

Analysis of Blood Utilization and ABO Compatibility in Stem Cell Transplant Patients at a Tertiary Care Hospital in Central India

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ABSTRACT

Background: Transfusion support is crucial for HSCT patients, especially with ABO incompatibility, where delayed erythroid engraftment and hemolysis increase RBC needs. The crossmatch-to-transfusion (C:T) ratio indicates transfusion efficiency. This study aims to evaluate PRBC utilization in HSCT patients using C:T ratio, assess transfusion thresholds, and analyze factors influencing PRBC use.

Materials and Methods: This retrospective study was conducted from October 2022 to September 2023 in the Department of Transfusion Medicine and Bone Marrow Transplant Unit at a tertiary care center in central India. It included 57 pediatric patients (age 2–19) undergoing allogeneic HSCT. Data included hemoglobin levels, PRBC units crossmatched and transfused, ABO compatibility status, stem cell source, and diagnosis. A hemoglobin threshold of 7 g/dL was followed. The C:T ratio was calculated.

Results: Among 57 allogeneic HSCT recipients (mean age 8.6 ± 4.5 years), thalassemia major was the main indication (61.4%), with bone marrow as primary stem cell source (86%). Of 485 PRBC units

crossmatched, 344 were transfused (C:T ratio 1.41). The transfusion threshold was 7.5 ± 0.4 g/dL, with PRBC utilization of 6 ± 3.5 units per patient. C:T ratios were similar across ABO groups: 1.4 in compatible, major mismatch, and minor mismatch transplants, and 1.2 in bidirectional mismatch. Major mismatch group had higher crossmatched units (11.5 ± 7), but RBC utilization showed no difference among ABO groups ($F(3,53) = 2.08$, $p = 0.113$). Age and RBC use showed no correlation ($\rho = 0.018$, $p = 0.897$), and utilization did not differ by stem cell source ($t(55) = 0.677$, $p = 0.501$). Despite higher C:T ratio in aplastic anemia (1.8) versus hemoglobinopathies (1.3) and leukemia (1.18), RBC use across diagnostic categories showed no difference ($F(6,50) = 1.58$, $p = 0.173$).

Conclusion: The study shows efficient PRBC use in pediatric HSCT patients through optimal C:T ratio. ABO incompatibility affects transfusion needs, with higher PRBC use in major ABO-incompatible transplants. Standardized transfusion strategies can improve efficiency and outcomes.

Keywords: Hematopoietic stem cell transplantation, Packed red blood cells, Crossmatch-to-transfusion ratio, ABO incompatibility, Pediatric HSCT, Transfusion medicine

INTRODUCTION

Hematopoietic progenitor cells (HPCs) are infused during hematopoietic stem cell transplantation (HSCT) to reconstitute the immune system and repair bone marrow components.^[1] Transfusion support for HSCT patients is critical as they lack blood cell production ability and challenging due to blood type transitions with allogeneic donors.^[1] Bone marrow transplant (BMT) patients need RBC transfusions due to anaemia from pre-transplant therapy. ABO group selection becomes intricate when the recipient and donor possess different blood types. Transplants with ABO mismatches often necessitate more transfusions due to delayed engraftment and red cell aplasia. The injection of HSC can lead to red cell hemolysis.^[2] Types of ABO mismatches in transplantation include:

- a.) Major ABO incompatible: Donor antigens are transferred to a recipient with pre-existing antibodies.
- b.) Minor ABO incompatible: The donor has antibodies against the recipient's antigens.
- c.) Bidirectional ABO incompatible: Both major and minor ABO mismatches are present.^[2]

Transfusion support is needed after transplantation, especially before red blood cell engraftment. This is crucial for ABO-incompatible hematopoietic stem cell transplantations (HSCTs). Compatibility between donor and recipient ABO groups guides blood component selection to minimize hemolysis risk until recipient antibodies disappear.^[3] For major ABO incompatibility, recipient-matched red blood cells should be used until recipient antibodies clear. In minor incompatibility, donor-type red cells can be given post-transplant, while recipient-type plasma and platelets are used until recipient red cells

disappear. For combined incompatibilities, group O red cells and AB plasma/platelets are used until problematic antibodies clear.^[4] ABO antigens exist on hematopoietic stem cells (HSCs) and red blood cells.^[5] Delayed erythrocyte recovery occurs when recipient immunity attacks donor red cells, extending transfusion needs. ABO incompatibility's impact on transplant outcomes remains controversial.^[4] Association for the Advancement of Blood & Biotherapies (AABB) guidelines recommend a restrictive transfusion strategy in which a transfusion is considered when the hemoglobin level is less than 7 g/dL. The crossmatch to transfusion ratio (CTR) evaluates transfusion laboratory efficiency. Optimal CTR is 1, while <2 is favorable per AABB guidelines.^[1] Higher values indicate over-ordering, requiring practice review.^[6] This study aimed to evaluate packed red blood cell utilization in HSCT patients using the crossmatch-to-transfusion (C: T) ratio. The objectives of the study to calculate the C:T ratio and assess transfusion thresholds in HSCT patients and to analyze factors, including ABO compatibility and primary diagnosis, influencing PRBC utilization.

MATERIALS & METHODS

Study Design and Setting

This was a Retrospective Study conducted in Department of Transfusion Medicine (IHBT) and Bone Marrow Transplant (BMT) Unit, M.G.M. Medical College and Associated hospital, Indore over the period of 12 months (from October 2022 till September 2023) after approval from the institutional ethical committee.

Study Population

57 patients included in study who underwent HSCT in the Bone Marrow Transplant (BMT) unit for various underlying diseases. Patients in the research varied in age from 2 to 19 years.

Patients admitted to the BMT unit for various hematological cancers who received allogeneic stem cell transplants, were included regardless of age, gender, specific

diseases or complications. Blood components transfused in clinical wards outside the BMT unit and patients who passed away before the HSCT transplantation phase were excluded from the study.

Patients in the BMT unit were evaluated for transfusion based on clinical status and labs. PRBC transfusion was indicated for hemoglobin below 7 g/dL. Blood requisition forms with EDTA and clotted blood samples were submitted for grouping and crossmatching. ABO and Rh grouping were performed and antibody screening, followed by AHG crossmatching using Ortho Vision immunohematology analyzer. PRBC units for BMT patients were leucodepleted and irradiated. Compatible units were issued with documentation. Transfusions were monitored for adverse reactions during and after administration (figure.1).

Data for the study were sourced from the crossmatch and issue registers maintained by the Department of Transfusion Medicine and Blood Centre. Additional patient details, such as transfusion records and

treatment information, were obtained from the online BMT data portal (BMT Plus), managed by the BMT unit staff. For each packed red blood cell (PRBC) transfusion request, patient medical records were reviewed. Extracted data included patient age, sex, underlying diagnosis, hemoglobin level at the time of transfusion, the number of PRBC units crossmatched and the number of units transfused. A C:T ratio of ≤ 2 was considered acceptable for the BMT unit. The PRBC transfusion threshold was set at a hemoglobin level of 7 g/dL, with clinical discretion permitted depending on patient condition.^[1] Crossmatch to Transfusion Ratio (C:T ratio) calculated. The C:T ratio represents the ratio of the number of blood crossmatches performed to the number of actual blood transfusions given to patients.^[7-8] Applied Formula:

$$\text{C:T ratio} = \frac{\text{Number of unit Crossmatched}}{\text{Number of units Transfused}}$$

- Interpretation: A C:T ratio of 2 or below suggests efficient blood usage, indicating that for every two crossmatches performed, one transfusion is administered.^[7-8]

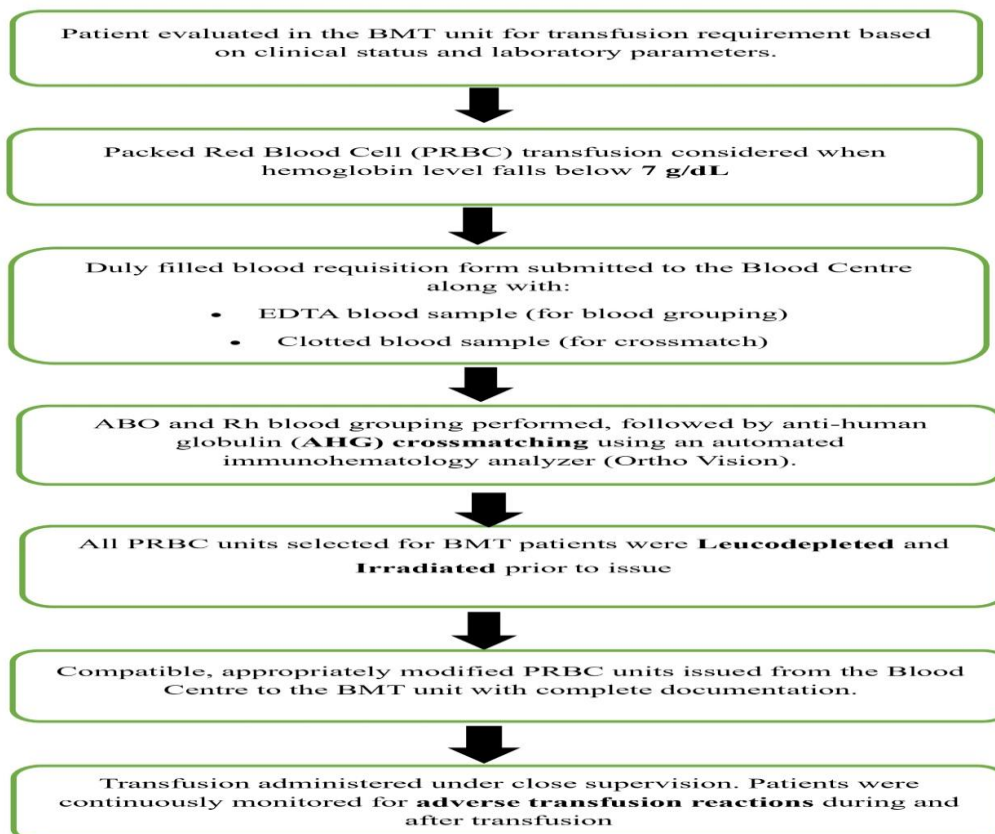


Figure 1. Workflow for Blood Ordering in the Bone Marrow Transplant Unit

Statistical Analysis

Statistical analysis was conducted using SPSS software (version 31.0.2). Continuous variables were presented as mean \pm standard deviation (SD) or Median. Before analysis, the normality of the distribution was checked. Spearman's rank correlation was employed to assess the link between age and RBC usage. An independent samples t-test was utilized to compare the average RBC usage between different stem cell sources. Variations in RBC usage among ABO compatibility groups and primary diagnostic categories were examined using one-way analysis of variance (ANOVA). Linear regression analysis was carried out to explore the connection between crossmatched and transfused PRBC units. Effect sizes were determined using Cohen's d for t-tests and omega-squared (ω^2) for

ANOVA. A p-value of less than 0.05 was considered statistically significant.

RESULT

All patients in the study underwent allogeneic transplantation (n=57, 100%), while no autologous transplants were performed. The study included a total of 57 patients (n=57), of whom 36 (63.16%) were male and 21 (36.84%) were female. The study population (n=57) had a predominantly pediatric age distribution. Patients ranged in age from 2 to 19 years, with a median \pm SD was 8.6 ± 4.5 years. Eleven patients (19.30%) were aged <5 years, 26 (45.61%) were between 5 and <10 years, 13 (22.81%) were between 10 and <15 years, and 7 (12.28%) were between 15 and <20 years.

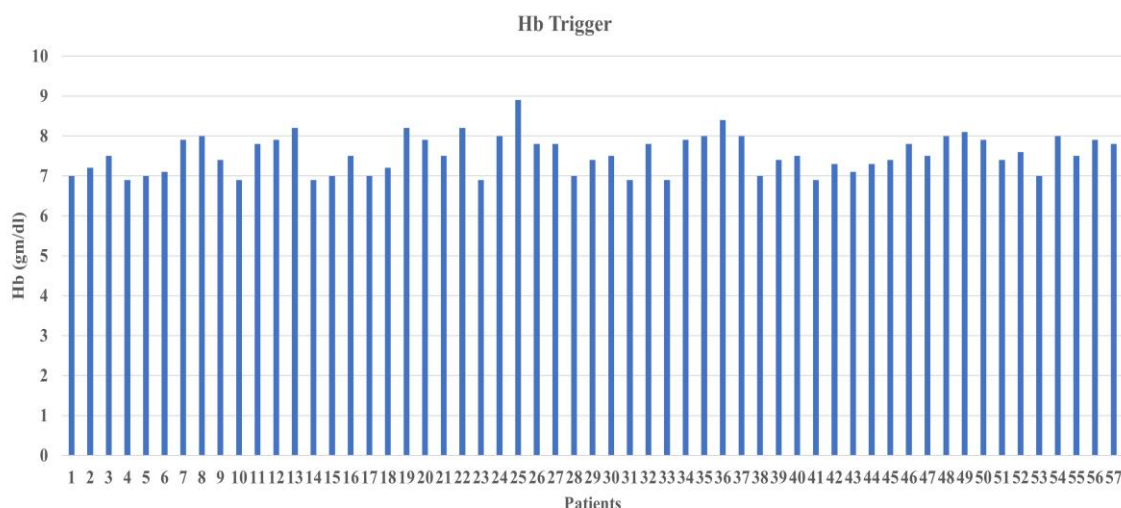


Figure 2. PRBC transfusion triggers in n=57 patients, with a mean haemoglobin threshold of 7.5 ± 0.4 g/dL (range 6.9–8.9 g/dL).

The mean \pm SD haemoglobin threshold for RBC transfusion was 7.5 ± 0.4 g/dL (figure. 2), following a restrictive strategy per standard guidelines. AABB guidelines advise restricting RBC transfusions to patients with haemoglobin below 7 g/dL, but evidence lacks clarity on optimal thresholds for hematology/oncology patients with severe thrombocytopenia. Trials show restrictive strategies (7–9 g/dL) yield similar outcomes compared to liberal thresholds (>10 g/dL). [1,9-10] In our study, the value of

C:T ratio of PRBC were 1.41. The median and range of PRBC utilisation based on the age groups were 6 (2-7) in less than 5 years old, 5 (1-18) in between 5 to 10 years, 5 (1-17) in between 10 to 15 years and 5(4-6) in between 15 to 20 years group respectively. The most common indication for Hematopoietic Stem Cell Transplant (HSCT) in our study was Thalassemia major with 35 number of patients (61.40 %) followed by Aplastic Anemia (21.06%), Sickle + β Thalassemia (8.78%), Sickle Cell

Anemia (3.51%), Myelodysplastic Syndrome (1.75%), Chronic Myeloid Leukemia (1.75%) and Acute Lymphoblastic Leukemia (1.75%) respectively (figure.3). Out of the 57

patients, 49 (85.96%) underwent HSCT using bone marrow as the source of stem cells, while only 8 (14.04%) received peripheral blood stem cell (PBSC) transplantation.

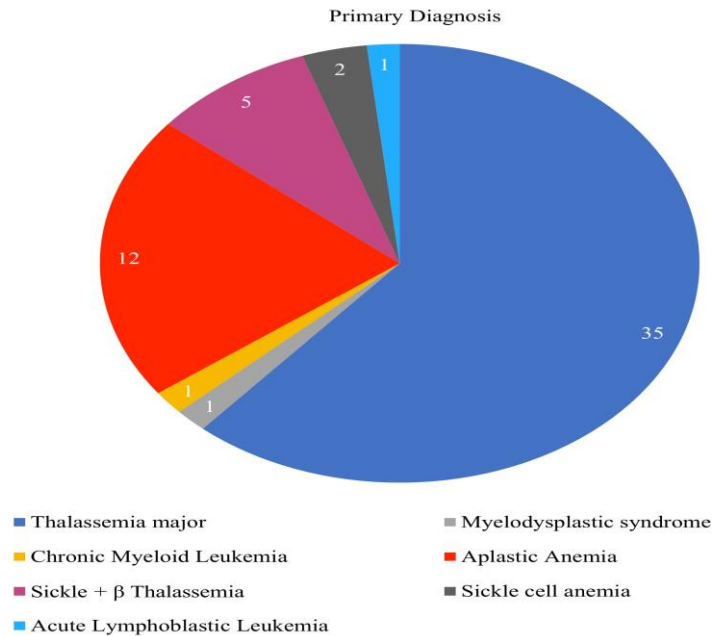


Figure 3. Frequency Distribution of Primary Diagnosis

The total number of crossmatched packed RBCs was $n=485$, with a mean \pm SD of 8.5 ± 5.3 , and the total number of RBCs transfused was $n=344$. The CT ratio was calculated to be 1.41. On average, 6 ± 3.5 PRBC units were used per patient. Figure 4 illustrates a strong positive linear relationship between the crossmatched and

transfused PRBC units ($R^2 = 0.64$), highlighting an efficient alignment between blood requisition and actual utilization. This correlation signifies effective blood inventory management, reducing unnecessary crossmatching and optimizing resource use.

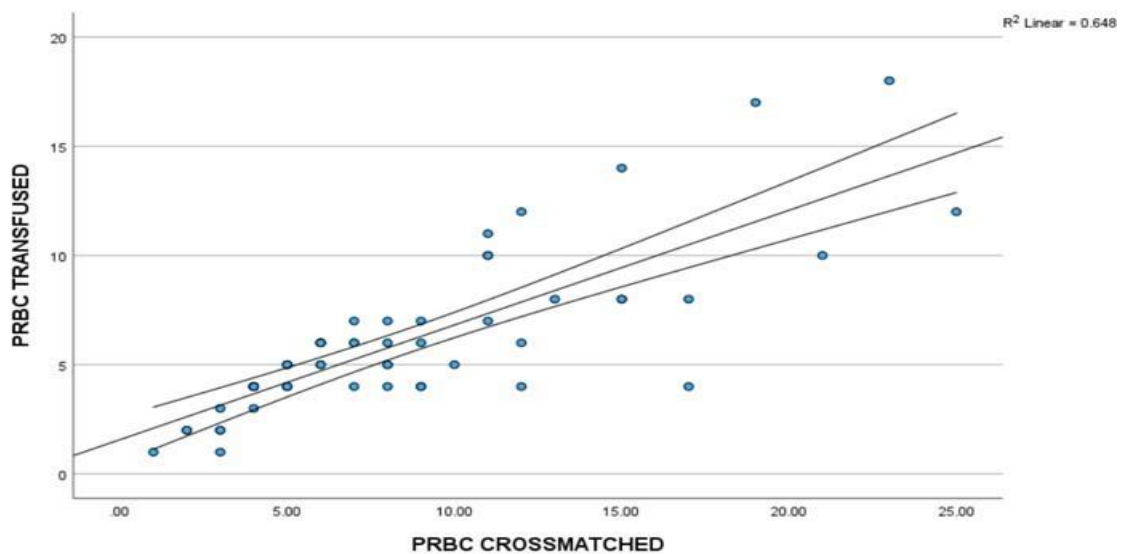


Figure 4. Correlation Between Crossmatched and Transfused Packed RBC (PRBC) Units

Table 1: Frequency distribution of ABO transplant type versus total crossmatched and transfused Packed RBC units

S. No	Type of ABO transplant (n)	Crossmatched PRBC units (n) (Mean±SD)	Transfused PRBC units (n) (Mean±SD)	C: T Ratio
1	ABO compatible (n=35)	263 (7.5±4.9)	182 (5.2±2.6)	1.4
2	Major mismatch (n=8)	92 (11.5±7)	64 (8±5.9)	1.4
3	Minor Mismatch (n=9)	83 (9.2±6.0)	59 (6.5±3.8)	1.4
4	Bidirectional (5)	47 (9.4±3.6)	39 (5±1.8)	1.2
	Total n=57	485 (8.5±5.3)	344 (6±3.5)	1.41

ANOVA F (3,53) = 2.08, p = 0.113

A total of 57 patients were analyzed. The C:T ratio for the patients who underwent ABO compatible, Major mismatch, Minor mismatch and Bidirectional incompatible type of transplant were 1.4, 1.4, 1.4 and 1.2 respectively (Table.1). The mean crossmatched PRBC utilization was highest in the major mismatch group (11.5 ± 7 units) compared to other groups. However, one-way ANOVA revealed no statistically significant difference among ABO transplant types, F (3,53) = 2.08, p = 0.113. The overall C:T ratio was 1.41, indicating efficient blood utilization.

In our research, Spearman correlation analysis showed no association between age and RBC use ($\rho = 0.01$, p = 0.89). There was no significant difference in RBC

utilization between stem cell sources (t (55) = 0.67, p = 0.50). The effect size was small (Cohen's d = 0.26, 95% CI -0.49 to 1.01). For patients primarily diagnosed with Hemoglobinopathy, Leukemia, and Aplastic anemia who underwent HSCT, the C:T ratios were 1.3, 1.18, and 1.8, respectively (table 2). It was observed that Aplastic anemia had the highest C:T ratio at 1.8, compared to those with Hemoglobinopathies and patients undergoing HSCT for Leukemia. There was no significant difference in RBC utilization among the primary diagnostic groups (F (6,50) = 1.58, p = 0.17; $\omega^2 = 0.05$), suggesting that transfusion needs were similar across these diagnoses.

Table 2: Frequency Distribution of Primary Diagnosis and C: T of blood utilisation

S. No	Primary Diagnosis (n)	Crossmatched PRBC units (n) (Mean±SD)	Transfused PRBC units (n) (Mean±SD)	C:T ratio
1	Hemoglobinopathies (Thalassemia major, Sickle cell anemia, Sickle cell plus β Thalassemia) (n=42)	376 (6.9±5.3)	282 (5.1±3.4)	1.3
2	Leukemia (CML, ALL, MDS) (n=3)	13(7±5.3)	11(5±3.2)	1.18
3	Aplastic Anemia (n=12)	96(7.3±5.6)	51(5±3.3)	1.8

ANOVA F (6,50) = 1.58, p = 0.173

DISCUSSION

In our study, we retrospectively analysed 57 patients who underwent HSCT with the blood components transfused such as Packed Red Blood Cells, and observed that the comprehensive value of C:T ratio 1.41. The C:T ratio used for the study passed the defined criteria indicating that the packed RBC are judiciously and efficiently used in the Bone Marrow Transplant (BMT) unit.

Similarly, a retrospective study by Ali N on analysis of packed red cell utilisation for twenty-five stem cell transplant patients over one year period, found that the C:T ratio of packed RBC utilisation was 1.26. [6] Karbasian F et al evaluated the effect of using standard regulations on blood transfusion indices following three years of workshops and training. They saw a 41% rise in the transfusion rate, a 31% increase

in requests, and a 6% drop in the cancellation of blood products. Furthermore, the C:T ratio was 1.33. The study demonstrated that educating and providing scientific training for staff, technicians, and physicians significantly improved the utilisation of blood products in the hospital. [11]

In their retrospective study, Xenocostas et al. evaluated the utilisation and risk factors for RBC transfusions and found that patients with a major ABO incompatible transplant had an increased need for transfusion support. Other significant factors included the patient's hemoglobin level before BMT, advanced disease status, unrelated donors, older age, and female sex. [12] In contrast, Zhang X et al found a substantial correlation between the support for RBC transfusion and the ABO compatibility of the HSC donor and recipient, as well as the presence of infection. Their investigation revealed that the effectiveness of RBC transfusion is unaffected by variables including GVHD, age and serious illnesses. [13] Vaezi M et al. observed that both minor and bi-directional incompatible groups necessitated higher packed cell infusions than ABO compatible groups. They also observed higher transfusion requirements, decrease in overall survival and greater incidence of Pure Red Cell Aplasia in patients undergoing ABO incompatible HSCT. [14] Despite being incongruous, certain research has demonstrated that ABO incompatible groups did not require more transfusions than ABO identical groups. [15-16]

Griffith LM et al in their multivariable study revealed that the quantity of RBC transfusions was significantly and independently linked to pre-transplant RBC levels, CD34+ dose, disease type, ABO compatibility, and the year of transplant. Furthermore, patients with a major ABO mismatch needed more time to become independent of RBC transfusion support. [17] La Rocca et al. found that ABO incompatible transplants were linked with an increased requirement for extended red cell support, linked to factors such as HLA

disparity and the development of hemorrhagic cystitis. [18] Similarly, Ojha et al identified major ABO incompatibility, allogeneic HSCT, haploidentical donor type, and leukemia as predictors of an increased need for blood products, [19] while Borhany et al also concluded that ABO incompatible transplants necessitated more transfusions. [20] Consequently, having an ABO blood type is not seen as a discrepancy to HSCT. [13]

In our study, although there was no correlation found between the patient's age ($p = 0.897$), or the stem cell source ($p = 0.50$) with the total amount of blood transfused. In our study, we observed that Aplastic anemia exhibited the highest C:T ratio with 1.8 as compared to Hemoglobinopathies and Leukaemia HSCT patients.

Ojha et al found that the patients with leukemia, aplastic anemia and myelodysplastic syndromes typically require more packed red blood cell support than those with myeloma or lymphoma. [19] It is noteworthy that although most transplant patients in the study were diagnosed with hemoglobinopathies, our research did not find any statistically significant differences ($p = 0.173$) in the use of blood components based on the primary diagnosis. This absence of significant variation implies that the condition prompting the transplant might not play as crucial a role in determining transfusion requirements as previously assumed.

The limitations of the study include a small sample size and a concentration on a particular group of patients. To confirm these results and achieve a broader understanding of blood component usage, future studies should aim to include larger and more varied populations.

CONCLUSION

Our study identified an optimal balance between transfusion practices and the needs of HSCT patients, thereby enhancing the overall efficiency and effectiveness of packed RBC usage in the HSCT patients. It

was found that ABO incompatibility type had a greater influence on blood component requirements. The study revealed no significant correlation between the patient's age, the stem cell source or the primary diagnosis with the total amount of blood transfused in these patients. Additionally, the ABO transplant type did not significantly affect the duration of hospitalization following HSCT. Ultimately, this study underscores the critical need for well-formulated transfusion strategies aimed at optimizing patient outcomes in stem cell transplantation. Implementing a standard National Guideline on approaches to immuno-hematological support and transfusion practices for HSCT patients could significantly enhance treatment effectiveness and improve the overall standard of care for patients undergoing bone marrow transplants.

Declaration by Authors

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