Africa Sanguine 2020, Volume 22, Number 1

Original Research

A Review of Massive Blood Transfusion and its Associated Syndromes in Zimbabwe

Une revue de la transfusion sanguine massive et de ses syndromes associés au Zimbabwe

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Conflict of Interest:
The authors report no conflict of interest.

Cite as: Hlatwayou F, *et. al.* A Review of Massive Blood Transfusion and its Associated Syndromes in Zimbabwe *Africa Sanguine.* 2020;22(1):30-37. https://dx.doi.org/10.4314/asan.v22i1.5

Keywords: Africa, massive transfusion protocols, massive transfusion syndromes, Mortality, review

Mots clés: Afrique, protocoles de transfusion massive, syndromes de transfusion massive, Mortalité, revue

ABSTRACT

Background and objectives: Massive blood transfusion is defined as transfusion approximating or exceeding a patient's total blood volume (5 -6 litres in adults) within 24-hours. This procedure is used to manage severely anaemic and bleeding patients. Negative outcomes associated with acidosis, hypothermia and coagulopathy may result. The study was carried out to review the management of massive transfusion in Zimbabwe.

Materials and methods: A 4-year retrospective clinical laboratory-based study was carried out on patients who had massive blood transfusion at a Zimbabwean hospital, from January 2014 to December 2017. Data was collected from patients' hospital records after permission from the hospital director.

Results: Of the 180 patient records, 145 (80.6%) were from female and 35 (19.4%) from male patients. Massive blood transfusion was done mostly on obstetric patients. Full blood count was the most commonly requested laboratory test, with 155 (86%) requests. Some of the patients had severe anaemia. Routine coagulation tests were significantly abnormal. All patients received packed red cells during the first 24 hours, followed by fresh frozen plasma (57.8%). Platelets, cryoprecipitate and whole blood were infrequently transfused (22%, 3% and 2% respectively). The mortality rate was 25.6% within 24 hours after transfusion. Transfusion of packed red cells alone was significantly associated with mortality ($p<0.001$) which increased significantly with the use of high numbers of packed red cell units.

Conclusion: Massive blood transfusion is associated with a high mortality rate in Zimbabwe. Transfusion of packed red blood cells alone resulted in highest mortality. There was an insufficient use of laboratory tests to monitor massive blood transfusion. This potentially can be addressed by establishing a national massive transfusion protocol for Zimbabwe.

RÉSUMÉ

Contexte et objectifs: La transfusion sanguine massive est définie comme une transfusion se rapprochant ou dépassant le volume sanguin total d'un patient (5-6 litres chez l'adulte) dans les 24 heures. Cette procédure est utilisée pour gérer les patients gravement anémiques et hémorragiques. Des résultats négatifs associés à l'acidose, l'hypothermie et la coagulopathie peuvent en résulter. L'étude a été réalisée pour examiner la gestion de la transfusion massive au Zimbabwe.

Matériel et méthodes: Une étude rétrospective clinique en laboratoire de 4 ans a été menée sur des patients ayant subi une transfusion sanguine massive dans un hôpital du Zimbabwe, de Janvier 2014 à Décembre 2017. Les données ont été collectées à partir des dossiers des patients de l'hôpital après autorisation du Directeur de l'hôpital.

Résultats: Sur les 180 dossiers de patients, 145 (80,6%) provenaient de femmes et 35 (19,4%) de patients de sexe masculin. Une transfusion sanguine massive a été effectuée principalement sur des patientes obstétricales. L'hémogramme complet était le test de laboratoire le plus demandé, avec 155 (86%) demandes. Certains patients souffraient d'anémie sévère. Les tests de coagulation de routine étaient significativement anormaux. Tous les patients ont reçu des concentrés de globules rouges au cours des 24 premières heures, suivis de plasma frais congelé (57,8%). Les plaquettes, le cryoprécipité et le sang total ont été rarement transfusés (22%, 3% et 2% respectivement). Le taux de mortalité était de 25,6% dans les 24 heures suivant la transfusion. La transfusion de concentrés de globules rouges seule était significativement associée à la mortalité ($p<0,001$) qui augmentait significativement avec l'utilisation d'un nombre élevé d'unités.

Conclusion: La transfusion sanguine massive est associée à un taux de mortalité élevé au Zimbabwe. La transfusion de concentrés de globules rouges seule a entraîné la mortalité la plus élevée. Les tests de laboratoire étaient insuffisants pour surveiller les transfusions sanguines massives. Cela peut potentiellement être résolu en établissant un protocole national de transfusion massive pour le Zimbabwe.

INTRODUCTION

Massive transfusion is defined as transfusion approximating or exceeding a patient's total blood volume (5-6 litres in adults) or of a minimum of 10 units in an adult within a 24-hour interval.[1] However, alternative definitions of massive transfusion do exist. This procedure is used mainly to manage severely anaemic and bleeding patients. Patients may also receive massive blood transfusion as a consequence of trauma, liver transplantation, abdominal aortic aneurysm, obstetric complications, abdominal surgery or gastrointestinal bleeding.[1-5]

Despite the clinical benefits of massive blood transfusion, there are several significant negative outcomes associated with it. These include acidosis, hypothermia, coagulopathy, hypocalcaemia, hyperkalaemia and acute respiratory distress syndrome (ARDS). Massive blood transfusion alters physiology resulting in the abovementioned outcomes which may cause morbidity and mortality. Massive transfusion in trauma, surgical and other critical care settings such as cardiac surgery, general surgery, road traffic accidents (RTA), obstetrics and upper gastrointestinal (UGI) bleeding has been found to be associated with multiple organ failure and other abnormal conditions.[6]

Haemorrhage is the most common cause of death in patients receiving large volumes of blood within a short period of time, and it is primarily caused by a combination of thrombocytopaenia and dilution of coagulation factors by transfused blood. Therefore, massive transfusion therapy of platelets and coagulation factors is necessary to stop uncontrolled blood loss. In Zimbabwe, most cases requiring massive blood transfusion are due to RTA, although no substantial evidence is available. However, excessive blood transfusion can lead to mortality due to coagulopathy, acidosis, transfusion related acute lung injury (TRALI), hypothermia and transfusion transmitted infections (TTIs). [7-11]

The above manifestations are defined as massive transfusion syndromes. Acidosis is mainly caused by impaired oxygen supply to the tissues due to decreased 2-3 diphosphoglycerate (2-3 DPG) in stored blood. It is also caused by disturbances in body pH due to the effect of citrate which is used as an anticoagulant in blood collection. Acidosis has been found to affect the enzymatic activities of the coagulation system leading to coagulopathies. Coagulopathies may also occur when the patient's coagulation factors are severely diluted by massive blood transfusion, resulting in haemorrhage. Hypothermia may be worsened by the introduction of cold blood products into the recipient's circulatory system. Hypothermia is a well-known risk factor for thrombosis.[12] TRALI has been associated with increased morbidity and mortality in patients undergoing massive blood transfusion, and it occurs within two hours after transfusion. The incidence is usually one in every five thousand transfusions. The main cause of TRALI is transfusion of blood with anti-leucocyte antibodies, mediators of inflammatory activities and micro aggregates in stored blood. TRALI usually results in severe hypoxaemia.[12- 14]

Although massive blood transfusion therapy is important for the resuscitation of uncontrolled blood loss, it can lead to high morbidity and mortality due to the so called 'lethal triad' (coagulopathy, acidosis and hypothermia). [6- 8, 10-12] Acidosis is mainly due to the introduction of citric acid which is used as an anticoagulant for donor blood. Coagulopathies may be caused by the dilution of patient's own coagulation factors by large volumes of transfused blood. Hypothermia may be due to the introduction of cold blood products into the patient's circulatory system. In addition, massive transfusion may cause several biochemical changes such as acid base imbalances, hypo-or hyperkalaemia and hypocalcaemia, resulting in abnormal body functioning.[12] Therefore, there is great need for guidelines to monitor massive blood transfusion to avoid some of

these outcomes in resource limited settings, such as Zimbabwe, in order to reduce morbidity and mortality caused by massive blood transfusion syndromes. In other countries, the establishment of massive transfusion protocols (MTPs) has been found to reduce mortality by early provision of blood replacement in situations of severe blood loss. MTPs are used to coordinate care for those patients who need massive blood transfusion. They facilitate communication among various healthcare services such as clinical settings, transfusion centres and laboratories in order to avoid delays in patient care. MTPs specify standards by which patients in critical condition are handled. Use of MTPs has demonstrated improved patient survival and reduced the rates of organ failure and other complications.[15-16]

Good MTPs should include information about the person responsible for the protocol, how the transfusion service and laboratory should be notified when to start and stop massive blood transfusion, laboratory test interpretation and blood product preparation and delivery. Other patient clinical needs should be included. Good MTPs should also have predefined ratios of packed cells, fresh frozen plasma (FFP) and platelet units of 1:1:1 or 2:1:1 for transfusion. Based on the protocol, the blood bank should ensure rapid delivery of blood components to facilitate resuscitation. However, MTPs are not always standardized. The packed cells: FFP: platelet ratio is controversial and varies from centre to centre. They can also result in wastage of blood products if used where there is no severe blood loss. [6, 16-19]

Laboratory tests are essential before massive blood transfusion. These include full blood count, blood grouping, antibody screening and identification, and compatibility testing. In cases of emergency, blood group O negative packed red blood cells can be transfused before laboratory results are available. Baseline biochemistry (electrolytes, calcium and magnesium levels and pH), haematology (haemoglobin and platelet count) and coagulation screening tests, such as prothrombin time (PT), activated partial thromboplastin time (aPTT) and thrombin time (TT) should be done. The introduction of point-of-care testing devices such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM) for routine laboratory based coagulation testing has allowed bedside analysis and reduced turnaround time for transfusion.[2, 5-6]

Published studies of practical guidelines for the management of haemorrhage have recommended early recognition of major blood loss by the clinicians and for hospitals to have adaptable MTPs. Communication between anaesthetists, haematologists and laboratory scientists was found to be useful once the protocols have been established.[20] Blood products should be readily available, together with emergency blood group O packed red blood cells in every hospital. Routine haemostatic tests such as platelet count, PT, aPTT and fibrinogen should be done frequently to ensure appropriate use of blood products. However, this may delay management of massive transfusion syndromes in resource limited settings, as some blood products may not even be available. FFPs should be part of the initial resuscitation procedures. A ratio of packed red blood cells: FFPs should be 2:1 until coagulation results become available. Coagulation results will indicate which factors are deficient, and which blood product should be given (FFPs or cryoprecipitate) to the patient.[12] MTPs also recommend the transfusion of cryoprecipitate and platelets when fibrinogen levels fall below 1.5 g/L and platelet count is very low ($<50x10^3$/uL) respectively.[21]

Most information on MTPs has been published in developed countries to ensure effective management of haemorrhaging patients and standardisation of blood transfusion.[10] Currently, there is no adequate information about the management of massive blood transfusion, in general, and massive transfusion syndromes, particularly, in Zimbabwe. This study aimed to determine how massive blood transfusion and associated syndromes are managed in Zimbabwe. The study also evaluated blood components used during massive blood transfusion and the mortality rates associated with massive blood transfusion from the time of admission.

MATERIALS AND METHODS

A retrospective clinical and laboratory study was carried out on patients receiving massive blood transfusion at the Parirenyatwa Group of Hospitals (PGH) after approval from the Joint Research Ethics Committee of the Parirenyatwa Group of Hospitals and University of Zimbabwe College of Health Sciences (***JREC /386/17***). Electronic data and archived written records from January 2014 to December 2017 were used for the study. Access to patient clinical information and laboratory data at Parirenyatwa Group of Hospitals and Blood Bank was granted by the Clinical Director and the Chief Medical Laboratory Scientist of the hospital respectively.

The collected data was used for research study purposes only. Strict confidentiality of the records was maintained by recording all results and saving the information on memory storage devices and use of a password protected computer that were only accessed by the researchers. The records consisting of patients who received massive blood transfusion for trauma, cardiac surgery, RTA, obstetric conditions and UGI bleeding were used in the study. Males and females of all age groups were included in the study. The Parirenyatwa Blood Bank database was used to identify patients who had received massive blood transfusion. Additional information on preoperative characteristics, intraoperative and postoperative outcomes was extracted from archived and computerized clinical records.

The *inclusion criteria* were**:** Patients who had received ≥4 units of blood in one hour or those who had received ≥10 units of blood in 24 hours in different critical care settings. The e*xclusion criteria* were*:* Patients with pre-existing coagulation disorders; hepatic failure; other related medical conditions. A minimum sample size of 143 was determined using the *Dobson's* formula.[22] Laboratory data was collected retrospectively from the Parirenyatwa Blood Bank database. The clinical records were used to find patients' information using data collection forms which were designed for this purpose and consisted of 24 variables. The variables were grouped into four categories after having been reviewed for completeness and validity. The categories were patient demographic characteristics, type and volume of blood components transfused, laboratory tests carried out and the outcomes of massive blood transfusion. Vital information required for the study included hospital number, age, sex, diagnosis, laboratory tests done, blood products given, time of transfusion in hours, hospital stay in days and outcomes of massive blood transfusion (death or survival). Patient diagnosis was grouped into six categories; obstetric, trauma, RTA, UGI bleeding, cardiac surgery and general surgery, for easy analysis. The general surgery group was made up of excision surgery, fibroid surgery and neurosurgery, while the cardiac surgery group was composed of cardiovascular surgery.

The collected data was captured using the Microsoft Excel spreadsheet after double checking for possible errors. The data was then statistically analysed using the *Epi info version: 7.2.2.2* and *Stata version 13.1* (Statacort, Texas 77845 USA). Normally distributed variables were summarised using mean and standard deviation. Median was used for abnormally distributed variables. Comparison between death and survival was done by *t-test* for mean values of continuous variables and *chi-square* or *Fisher's exact test* for categorical variables. Analysis of risk factors for death among patients with massive blood transfusion analysis was done by logistic regression and *Kaplan-Meier* survival curves without adjusting for covariates. The 2 sided $p<0.05$ was set as the statistically significant level.

RESULTS

Although the calculated minimum sample size was 143, this study was done on 180 patient records. There were 145 (80.6%) and 35 (19.4%) female and male patient records respectively. Ages ranged from 14 to 81 years with a median age of 31 years ($p<0.001$). There was a statistically significant difference ($p<0.001$) between the mean ages for females and males in patients admitted in different critical care settings (Table 1). There were no statistically significant differences ($p=0.144$) in transfusion times (hours) of patients admitted in different critical care settings. Massive blood transfusion was done mostly in obstetric patients. Patients involved in RTA had the shortest hospital stay after massive blood transfusion (Table 1).

One hundred and fifty-five (86%) of the massive blood transfusion patients had full blood count (FBC) requested as pre-transfusion laboratory test, while coagulation test requests varied significantly in different critical care settings ($p<0.005$). Some patients requiring massive blood transfusion in these settings exhibited severe anaemia (Hb<5 g/dL and HCT<30%). PT and aPTT results were significantly abnormal in Trauma and Obstetrics patients (Table 2)**.** Packed red blood cell transfusion ranged from 4 to 18 units (median=5.5), and was done in all (100%) patients in different critical care settings. FFPs were the second most (57.8%) widely used blood product ranging from 1 to 18 units in 24 hours. Transfusion of platelets, cryoprecipitate and whole blood were less frequent, at 22.2%, 2.8% and 1.7% respectively (Table 3). Use of FFPs decreased as the number of packed red blood cells became available for transfusion (Figure 1).

The mortality rate during massive blood transfusion was 25.6%, with 14.4% and 11.2% of these patients dying after 24 hours and within 24 hours respectively. There was no association ($p>0.05$) between diagnosis and mortality during massive blood transfusion. Transfusion of packed red blood cells alone was significantly associated with mortality. The survival rates decreased significantly with increasing number of packed red blood cell transfusions ($p<0.001$) (Figure 2). Packed red blood cell transfusion was a risk factor for mortality odds ratio=1.54, confidence interval 1.24-1.92, ($p<0.001$). Units of transfused platelets, time of transfusion and hospital stay were also significantly associated with mortality during massive blood transfusion (Table 4).

Table 1: Demographic and clinical characteristics of patients

	Trauma	Cardiovascular surgery	General surgery	RTA	Obstetrics	UGI bleeding	*p-values*
Number of patients, n (%)	18(10.0%)	20(11.1%)	8(4.4%)	14(7.8%)	112(62.2%)	8(4.4%)	<0.001
Males, n (%)	10(28.6%)	8(22.9%)	5(14.3%)	10(28.6%)	0(0.0%)	2(5.7%)	<0.001
Females, n (%)	8(5.5%)	12(8.3%)	3(2.1%)	4(2.8%)	112(77.2%)	6(4.4%)	<0.001
Age (years) mean ±SD	35.9±17.1	40.9±15.7	44.8±10.4	31.3±11.1	30.1±6.2	34.9±15.4	<0.001
Transfusion time (Hours) mean ±SD	2.3±1.6	2.4±1.3	2.1±1.6	2.7±1.9	2.0±1.3	3.1±1.7	0.144
Length of hospital stay (Days) mean ±SD	5.7±5.3	4.0±1.8	6.0±6.2	2.2±1.4	3.7±2.1	4.6±4.1	0.005

Table 2: Median Values of Pre-transfusion Haematology Laboratory Tests in different Clinical Settings

Results	Trauma	Cardiovascular surgery	General surgery	RTA	Obstetrics	UGI bleeding	*p-values*
RBC×10^{12}/L ($3.6-6.5\ 10^{12}$/L)	2.8±0.9	3.0±1.2	3.1±0.8	3.0±1.3	2.7±0.9	2.8±1.1	0.706
Hb in g/dL, (12-18 g/dL)	6.9±2.0	6.8±2.7	8.3±2.4	8.6±3.0	7.2±2.7	7.8±3.2	0.441
HCT as % (36-55%)	25.3±10	24.0±7.5	27.1±7.4	25.3±10.1	23.7±7.7	24.8±8.7	0.729
Plt ×10^9/L ($122-390x10^9$/L)	179.5±119.4	191.6±170.2	246.7±147.3	174.5±78.8	197.6±107.6	279.5±150.5	0.348
PT (10-15 sec)	23.2±11.3	17.1±4.0	12.1±2.2	17.1±0	28.8±10.0	17.2±0	<0.001
aPTT (35-45 sec)	60.6±35.3	35.9±8.3	-	-	59.9±27.2	42.9±0	<0.001
TT in sec, (10-14 sec)	-	5	-	-	-	-	-
INR, mean (0.8 - 1.1)	1.7±0.7	1.3±0.4	1.0±0.03	1.3±0	1.6±0.6	1.3±0	<0.001

Table 3: Blood Components used during Massive Transfusion

Blood Product	Trauma	Cardiovascular surgery	General surgery	RTA	Obstetrics	UGI bleeding	*p-values*
Packed cells, median U in 24h	6	6	5.5	6	5	6	0.7915
FFP, median U in 24h	3	4	3	4	5	6	0.0877
Platelets, median U in 24h	3	1	2	3	4	6	0.2578
Mean U of packed cells per patient	5.3	5.6	5.3	5.9	5.6	6.3	0.7976
Number of patients using packed cells, n,%	18(100%)	20(100%)	8(100%)	14(100%)	112(100%)	8(100%)	-
Mean U of FFP unit per patient	4.5	5.4	3.4	7.4	5.8	4.7	0.2289
Number of patients using FFP, n, %	10(56%)	14(70%)	5(63%)	7(50%)	65(58%)	3(38%)	0.703
Mean U of platelets per patient	3.5	2.2	2	3	4.3	6	<0.001
Number of patients using platelets, n, %	4(22%)	5(25%)	1(13%)	4(29%)	24(21%)	2(25%)	0.958
Number of patients using cryoprecipitate	0(0%)	0(0%)	0(0%)	1(7.1%)	4(4%)	0(0%)	-
Number of patients using whole blood	0	0	0	0	3(3%)	0	-
Mean PC:FFP ratio	1:0.43	1:0.76	1:0.60	1:0.95	1:0.79	1:0.55	0.0890

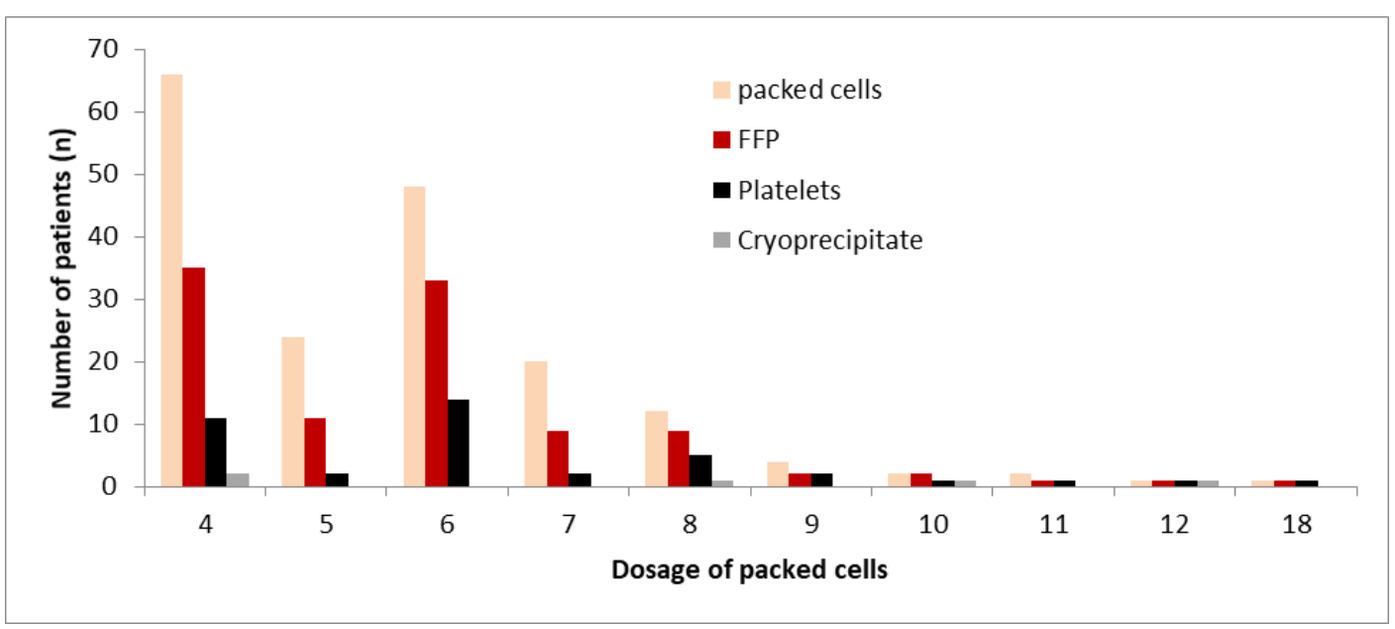

Figure 1: Comparison of transfused Blood Products

Table 4: Logistic Regression Analysis for Mortality

Variable	Odds ratio estimates	95% Confidence Interval limits	*P-value*
Age	1.01	(0.98 -1.04)	0.664
Sex (M/F)	1.21	(0.53 -2.76)	0.651
RBC $\times 10^{12}$/L	0.66	(0.44 -0.99)	0.043
Hb in g/dL	0.89	(0.77 -1.03)	0.112
Platelets $\times 10^{9}$/L	1.00	(0.99 -1.00)	0.224
Packed cells (units)	1.54	(1.24 -1.92)	<0.001
FFP	1.14	(1.00 -1.31)	0.057
PC:FFP ratio	0.98	(0.66-1.45)	0.927
Platelets	1.52	(1.09 -2.13)	0.010
PT (seconds)	1.14	(0.99 -1.32)	0.069
aPTT (seconds)	1.14	(0.95 -1.39)	0.167
Time of transfusion (hours)	1.54	(1.22 -1.94)	<0.001
Hospital stay (days)	0.73	(0.60 -0.89)	0.002

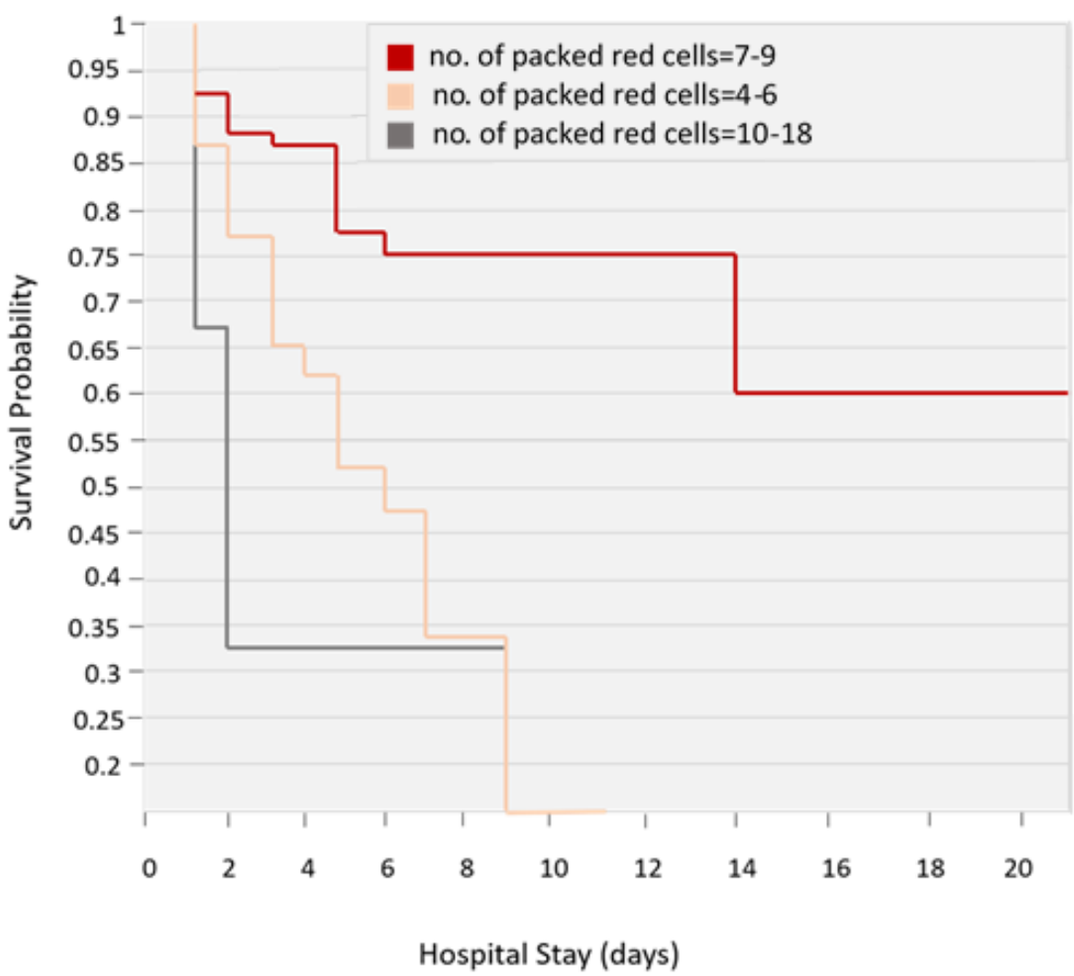

Figure 2: Survival Analysis of Mortality by number of transfused Packed Red Cells

DISCUSSION

There were more females who required blood than males. Although there is currently no information about the gender differences in transfusion needs, this could have been associated with factors that cause females to require blood, such as blood loss during menstruation, pregnancy and postpartum haemorrhage.[23] The median age suggested that the majority of those needing blood were young adults. Bleeding patients received massive blood transfusion as a result of RTA, trauma, cardiovascular surgery, obstetrics and general surgery. Most of these patients were females of young age compared to males. This was probably due to the fact that most of the patients were in the obstetrics setting as a result of post-partum haemorrhage.[23] However, other studies have shown that massive blood transfusion was most common in males of young age because of haemorrhage arising from interpersonal violence and RTAs.[4, 10, 24]

Transfusion periods (hours) did not show any statistically significant difference across different disciplines. However, protracted transfusion times were associated with higher mortality. This showed a lack of standardisation in managing massive blood transfusion. In standardised massive transfusion management, it is required that every aspect of transfusion must be done on time. This includes communication among critical healthcare givers, processing and delivery of blood products and preparation of blood product ratios for effective massive blood transfusion. Studies have also indicated that timing is one of the most crucial aspects of massive blood transfusion.[25] Obstetrics had the largest number of patients requiring massive blood transfusion. This could be due to postpartum haemorrhage. Post–partum haemorrhage was found to be the leading cause of mortality among women in Japan and it is treated by transfusion of several haemostatic blood products.[26]

Patients involved in RTAs had the shortest hospital stay after massive blood transfusion. It is not clear why this was the case, but it is thought these patients may only require massive transfusion to prevent severe haemorrhagic shock after accidents.[6] Those who sustain abdominal and pelvic injuries (APIs) often require longer hospitalization.[27] Full blood count (FBC) was the most requested pre-transfusion laboratory test. FBC results may give additional information helpful in the management of most diseases. Haemoglobin and haematocrit are used to evaluate anaemia during massive blood transfusion. FBCs also allow for the evaluation of platelets to identify bleeding due to dilutional thrombocytopaenia in these patients. Values for these three haematological parameters are often used as transfusion triggers. Transfusion of packed red blood cells is strongly indicated in order to facilitate rapid oxygen (O_2) supply to the tissues in bleeding patients.[12, 28] However, there is need to use more laboratory tests for the assessment of massive transfusion syndromes.

PT and aPTT results were significantly abnormal in Obstetric and Trauma patients. This was expected because patients in these critical care settings may lose a lot of blood. Therefore, coagulopathies are common due to dilution of coagulation factors and interferences caused by low calcium and pH imbalances. The hypocalcaemia was caused by the trapping of calcium by sodium citrate. The sodium citrate, as an acid, caused pH imbalances. These resulted in abnormal PT and aPTT.[12] Biochemical measurement of calcium and pH would have assisted in the study. Packed red blood cells were used by all who required transfusion in critical care settings. These are the most widely used blood products for the treatment of anaemia.[28]Therefore, this is one of the most important products in transfusion practice.

FFPs were the second most widely used blood product. These are effective in the treatment of bleeding, whether transfusion induced or not. Platelet concentrates, cryoprecipitate and whole blood were less frequently used. Transfusion of whole blood is not recommended because of its tendency to cause severe adverse transfusion outcomes due to incompatibilities between donor and recipient, plasma and red blood cells respectively.[12] Massive transfusion protocols recommend the use of a 1:1:1 or 2 ratio for platelet, fresh frozen plasma and red blood cells respectively, to avoid excessive or under-transfusion of any one blood product.[16]

Death rates of more than a quarter of massively transfused patients are not acceptable. The absence of an association between the deaths and the underlying diagnosis points to the significant challenges and dangers associated with massive blood transfusion. Since transfusion of packed red blood cells alone was significantly associated with increased mortality, it means the ratio system, as recommended in transfusion protocols, was not used for adequate resuscitation. Reduction of transfusion related mortality can be achieved by recognizing patients who really need blood products, and proper identification of the products is required. Maximal involvement of critical care specialists such as anaesthetists and haematologists, and establishment of a locally designed WHO recommended massive transfusion protocol should be urgently considered.[29-30]

CONCLUSION

Although massive blood transfusion has significantly reduced mortality in critical care settings, deaths continue to occur, and it has contributed significantly to the high mortality rate. Transfusion of packed red blood cells without other blood products was responsible for most deaths. There was insufficient use of laboratory tests to monitor massive blood transfusions, contributing to high mortality. There is an urgent need to establish a local MTP in order to reduce mortality associated with this procedure. Predefined massive transfusion protocols have been found to significantly reduce mortality associated with organ failure.[31]

LIMITATIONS

There was limited essential clinical and laboratory information in the patient records. The severity of coagulopathy, hypocalcaemia, acidosis, hyperkalaemia and hypokalaemia could not be measured and evaluated as necessary coagulation and biochemical test results were not easily available.

RECOMMENDATIONS

The results of the current study support the following recommendations:

- The urgent establishment of a local protocol on massive transfusion.
- Strong communication among health care personnel in critical care settings.
- Urgent laboratory tests during massive blood transfusion to monitor possible complications.
- Critical care experts such as anaesthetists and haematologists are to be consulted as soon as a massive transfusion scenario is suspected or required.
- Regular institutional review of massive transfusion cases, their management and outcome.
- Regular consultations with Hospital Transfusion Committees (HTCs).

REFERENCES

1. Pham HP, Shaz BH, Hemmings HC. Update on Massive Transfusion. *British Journal of Anaesthetics*. 2013; 111 (1): i71-i82.
2. Hess J, Silvergleid A, Tirnauer J. Massive Blood Transfusion [Internet]. 2014. Available from: https://www.scribd.com/document/332895233/ UpToDate-Massive-Blood-Transfusion.
3. Sun Y, Jin Z-K, Xu C-X, Dang Q-L, Zhang L-J, Chen H-N, *et al*. Investigation of the current situation of massive blood transfusion in different surgical departments: a large multicentre study in China. *International Journal of Clinical Experimental Medicine*. 2015*;* 8 (6): 9257–65.
4. Rangarajan K, Subramanian A, Pandey R M. Determinants of mortality in trauma patients following massive blood transfusion. *Journal of Emergency Trauma Shock*. 2011; 4 (1): 58–63.
5. Sinha R and Roxby D. Transfusion practices in massive haemorrhage in pre-intensive and intensive *care: Transfusion practices in massive haemorrhage. Vox Sang*. 2011; 101 (3): 230–6.
6. Sihler KC, Napolitano LM. Complications of massive transfusion. *Chest*. 2010*;* 137 (1): 209-220.
7. Maegele M, Lefering R, Paffrath T, Tjardes T, Simanski C, Bouillon B, *et al*. Red blood cell to plasma ratios transfused during massive transfusion are associated with mortality in severe multiply injury: a retrospective analysis from the Trauma Registry of the Deutsche Gesellschaft für Unfallchirurgie. *Vox Sang*. 2008; 95 (2): 112–9.
8. Vymazal T. Massive haemorrhage management–a best evidence topic report. *Ther Clin Risk Manag*. 2015; 11: 1107–11.
9. Bell DG and McCann ET. Transfusion in trauma. *Current Pulmonary Report*. 2016; 5 (2): 94-100.
10. Ortega-Gonzalez MDC, Monzon-Torres BI. Value and impact of massive blood transfusion protocols in the management of trauma patients. *South Afr J Anaesth Analg*. 2011; 17(4), 282–5.
11. Rutsate R, Mandisodza A, Chikwasha V, Emmanuel J, Mavunganidze G. An assessment of the potential risk of transfusion transmitted infections in patients transfused in Zimbabwean Hospitals. *IJRDO-Journal of Health Sciences and Nursing.* 2017*; 2 (10):126-136.*
12. Petz L, Swisher SN, Kleinman S, Spence RK, Strauss RG. Diagnosis and Management of Transfusion Reactions. *Clinical Practice of Transfusion Medicine*. 1996*; 3rd Edition:* 905- 929.
13. Napolitano LM. Kurek SDO, Luchette FA, Corwin HL, Barie PS, Tisherman SA et al. Clinical practice guidelines: Red blood cell transfusion in adult trauma and critical care. *Critical Care Medicine*. 2009; 37 (12): 3124-3157.
14. Maxwell MJ, Wilson MJA. Complications of blood transfusion. *Continuing Education in Anaesthesia Critical Care and Pain.* 2006; 6 (6): 225-229.
15. Hsu Y, Haas T, Cushing M. Massive transfusion protocols: current best practice. *International Journal of Clinical Transfusion Medicine.* 2015; 4: 15-27.
16. Kamal S. Massive transfusion protocol [Internet]. 2015. Available from: https://fr.slideshare.net/ DRSHDABKAMAL/massive-transfusion-protocol.
17. Kaur P, Basu S, Kaur G, Kaur R. Transfusion protocol in trauma. *Journal of Emergency Trauma Shock*. 2011; 4 (1): 103–8.
18. Hardcastle T C. Complications of massive transfusion in trauma patients. *ISBT Sci Se.* 2006; 1 (1): 180–4.
19. Patil V, Shetmahajan M. Massive transfusion and massive transfusion protocol. *Indian J Anaesth*. 2014; 58 (5): 590–5.
20. Jain K, Jain S, Sood N, Puri A. Massive blood transfusion: A case report of transfusion of 70 units of blood and blood products in 24 hours. *Case Report.* 2018; 3 (1): 68-71.
21. Hunt B J, Allard S, Keeling D, Norfolk D, Stanworth S J, Pendry K, *et al*. A practical guideline for the haematological management of major haemorrhage. *Br J Haematol*. 2015; 170 (6): 788–803.
22. Nyi Nyi Naing. Determination of Sample Size. *Malays J Med Sci.* 2003;10(2): 84–86.
23. Gombotz H, _Schreier G, _Neubauer S, Kastner P, l Hofmann Axe. Gender disparities in red blood cell transfusion in elective surgery: a post hoc multicentre cohort study. *BMJ Open.* 2016; 6(12): e012210
24. Yang J-C, Wang Q-S, Dang Q-L, Sun Y, Xu C-X, Jin Z-K, *et al*. Investigation of the status quo of massive blood transfusion in China and a synopsis of the proposed guidelines for massive blood transfusion. *Medicine (Baltimore)*. 2017; 96(31): e7690.
25. O'Reily KB, Lockhart E, Holcomb JB. Massive transfusion: a question of timing, detail, a golden ratio. CAPTODAY. [Internet] 2014. Available from: http://captodayonline.com/massive-transfusion-question-timing-detail-golden-ratio/.
26. Tanaka H, Matsunaga S, Yamashita T, Okutomi T, Sakurai A, Sekizawa A, *et al*. A systematic review of massive transfusion protocol in Obstetrics. *Taiwanese Journal of Obstetrics and Gynaecology*. 2017; 56 (6): 715-718.
27. Cheynel N, Gentil J, Freitz M, Rat P, Debalon PO, Kopp CB. Abdominal and Pelvic Injuries caused by Road Traffic Accidents: Characteristics and Outcomes in a French Cohort of 2009 Casualties. *World Journal of Surgery*. 2011*;* 35 (7): 1621-1624.
28. Liumbruno G, Bennardello F, Lattanzio A, Piccoli P, Rossetti G. Recommendations for the transfusion of red blood cells. *Blood Transfusion*. 2009*;* 7 (1): 49-64;
29. Thomas D, _Wee M, _Clyburn P, Walker I, Brohi K, Collins P*, et al*. Blood transfusion and the Anaesthetist: management of massive haemorrhage. *Anaesthesia*. 2010*;* 65 (11): 1153–1161.
30. Federicks C, Kubasiak JC, Mentzer CJ, Yon JR. Massive Transfusion: An update for the anaesthesiologist. *World Journal of Anaesthesiology*. 2017; 6 (1): 14-21.
31. Cotton B, Au BK, Nunez TC, Gunter OL, Robertson AM, Young PP. Predefined Massive Transfusion Protocols are Associated with a reduction in Organ failure and Post-injury Complications. *Journal of Trauma: Injury, Infection and Critical Care*. 2009; 66 (1): 41-49.