such patients is challenging.^[1] It requires an effective interaction between clinicians

and transfusion medicine services and has recently advanced from supportive treatment with crystalloid and red blood cell therapy to use of standardized massive transfusion protocols (MTPs).^[2]

Massive blood transfusion refers to the replacement of large volume of blood with blood products over a short period of time to a patient with uncontrolled hemorrhage. Several definitions are in existence based

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on the volume of blood products and the time frame of transfusion.^[3-5] The most common among them are:^[3,6,7]

- Transfusion of more than 10 packed red blood cell (PRBC) units within 24 h
- Transfusion of more than 4 PRBC units within 1 h with anticipation of continued need for blood products
- Replacement of more than 50% of total blood volume within 3 h.

The present study defines massive transfusion (MT) as transfusion of more than 4 PRBC units within 1 h with anticipation of continued need for blood products.

A large proportion of clinical settings such as trauma, obstetrics, and major surgery calls for MT. In traumatic injuries, exsanguinations are the most common cause of morbidity and also account for 50% of deaths within 24 h of injury and 80% of intraoperative mortalities.^[8-10] Como *et al.* noticed that 99% of the patients admitted to trauma center receiving <10 units of PRBC survived, whereas only 60% of the patients receiving more than 10 units of PRBC survived, thus focusing on the fact that transfusion ratios are associated with mortality.^[11] Obstetrical hemorrhage is the leading cause of maternal mortality, and MT plays an integral role in the acute management.^[1] Other scenarios that can require the need for massive blood transfusion are gastrointestinal (GI) bleeding, orthopedic, cardiorespiratory, and liver surgeries.^[12]

Patients undergoing massive hemorrhage experience dynamic changes in hemostasis due to many factors such as crystalloid use, transfusion of blood components, and certain etiology-specific causes.^[13] In trauma, early trauma-induced coagulopathy (TIC), caused by a combination of tissue injury and shock, can lead to systemic anticoagulation and hyperfibrinolysis and is presumed to be present in 56% of severely injured patients within 30 min of injury even before any crystalloid or component usage.^[14-16] Obstetric hemorrhage, on the other hand, leads to an acquired fibrinogen deficiency^[17] compounded by hyperfibrinolysis, with uterine atony and accretism being the contributing factors.

Early recognition and rapid treatment of initial coagulation disturbances improves survival in massively bleeding patients. Damage control resuscitation through MTP with predetermined and standardized ratios of blood components is the current thought to actively address the issues of rapid blood loss and thus improve the clinical outcome of such patients.^[21-23] Therefore, developing an institutional MTP requires communication between different clinical services, transfusion practitioners, nursing care, and laboratories. Thus, evaluation of an MTP requires consideration of both protocol and

compliance before concluding its effectiveness on patient outcomes.

Despite a number of retrospective cohort studies, the overall clinical value of the approach of a ratio of 1:1:1 PRBC: plasma: platelet is still unclear. Many literatures support higher plasma and platelet ratios when compared to PRBC to be associated with better patient outcomes in terms of survival.^[24,25] However, the benefit regarding higher ratios of plasma and platelet cannot be fully justified since increased incidences of acute respiratory distress syndrome (ARDS), abdominal compartment syndrome, and multiorgan failure (MOF) have been reported, though no statistical significance has been obtained.^[26]

Although the institution of the present study advocates the use of 1:1:1 ratio of PRBC: FFP: platelet, there is lack of adherence to such a protocol. The clinicians in view of the clinical scenario initiate blood components in varied ratios which is grouped in the present study as high (>1), equal (=1), and low (<1) ratios of both FFP: PRBC and platelet: PRBC. All the ratios are individually and extensively compared to the clinical outcome in terms of mortality.

Aim and objectives

1. To evaluate the relationship between the ratios of blood components transfused and mortality
2. To assess the other factors affecting mortality in patients following MT.

Methodology

This study was a prospective, observational study involving the participation of various specialties including the department of emergency medicine, obstetrics and gynecology, surgery, orthopedics, critical care, and laboratory services. The study was conducted after obtaining clearance from the institutional ethics committee. Written informed consent was taken from each patient included in the study after detailing them about their role in the study.

MT was defined as receiving more than 4 PRBC units within 1 h with the anticipation of continued need for blood products. Using this definition, all the massively transfused patients above 13 years of age regardless of the cause of bleed were included in the study. The study was carried out for 1 year and 10 months from December 2015 to October 2017. Patients who received blood transfusion from other centers before reaching our hospital and death within 30 min of admission were included under the exclusion criteria of the study. A total of 61 patients who satisfied the inclusion and exclusion criteria were included in the study. Although our institution advocates

the use of 1:1:1 ratio of PRBC: FFP: platelet, there is lack of strict adherence to such a protocol.

The clinicians in view of the clinical scenario initiate blood components in varied ratios which is grouped in the present study as high (>1), equal (=1), and low (<1) ratios of both FFP: PRBC and platelet: PRBC. There are no definite criteria or score *per se* that is used for initiating the MTP. Only in trauma patients, the department of emergency medicine follows a criterion that takes into account pulse rate (PR), blood pressure (BP), type of trauma, and Focused Assessment with Sonography for Trauma (FAST) findings, but this is not generalized to the other causes of massive hemorrhage such as obstetrics and GI bleeds. In effect, there was lack of a standardized institutional MTP and hence the need of the present study. Point-of-care testing (POCT) devices such as thromboelastography or rotational thromboelastometry which are considered the gold standard for predicting the need of MT were unavailable at our center. To standardize and optimize the MTP at our center, the clinical outcome of all the massively transfused patients was assessed in terms of mortality. Since the study population involved patients of different etiologies including obstetric causes, trauma, GI bleed, major surgery, and orthopedic surgery, subgroup analysis of mortality with respect to the different etiologies was carried out for obtaining significant results. The overall 7-day mortality was studied among the different subgroups. In addition to these, demographic characteristics of all the massively transfused patients were also studied; which are as follows:

1. Age
2. Gender
3. Criteria of admission including emergency and elective criteria of admission
4. Preliminary clinical signs before transfusion
5. Diagnosis.

All these demographic characteristics with respect to each subgroup, i.e., the different etiologies of admission, were analyzed, and its relationship with the clinical outcome in terms of mortality was also assessed.

Algorithm in a massively bleeding patient

1. The decision regarding activation of MTP is carried out by the treating physician
2. The criteria to activate MTP in the department of emergency medicine at our institution is:
 - a. PR >120/min
 - b. Systolic BP (SBP) <90 mm of Hg or mean arterial pressure <60
 - c. Penetrating trauma to abdomen
 - d. FAST positive
 - e. If more than two criteria are present, the physician takes the call for activation of MTP in a trauma setting.

Note: This is not a generalized criterion, and the activation of MTP in other cases of massive bleed is strictly based on the clinicians' instinct after considering the deranged vitals, amount of blood loss at the moment, and anticipation of further blood loss.

3. The transfusion medicine and laboratory services are notified immediately over the phone or by a documented urgent request
4. Intravenous access using a large bore needle (14/16-gauge) is maintained and blood specimens are sent to the blood bank for ABO grouping, Rh typing, and cross-matching. Another set of blood samples is sent to the laboratory for the assessment of complete blood count, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen, arterial blood gas analysis, and electrolytes (Na⁺, K⁺, and Ca²⁺)
5. Until the cross-matched units are available, uncross-matched O-negative units are issued. The consent for each event of transfusion is taken. As soon as the blood group of the patient is determined, switching over to respective blood group is carried out
6. The blood bank issues blood products in predetermined packs as per the physicians' order consisting of PRBC and FFP units, keeping in view the complete blood count and coagulation profile
7. Administration of blood components is done using blood warmers
8. Proper identification of the patient before the start of transfusion is very essential
9. Additional blood components are issued in packs based on the laboratory results, i.e., platelet count <50,000/cumm, PT >60 s, international normalized ratio >1.5 times the control value, and fibrinogen <100 mg/dL. These include platelet and cryoprecipitate. Cryoprecipitate is usually issued in packs of 10, 20, etc., based on the formula:
 - a. Dose (units) = (desired fibrinogen increment [mg/dL] × plasma volume)/250 mg/unit
10. Our aim is to:
 - a. Keep temperature >35°C
 - b. Keep platelet count >50,000/cumm
 - c. Keep fibrinogen >150 mg/dL
 - d. Keep PT and APTT <1.5 times the normal value.
11. The protocol is terminated only when notified by the treating physician. After termination of the protocol, subsequent blood products are released only on demand by the physician.

Figure 1 shows schematic representation of the algorithm.

Statistical analysis

The demographics, clinical data, and details of PRBC, FFP, platelet transfusion, and laboratory data were collected and checked with the patient records and

hospital computer information system. These data were entered into a Microsoft Office Excel 2010, and data were analyzed with the SPSS Software Program (Version 20.0, SPSS Inc., Chicago, IL, USA). Results were expressed as mean ± standard deviation; categorical measurements are expressed in number and percentage. Comparisons were performed using Chi-square test. Results were analyzed and some was considered significant when $P < 0.01$ and some when $P < 0.05$.

Results

During the study, all the massively transfused patients in our institution were included. This accounted for a total of 61 patients above 13 years of age over the study period of 1 year and 10 months. The mean age of the study population was 33.4 ± 8.3 years (male - 37.6 years and female - 30.1 years). The study population included 30 males and 31 females. Of the 31 females, 28 belonged to the obstetric group, 2 belonged to the major surgery group, and 1 belonged to the trauma group. Figures 2 and 3 demonstrate the percentage distribution of the sample according to age and gender, respectively.

Out of the 61 massively transfused patients, 34 patients were included in the emergency category of admission to the casualty, whereas 27 were elective cases [Figure 4]. The most common cause for emergency admission was blunt trauma which accounted for 58.8% followed by GI bleed with 11.6%. Among the elective cases, the most common indication for MT was among the obstetric cases (73%), with placenta accreta (44.4%) being the most common cause.

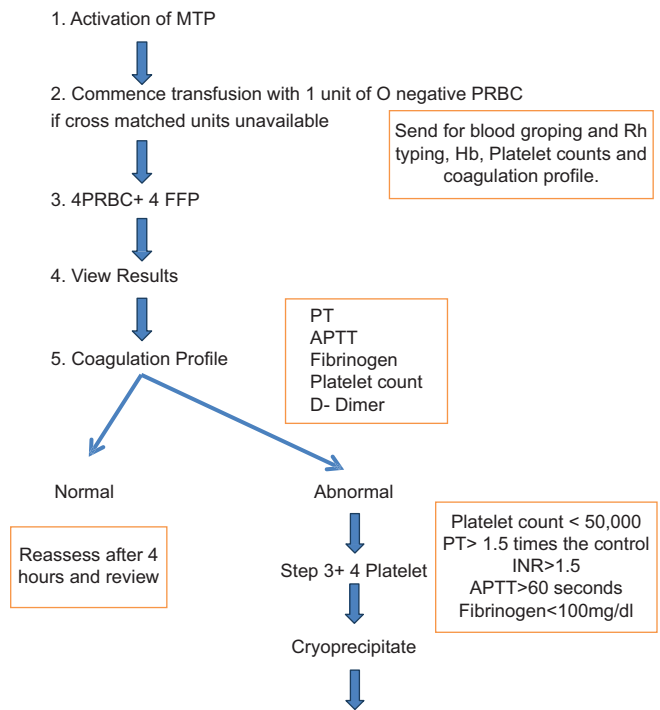


Figure 1: Schematic representation of the algorithm

The etiologies leading to the initiation of MT in the study population were heterogeneous. Obstetric causes accounted for the highest percentage (45.9%), with placenta accreta being the most common indication. This was followed by trauma (36.1%), with most common causes being blunt trauma, GI bleed (6.6%), major surgery (6.6%), and orthopedic surgery (4.9%) [Figure 5]. Table 1 shows the distribution of study sample according to age, gender, criteria of admission, and diagnosis.

Of the 61 patients with heterogeneous diagnosis studied, 5 were nonsurvivors with 4 males and 1 female. The overall 7-day hospital mortality rate was 8.1% with 100% mortality observed among patients with penetrating trauma followed by 25% in patients with

Table 1: Distribution of study sample according to age, gender, criteria of admission, and diagnosis

	Count (%)
Age	
15-30	34 (55.7)
31-45	21 (34.4)
46-60	6 (9.8)
Mean±SD	33.4±8.3
Gender	
Male	30 (49.2)
Female	31 (50.8)
Criteria for admission	
Emergency	34 (55.7)
Elective	27 (44.3)
Diagnosis	
Obstetrics	28 (45.9)
Placenta accreta	12 (19.7)
Placenta percreta	6 (9.8)
PPH	7 (11.5)
Obstetric (others)	3 (4.9)
Trauma	22 (36.1)
Blunt	20 (32.8)
Penetrating	2 (3.3)
GI bleed	4 (6.6)
Orthopedic	3 (4.9)
Major surgery	4 (6.6)

SD=Standard deviation, GI=Gastrointestinal, PPH=Post Partum Hemorrhage

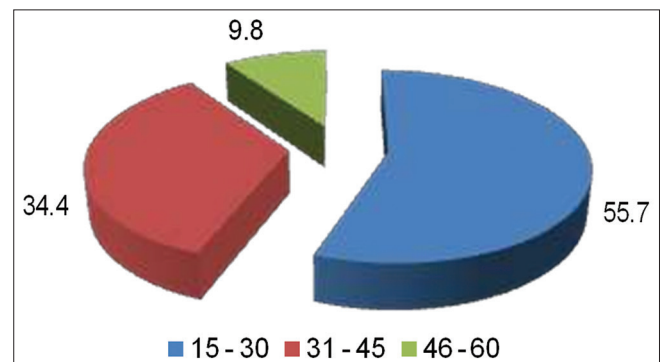


Figure 2: Percentage distribution of the sample according to age

GI bleed and 10% in patients who suffered from blunt trauma [Figure 6]. The cause of death was MOF and sepsis (one patient) and massive hemorrhage, acidosis, and shock (four patients); 4 out of the 5 nonsurvivors died within the first 24 h of admission. Only one nonsurvivor (male patient with history of blunt trauma, MOF) died after more than 25 days of hospital stay. Figure 7 shows the distribution of diagnosis based on survival.

These factors were compared to the clinical outcome in terms of mortality. Except for the criteria of admission, there was no significant relationship between age, gender, and diagnosis with the survival status. All the five nonsurvivors were emergency cases and 100% survivorship was observed among the elective cases, and these data attained statistical significance. Table 2 gives a comparison of the survival status based on the criteria of admission.

Certain common preliminary signs and investigation done before initiation of MT among the different etiologies were analyzed. These included heart rate (HR), SBP, and FAST. FAST was performed only for admissions to the casualty, and hence, its importance cannot be fully estimated. Estimate of blood loss (EBL)

could be analyzed only for obstetric patients based on the mop count, and therefore, its significance was also limited. Figure 8 demonstrates the etiology-specific distribution of the preliminary investigations. There was no statistical significant relationship between HR, FAST, and EBL to survivorship among the different diagnosis studied. However, all the nonsurvivors irrespective of the etiology of mortality had a SBP of <90 mm of Hg, and the analysis was statistically significant suggesting that hypotension before initiation of MT can have a detrimental effect on survival. Table 3 compares preliminary investigations to survival status.

The turnaround time (TAT) from the time of request to the time of issue of PRBC unit in the MT protocol was calculated, and the mean TAT was estimated to be 9.4 ± 2.1 min (range 8–17 min). 54.1% of the patients received PRBC unit in <10 min. 61.8% of the emergency cases irrespective of diagnosis received the PRBC unit in <10 min, and this analysis attained statistical significance indicating efficient communication of the treating physicians and the transfusion medicine services. Table 4 gives a comparison of selected variables on TAT.

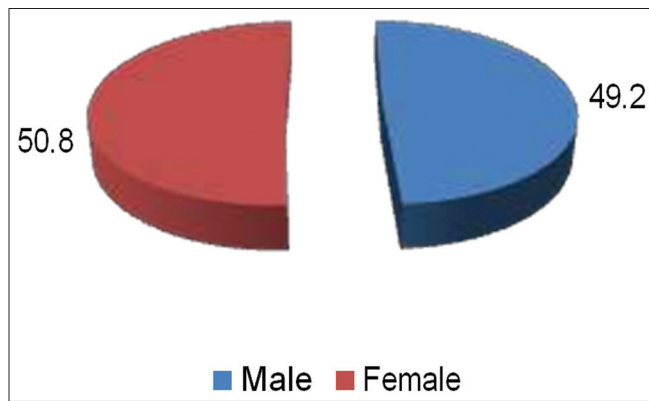


Figure 3: Percentage distribution of the sample according to gender

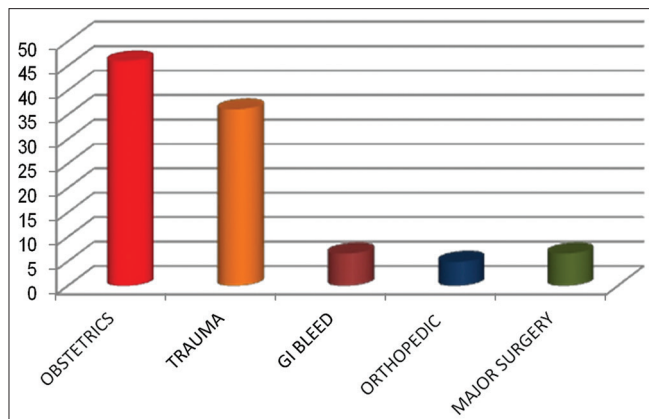


Figure 5: Percentage distribution of the sample according to diagnosis

Table 2: Comparison of the survival status based on criteria of admission

Survival status	Count (%)		χ^2	P
	Emergency	Elective		
Nonsurvivor	5 (14.7)	00	4.33*	0.038
Survivor	29 (85.3)	27 (100.0)		

*Significant at 0.05 levels

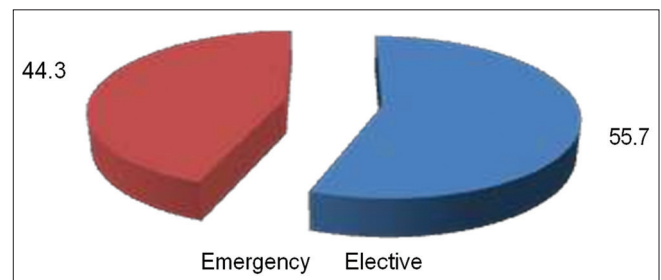


Figure 4: Percentage distribution of the sample according to criteria for admission

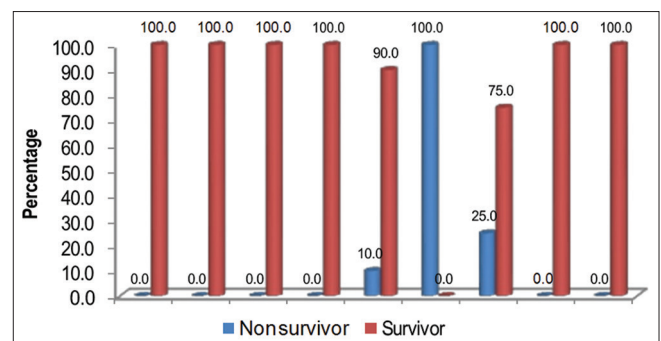


Figure 6: Comparison of the survival status based on different ratios of platelet:packed red blood cell

A total of 428 units of PRBC, 400 units of plasma, 324 units of random donor platelet, and 420 units of cryoprecipitate were transfused among the massively bleeding patients included in this study. Although the institution of this study advocates the use of 1:1 ratio of FFP: PRBC and platelet: PRBC, there was lack of strict adherence to such a protocol and physician-initiated varied ratios were witnessed in this study population. The present study achieved a mean FFP: PRBC ratio of

0.98 and a mean platelet: PRBC ratio of 0.95. Figures 9 and 10 illustrate the percentage distribution of the sample according to FFP:PRBC and platelet:PRBC.

Table 3: Comparison of the preliminary investigations on survival status

	Count (%)		χ^2	P
	Nonsurvivor	Survivor		
HR				
>120	4 (13.3)	26 (86.7)	2.07	0.150
<120	1 (3.2)	30 (96.8)		
SBP				
>90	0	30 (100.0)	5.27*	0.022
<90	5 (16.1)	26 (83.9)		
FAST				
Positive	4 (18.2)	18 (81.8)	-	-
Negative	0	0		
Estimate blood loss				
<4000	0	13 (100.0)	-	-
>4000	0	15 (100.0)		

*All the nonsurvivors had a SBP of <90 mm of Hg and the analysis was statistically significant (P=0.02). HR=Heart rate, SBP=Systolic blood pressure, FAST=Focused assessment with sonography for trauma

Table 4: Comparison of selected variables on turnaround time

	Count (%)		χ^2	P
	<10 min	10–15 min		
Criteria for admission				
Emergency	21 (61.8)	13 (38.2)	7.78**	0.005
Elective	7 (25.9)	20 (74.1)		
Length of hospital stay (days)				
<25	19 (45.2)	23 (54.8)	0.02	0.877
>25	9 (47.4)	10 (52.6)		
Survival status				
Nonsurvivor	4 (80.0)	1 (20.0)	2.55	0.110
Survivor	24 (42.9)	32 (57.1)		

**Significant at 0.01 level

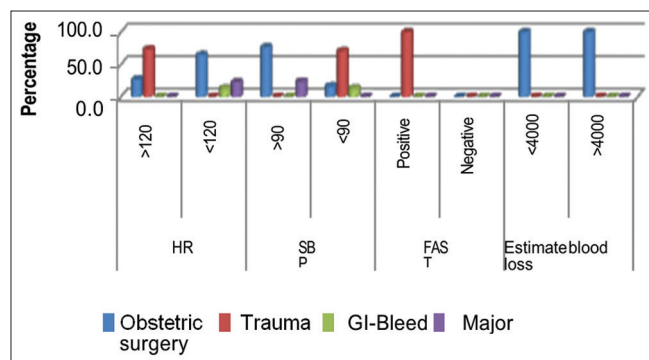


Figure 7: Distribution of diagnosis based on survival status

Keeping in mind the goal of the study, these different ratios of FFP:PRBC and platelet:PRBC were compared to the survival status. The analysis showed that majority of the survivors received equal ratios of FFP:PRBC and platelet:PRBC. All the five nonsurvivors received low ratios of FFP:PRBC. All these analyses were statistically significant indicating a better clinical outcome in terms of mortality with 1:1:1 ratio of FFP:PRBC: platelet. Figures 6 and 11 give a comparison of the survival status based on different ratios of FFP:PRBC and platelet:PRBC, respectively.

Discussion

In the present study, the study population comprised several group of patients including different etiologies leading to the initiation of the MTP. Among a total of 61 patients studied, majority were obstetric causes (45.9%) followed by trauma (36.1%), GI bleed (6.6%), major surgery (6.6%), and orthopedic surgery (4.9%). Literature analysis showed that optimization, activation, and outcomes of the MT protocols have been widely studied in the context of trauma, but implication of the same in a nontrauma setting still remains a concern. Still, there is lack of evidence to validate and adopt a uniform MTP, irrespective of the etiology of bleed.

The 7-day overall mortality rate in the present study was 8.1% with 100% mortality observed among patients with penetrating trauma followed by 25% in patients with GI bleed and 10% in patients who suffered from blunt trauma. This was lower than the 26.1% mortality rate observed by Yoon *et al.* in a population consisting of 334 trauma patients for 5 years.^[27] Study of MTP use by Sinha *et al.* in a similar heterogeneous setting also showed a higher mortality rate of 29% among their

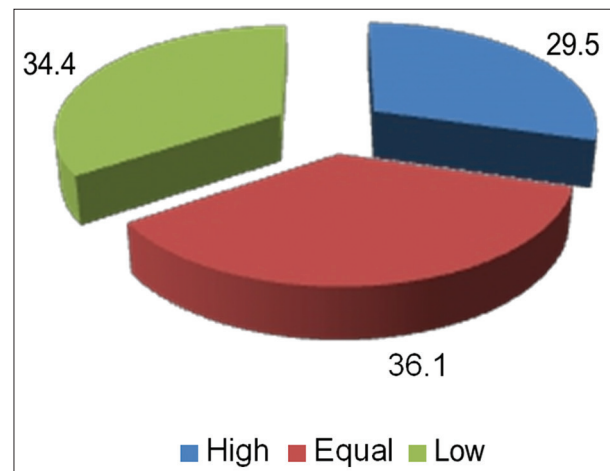


Figure 8: Comparison of selected variables based on diagnosis

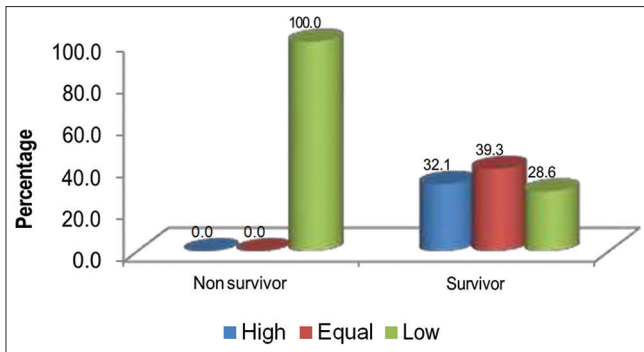


Figure 9: Percentage distribution of the sample according to fresh frozen plasma:packed red blood cell

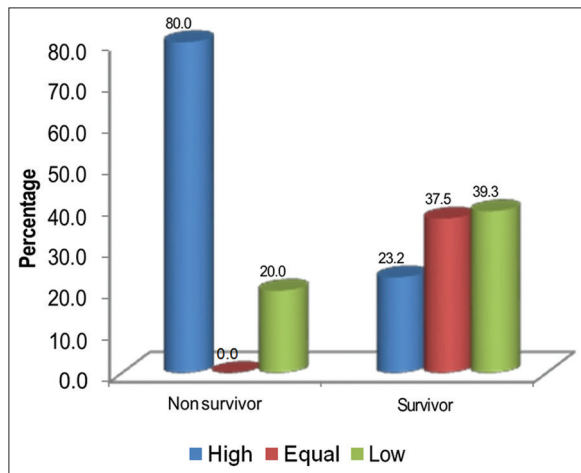


Figure 10: Percentage distribution of the sample according to platelet:packed red blood cell

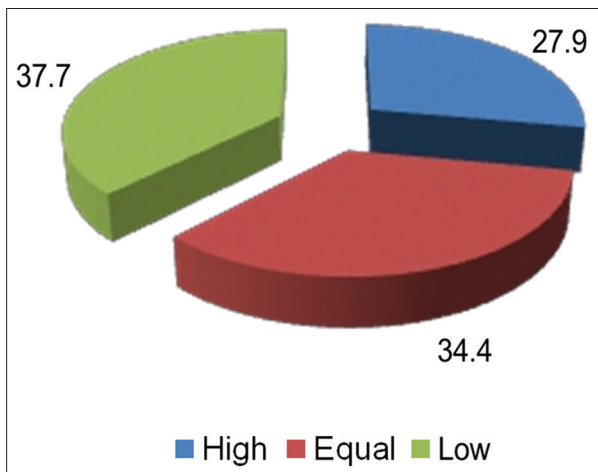


Figure 11: Comparison of the survival status based on different ratios of fresh frozen plasma:packed red blood cell

study cohort when compared to our study.^[28] This difference in the mortality rates from our study might be due to fewer number of patients included in each group in our study and short time period of the study. Study by Morse *et al.* supported the finding that the mortality risk among such heterogeneous populations

is also associated with the underlying disease and not the MTP alone.^[29]

In the present study, among the demographic characteristics studied, emergency admission was an independent risk factor for mortality ($P < 0.05$) among the massively transfused patients. This analysis was supported by the study by Yoon *et al.* where emergency admission was an independent predictor for survival with an odds ratio of 2.6 ($P < 0.001$).^[27]

Prehospital parameters are considered as important predictors of TIC and also for predicting the need for MT. The injury severity score, shock index (SBP/HR), and pretransfusion administration of fluids help in predicting TIC and need for MT. However, validated scores are only available for trauma settings. And therefore, generalization of such scores in a nontrauma setting is not accepted to date. In the present study, the prehospital parameters including HR, SBP, FAST, EBL, and preadministration of fluids were analyzed individually and their effect on mortality was looked upon. All the nonsurvivors irrespective of the etiology had an SBP of <90 mm of Hg suggesting hypotension as a result of massive hemorrhage before the initiation of MT can have a detrimental effect on survival. This result was supported by the study by Zenati *et al.* which states that duration and episodes of hypotension in massively bleeding patients are associated with increased mortality.^[30]

Early recognition of the ongoing massive hemorrhage and prompt delivery of the components is the key to survival in a massively bleeding patient. Several literatures illustrate the importance of TAT in the initiation of MTP and its effect on mortality. In the present study, the mean TAT for a PRBC unit was estimated to be 9.4 ± 2.1 min. 54.1% of the patients received the blood component pack in <10 min. 61.8% of the emergency cases which also included 4 out of the 5 nonsurvivors, irrespective of diagnosis, received the blood components in <10 min. This is in accordance with the study by McClain *et al.* where the mean TAT in emergency blood issue was 10 ± 3.8 min at one center and 14 ± 7.2 min at another center.^[31] There was no association of TAT with mortality in the present study. Literatures are in view that early recognition and rapid availability of blood components improves survival in massively bleeding patients, but an exact guideline for TAT has not been emphasized.^[21-23]

Despite the fact that the institution of the present study advocates the use of 1:1:1 ratio of FFP:PRBC: platelet, there is lack of adherence to the same and physician-initiated varied ratios as per the need of the clinical scenario are widely implemented. The present study was carried out to look into the various trends in the clinical outcome associated with the different ratios

administered and thus formulate an effective MTP in the institution. The present study achieved a mean FFP:PRBC ratio of 0.98 and a mean PLT:PRBC ratio of 0.95 which was comparable to the 1:1 ratio advocated by the institution and various retrospective studies. The different ratios were grouped as high (>1), equal (=1), and low (<1) ratios of FFP:PRBC and platelet: PRBC, respectively, and its effect on mortality and morbidity was extensively studied.

Majority of the survivors irrespective of the etiology received equal ratios of FFP:PRBC and platelet:PRBC. These analyses were statistically significant indicating a better clinical outcome in terms of mortality with equal ratio of FFP:PRBC and platelet:PRBC. This was in accordance with the current randomized control. One such trial is the Pragmatic Randomized Optimal Platelet and Plasma Ratios trial which compared the 1:1:1 and 2:1:1 ratio of PRBC: plasma: platelet with 24-h and 30-day mortality. No significant difference in mortality was found between the two ratio groups. However, patients in the 1:1:1 group attained better hemostasis and the death due to bleeding was less.^[32] Studies by Dzik *et al.* and Yoon *et al.* and many more studies favored the 1:1:1 protocol.^[27,33] However, another randomized control study, The Prospective Observational Multicenter Major Trauma Transfusion study observed that higher ratios of plasma or platelet were associated with decreased in hospital mortality when transfused early, i.e., in the first 6 h of admission.^[34] Literatures have also put forward the collateral damage associated with 1:1 protocols. This is because stringency with these protocols results in unnecessary transfusion of FFP in patients with no need which result in complications of fluid overload, i.e., edema, ARDS, and abdominal compartment syndrome, leading to MOF.^[35-38]

Contrasting literatures are also available in this regard. Gunter *et al.* reviewed a total of 259 patients who received more than 10 units of PRBC in the first 24 h and found that there was 62% reduction in the 30-day mortality in the low ratio group of plasma to PRBC compared to 41% in the high ratio group.^[39] Similarly, Kudo *et al.* found a similar end point, with increased mortality (44.4%) among the high ratios of plasma to PRBC transfusion when compared to low ratios (33.3%).^[40]

The challenge observed in the present study was that the population studied is invariably heterogeneous and most of the literatures comparing the different ratios of blood components to the clinical outcome are retrospective studies and are conducted mainly in the trauma settings. This limited the scope of our findings; however, since the data were statistically significant, the current study emphasizes the adoption of the 1:1:1 ratio of PRBC:FFP: platelet for a better clinical outcome in terms of mortality.

Limitations of the study

- Small sample size
- Heterogeneous population
- Variable distribution of population in each subgroup
- No statistical analysis could be established between the various subgroups and ratio of blood components with respect to the clinical outcomes because of a highly variable number of patients in each subgroup
- Mortality influenced by the disease conditions of the patients could not be ruled out since different etiologies in the study
- Lack of POCT creates a gap in the early estimation of coagulopathy and hence prompt action
- Effect of cryoprecipitate transfusion on the clinical outcome was not assessed since all the patients did not necessitate the need
- Poor documentation in the clinical records.

Conclusion

- Institutional definition of MT for all massively bleeding cases irrespective of the etiology should be formulated
- An institutional MTP with fixed ratios approximating a ratio of 1:1:1 ratio of PRBC: FFP: platelet need to be designed
- Better methods such as introduction of POCT for prediction of MT requirement
- Strict compliance to the MTP.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Young PP, Cotton BA, Goodnough LT. Massive transfusion protocols for patients with substantial hemorrhage. *Transfus Med Rev* 2011;25:293-303.
2. Pham HP, Shaz BH. Update on massive transfusion. *Br J Anaesth* 2013;111 Suppl 1:i71-82.
3. Raymer JM, Flynn LM, Martin RF. Massive transfusion of blood in the surgical patient. *Surg Clin North Am* 2012;92:221-34, vii.
4. Levy JH. Massive transfusion coagulopathy. *Semin Hematol* 2006;43:S59-63.
5. Malone DL, Hess JR, Fingerhut A. Massive transfusion practices around the globe and a suggestion for a common massive transfusion protocol. *J Trauma* 2006;60:S91-6.
6. Diab YA, Wong EC, Luban NL. Massive transfusion in children and neonates. *Br J Haematol* 2013;161:15-26.
7. Seghatchian J, Samama MM. Massive transfusion: An overview of the main characteristics and potential risks associated with substances used for correction of a coagulopathy. *Transfus Apher Sci* 2012;47:235-43.
8. Sauaia A, Moore FA, Moore EE, Moser KS, Brennan R, Read RA, *et al.* Epidemiology of trauma deaths: A reassessment. *J Trauma* 1995;38:185-93.

9. Kauvar DS, Lefering R, Wade CE. Impact of hemorrhage on trauma outcome: An overview of epidemiology, clinical presentations, and therapeutic considerations. *J Trauma* 2006;60:S3-11.
10. Acosta JA, Yang JC, Winchell RJ, Simons RK, Fortlage DA, Hollingsworth-Fridlund P, et al. Lethal injuries and time to death in a level I trauma center. *J Am Coll Surg* 1998;186:528-33.
11. Como JJ, Dutton RP, Scalea TM, Edelman BB, Hess JR. Blood transfusion rates in the care of acute trauma. *Transfusion* 2004;44:809-13.
12. Friedman AJ. Obstetric hemorrhage. *J Cardiothorac Vasc Anesth* 2013;27:S44-8.
13. Reiss RF. Hemostatic defects in massive transfusion: Rapid diagnosis and management. *Am J Crit Care* 2000;9:158-65.
14. Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *J Trauma* 2003;54:1127-30.
15. Floccard B, Rugeri L, Faure A, Saint Denis M, Boyle EM, Peguet O, et al. Early coagulopathy in trauma patients: An on-scene and hospital admission study. *Injury* 2012;43:26-32.
16. Patregnani JT, Borgman MA, Maegele M, Wade CE, Blackbourne LH, Spinella PC. Coagulopathy and shock on admission is associated with mortality for children with traumatic injuries at combat support hospitals. *Pediatr Crit Care Med* 2012;13:273-7.
17. Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. *Br J Anaesth* 2012;109:851-63.
18. Lier H, Krep H, Schroeder S, Stuber F. Preconditions of hemostasis in trauma: A review. The influence of acidosis, hypocalcemia, anemia, and hypothermia on functional hemostasis in trauma. *J Trauma* 2008;65:951-60.
19. Watts DD, Trask A, Soeken K, Perdue P, Dols S, Kaufmann C. Hypothermic coagulopathy in trauma: Effect of varying levels of hypothermia on enzyme speed, platelet function, and fibrinolytic activity. *J Trauma* 1998;44:846-54.
20. Martini WZ, Holcomb JB. Acidosis and coagulopathy: The differential effects on fibrinogen synthesis and breakdown in pigs. *Ann Surg* 2007;246:831-5.
21. Holcomb JB. Damage control resuscitation. *J Trauma* 2007;62:S36-7.
22. Cotton BA, Gunter OL, Isbell J, Au BK, Robertson AM, Morris JA Jr., et al. Damage control hematology: The impact of a trauma exsanguinations protocol on survival and blood product utilization. *J Trauma* 2008;64:1177-82.
23. Tieu BH, Holcomb JB, Schreiber MA. Coagulopathy: Its pathophysiology and treatment in the injured patient. *World J Surg* 2007;31:1055-64.
24. Borgman MA, Spinella PC, Perkins JG, Grathwohl KW, Repine T, Beekley AC, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007;63:805-13.
25. Spinella PC, Perkins JG, Grathwohl KW, Beekley AC, Niles SE, McLaughlin DF, et al. Effect of plasma and red blood cell transfusions on survival in patients with combat related traumatic injuries. *J Trauma* 2008;64:S69-77.
26. Sperry JL, Ochoa JB, Gunn SR, Alarcon LH, Minei JP, Cuschieri J, et al. An FFP: PRBC transfusion ratio $\geq 1:1.5$ is associated with a lower risk of mortality after massive transfusion. *J Trauma* 2008;65:986-93.
27. Yoon S, Park AJ, Kim HO. Clinical observation study of massive blood transfusion in a tertiary care hospital in Korea. *Yonsei Med J* 2011;52:469-75.
28. Sinha R, Roxby D, Bersten A. Experience with a massive transfusion protocol in the management of massive haemorrhage. *Transfus Med* 2013;23:108-13.
29. Morse BC, Dente CJ, Hodgman EI, Shaz BH, Winkler A, Nicholas JM, et al. Outcomes after massive transfusion in nontrauma patients in the era of damage control resuscitation. *Am Surg* 2012;78:679-84.
30. Zenati MS, Billiar TR, Townsend RN, Peitzman AB, Harbrecht BG. A brief episode of hypotension increases mortality in critically ill trauma patients. *J Trauma* 2002;53:232-6.
31. McClain CM, Hughes J, Andrews JC, Blackburn J, Sephel S, France D, et al. Blood ordering from the operating room: Turnaround time as a quality indicator. *Transfusion* 2013;53:41-8.
32. Holcomb JB, Tilley BC, Baraniuk S, Fox EE, Wade CE, Podbielski JM, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs. a 1:1:2 ratio and mortality in patients with severe trauma: The PROPPR randomized clinical trial. *JAMA* 2015;313:471-82.
33. Dzik WH, Blajchman MA, Fergusson D, Hameed M, Henry B, Kirkpatrick AW, et al. Clinical review: Canadian national advisory committee on blood and blood products – Massive transfusion consensus conference 2011: Report of the panel. *Crit Care* 2011;15:242.
34. Holcomb JB, del Junco DJ, Fox EE, Wade CE, Cohen MJ, Schreiber MA, et al. The prospective, observational, multicenter, major trauma transfusion (PROMTTT) study: Comparative effectiveness of a time-varying treatment with competing risks. *JAMA Surg* 2013;148:127-36.
35. Hannon T. Trauma blood management: Avoiding the collateral damage of trauma resuscitation protocols. *Hematology Am Soc Hematol Educ Program* 2010;2010:463-4.
36. Johnson JL, Moore EE, Kashuk JL, Banerjee A, Cothren CC, Biffl WL, et al. Effect of blood products transfusion on the development of postinjury multiple organ failure. *Arch Surg* 2010;145:973-7.
37. Sambasivan CN, Kunio NR, Nair PV, Zink KA, Michalek JE, Holcomb JB, et al. High ratios of plasma and platelets to packed red blood cells do not affect mortality in nonmassively transfused patients. *J Trauma* 2011;71:S329-36.
38. Inaba K, Branco BC, Rhee P, Blackbourne LH, Holcomb JB, Teixeira PG, et al. Impact of plasma transfusion in trauma patients who do not require massive transfusion. *J Am Coll Surg* 2010;210:957-65.
39. Gunter OL Jr., Au BK, Isbell JM, Mowery NT, Young PP, Cotton BA. Optimizing outcomes in damage control resuscitation: Identifying blood product ratios associated with improved survival. *J Trauma* 2008;65:527-34.
40. Kudo D, Sasaki J, Akaishi S, Yamanouchi S, Koakutsu T, Endo T, et al. Efficacy of a high FFP: PRBC transfusion ratio on the survival of severely injured patients: A retrospective study in a single tertiary emergency center in Japan. *Surg Today* 2014;44:653-61.