

A Study of Frequency and Pattern of Adverse Transfusion Reactions at a Blood Bank in a Tertiary Care Hospital: Towards Hemovigilance

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ABSTRACT

Background: Adequate and safe transfusion facility of blood and its components is necessary as blood transfusions are a part of life saving measures in medical and surgical emergencies. However, transfusion practice could result in non-fatal to fatal adverse transfusion reactions (ATR). Therefore, it is important to identify various adverse reactions so that steps can be taken to minimize such reactions and ensure safer transfusion being carried out.

Methods: All ATRs reported to the blood bank from January 2013 to December 2016 were reviewed and analysed. The frequency of ATRs and its association with various component types were assessed.

Result: During the study period, a total of 199106 units of blood were issued from the blood bank out of which there was an incidence of 77 (0.12%) transfusion reactions. Chills/rigors was the most common symptom (27.3%) of the symptomatic cases followed by pruritis (23.4%)

Majority of the transfusion reaction were non haemolytic, 76 (98.7%) cases. One case was of haemolytic transfusion reaction. Among the non-haemolytic transfusion reactions, febrile non haemolytic transfusion reaction (FNHTR) constituted 28 (36.4%) and allergic reactions constituted 41 (53.2%). Other transfusion reactions including hypotensive transfusion reaction (HTR), 1 (1.3%) case and transfusion associated dyspnoea (TAD), 6 (7.8%) cases were also seen. The frequency of ATRs was highest with packed red cells (PC) being 75.3% and least with platelet concentrate (PLTC) being 11.7%.

Conclusion: The frequency of ATRs in our blood bank was found to be on a lower scale when compared to that of most of the similar studies. Allergic reactions and FNHTR were the most common ATRs seen, introduction of leukoreduction filters would help reduce FNHTRs.

Keywords: Adverse Transfusion Reaction, Hemovigilance, Febrile Non Hemolytic Transfusion Reaction

Introduction

Adequate and safe transfusion facility of blood and its components form part and parcel of any health care setup. They often form a part of life saving measure in medical and surgical emergencies.^[1] However, transfusion practice could be double-edged sword as it can result in non-fatal to fatal adverse transfusion reactions (ATR).^[1-3]

ATR can be infectious or non-infectious and could be immediate or delayed type. The risk of infectious ATRs has dramatically decreased by approximately 10,000-fold because of strict donor screening and the development of improved techniques such as nucleic acid amplification tests and chemiluminescent immunoassays for detecting infectious agents.^[4] But non-infectious complications like transfusion associated lung injury, haemolytic transfusion reactions are a cause of considerable mortality and morbidity.^[5-7] The acute transfusion reactions present as adverse signs or symptoms during or within 24 hours of a blood transfusion. The most frequent symptoms of the reactions are fever, chills, pruritus, or urticaria, which typically resolve promptly without specific treatment or complications.^[4,5]

There are no definite known predictive factors which may predispose the patients to develop reaction during transfusion.^[8] It is important to identify various adverse reactions so that steps can be taken to minimize such reactions and ensure safer transfusion being carried out. In this study, we measured the frequency and pattern of non-infectious ATRs at a tertiary care hospital and assessed the possible factors affecting these reactions with an aim to contribute to improved patient safety during transfusion.

Materials and Methods

The study was conducted in the Blood Bank, KMC Hospital Ambedkar Circle, Mangaluru, attached to Kasturba Medical College, Mangaluru. After obtaining institutional ethical clearance, the data from January 2013 to December 2016 was retrieved from the archival records and was analyzed.

The data included all the adverse transfusion reactions reported and transfusion work up done in the blood bank as well as the total blood components issued from the blood bank. The reaction was categorized as acute transfusion

reaction on the basis of the adverse symptoms developing within 24 hours after the onset of transfusion. The cases with incomplete or limited clinical records were excluded.

Additional clinical details about the patient were collected from the medical records. Information regarding the details of the ATRs reported were collected that included: a) Pertinent demographic and clinical information of the recipient reporting the reaction, b) Indication for transfusion and type of component transfused, c) Clinical signs and symptoms of reactions, d) Transfusion reaction workup details that included possible clerical error, gross appearance of patient's post transfusion sample for hemolysis and comparison with pre-transfusion sample. Also, in case of suspected hemolytic reaction, further investigations results done (in our laboratory) was recorded namely plasma haemoglobin level, hemoglobinuria by gross visual examination and urine haemoglobin by dipsticks, total and direct serum bilirubin, peripheral blood smear examination for the presence of schistocytes and spherocytes. Results of compatibility tests repeated on pre, post-transfusion sample and in the sample remaining in the unit used for transfusion were recorded. Similarly results of forward grouping, reverse grouping and cross matching, direct antiglobulin test, results of the bacteriological testing by the culture of the unit sample, if done, details like prior transfusion history, co-morbid clinical conditions if any were also recorded. Details of relevant donor history was taken. The data was analyzed by tables, graphs, proportions and ratios using SPSS version 25.0. 'Z' test for single proportion was used and a 'p' value < 0.005 was considered significant.

Result

During the study period of January 2013 to December 2016, a total of 199106 units of blood components were issued from the blood bank out of which there was an incidence of 77 (0.12%) transfusion reactions that fulfilled the inclusion

and exclusion criteria. None of the delayed transfusion reactions were reported during the study period.

Among those who had reaction 42 (54.5%) were females and 35 (45.5%) were males. The recipients in the age group of 51-50 showed highest number (22) of ATRs.

Pattern of clinical signs and symptoms

Fever ($\geq 1^\circ\text{C}$ increase) and chills/rigors were present in 7.8% and 27.3% of the symptomatic cases, respectively. The incidence of clinical signs and symptoms related to allergic reactions like urticaria, rash, and pruritus in symptomatic cases was 23.4%, 1.3% and 23.4% respectively.

Other symptoms like chest pain, dyspnoea, hypotension, periorbital swelling, red urine, tachypnea were 27.3%, 7.8%, 1.3%, 1.3% and 1.3% respectively. Table 1

Classification of ATRs by the blood bank physicians.

Majority of the transfusion reaction were non haemolytic, 76 (98.7%) cases. There was an incidence of haemolytic transfusion reaction in one case. (Table 2). Among the non-haemolytic transfusion reactions, the number of cases classified as FNHTRs and allergic reactions were 28 (36.4%) and 41(53.2%), respectively. Other transfusion reactions were classified as Hypotensive transfusion reaction (HTR) and Transfusion associated dyspnoea (TAD), which occurred at a frequency of 1 (1.3%) and 6 (7.8) cases respectively. Fig 1. Blood culture done of the remaining bag for suspected bacterial sepsis was negative.

The frequency of ATRs was compared according to the types of blood components transfused i.e. fresh frozen plasma (FFP), PC and platelet concentrate (PLTC). Majority were due to packed red cells (PC). (Fig 2). Fig 3 shows the frequency of various departments that reported transfusion reactions. The proportion of the transfusion reactions with respect to number of each component transfused was analysed statistically which showed the incidence of reactions with PC, FFP and PLTC to be statistically significant. (Table: 3)

Table 1: Frequency distribution of clinical features of the transfusion reactions.

SYMPTOMS	Frequency	Percent
Chest Pain	2	2.6
Chills/Rigor	21	27.3
Dyspnoea	6	7.8
Fever	6	7.8
Hives/Urticarial	18	23.4
Hypotension	1	1.3
Itching and Rashes	1	1.3
Periorbital Swelling	1	1.3

SYMPTOMS	Frequency	Percent
Pruritis/ itching	18	23.4
Rashes	1	1.3
Red urine	1	1.3
Tachypnea	1	1.3
Total	77	100.0

Table 2: Different types of transfusion reactions according to the type of components (percentage of the type of reaction in bracket). PC: Packed red cells, FFP: Fresh frozen plasma, PLTC: Platelet concentrate, CRYO: Cryoprecipitate, ATR: Acute transfusion reaction.

Type of transfusion reaction	PC (n=75913)	FFP (n=75335)	PLTC (n=45939)	CRYO (n=1919)	Total ATR(n=77)
Allergic reactions	28 (0.03)	7(0.009)	6 (0.13)	0	41
FNHTR	23(0.03)	3(0.003)	2(0.04)	0	28
Hemolytic transfusion reaction	1(0.001)	0	0	0	1
Transfusion associate dyspnoea	5(0.006)	0	1(0.002)	0	6
Hypotensive transfusion reaction	1(0.001)	0	0	0	1
Total (77)	58	10	9	0	77

Table 3: Number of transfusion reactions with various components and the 'p' value. PC: Packed red cells, FFP: Fresh frozen plasma, PLTC: Platelet concentrate, CRYO: Cryoprecipitate.

Blood components	Total number of units transfused	Number of reactions	Percentage of reactions due to individual component	'p' value
PC	75913	58	75.3	<0.0001
FFP	75335	10	13	<0.0001
PLTC	45939	9	11.7	<0.0001
CRYO	1919	0	0	
Total	199106	77		

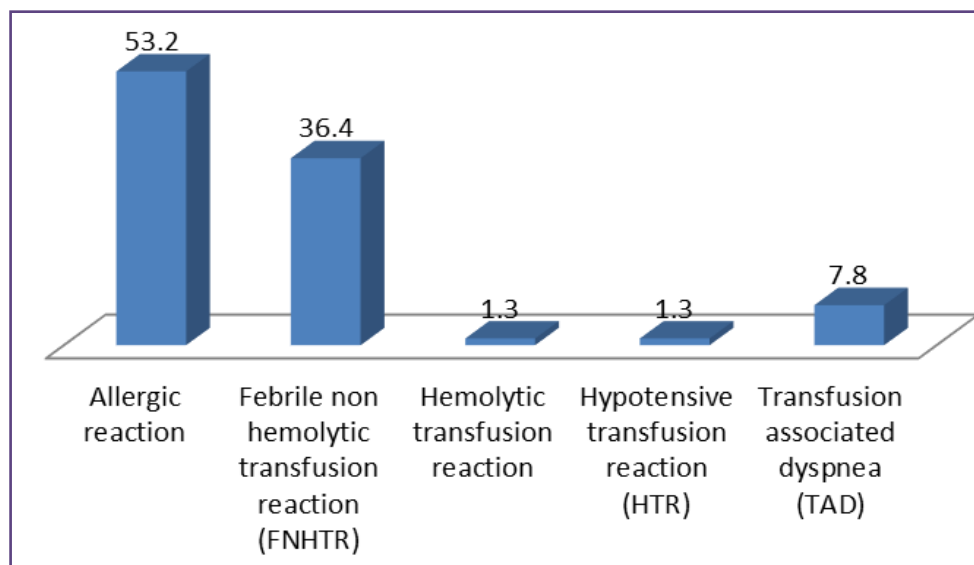


Fig. 1: Frequency of various types of acute transfusion reactions in percentage.

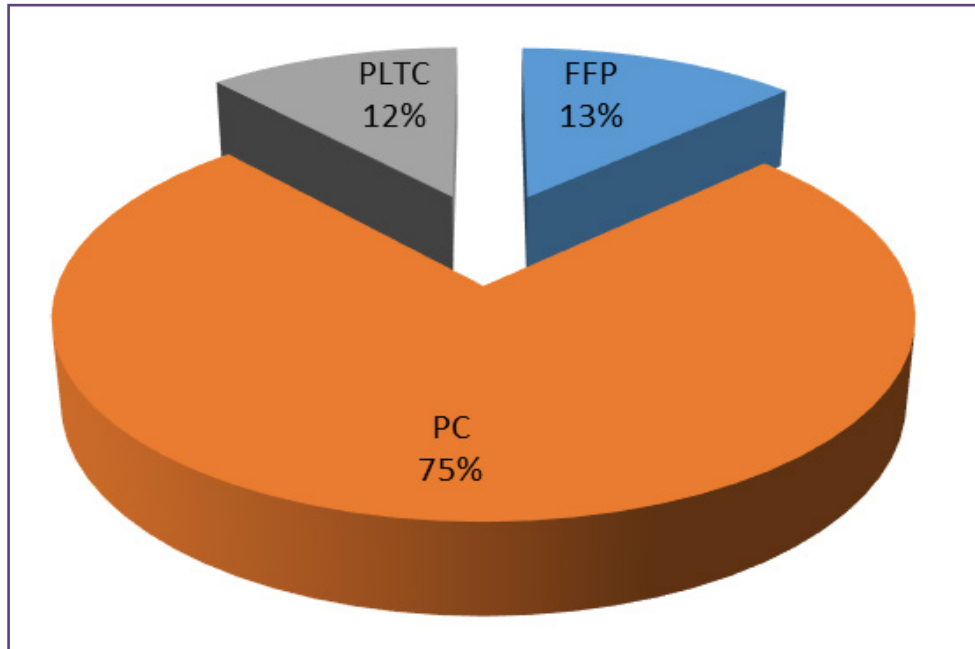


Fig. 2: Proportion of different components causing adverse transfusion reactions PC: Packed red cells, FFP: Fresh frozen plasma, PLTC: Platelet concentrate.

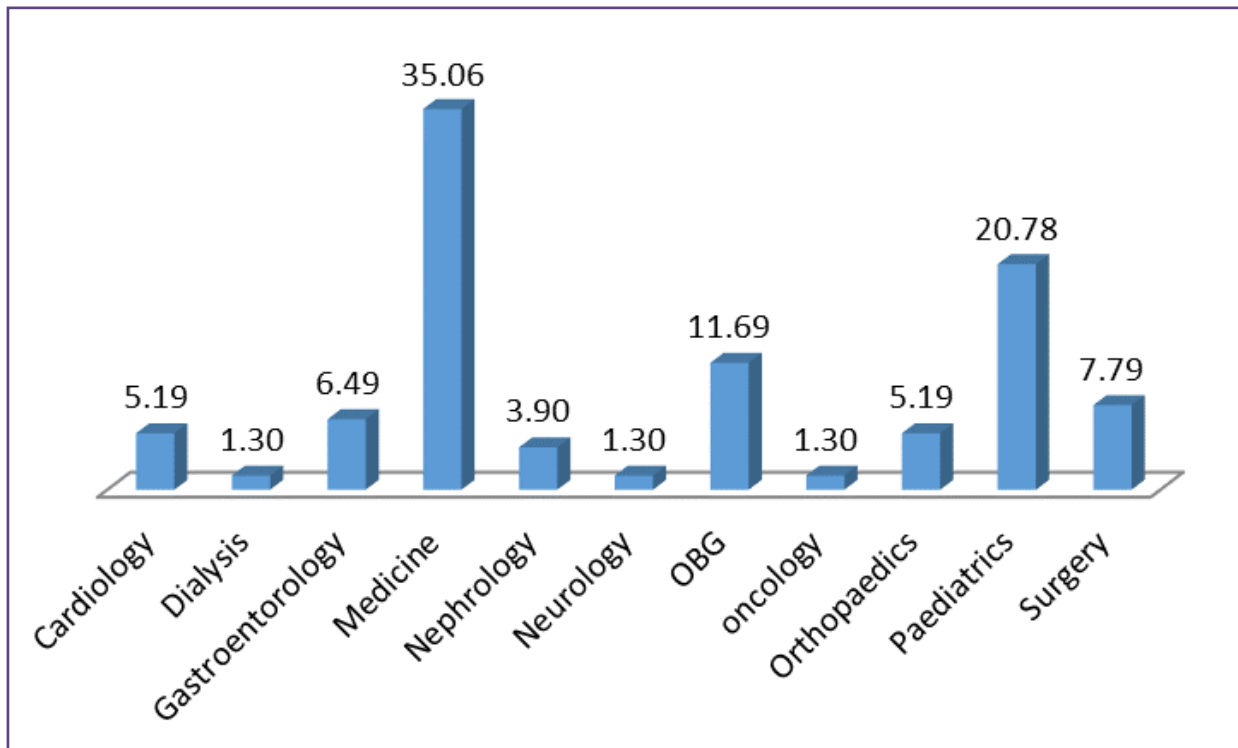


Fig. 3: Comparison of frequency of various departments reporting the transfusion reactions. OBG: Obstetrics and Gynaecology.

Discussion

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.^[9] Every component or blood transfusion carries a minute risk of transfusion reactions.

In this study, the frequency of ATRs was observed to be 0.12%. In a similar study by Bhattacharya *et al.*, incidence of adverse transfusion reaction was 0.18% (105 reactions out of 56,503 units of blood and blood component transfused).^[10] Two other studies done by Sinha *et al.*^[11] and Prakash *et al.*^[12], the frequency of transfusion reactions were 0.27% (15/5535) and 0.2% (66/31287) respectively.

The frequency was more in females (54.5%) than males (45.5%). Other studies have also shown more incidence of transfusion reaction in females in Sikkim (59.4%), Saudi Arabia (59.4%).^[1] Studies by Sinha *et al.* showed a female predominance,^[10] while the study by Prakash *et al.*^[11] showed an almost equal frequency. However, studies done by Kumar *et al.* and Bhattacharya *et al.* in India show a lower incidence of transfusion reactions in females (45.7% and 34.2% respectively).^[2,9]

Majority of reactions occurred due to packed red cells in our study which was significant ('p' <0.0001). Similar occurrence was found in study by Prakash *et al.*^[11] and Sharma *et al.*^[1]

Majority of the transfusion reaction were non haemolytic, out of which the common ones were allergic reactions and FNHTR being 53.2% and 36.4% respectively. Fig 1. Similar incidence was founded by some studies.^[1, 11,] Some studies observed FNHTR to be commoner^[12,13] while others reported more reactions with single donor platelets.[Saha]

Allergic reaction is defined as urticaria, pruritus, rash, oedema, or flushing within the first four hours of transfusion and/or itching sensation without any evidence of other conditions causing allergic reactions.^[12,13] Most of our recipients had either single or combination of hives, itching and periorbital edema. Majority were due to PC followed by due to FFP. Allergic reactions were observed with all types of components in most studies like that of ours.^[1-2,12-13] attributing it to plasma proteins in the component. The allergens implicated are IgA and haptoglobin of the donor component. Although this reaction is common in Ig A deficient individuals albeit it may occur in those with normal Ig A levels. Since these reactions are mild, testing for Ig A levels is not done in most centres and mild symptoms are treated symptomatically.^[14]

Febrile non-haemolytic transfusion reaction (FNHTR) which is defined as fever ($\geq 1^{\circ}\text{C}$ increase and $\geq 38.0^{\circ}\text{C}$ body temperature) within the first four hours of transfusion and/or chills/rigors without any evidence of infection or other conditions causing fever.^[15]

FNHTRs are due to the cytokines released from leukocytes during storage or due to antibodies to donor leukocytes.^[16] The incidence in our study was 36.4%. This is comparable to studies done by Sharma *et al.*^[1] and Pahuja *et al.*^[13] This type of ATR was more common with PC in our study which was similarly observed by Vasudev *et al.*^[16] Many studies show that the incidence of FNHTRs can be decreased through leukocyte reduction.^[17] The relative high incidence of FNHTR could be because of lack of leukoreduction of the components in our blood bank.

Acute haemolytic reaction occurs during or within 24 h after administration of a blood product are usually caused by transfusion of incompatible red blood cells (RBCs), and, more rarely, of a large volume of incompatible plasma.^[18]

One case of haemolytic transfusion reaction was observed in the OBG department where the patient presented with haematuria and haemoglobinuria. The transfusion reaction was stopped and reported. There was no incompatibility detected. Haemolytic transfusion reaction in the absence of demonstrable incompatibility has been reported by others. These reactions may have occurred if the antibody was absent at the time of cross match, being fixed in tissues. Another possibility is that the antibody was present in such low titres that it could not be detected while cross matching but was enough to cause the acute haemolytic transfusion reaction.^[15] Hemolysis could also occur due to improper storage of the component outside the blood bank.^[16]

Hypotension during transfusion although could be one of the manifestations of haemolytic reaction, septicemia, TRALI or anaphylactic reaction,^[19] many a times it is reported as an isolated sign as that in our case. The incidence was 0.001% which is very low compared to that observed with Saha *et al.*^[14] and Metcalf RA *et al.*^[20] Also in our case, hypotension may only partly be attributed to blood transfusion as the recipient was undergoing an open reduction and internal fixation surgery and was on spinal anaesthesia, which is known to cause postural hypotension.

There was absence of any adverse reaction attributed to bacterial contamination of the components in our study. Stringent quality measures in place at collection and processing of the units could be the reason.

Active surveillance for transfusion reactions provides a true incidence of the reactions which could help further improve

on the services.^[21] As a limitation, active surveillance was not done in our study, which otherwise would have brought into light the under reporting of any ATR. This could also contribute on possible bias on the absence of delayed transfusion reactions in our study.

Conclusion

The frequency of transfusion reactions in our blood bank was found to be on a lower scale when compared to that of most of the similar studies. Allergic reactions and FNHTR were the most common ATRs seen and introduction of measures of leukoreduction would help reduce FNHTRs.

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Competing Interests

There are no conflicts of interest

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