Original Article

Transfusion-related adverse events at the tertiary care center in North India: An institutional hemovigilance effort

Prasun Bhattacharya, Neelam Marwaha[1], Hari Krishan Dhawan[1], Pallab Roy[2], R. R. Sharma[1]

Departments of Transfusion Medicine, Medical College and Hospital, Kolkata, [1]Department of Transfusion Medicine, [2]Medical Microbiology, PGIMER, Chandigarh, India

Abstract:

Aim: This study was designed to analyze the incidence and spectrum of adverse effects of blood transfusion so as to initiate measures to minimize risks and improve overall transfusion safety in the institute. **Materials and Methods:** During the period from July 2002 to July 2003 all the adverse events related to transfusion of blood and blood components in various clinical specialties were recorded. They were analyzed and classified on the basis of their clinical features and laboratory tests. Attempt was also made to study the predisposing risk factors. **Results:** During the study period 56,503 blood and blood components were issued to 29,720 patients. A total of 105 adverse reactions due to transfusion were observed during the study period. A majority of the adverse reactions was observed in hemato-oncology patients 43% ($n = 45$) and in presensitized patient groups 63% ($n = 66$). FNHTR 41% ($n = 43$) and allergic reactions 34% ($n = 36$) were the most common of all types of adverse transfusion reactions, followed by AcHTR 8.56% ($n = 9$). Majority of these AcHTR were due to unmonitored storage of blood in the refrigerator of wards resulting in hemolysis due to thermal injury. Less frequently observed reactions were anaphylactoid reactions ($n = 4$), bacterial sepsis ($n = 4$), hypervolemia ($n = 2$), hypocalcemia ($n = 2$), TRALI ($n = 1$), DHTR ($n = 1$), and TAGvHD ($n = 1$). **Conclusion:** Analysis of transfusion-related adverse outcomes is essential for improving safety. Factors such as improvement of blood storage conditions outside the blood bank, improvement in cross-matching techniques, careful donor screening, adherence to good manufacturing practices while component preparation, bedside monitoring of transfusion, and documentation of adverse events will help in reducing transfusion-related morbidity and mortality.

Key words:

Hemovigilance, transfusion reaction, adverse events of transfusion, haemolytic transfusion reaction, risk associated with transfusion

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Correspondence to:
Dr. Neelam Marwaha,
Department of Transfusion Medicine, PGIMER, Chandigarh - 160 012, India.
E-mail: neelam2918@yahoo.com

Introduction

Prior to the discovery of blood group antigens, approximately one third of human transfusions resulted in adverse outcome, often death.[1] With the discovery of blood group antigens in 1901, by Karl Landsteiner, transfusion therapy changed from a hazardous proposition to a relatively safe procedure. Safety from transfusion transmitted diseases improved with advancement of technology. The recent testing facilities have lowered the incidence of transfusion-transmitted diseases to minimum; however, the incidence of adverse events due to human errors, ABO incompatibility, alloimmunization, bacterial contamination, and immunomodulation phenomena remain a matter of concern.

The concept of hemovigilance emerged from an already existing system of pharmacovigilance. Hemovigilance is aimed to detect and analyze all untoward effects of blood transfusion in order to correct their cause and prevent recurrence. Many countries in the developed world have established national hemovigilance systems, a few developing countries are setting it up. In India, establishment of a hemovigilance system is included in the National Blood Policy, but is yet to be implemented. Moreover there is marked paucity of data from country on transfusion-related adverse events.

In present study we have tried to detect and analyze transfusion-related adverse events as a pilot institutional effort toward hemovigilance.

Materials and Methods

During the period from July 2002 to July 2003 all the adverse events related to transfusion of blood and blood components in various clinical specialties and superspecialties were studied in the Department of Transfusion Medicine PGIMER. The study was approved by the ethics committee of the institute.

Any transfusion-related adverse event was worked up as outlined in the department's standard operating procedures prepared in accordance with the guidelines laid down by the Directorate General of Health Services (DGHS) Technical Manual,

Ministry of Health, Government of India. Instructions to the clinical residents and nursing staff in wards were given regarding reporting of the adverse events related to transfusion. During issue of each of the unit of blood/component a compatibility form was issued containing written guidelines regarding bedside monitoring of the transfusion event and the procedure of reporting of the transfusion-related adverse event. The compatibility form also bore the contact number of transfusion medicine resident.

Investigation of transfusion-related adverse event

1. The patient's name and identification number (Central registration number i.e. C.R. No.) both on the vial and requisition form were rechecked to rule out the possibility of wrong sampling or bedside transposition. Most recent results of blood typing and antibody screening were compared with the patient's previous transfusion records (if patient was transfused previously) and results written in the blood requisition form.
2. Verification of the patient's clinical records and his/her red cell ABO and Rh typing records at the bedside and in the department.
3. The implicated unit's identity was verified by checking its number and ABO and Rh type and confirming that if it was issued to the intended recipient. This revealed any error during the issue of blood/component from the blood bank.
4. Relevant clinical history of the patient regarding the indications of blood/component transfusion(s) and similar episodes of adverse reactions in the past during transfusion was recorded; this also included history of pregnancy and drug intake if any.
5. Nature of transfusion reactions: These included the clinical signs and symptoms (i.e., fever, chills, hypotension, rigors, cola-colored urine, rashes, respiratory discomfort and any other untoward events developed during the course of transfusion or following transfusion) and their duration and management. This information was used in classification of the transfusion reaction, whether immediate or delayed in onset and with or without any evidence of hemolysis. Any transfusion-related adverse events occurring within 24 hours were considered as acute transfusion reactions.
6. Collection of patient's blood sample: Two milliliters (2 ml) of posttransfusion blood sample of the patient was collected carefully in an EDTA vial, by the clean venipuncture technique using a wide-bore needle to prevent mechanical hemolysis, in all patients with adverse events. Other samples were drawn depending on the nature of reactions.
7. Laboratory investigations in the Department of Transfusion Medicine:
   (i) Gross examination
      (a) Blood bag and transfusion set were examined for any abnormal findings namely discoloration, clot, and hemolysis or foul smell.
      (b) The patient's blood sample was centrifuged and supernatant plasma after centrifugation was observed for evidence of hemolysis by appearance of pink or reddish tinge.
   (ii) Serological testing on pre and posttransfusion samples
      (a) ABO and Rh typing of the patient by both cell (using commercial monoclonal anti-sera) and serum (using freshly prepared reagent A, B, O, cells against patient's serum) grouping.
      (b) Reconfirmation of the ABO-Rh type of the implicated blood component
      (c) Evidence of mixed-field agglutination in the blood sample of the patient by visualizing saline suspension of both the pre- and posttransfusion blood sample under a microscope.
      (d) Rechecking of compatibility was done by an immediate-spin compatibility test, saline indirect antiglobulin test (IAT), and enhancement-technique low ionic strength solution (LISS) with the patient's pre- and post- transfusion sample.
8. Bacterial culture: Bacterial culture from the blood bag(s) and patient's blood was taken in suspected cases of bacterial sepsis and sent to the Department of Microbiology. Bacterial sepsis was confirmed if the blood culture of the patient and the transfused component contained the same organism and had the same pattern of antibiotic sensitivity, i.e., same antibiogram.
9. Other supportive laboratory investigations of hemolytic reaction:
   (a) Quantitative estimation of plasma hemoglobin by the peroxidase method. Here every effort was made to prevent hemolysis during collection of the blood sample.
   (b) Urine for hemoglobinuria by gross visual examination and if negative on visual examination, then the urine sample tested for hemoglobin estimation as a part of hemolytic work-up.
   (c) Peripheral blood smears examination for the presence of schistocytes and spherocytes.
   (d) Estimation of hemoglobin and bilirubin was done after 24 hours following repeat blood transfusion in cases where blood transfusion was given following the preliminary completion of transfusion reaction work-up.
10. Circumstantial evidences for thermal, oncotic, and osmotic injury was looked for by reviewing the mode of storage and storage conditions of the issued unit after it was released from the blood bank and whether any medication was given to the patient along with blood transfusion especially through the same i.v. blood transfusion set.
11. In nonhemolytic transfusion reactions investigations were done according to their clinical presentationsnamely in:
   (a) Transfusion-related acute lung injury (TRALI): Chest X-ray;
   (b) Estimation of serum calcium in suspected hypocalcemia;
   (c) Skin biopsy in suspected transfusion associated graft vs. host disease (TAGvHD).

Febrile nonhemolytic transfusion reaction (FNHTR) and allergic and anaphylactoid reactions were diagnosed by their clinical features namely fever, rigors, chills, and rashes which had no primary causes for their manifestation.

Definition of FNHTR as given in American Association of Blood Banks technical Manual 16th ed. "A body temperature rise of >1°C or more occurring in association with transfusion and without any other explanation" such reactions are often associated with rigor and chills. Rigors and other symptoms in the absence of fever are also included as FNHTR because of a presumed common mechanism.[2]

Simple allergic reaction was differentiated from anaphylactoid reaction by the absence of systemic manifestations such as

bronchospasm, hypotension as seen in anaphylactoid reaction.

Results

During the 1-year study period 56,503 units of blood and blood components were transfused to 29,720 patients admitted in various clinical specialties. Out of the 29,720 patients who received transfusions, 105 patients had adverse events during the course of or after transfusion. A total of 144 units of blood and blood components were transfused to these 105 patients who had adverse outcomes. The implicated units were as follows: 66 whole blood, 39 packed RBC, 25 platelet concentrate, 13 FFP, and 1 cryoprecipitate.

Of the 105 patients who had transfusion-related adverse outcomes, 69 were males and 36 were females. The age of the patients ranged from day 3 of life (3/365 years) to 81 years. Clinical indications for transfusion in these patients are shown in Figure 1.

History of previous transfusions was present in 55 out of total 105 (52.38%) patients. Of the 36 female patients, 27 (75%) had a history of pregnancy prior to or during transfusion. Six were pregnant at the time when the transfusion reaction occurred.

Categorization of transfusion-related adverse reactions

Transfusion-related adverse events were classified according to their time of onset: (1) acute (onset within 24 hours), (2) delayed (onset after 24 hours). Acute reaction along with features of delayed reaction was classified as the mixed type.

Table 1 shows the frequency of transfusion-related adverse events observed during the study period. Acute reactions comprised 96% (101 of 105) of total transfusion-related events.

Acute hemolytic transfusion reactions (AcHTR)

Nine patients had AcHTR, four were males and five females. Of these nine reactions, three were reported from hemato-oncology, two each from elective surgery and surgical emergency, and two from obstetrics unit. Clinical signs and symptoms as observed in accordance with the decreasing order of frequency were hemoglobinuria 67% ($n = 6$), rigors 44.4% ($n = 4$), fever 11% ($n = 1$) and jaundice 11% ($n = 1$). Acute renal failure occurred in three patients and all three of these patients had a fatal outcome. AcHTR was immune mediated in three cases and nonimmune mediated in six cases [Figure 2]. Out of three immune-mediated Ac HTR one was due to a major ABO mismatched blood transfusion event which occurred in a 40-year-old female suffering from cold agglutinin disease. She was referred from a peripheral health care facility as AB Rh(D) positive and had been transfused with AB Rh(D) positive blood. The actual blood group of the patient on investigation was detected to be B Rh(D) positive. Two patients who received ABO-matched blood had an AcHTR due to non-ABO mismatch. One was a multiparous woman of P_1 negative blood group having saline reacting anti-P_1 of high thermal amplitude. The second patient was a multitransfused multiparous woman having anti-c antibody reactive in saline phase. Out of six nonimmune hemolysis cases, in five patients the implicated red cell units were damaged due to thermal injury as a result of storage in the unmonitored domestic refrigerator in the wards The mean storage period of these blood units in wards was 48.13 hours (range 8 hours to 6 days),. In one unit there was bacterial contamination, again as a result of unmonitored storage.

Febrile nonhemolytic transfusion reactions

Forty-three patients had signs and symptoms of FNHTR. In our study fever was observed in 25 patients out of 43 characterized

Table 1: Classification of transfusion-related adverse events in 105 patients

Type of transfusion reaction	Number of patients	
	Total	Percentage
(A) Acute transfusion reaction	101	96
1. Acute hemolytic transfusion reaction	9	8.56
2. Acute nonhemolytic transfusion reaction	92	87.61
(a) FNHTR	43	41
(b) Allergic reaction	36	34
(c) Anaphylactoid reactions	4	3.8
(d) Bacterial sepsis	4	3.8
(e) Hypervolemia	2	1.90
(f) Hypocalcemia	2	1.90
(g) TRALI	1	0.95
(B) Delayed transfusion reaction	2	1.90
(a) DHTR	1	0.95
(b) TA-GvHD	1	0.95
(C) Mixed reaction	1	0.95
Allergic with DHTR	1	0.95
(D) Unclassified acute reaction	1	0.95

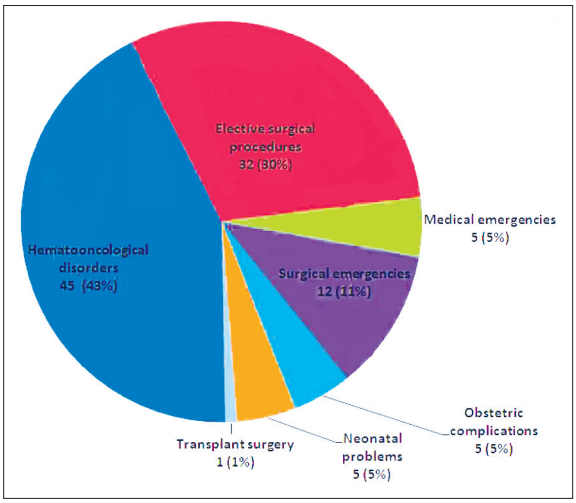

Figure 1: Clinical indications of transfusion in patients with transfusion-related adverse events

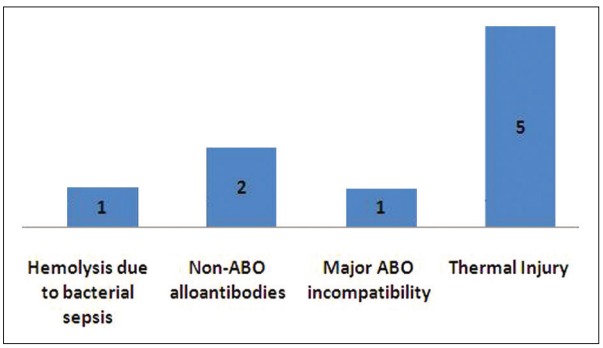

Figure 2: Causes of acute hemolytic transfusion reaction n = 9

as FNHTR. Clinical signs and symptoms observed in decreasing order of frequency were chills 66% (n = 28), rigors 63% (n = 27), fever 58% (n = 25), hypotension 14% (n = 6), vomiting 10% (n = 4), myalgia 7% (n = 3), and cough 2% (n = 1). The mean rise in body temperature as observed in 25 patients was 1.36 ± 1.07°C (range 0.5-2.1°C). Thirty-six patients developed FNHTR after transfusion of PRBCs and whole blood. Three patients had a reaction after platelet transfusions. Four patients developed FNHTR after FFP and cryoprecipitate transfusion.

Allergic reactions

They were noted in 36 patients, 24 males and 12 females. Clinical signs and symptoms that appeared in patients of allergic reactions according to the decreasing order of frequency were rash 76% (n = 28), pruritus 33% (n = 12), periorbital edema 10.8% (n = 4), wheals 8% (n = 3), cough 5.4% (n = 2), chills 2.7% (n = 1), and vomiting 2.7% (n = 1). WB and PRBC were implicated in 27 cases, platelets are implicated in 6 cases, and plasma was implicated in 3 cases.

Anaphylactoid reactions

Of four patients, three were males and one female. Of the four reactions two were from hemato-oncology, one each from surgical specialty and neonatology. Clinical signs and symptoms in decreasing order of frequency were rash 75% (n = 3), hypotension 50% (n = 2), respiratory distress 50% (n = 2), and flushes 25% (n = 1). The mean time interval between the onset of transfusion and appearance of clinical signs and symptoms was 85 ± 23.5 minutes. All of them recovered uneventfully. Three of the implicated units were whole blood and one was a packed red cell unit.

Bacterial sepsis

Bacterial sepsis was suspected in five patients with transfusion reactions. *E. Coli* was detected in three cases, *Enterobacter aerogenes* and *Klebsiella pneumonia* in one cases each. Sepsis resulted in three deaths; one patient recovered following a hemolytic episode. Outcome was not known in fifth patient as the patient absconded. Of the five implicated units three were whole blood, one unit was packed RBC, and one was platelet concentrate. Clinical signs and symptoms in decreasing order of frequency were fever 60% (n = 3), rigors 40% (n = 2), hypotension 40% (n = 2), oliguria 20% (n = 1).

Hypervolemia

Hypervolemia was observed in two patients, one in a 6-day-old neonate during double volume exchange transfusion (DVET). This neonate developed sudden onset, acute respiratory distress, and cyanosis, which were relieved with diuretics. The second patient was a 2-year-old male with severe anemia who received two units of whole blood in less than 3 hours. At the end of transfusion, he developed orthopnoea, frothy cough, and gallop sound on auscultation, which were relieved with diuretics and oxygen. Both the patients recovered on symptomatic management.

Hypocalcemia

Hypocalcemia was observed in two neonatal patients (D3 and D4 of life), during DVET. Both the babies developed bradycardia and one of them had a cardiac arrest, but was revived. Estimation of serum calcium in posttransfusion blood samples in both of them were below the normal range (7.5 mg/dl and 7.0 mg/dl, whereas their pretransfusion serum calcium levels were 9.5 mg/dl and 10 mg/dl respectively).

Transfusion-related acute lung injury

It was noticed in a 10-year male child who received multiple transfusions of blood and platelets for pancytopenia due to aplastic anemia. The patient received one unit of whole blood and two units of platelets 48 hours before the transfusion of the implicated units. He developed sudden onset of respiratory distress and cyanosis within 2 hours following transfusion of two units of platelet rich plasma (PRP), which were 1 day old. The patient expired after 24 hours of transfusion of PRP. His pretransfusion chest X-ray was normal, but posttransfusion chest X-ray showed bilateral pulmonary edema.

Delayed reactions

Delayed hemolytic transfusion reactions (DHTR)

This occurred in a 14-year-old multitransfused thalassemic male, presenting with a history of recurrent attacks of jaundice following blood transfusion. Initially the patient received transfusion at intervals of 4 weeks but gradually over a period of 8 months, this interval decreased to 3 weeks. Both the pre- and posttransfusion samples were compatible with the donor unit in saline antihuman globulin phase (AHG) but incompatible in the LISS AHG phase. Antibody specificity could not be detected.

Transfusion associated graft vs host disease

This was suspected in a 5-year-old female child who was on chemotherapy for acute lymphoblastic leukemia (ALL). She developed erythematous rash over palms and soles, loose stools and unconjugated hyperbilirubinemia (unconjugated hyperbilirubinemia = 6.3 mg/dl) on the 8th day following transfusion of 2 units of fresh packed red cells (<2 days old) and 2 units platelets (day 0). Her skin biopsy features were suggestive of Transfusion associated graft vs host disease (TAGvHD). The patient recovered with steroid therapy.

Mixed reaction

This occurred in a 50-year-old male, a patient of aplastic anemia. He, on receiving 100 ml of PRBC, initially developed clinical features suggestive of allergic reactions (rash, pruritus). A transfusion reaction work-up showed the posttransfusion sample to be direct antiglobulin test (DAT) positive and the pretransfusion sample was incompatible with the donor unit by the LISS technique. This patient developed jaundice with unconjugated hyperbilirubinemia (5.2 mg/dl) after 36 hours of blood transfusion (PRBC). Antibody specificity could not be detected. This reaction was classified as a mixed type having features of allergy and delayed hemolytic reaction. This patient had received two units of blood 6 months prior to admission in the institute.

Unclassified reaction

A three-and-a-half-year-old male child, with diagnosis of septicemia, severe anemia, and disseminated intravascular coagulation (DIC), developed rash during transfusion of whole blood (100 ml). The rash did not subside on antihistaminics and within 2 hours, the patient died. The preliminary work-up of the transfusion reaction was not suggestive of any incompatibility. Reaction could not be categorized; the cause of death might be due to the underlying disease itself.

Table 2: Estimated risk of various types of transfusion reactions per 1,000 units of blood components transfused

Type of reaction	RBCs (WB/ PRBCs)	Platelets	Plasma and cryoprecipitates
FNHTR	1.14	1.43	0.56
Allergic reaction	0.87	2.45	0.47
AcHTR	0.21	NR	NR
Bacterial sepsis	0.08	0.2	NR
Anaphylactoid	1.02	NR	NR
Hypervolemia	0.06	NR	NR
Hypocalcemia	0.16	NR	NR
TRALI	NR	0.41	NR
DHTR	0.10	NR	NR
TAGvHD	0.10	0.41	NR

NR: Not reported in this series because the particular type of reaction was not observed with particular blood component.

Estimation of risk for various transfusion reactions]

The total number of blood component transfused during the study was 56,503 (35,550 PRBC and whole blood, 4,899 platelets, 14,056 plasma and cryoprecipitates. The risk of transfusion reaction was expressed per 1,000 units of blood component transfused by following formula: Risk of Transfusion reaction = n/a × 1,000 where "n" is the total number of reactions in each category and "a" is the total number of blood components transfused [Table 2].

Outcome of acute transfusion reactions

FNHTR (41%) and allergic reactions (34%) were the two most frequent adverse reactions observed with transfusion of blood and blood components. Hemolytic transfusion reactions were the third most common category. Mortality was associated with AcHTR, bacterial sepsis, and Transfusion-related acute lung injury (TRALI). In other cases, the transfusion reactions were successfully managed.

Discussion

The means of determining risks for allogenic transfusion was by case reporting of adverse outcomes and laboratory work-up of the adverse events. Unfortunately, clinical case reporting has several limitations as a source of comprehensive information about incidence of transfusion reactions. The most important concerns are the dependence on the awareness of physicians and other health care workers to (1) look for adverse effects and their reporting, (2) determine whether the effects could have been caused by transfusion. It is less difficult to identify the adverse effects within a short time of transfusion event. However, the longer the time of events to occur after the transfusion, the less likely they are to be reported (especially if they are mild and nonspecific). The accurate figures for the number of recipients transfused was difficult to obtain, so the risk estimate was calculated based on the number of units transfused.

Risk factors, which were observed to be responsible for acute hemolysis, were unmonitored storage conditions in the wards. The mean storage period was 48.13 hours (range 8 hours to 6 days), technical errors and less sensitive techniques (immune hemolysis) and bacterial contaminations. A majority of acute hemolytic reactions observed in this study were due to improper storage conditions 66% (6 out of 9). Overall risks for acute hemolytic reactions which were observed in different studies ranges from 0.02 to 0.07[3-5] per 1,000 red cell units transfused. In the present study, the risks for AcHTR (9 out of 37,550) are estimated to be 0.23 per 1,000 red cell units transfused. Non-ABO incompatibilities were observed in two patients, one due to anti-P_1 and anti-c antibody in the other. The antibodies involved in both of them were saline reactive, the cause for failure to detect them by an immediate-spin compatibility test was related to technical error. The overall higher incidence of AcHTR observed in our study seems to be due to the higher number of nonimmune hemolysis which were comparatively rare in the above-quoted studies. Improper storage conditions in unmonitored refrigerators outside the department led to deterioration of red cell units. Hence awareness among the bedside staff is essential to reduce this risk. A hand book about handling and storage of blood and components for the resident staff has been developed by the department and is issued to all clinical residents at the time of their entry into the institute.

In our study fever was observed in 25 patients out of 43 characterized as FNHTR. In one study of 108 reactions characterized by chills, cold or rigors, only 18 involved a rise in temperature.[6] Data on the incidence of FNHTR vary greatly in the literature. Possible reasons for this variation include differences in recording of symptoms by the bedside staff, case ascertainment, and use of pretransfusion medications to control fever. With the concept of universal leukoreduction there is dramatic risk reduction for FNHTR. The most common quoted rate for FNHTR is 0.5-1%[7] for the general populations of patients with red cell (WB/PRBC) transfusion. In other studies it varies from 0.08% to 6.8%.[8,9] A comparative study on incidence of FNHTR in leukoreduced vs. nonleukoreduced blood components showed that the incidence is 0.12% in nonleukoreduced and 0.08% in prestorage leukoreduced blood.[9] The present study with transfusion of the nonleukoreduced red cells (WB/PRBC) has shown the overall risks for FNHTR to be 0.114% (43 out of 37,550) which is comparable to the reported data of nonleukoreduced blood components.

Definitions of allergic reactions vary greatly in literature and there are a few data on incidence of allergic reactions on well-designed studies in the general patient population. Moore *et al.*[10] reported a 3% rate of mild allergic reactions from Mayo Clinic. This mild allergic reaction was defined as hive or localized urticaria. Incidence in other studies varies from 0.2% to 3%.[5,9-11] Higher incidence of allergic reactions 3-4.8%[5,8] is reported in studies with platelet transfusion in hemato-oncology patients. In the present study it was 0.87% with red cells, 2.45% with platelets, and 0.47% with FFP. Higher incidence with platelet transfusion was seen in hemato-oncology patients, similar to reported studies.

Anaphylactoid reaction was observed in four patients after transfusion. Estimation of plasma IgA could not be done in any of the four patients. Pineda *et al.*[10] reported an incidence of 0.0021 per 1,000 units of transfusion of blood components (red cells, platelets, and plasma). In the present study all of these four patients received red cell transfusions (WB/PRBC) and the overall risk for anaphylactoid reactions was observed to be 1.02 per 1,000 red cell units. A previous study reported hypotensive reactions with platelet transfusions. The present study further adds to this observation that hypotension can also be observed with red cell (WB/PRBC) transfusions, which was also observed by Domen *et al.*[12]

Bacterial contamination remains an important cause of

transfusion-related morbidity and mortality. Sources of bacteria are believed to arise from donor either from venepuncture site or from unsuspected bacteremia and during component preparation.[13] Bacterial sepsis was suspected in five patients; the blood components implicated were four red cell units (WB/PRBC) and 1 platelet unit (age day 1). The incidence of transfusion-associated bacterial contamination (TABC) varies from 0.0002 to 0.003 for PRBC and 0.01 to 0.44 for platelets per 1,000 units of blood component transfused.[5,14] Incidence of TABC in present study per 1,000 blood component transfused is 0.08 for PRBC and 0.20 for platelets. The prevalence of bacterial contamination of blood components is higher for platelets than for red cells (WB/PRBC), but risk estimates are highly variable and depend on methods of culture, processing, and storage. The pathogens isolated from two cases of confirmed TABC in the present study were enterobacter aerogens (red cell unit) and klebsiella pneumonia (platelet unit) and both of these patients succumbed to sepsis. Predisposing factors, which might be responsible for bacterial contamination in this study, contribute to collection through skin flora, asymptomatic donor bacteremia, and extended storage of blood component outside the blood bank, mean 44 hours (range 1-96 hours). The majority of the suspected cases of bacterial sepsis (four out of five patients) occurred in the summer and monsoon season, which suggest sweating and humidity might be a factor for bacterial proliferation in the donor skin flora.

There were two reactions of hypervolemia observed in this study and both of them were associated with red cell transfusions (WB). Very few studies had estimated the risks of hypervolemia due to transfusion and it varies from 0.31 to 0.42[5,15] per 1,000 recipients of transfusion. Our observed incidence (0.06) is much lower than the previous two studies. Both the patients belonged to the pediatric age group. The predisposing factors observed in this study were faulty transfusion administering techniques, which resulted in volume overload (i.e., rapid infusion of whole blood in both cases). No underlying causes precipitating acute volume overload (i.e., cardiac or pulmonary disease) were present in these patients.

Hypocalcemia was noted in two patients, both of them were newborns, undergoing DVET. Both of them developed bradycardia at the end of transfusion. There is always a possibility of this adverse transfusion reaction especially during exchange transfusion due to citrate toxicity. The already jaundiced, premature newborns are more susceptible to citrate overload due to depressed liver functions.

There was a single case of suspected TRALI. Thus, the overall risk for TRALI appeared to be 0.04%. The incidence of TRALI is rare in the Indian subcontinent where most donors are male (95% in the present study). The incidence of TRALI reported in various studies from Western literature ranged from 0.014% to 0.08%[16] per units transfused. However, it is generally agreed that TRALI is underdiagnosed. This is likely because of poor awareness, lack of recognition of the condition, and/or because TRALI is easily confused with other conditions, e.g., adult respiratory distress syndrome (ARDS), hypervolemia, and congestive heart failure. This case has already been reported.[17]

The overall risk estimates of DHTR cited in various studies vary from 0.007 to 0.6907[2-4] per 1,000 red cell units transfused. In the present study in the institute, we found the incidence of DHTR to be 0.10 per 1,000 WB/PBRC units (4 out of 37,550), though the case reports were only two (who received 4 units of PRBCs). The data on overall incidence of DHTR vary in different studies because DHTR is difficult to diagnose and most often, it is asymptomatic or may even be similar to the clinical signs and symptoms of the patient so that it remains underdiagnosed and underreported. The lower incidence of DHTR in our study seems to be due to underreporting.

Only single incidence of TAGvHD was suspected in a multi-transfused 5-year female child on chemotherapy for ALL. Risk factors observed in this study could be immunosuppression and transfusion of relatively fresh units of blood and platelets. To the best of our knowledge, no incidence data have been reported from any country. The literature contains individual case reports and defines the risk factors for development of TAGvHD.

The highest number of reactions was observed in hemato-oncological patients. FNHTR and allergic reactions were the commonest type of adverse events observed almost in all patient groups (incidence 41% and 34% respectively). DHTR, TRALI, and TAGvHD were seen only in hemato-oncology patients, which might be due to their higher incidence of prior exposure to sensitization, immunosuppression, and/or due to increased awareness of clinicians to report the adverse events.

Hemovigilance data are highly valuable for initiating changes to improve blood safety. Over 12 years of reporting, the trends observed by SHOT, UK (serious hazards of transfusion) have revealed the outcome of an effective hemovigilance system. The number of events reported has risen, while the frequency of the most serious events, and the mortality directly related to transfusion, has fallen.

Conclusion

Acute transfusion reactions constituted 96% of all reported reactions, majority were FNHTRs and allergic reactions. These were reported with a higher frequency in hematooncology patients, who require repeated blood transfusion. The incidence of AcHTR was higher than in most reported studies and improper storage at bedside was a more common cause than immunological incompatibility. TRALI, TAGvHD, and DHTRs were rare, possibly due to underreporting. The hemovigilance system plays a very important role in improving blood safety. The preliminary hemovigilance data highlight the importance of establishing functional hospital transfusion committees at institute level and at the same time developing a national hemovigilance program for policy making in transfusion services. An encouraging environment for reporting of adverse events and near-misses in a supportive, nonblaming learning culture is required to have an effective hemovigilance system. Vigilance in hospital transfusion practice and analysis of these data are of paramount importance to improve transfusion safety.

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