

Trends in the Utilization of Blood Components in The Intensive Care Unit in A Tertiary Care Hospital

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Cite this paper as: Dr. Bethany G Neumann, Dr. Rajat Mondal, Dr. Debarshi Saha, Dr. Deepa Sowkur Anandarama Adiga, Dr. Nikhil Kumar, Dr. Arnab Ghosh, (2025) Trends in the Utilization of Blood Components in The Intensive Care Unit in A Tertiary Care Hospital. *Journal of Neonatal Surgery*, 14 (32s), 7649-7657.

ABSTRACT

Background: Guidelines for component transfusion are often not followed. Risks are also associated with transfusion and vary with different investigators.

We evaluated the utilization of blood and its components among intensive care unit (ICU) patients and studied the association between transfusion and increased morbidity and mortality.

Methods: Retrospective study on total 250 patients in ICU >24 hours with 694 transfusion events for 7 months. Components (number and type) transfused, length of stay (LOS) in ICU and hospital, complications and mortality were recorded.

Results: A total of 250 of 2102 ICU patients were transfused. Of these 516 (31.40%) were packed cell (PC), 415 (25.26%) platelets concentrate (PLTC), 686 (41.76%) were fresh frozen plasma (FFP), totaling 1643 transfusions. Of the PC transfusions, 60(33%) patients had hemoglobin (Hb)<7g/dl and 77(42.3%) had Hb between Hb 7-9g/dl. Sixty-six (26.4%) of 250 patients were transfused with PLTC of which 53(80.3%) had platelet count<20000/cu.mm. There were 120/250(48%) FFP transfusions of which 83(69.2%). Hb ≤ 9.0g/dl for PC, platelets ≤ 20000/cu.mm for PLTC, INR ≥ 1.6 (PT ≥ 17s) for FFP were the triggers for respective component transfusion.

The mortality among the transfused patients is 22.4%(56/250) compared to that 19.8%(248/1852) of the non-transfused (p=0.00001, significant). The transfusion of PC & PLTC together showed 3.76 (odds ratio) times higher mortality than any other component transfused, either singly or in combination.

Conclusions: Transfusion triggers largely agreed with other studies. Mortality is significantly associated with transfusion. The ICU stay increased with PC transfusions i.e. the more the ICU stay, the more likely is the increase in patients being severally transfused.

Keywords: Blood components, ICU patients, Utilization, Triggers, Mortality.

1. INTRODUCTION

The World Health Organization (WHO) defines anemia as hemoglobin (Hb) < 13g/dl and < 12g/dl, among men and women respectively.^[1, 2] Though it may seem obvious that red blood cell packed cell (PC) transfusions save lives, numerous studies have attested to risks outweighing the benefits of such transfusion.^[3,4,5] Due to alteration of physiological responses, extremely sick patients may maintain adequate tissue oxygenation at Hb <7g/dl, but this also constitutes a trigger for transfusion.^[6,7] The restrictive policy of PC transfusion reduced overall mortality and needs to be validated by other studies.^[8] That PC transfusion increased morbidity also needs to be confirmed by other studies.^[4]

Transfusion of FFP has been shown to be of little help to rectify mild increments of international normalized ratio (INR).^[9] Apparently, heavy bleeding and presumptive measures to control bleeding in planned invasive procedures comprise the main indications for FFP transfusion.^[11] Since INR>1.7 increased bleeding risk^[12], what constitutes the trigger in the ICU patients needs to be seen. Transfused singly, FFP was associated with the highest mortality^[13, 14] which also requires validation.

In critically ill patients, platelets concentrate (PLTC) is transfused to alleviate the risk of bleeding in complex coagulation defects, anticipated surgery in patients taking antiplatelet agents or with renal insufficiency. Patients admitted to ICU have a 35-45% incidence of developing thrombocytopenia and 15-30% of them may be administered PLTC^[15, 16, 17] Since Platelet count>50000/mm³ is considered safe for surgery^[18], ICU practice could be different and needs investigation. PLTC transfusions were generally not associated with increased mortality^[19] but require validation from other studies.

This study aims to define transfusion practices regarding all the components viz. PC, FFP and PLTC among the critically ill patients. The primary endpoint of the study is to assess mortality among the transfused patients and assess whether it differs significantly from that of the non-transfused patients.

2. METHODS

Design and Setting

The study was conducted over seven months after obtaining approval from the institute's ethics committee. The study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional review board (Institute ethics committee [IEC]). Informed written consent of the patients was waived by the IEC since it required no interaction with patients and only the blood bank and non-specific medical records department data was required.

Patients remaining in ICU for >24 hours were enrolled in our study. The outcome was death or discharge from the hospital. The patients requiring PRBC were divided into three categories viz. ≤ 7 g/dl, 7-9g/dl and ≥ 9 g/dl hemoglobin levels prior to transfusion. The patients requiring FFP were divided into those with INR ≤ 1.6 and with INR ≥ 1.6 . The patients requiring platelets were divided into 4 groups viz. ≤ 20000 /cu mm, 20000-30000/cu. mm, 30000 – 50000/cu. mm and > 50000/cu. mm.^[20] A total of 250 patients with 694 transfusion events were studied. A transfusion event is defined as an episode of transfusion wherein one to multiple units of the same or different components was administered. Cases where inadequate data was available and cases of thalassemia or other morbidities that are obligatorily dependent on transfusion of components were also excluded from the study.

Data collection

Patient demographics, admitting clinical diagnoses, any past or present comorbidities, pre-transfusion prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin (APTT), platelet counts and hemoglobin (Hb) levels as applicable were documented. The number of any components transfused, length of stay (LOS) in ICU and hospital, complications and mortality (if encountered) were also recorded.

Statistical analysis

Descriptive statistics was used for the quantitative variables. Means were described with standard deviations (SD) and medians with interquartile ranges. Chi-square test was used to determine statistical significance between categorical variables. $p < 0.05$ was taken as statistically significant. Statistical calculations were performed using SPSS v. 16.0, Armonk, New York: IBM Corporation.

3. RESULTS

Patient and intensive care unit (ICU) characteristics

In the seven-month study period, 2102 patients were admitted to the ICU, of which 250 patients were transfused at least one

component (Table: 1))

Table1. Patients' characteristics (n=250)

Variable	Mean $\pm$ SD	Median[IQR]
Age, years	43.53 $\pm$ 2.47	47.0 [24.8, 62.0]
Gender, n (%)		
Male	169 (67.6)	
Female	81 (32.4)	
Age group, n (%)		
Adult	200 (80.0)	
Pediatric	50 (20.0)	
Outcome		
Length of stay in hospital, days	15.17 $\pm$ 15.06	10.50 [5.0, 20.0]
Length of stay in ICU, days	9.16 $\pm$ 8.84	6.0 [11.0, 3.0]
Discharged from ICU, n (%)	194 (77.6)	
Died in ICU, n (%)	56 (22.4)	
Transfusion reaction, n (%)	1 (0.4)	

ICU – Intensive Care Unit, SD – Standard Deviation, LQ – Lower Quartile, UQ – Upper Quartile

The overall mortality rate in the ICU was 14.46% (304 of 2102 patients) of which 56 were transfused. The total number of units transfused were 1643, of which PC were 516 (31.40%), PLTC were 415 (25.26%) and FFP were 686 (41.76%). The total transfusion events were 694 of which 349 (50.29%) were PC events, 120 (17.29%) were PLTC events and 218 (31.42%) were FFP events.

RBC packed cell (PC) transfusions

The details of PC transfusion along with indications for transfusion are shown in (Table: 2). A patient with a pre-transfusion Hb <7 g/dl is significantly likely to be multiply transfused (p = 0.001)

Table 2. Indications for Packed Cell (PC) Transfusions

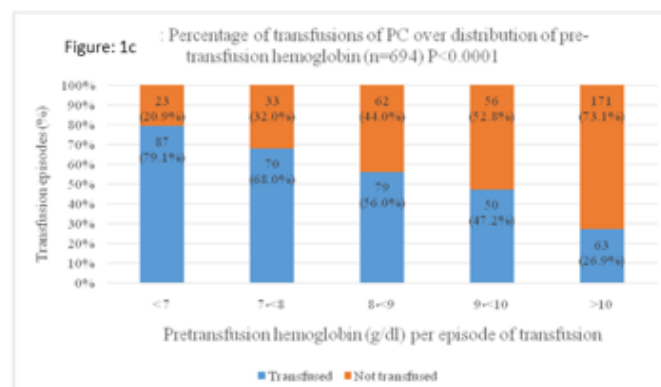
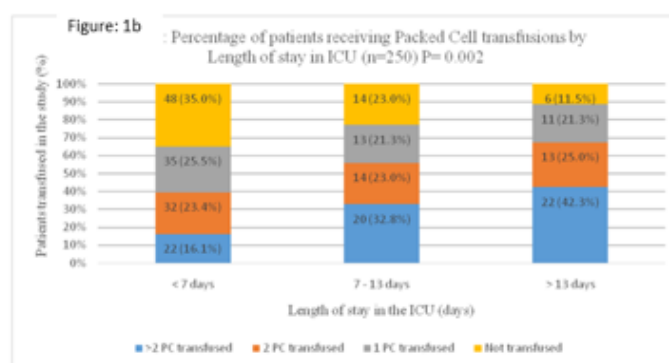
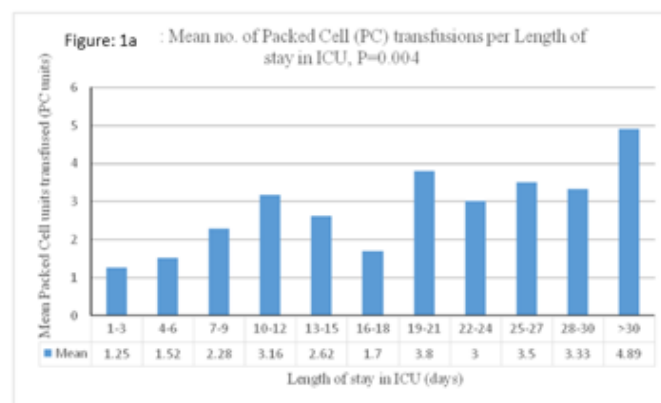
Characteristics	Mean $\pm$ SD	LQ/Median/UQ
Total PC units transfused	516	
Patients with PC transfusions, n (%)	182 (72.8%)	
No. of PC units transfused (n=182)	2.84 $\pm$ 2.77	1.0/2.0/3.0
Hemoglobin among transfused, g/dl (n=182)	7.96 $\pm$ 2.09	6.8/7.9/8.9
Indication for transfusion, n (%)		
Low hemoglobin	83 (45.6)	
Active bleeding	33 (18.1)	
Surgical procedure	47 (25.8)	
Hemodynamic instability	17 (9.3)	
Hemodialysis	2 (1.1)	

Pre-transfusion Hb, g/dl, n (%)		
≤ 7	60 (33.0)	
7-9	77 (42.3)	
> 9	45 (24.7)	

PC, Packed Cells; SD, Standard Deviation; LQ, Lower Quartile; UQ, Upper Quartile

Thus, as the LOS increased, the number of PC transfusions per patient increased and was statistically significant ($p = 0.004$; Fig: 1a)

Again, the number of patients requiring PC transfusion correlated significantly with the number of days spent in ICU ($p = 0.002$; Fig: 1b).



The <9g/dl Hb level was most commonly used as the transfusion trigger ($p<0.0001$; Fig: 1c) unless active bleeding, ischemic/coronary heart disease or tissue oxygenation due to some other causes did not complicate the situation.

Platelet concentrate (PLTC) transfusion

PLTC were given to 66 patients of 250 totally transfused, the minimum pre-transfusion value being 3000/cu. mm and maximum being 348000/cu. mm. The indications and triggers for platelet transfusions are shown in Table: 3. PLTC transfusions did not correlate significantly with LOS.

Table 3. Indications and triggers for Platelet Concentrate (PLTC) transfusions

Characteristics	Mean	LQ/Median/UQ
Total Platelet conc. units transfused	415	
Patients with PLTC transfusions, n (%)	66 (26.4%)	
No. of PLTC units transfused (n=66)	6.29±4.90	3.8/4.0/8.0
Platelet count among transfused, X 10 ⁹ /L (n= 66)	29.4±5.62	6.8/14.5/27.3
Indication for transfusion, n (%)		
Low platelet count	53 (80.3%)	
Hemorrhage	4 (6.1)	
Surgical procedure	6 (9.1)	
Other	3 (4.5)	
Pre-transfusion Platelet count, X 10 ⁹ /L, n (%)		
≤ 20	41 (62.1)	
20-30	12 (18.2)	
30-50	5 (7.6)	
>50	8 (12.1)	

PLTC, Platelet Concentrate; SD, Standard Deviation; LQ, Lower Quartile; UQ, Upper Quartile

Regarding PLTC transfusion events, a trigger of 20000/cu mm was being followed with majority of the patients (Table: 3). In those patients where a trigger was not being followed, active bleeding, falling platelet counts due to malaria/dengue and surgery were the indications.

FFP transfusion

In the current study, 120 patients received FFP, characteristics of which are shown in Table 4.

Table 4. Indications and triggers for Fresh Frozen Plasma (FFP) transfusions

Characteristics	Mean ±SD	LQ/Median/UQ
Total FFP units transfused	686	
Patients with FFP transfusions, n (%)	120 (48.0%)	
No. of FFP units transfused (n=120)	5.72±5.54	2.0/4.0/6.0
International Normalized Ratio (INR) among transfused (n= 120)	3.31±2.3	1.46/2.15/3.35
Prothrombin Time (PT) among transfused (n=120)	35.38±30.95	18.98/25.75/37.73
Activated Partial Thromboplastin Time (APTT) among transfused (n=60)*	60.17±31.74	41.72/50.60/63.30

Indication for transfusion, n (%)		
Elevated PT/INR/APTT	89 (74.2)	
Active bleeding	6 (5.0)	
Surgical procedure	11 (9.2)	
DIC	9 (7.5)	
Other	5 (4.1)	
Pre-transfusion INR, n (%)		
≤ 1.6	37 (30.8)	
>1.6	83 (69.2)	
Pre-transfusion PT, n(%)		
≤ 17	17 (14.2%)	
> 17	103 (85.8%)	

* There were 60 cases where APTT values were not recorded in the case sheets

FFP, Fresh Frozen Plasma; INR, International Normalized Ratio; PT, Prothrombin Time; APTT, Activated Partial Thromboplastin Time; DIC, Disseminated Intravascular Coagulation; SD, Standard Deviation; LQ, Lower Quartile; UQ, Upper Quartile

Mean numbers of FFP transfused did not correlate significantly with LOS. The trigger of INR >1.6 for FFP transfusion was not followed in many patients. Most patients of cardiothoracic surgery and general surgery who had a transfusion event were administered FFP.

Mortality

Transfusion of any component is significantly associated with higher mortality, 56/250 died among the transfused as opposed to 248/1852 among the non-transfused ($\chi^2=14.4514$, $p=0.0001$)

The type of component transfused correlates significantly with mortality ($\chi^2=13.268$, $p=0.039$) when individually considered, mortality due to FFP transfusion was the highest among the three components (11 of 35, 31.4%; , whereas mortality due to PC (12 of 93, 12.90%) and PLTC (6 of 25, 24%). When combination of components considered mortality due to PC and PLTC was the highest (6 of 12, 50%).

Risk of mortality

Patients who received Platelets and FFP showed significant risk of mortality, odds ratio (OR) 1.11 and 1.73 respectively while patients with PC transfusion showed OR 0.38.

The combined transfusion of PC and PLTC carried the highest risk of mortality (OR 3.76) followed by PLTC and FFP (OR 1.16) in contrast to patients who received PC and FFP, the risk of mortality was insignificant (OR 0.93).

The patients who received combination of all the three components the risk of mortality is significant (OR 1.84).

4. DISCUSSION

Anemia, hemorrhage and surgery are the main indications of transfusion in our study. The mean pre-transfusion Hb is 7.96 ± 2.09 g/dl in the current study, The RBC transfusion rate in our study is 182/2102 (8.6 %) and the trigger of 9g/dl of Hb was being followed for RBC transfusion. PC transfusion wasn't associated with any significant risk of mortality (OR 0.38)

ICU length of stay (LOS) correlated significantly with the number of mean PC units transfused in our study. With < 3, 4-6, 7-9 and 10-12 days of ICU LOS, the mean PC units transfused were 1.25, 1.52, 2.28 and 3.16 respectively. Among the transfused patients, with <7 days LOS, 65%, 7-13 days, 77% while >13 days, 88.5% were transfused with PC.

PLTC were given to 66 patients out of 250 totally transfused, the minimum pre transfusion value being 3000/cmm and maximum being 348000/cmm; only 8(12.1%) had platelet count >50000/cmm. Low platelet count (n=53, 80.3%) was the major cause of PLTC transfusion followed by surgical procedure (n=6, 9.1%) and hemorrhage (n=4, 6.1%) in our study. PLTC carried a moderate risk of mortality as seen in our study (OR 1.11)

In the current study, 120 patients received FFP, a deranged PT/INR/APTT/ accounted for most 89(74.2%) transfusions,

majority of the patients in our study had INR >1.6 ($n=83$, 69.2%) and PT >17 seconds ($n=103/120$, 85.8%). FFP transfusion carried the highest risk of mortality in our study (OR 1.73).

The combined transfusion of PC and PLTC carried the highest risk of mortality (OR 3.76) than any other combination of component transfusion in our study.

The indications of transfusion in our study comparable to the study by Rao et al.^[21] The mean pre-transfusion Hb in current study, is lower than that of Vincent et al (8.4g/dl)^[3] and a little higher than that of Al-Faris et al (7.08g/dl).^[22] The RBC transfusion rate in our study 8.6% compared to 21% and 40% in studies by Al-Faris et al^[22] and Vincent et al^[3] respectively. Thus, most patients in our ICUs were able to maintain adequate tissue perfusion and oxygenation in contrast to that of other studies.^[3, 4, 22]

Hebert et al (TRICC study) proved that a restrictive policy of RBC transfusion (Hb <7 g/dl) with the aim to maintain Hb between 7-9g/dl was associated with significantly less mortality^[8] also reiterated by the British journal of hematology guidelines. Transfusion trigger for RBCs (<9 g/dl)^[11] was being followed indicating partial compliance in our study.

Our study showed as the LOS increases, the number of PC transfusions per patient increased and number of patients requiring PC transfusion correlated significantly with the LOS, similar to the study by Corwin et al who showed, ≤ 3 days LOS, 30%, 4-6 days LOS, 40%, 7-13 days LOS, $>50\%$, >13 days LOS approximately 80% of patients received transfusion.^[4]

Generally, platelets $>50000/\text{cu mm}$ is considered safe for invasive surgery.^[18] in our study low platelet count (80.3%) was the major cause of PLTC transfusion similar to Rao et al. where the primary indication was low platelet count (39.5%).^[21]

One observational study documented that the platelet count did not even marginally increase post transfusion. The trigger for PLTC transfusion according to hematology and oncology patients' guidelines is 20000/cu mm in the presence of infections or hemostatic abnormality, to 10000/ cu mm if none of these reasons exist.^[15] Whether this guideline applies to general ICU patients is not yet decided.^[23]

The primary indications for FFP transfusion are prevention/ treatment of bleeding and elevated/ abnormal coagulation tests.^[23] The median increment in INR was 0.1 if INR was between 1 and 1.5, 0.4 for INR between 1.6-2.5, 1 for INR between 2.5-3.5, and 2.5 for INR >3.5 .^[24] Quantitative reduction of coagulation factors to $<30\%$, corresponding to INR >1.7 increases risk of bleeding.^[12]

Our study correlates with the study by Tantawy H et al. who did not find any significant statistical difference in up to 6-month mortality between 446 patients with 1 to 5 units of transfusion and 446 matched patients without PRBC transfusion.^[25] Carson JL et al. also showed that restrictive transfusion strategies did not improve the 30-day mortality rate compared with liberal transfusion strategies.^[26]

Our findings of moderate risk of mortality associated with PLTC (OR 1.11) differ from the confounder adjusted study by Ning S et al. where PLT transfusions were not associated with increased mortality in ICU (hazard ratio [HR], 0.78; 95% confidence interval [CI], 0.60-1.02; $p = 0.06$) or in hospital (HR, 0.89; 95% CI, 0.68-1.09; $p = 0.41$).^[19]

Our study correlates the results showed in their literatures by Li-Min Zhang et al.^[13] that mortality and worse outcomes were correlated with FFP transfusion and Glasgow Coma Scale score ($P < 0.05$). Luo Z et al. in his confounder adjusted study showed FFP transfusion was associated with in-hospital mortality (OR 1.09, 95% CI, 1.01-1.18; $p = 0.035$).^[14]

Strengths and limitations of the study

This study was conducted on 250 transfused out of 2102 ICU patients over one year. Mortality pertaining to PC, PLTC and FFP have been found out individually and in combination. Morbidity in terms of LOS has also been ascertained. OR concerning individual and combination component transfusion is established.

Disease diagnosis and severity in terms of Acute Physiology and Chronic Health Evaluation (APACHE) II or Sequential Organ Failure Assessment (SOFA) score hasn't been assessed while correlating mortality and LOS with component transfusion. This would have ensured confounder adjustment. The patients couldn't be followed after discharge. Thus, actual mortality rates could not be ascertained.

Conclusions

PC transfusions and the transfusion rate increase with increasing number of days of ICU stay.

A hemoglobin level of 9g/dl is usually followed as the trigger for PC transfusion whereas hemoglobin levels less than 7 g/dl usually induce multiple transfusions. A trigger of 20000/cu mm platelet count and a PT of 17 seconds over INR 1.6 is used as a trigger for FFP transfusion. Mortality is significantly associated with transfusion of any component. Considering single component transfusion, FFP transfusion carried the highest risk of mortality while a combined transfusion of PC and PLTC transfusion carried the highest risk of mortality.

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