ORIGINAL ARTICLE

Incidence and Pattern of Transfusion Reactions and its Association with Blood and its Components in a Tertiary Care Hospital

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Abstract

Objectives: Transfusion medicine has made substantial progress in research, and blood transfusions are now safer than ever before. Still, the inherent risk of transfusion reactions (TRs) continues with transfusion of blood and blood components. The study was designed to analyze the incidence and nature of TRs reported in the blood center.

Materials and methods: A retrospective review of all TRs reported to the blood center was retrieved from incident reporting forms from January 2020 to December 2022. All acute transfusion reactions (ATRs) were tabulated and analyzed by the blood transfusion officer and classified according to National Blood Transfusion guidelines. Data were described in terms of range, mean ± standard deviation (± SD), median (IQR), frequencies (number of cases), and relative frequencies (percentages), as appropriate.

Results: A total of 1,65,121 blood and blood components were issued, and ATRs reported were 296 (0.18%). The median (IQR) age of the patient was 45–60, with M:F of 1.3:1. Febrile nonhemolytic transfusion reactions (FNHTR) 151 (51%) were the most common ATRs, followed by allergic TRs 111 (37.5%). The estimated risk of transfusion reaction per 1,000 units was highest with whole blood (WB) 3.84 ($p = 0.038$), followed by packed red blood cells (PRBCs) 2.85 ($p = 0.001$), and single donor platelet (SDP) 1.47 ($p = 0.571$). The most common symptoms observed were fever 31.8%, followed by chills 28.7%, and rashes 27.4%. FNHTR (27/151) 17.8% were reported most frequently from gastroenterology, allergic (26/111) 23.4% from emergency, and delayed hemolytic transfusion reactions (DHTR) (9/9) 100% from thalassemia day care center ($p = 0.001$).

Conclusion: The overall incidence of TRs was 0.18%. The incidence of actual TRs remains underestimated due to lack of awareness regarding TRs among healthcare professionals.

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Introduction

Transfusion reactions (TR) are defined as adverse events associated with the transfusion of whole blood (WB) or one of its components. These may range in severity from minor to life-threatening. The estimated frequency of these adverse TR ranges from 0.2 to 10%, and their mortality is approximately 1 in 2,50,000.[1] The TRs can occur during the transfusion (acute TR) or days to weeks later (delayed TR) and may be immune or nonimmune depending upon the pathophysiology.[2] Hemovigilance is a systematic surveillance of adverse TR, and the primary objective of the program is to track adverse events associated with transfusion of blood and blood products. The lack of robust hemovigilance systems across the country makes it challenging to assess the true and actual incidence of these reactions.

Materials and Methods

A retrospective observational study was carried out in a tertiary care hospital from January 2020 to December 2022. This study was approved by the Ethics and Research Committee of Dayanand Medical College and Hospital in accordance with the World Medical Association Declaration of Helsinki, vide no. DMCH/IEC/2023/221 dated July 18th, 2023. All the reactions were analyzed as per the algorithm as shown in Figure 1.

The following work-up was performed after receiving the residual blood bag along with the blood transfusion set and the patient posttransfusion blood sample:

- Clerical check for identification error.
- Visual check of posttransfusion plasma for hemolysis.
- Comparing patient pre- and posttransfusion sample for proper identification.
- Performing ABO and Rh grouping and direct antiglobulin test (DAT) on posttransfusion sample and compare with pretransfusion samples.
- Bacteriological testing was done by sending the blood from blood bag for culture.
- Urine routine for examination of color/microscopic RBCs.

The purpose of the present study is to estimate the incidence and pattern of transfusion related events in our center.

Statistical Analysis

Data were described in terms of range; mean ± standard deviation (± SD), median (IQR), frequencies (number of cases), and relative frequencies (percentages), as appropriate. To compare categorical data, the Chi-squared (χ^2) test was performed. All statistical calculations were done using Statistical Package for the Social Sciences (SPSS) for Microsoft Windows 10 Pro.

Results

A total of 1,65,121 blood and its components were issued over a period of 3 years. These comprised 1,821 (1.10%) WB, 69,710 (42.2%) packed red blood cells (PRBCs), 69,200 (41.9%) fresh frozen plasma (FFP), 49 (0.02%) single donor plasma, 1,747 (1.06%) cryoprecipitate (CRYO), 17,161 (10.4%) random donor platelet (RDP), and 5,433 (3.3%) single donor platelet (SDP). The TRs were observed in 296 (0.18%) recipients.

The median (IQR) age of the patients was 45 years (31–60), with an M:F ratio of 1.3:1. The TRs were most frequent in the age-group >60 years (23.3%), followed by the age-group 41–50 years (20.6%), with 11.8% TRs in patients <21 years of age. B positive Rh blood group (37.2%) showed maximum TRs, followed by O Rh positive blood group (31.8%). PRBC transfusion (67.2%) showed a higher incidence of TRs, followed by FFP (24.3%). No reaction was observed with CRYO or single donor plasma. It was also observed

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that TRs were more in patients receiving multiple transfusions ($p = 0.010$), with a mean of 2.19 ± 2.57.

Transfusion reactions were observed most frequently within 30–60 minutes (33.4%) of starting transfusion, with a mean of 6.59 ± 42.18 minutes ($p = 0.010$). Nearly one-third of TRs were observed with as little as 20–60 mL of product transfused, with a mean of 113 ± 69.02 mL. Most TRs were reported in the department of gastroenterology ($n = 48$; 16.2%), followed by emergency ($n = 46$; 15.5%). The estimated risk of TRs per 1,000 units was maximum with WB 3.84 ($p = 0.038$), followed by PRBC 2.85 ($p = 0.001$), and minimum with RDP 0.58 ($p = 0.001$), as shown in Table 1.

The most common immune-mediated reactions encountered in our study were febrile nonhemolytic transfusion reaction (51%), followed by allergic transfusion reaction (37.8%), anaphylactic reaction (1.4%), hemolytic transfusion reaction (0.7%), and transfusion-related acute lung injury (TRALI) (0.3%). The nonimmune-mediated reactions recorded were transfusion-associated circulatory overload (TACO) (1%) and transfusion-associated hypotension (TAH) (2.4%). Delayed hemolytic transfusion reactions (DHTR) were seen in 3% of cases. All the recipients were multitransfused, transfusion-dependent thalassemia.

The common symptoms and signs observed during TRs are shown in Figure 2A. PRBC transfusions were associated with TR in 199 recipients (0.3%), the most common being febrile nonhemolytic transfusion reactions (FNHTR) ($n = 142$; 94%), as shown in Table 2. TRs were observed in 72 FFP transfusion recipients (0.1%), allergic reaction being the most frequent ($n = 64$; 57.1%). SDP and RDP transfusions were associated with only allergic reactions in 8/5,433 (0.14%) and 10/17,161 (0.05%) recipients, respectively. It was seen that in recipients younger than 21 years of age, FNHTR (57.1%), followed by DHTR (20%) and allergic (20%), were most common, whereas in older recipients, FNHTR (50.2%) and allergic (40.2%) were common ($p = 0.001$). FNHTR (27/151) was reported most frequently from the department of gastroenterology, allergic (26/112) from emergency, and DHTR (9/9) from thalassemia day care center ($p = 0.001$), as shown in Figure 2B. The year-wise risk of transfusion reaction per 1,000 units is shown in Figure 2C.

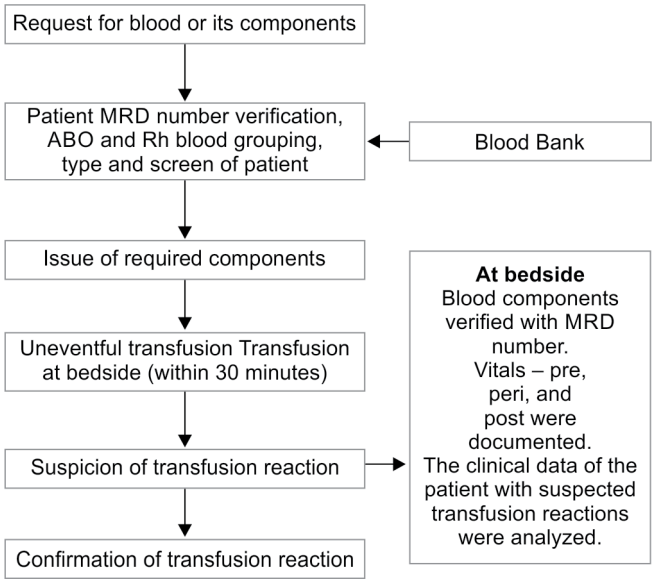

Fig. 1: Algorithm for work-up of issuing of blood and its components

Discussion

The safe transfusion of blood and its components requires strict adherence in maintaining the blood cold chain. The "blood cold chain" is the system for storing and transporting blood and its components so that they are kept at the correct temperature at all times from collection to transfusion. Any break in the blood cold chain increases the risk of a small number of contaminating bacteria growing in lethal numbers, especially platelets, which are kept at room temperature at 22–24°C, posing a threat of transfusion reaction. The blood and the blood components should be transfused within 30 minutes after issue from the blood bank.

The incidence of TRs observed in our study was 0.18%. Table 3 shows the frequency of TRs reported in various national and international studies, ranging from 0.73 to 9.45%.[3–11] The frequency of TRs in females was lower than in males (43.6 vs 56.4%), as shown in a similar study by Kumar et al. (45.7/54.3%).[3] The majority of TR occurred due to PRBCs (67.2%), as found in a similar study by Prakash et al. (42.8%).[12] Most of the TRs in our study were nonhemolytic, out of which the commonest was FNHTR, 51%, followed by allergic, 37.8%. In the study by Pahuja et al.[10] the frequency of FNHTR and allergic was 54.7/41.4%.

The most common TR observed in our study was FNHTR, 51%, as shown by Khalid et al., who reported 41.9%.[13] Ramanathan reported 51.4%.[14] It was observed with 94.0% PRBC, followed by 3.97% FFP and 1.98% WB in a similar study by Sidhu et al.[15] The most common presenting symptoms were fever, chills, and shivering. Nausea and headache were also seen in a few cases.

Human leukocyte antigen (HLA), granulocyte, and platelet-specific antibodies have been implicated in the pathogenesis of FNHTR. The recipient's antibodies react with

Table 1: The total supply and estimated risk of TR per thousand units of blood and blood components

	Total supply	*Total supply per 1,000*	*Reaction*	*Per 1,000 reaction*	*Chi-square value*	*p-value*
FFP	69200	41.9%	72	1.04	37.535	0.0001
PRBC	69710	42.2%	199	2.85	75.754	0.001
RDP	17161	10.4%	10	0.58	15.628	0.001
SDP	5433	3.3%	8	1.47	0.321	0.571
WB	1821	1.1%	7	3.84	4.306	0.038
CRYO	1747	1.1%	0	0.00	3.165	0.078
PPP	49	0.0%	0	0.00	0.008	0.767
Total	165121	100.0%	296	1.79		

$p < 0.05$ significant

Figs 2A to C: (A) Signs and symptoms of TRs; (B) TRs with respect to different clinical departments; (C) Year-wise risk of TR per thousand units of blood and blood components transfused

transfused antigens, leading to activation of the complement system and release of cytokines (IL-1), which is capable of causing fever. The most effective way to prevent FNHTR is prestorage leukocyte depletion, causing removal of WBC before the release of cytokines, by Heddle.[16]

Febrile nonhemolytic transfusion reactions was defined by the International Society of Blood Transfusion and the International Hemovigilance Network (IHN) as the presence of fever (body temperature ≥38°C, or an increase of >1°C from the pretransfusion temperature) during or within 4 hours after transfusion, or with fear of cold, chills, headache, nausea, and other symptoms, to the exclusion of hemolytic TR, bacterial contamination, and other potential factors.[17]

The patients were managed by immediately stopping the transfusion and giving antipyretics. The relatively high risk of FNHTR in our study could be because

Table 2: Number of TRs with respect to blood and its components

Type of reaction	*Component*										*Total*
	FFP		*PRBC*		*RDP*		*SDP*		*WB*		
FNHTR	6	3.97%	142	94.0%	0	0.0%	0	0.0%	3	1.98%	151
Allergic	64	57.1%	28	25.0%	10	8.9%	8	7.1%	2	1.78%	112
DHTR	0	0.0%	9	100%	0	0.0%	0	0.0%	0	0.0%	9
Hypotensive	1	14.2%	5	71.4%	0	0.0%	0	0.0%	1	14.2%	7
Anaphylactic	0	0.0%	4	100%	0	0.0%	0	0.0%	0	0.0%	4
TACO	0	0.0%	2	66.6%	0	0.0%	0	0.0%	1	33.3%	3
HTR	0	0.0%	2	100%	0	0.0%	0	0.0%	0	0.0%	2
TRALI	0	0.0%	1	0.5%	0	0.0%	0	0.0%	0	0.0%	1
Nonspecific	1	14.2%	6	85.7%	0	0.0%	0	0.0%	0	0.0%	7
Total	72		199		10		8		7		296

Table 3: Comparative studies of incidence of TRs

Name of the study	*Allergic reaction (%)*	*Anaphylactoid reaction (%)*	*FNHTR (%)*	*HTR (%)*	*Hypotensive reaction (%)*	*TACO (%)*	*TRALI (%)*	*Other (%)*	*Incidence (per 1,000 components)*
Kumar et al.[3]	51.1	5.1	35.7	2.6	–	0.5	0.5	2.5	0.5
Shajil et al.[4]	53.2	–	36.3	1.2	1.3	–	–	7.8	0.4
Payandeh et al.[5]	49.2	–	37.2	–	6.8	–	–	6.8	9.45
Mafirakureva et al.[6]	34	1.4	58.5	5.2	0.4	0.25	0.25	–	0.46
Bassi et al.[7]	24	–	73	1	1	–	–	1	3.98
Sharma et al.[8]	65.6	3.12	28.1	–	–	–	–	3.18	9.26
Philip et al.[9]	40.14	0.70	51.40	4.22	–	0.70	–	2.81	0.73
Pahuja et al.[10]	41.4	1.27	54.7	1.27	–	0.955	0.31	–	1.95
Saha et al.[11]	49.2	1	25.47	3	5.22	4	3	1.49	1.39
Present study	37.5	1.4	51	0.7	2.4	1	0.3	2.4	1.80

of the lack of universal leukoreduction of the components in our blood center. We have shifted to 80% leukoreduction, so most of the reactions reported are due to nonleukoreduced blood and its components. Leukoreduced PRBC and filters are being exclusively used for hemato-oncology patients in our hospital. The average time lapse from blood components issue to bedside transfusion of the components is within 30 minutes, thereby decreasing the possibility of TR.

Allergic reaction was the second commonest TR (37.8%) as shown in similar studies by Sidhu et al.[15] (41.5%) and Joy et al. (39.4%).[18] SDP and RDP transfusions were associated with only allergic reactions. The allergic reactions in SDP were probably due to sensitization to plasma constituents that cannot be filtered out. Majority of patients presented with rash, itching, and urticaria. Fever and periorbital edema were also seen in a few cases. FFP (64/112; 57.1%) was the most common component ordered by the physician for patients with deranged coagulation profile and thawed in a plasma water bath at 37°C. Allergic reactions are commonly due to transfusion of allergens (e.g., donor-ingested food and medications) and polymorphic serum proteins like haptoglobins, C3, C4, transferrin, albumin, etc., which react with IgE antibody bound to basophils or mast cells in the recipient's blood. This interaction results in release of C3a, C5a, histamine, prostaglandins D_2, leukotrienes C and D_4, causing increased vascular permeability. Histamine release causes rashes, itching, and edema.

Anaphylactic reactions were seen in 4/1,65,121 (0.002%) patients with transfusion of PRBCs. Patients presented with rashes, itching, and hypotension in a similar study by Salmani et al.[19] It is due to IgA deficiency of the recipient and subsequent formation of anti-IgA by Sandler et al.[20] These reactions can be reduced by giving washed leukodepleted PRBCs.

A single case of TRALI was reported in our study in a female patient, with an incidence of 0.0006%. TRALI reported in various studies in Western literature ranges from 0.014 to 0.08%.[21] It was seen with PRBC transfusion. Patient presented with fever, dyspnea, and tachycardia, as shown in a similar study by Joy et al.[18] X-ray of the patient showed bilateral infiltrates. The donor sample could not be evaluated for antineutrophilic antibodies. TRALI is rare but an important mortality associated with transfusion. It is a great mimicker of a variety of clinical conditions and is often underdiagnosed. It can be reduced by careful selection of donors, using plasma from male donors, and screening female donors for HLA and human neutrophilic antibodies, which are strong risk factors.

Acute hemolytic transfusion reaction was seen in 0.001% of all transfusions. One reaction was due to ABO mismatch, as B positive blood was transfused to an A positive patient by human error. Baele et al.[22] reported bedside transfusion error in 12.4 per thousand transfusions. In order to reduce the chances of human error, our hospital policy recommends a trained and competent healthcare worker to collect blood from the blood center with appropriate documentation using patient identifier, and final check to be conducted next to the patient at bedside by a trained staff who administered the product using the same identifier. The other case was due to alloimmunization. The antibody was present in low titer and could not be detected during routine crossmatching, as shown in a similar study by Shajil et al.[4] who reported an incidence of 1.29%. HTR was seen with only PRBC transfusion, and patients presented with

fever, chills, abdominal pain, and dark-colored urine in our study.

Among the nonimmune-mediated TR, TAH and TACO were also seen in our study. TAH is defined as a drop in systolic BP ≥30 mm Hg and a systolic BP ≤80 mm Hg. TAH was seen in 2.4% in our study. It was seen with 71.4% of PRBC, 14.2% of WB, and 14.2% of FFP transfusions in our study. The reported incidence of TAH varied in literature, as shown by Shajil et al.[4] (1.3%) and Saha et al.[11] (6.4%). TAH was observed as isolated findings with no underlying cause and responded to supportive treatment.

Transfusion-associated circulatory overload was seen in three (0.002%) recipients, two of whom had underlying diabetes, hypertension, history of myocardial infarction, and reduced ejection fraction. Patient presented with dyspnea and decreased oxygen saturation levels (dropped to 60% on room air) after PRBC transfusion. Brain natriuretic peptide (BNP) levels were 286 pg/mL posttransfusion in two cases. Another case was an elderly female who came for orthopedic surgery and developed TACO post-WB transfusion. Joy et al.[18] reported incidence of 0.008%.

Delayed hemolytic transfusion reactions was seen in 0.005% recipients. It was seen with 100% of PRBCs. The most common presenting symptoms and signs were back pain, nausea, abdominal pain, and mild hematuria, as shown in a similar study by Sidhu et al.[15] All patients had underlying thalassemia and were on regular transfusion. DHTR is a side effect of blood transfusion due to recipient RBC autoantibodies and alloantibodies. This can be reduced by giving extended phenotype-matched leukodepleted blood. There was no incidence of transfusion-associated graft-vs-host disease (TAGVHD) in our study.

Nonspecific reactions were 7/1,65,121 (0.004%) of transfusions. These could not be categorized into any TR and were probably because of underlying medical conditions of the patient. Safe blood transfusion forms an indispensable part of quality parameter in transfusion services. Continuous hemovigilance is aimed at identifying the adverse events related to transfusion, which in turn guides in setting up measures to mitigate the frequency of such events. Our blood center is also a part of the Hemovigilance Program of India.

Conclusion

The overall incidence of TR in our study was 0.18%. The risk of reaction per 1,000 components transfused was maximum with WB 3.84 and PRBC 2.85, and minimum with RDP 0.58. Though consumption of WB is reduced, it is still used in patients who need all the components of blood, such as in significant blood loss due to trauma/surgery and cardiovascular surgeries. Nowadays, reconstituted-WB is used, also known as reconstituted red blood cells. This is a combination of red blood cells and plasma to achieve a specific volume of a targeted hematocrit. It is immunologically safer and better than using WB. DHTRs are often missed, as the temporal relationship with transfusion is overlooked. Every hospital should have a hospital transfusion committee who has the overarching responsibility to maintain safe hospital transfusion practices by investigating transfusion events and developing strategies for reduction and improvement. Our main aim is to improve the reporting of transfusion reaction and data collection, followed by evidence-based improvement in blood transfusion practices.

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