

## Research Article

# A study of transfusion related adverse events at a tertiary care centre in North India: an initiative towards hemovigilance

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## ABSTRACT

**Background:** The goal of hemovigilance is to improve the transfusion safety. The present study was undertaken to detect and analyze the transfusion related adverse events as a pilot effort towards hemovigilance from the institution.

**Methods:** The present retrospective study was conducted in the Department of Transfusion Medicine, Government Medical College, Jammu from Jan 2014- Dec 2014. All the adverse events related to transfusion of blood and blood products reported to the department were recorded and analyzed as per Departmental Standard operating procedures.

**Results:** During 1 year study period 33,852 blood and blood components were issued to various clinical departments. Ninety four reactions were reported, the type of reaction observed were allergic reactions in 41.5%, followed by febrile non hemolytic transfusion reaction(FNHTR) in 35.5%, Acute hemolytic reactions in 11.7%, delayed hemolytic transfusion reactions(DHTR) in 4.2%, transfusion associated cardiac overload (TACO) in 4.2% and Bacterial sepsis in 2.1%.

**Conclusion:** The frequency of transfusion in our patients was found to be 0.27%. Factors such as rational use of blood components, improving storage conditions, bedside monitoring of transfusion and documentation of adverse events will help in improving transfusion safety.

**Keywords:** Hemovigilance, Transfusion reaction, Adverse events

## INTRODUCTION

The term hemovigilance was coined in France in the early 1990s, has been developed and adopted internationally and is now an integral part of transfusion practices. It is a systemic surveillance of adverse transfusion reaction and events, encompassing the whole transfusion chain and aimed at improving the safety of the transfusion process, from donor to recipient “vein to vein”.<sup>1</sup> First hemovigilance surveillance system was implemented in France in 1994 as mandatory reporting as required by updated French regulation. Serious hazards of transfusion (SHOT) were established in United Kingdom shortly after 1996 as voluntary reporting. In United Kingdom and Ireland, 366 reports of deaths or major complications of transfusions were reported as a part of

SHOT initiative. The most common adverse event was (52%) giving wrong blood to the patients.<sup>2</sup> Indian pharmacopoeia commission in collaboration with National institute of biological has launched a Hemovigilance Programme of India on 10<sup>th</sup> December 2012. The main objectives of the programme are to track adverse reactions/events and incidence associated with transfusion of blood and blood product and to help identify trends, recommends best practices and interventions required to improve patient care and safety, while improving the overall health care.<sup>3</sup> Sixty medical colleges will be enrolled in it including Government Medical College, Jammu. The present study was undertaken to detect and analyze the transfusion related adverse events as a pilot effort towards hemovigilance from the institution.

## METHODS

The present retrospective study was conducted in the Department of Transfusion Medicine, Shri Maharaja Gulab Singh Hospital, Jammu from Jan 2014- Dec 2014. All the adverse events related to transfusion of blood and blood products reported to the department were recorded on transfusion reaction reporting forms and analyzed as per laboratory investigation form for investigating the transfusion reactions as per standard operating procedures of the Department prepared in accordance with the guidelines laid down by the Director General of Health Services Technical Manual, Ministry of Health And Family Welfare, Government of India.

### Investigation of transfusion related adverse event

1. Patients name, central registration number (C.R. No), red cell ABO and Rh D typing are rechecked on requisition form, pretransfusion sample and transfusion reaction reporting form to rule the possibility of wrong sampling or bedside transposition.
2. Relevant clinical history of the patient regarding the indication of blood /blood component transfusion(s) and similar episodes of adverse reactions in the past during transfusion, previous history of pregnancy and transfusions were also recorded.
3. Clinical features due to transfusion reactions were also recorded i.e. fever, chills, rigors, hypotension, pain abdomen, urine color, urticaria, rashes ,respiratory discomfort, jaundice and any other sign or symptoms related to transfusion reactions.
4. Implicated blood component is checked for discoloration, clots, foul smell and any leakage
5. Post -transfusion blood sample of the patients was obtained in EDTA vial for laboratory investigations in transfusion medicine laboratory.
6. After centrifugation plasma is checked for evidence of hemolysis by presence of pink or red tinge.
7. Serological tests performed on pretransfusion and posttransfusion sample are to rule out hemolytic transfusion reactions:
  - a. ABO and RhD typing both cell and serum grouping on patients samples.
  - b. ABO and RhD typing both cell and serum grouping implicated blood component.
  - c. Repeat compatibility testing by immediate spin method and LISS gel Diamed cards.
  - d. Antibody screening
  - e. Direct Antiglobulin test
8. Bacterial culture of the blood bag and patients blood. Blood sepsis is confirmed if the blood culture of the patient and transfused component is same
9. Other supportive tests like:
  - a. Urine for hemoglobinuria

- b. Complete blood counts, peripheral blood smears for schistocytes and spherocytes, reticulocyte count.
  - c. Serum bilirubin direct and indirect
  - d. Blood urea And Serum creatinine
  - e. Promthrombin time, Activated partial thromboplastin time.
10. X-ray chest, ECG etc.

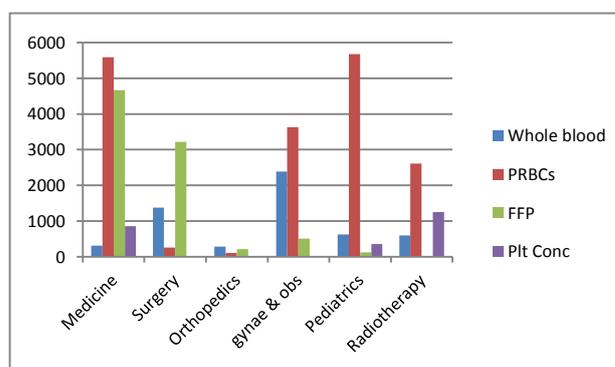
Febrile non hemolytic transfusion reactions (FNHTR) is defined according to American Association of Blood Bank Technical manual as “A body temperature rise of  $>1^{\circ}$  C or more occurring in association with transfusion and without any other other explanation” such reactions are often associated with chills and rigors.<sup>4</sup>

## RESULTS

During 1 year study period, 33,852 blood and blood components were issued to various clinical departments. The number of different products issued from blood transfusion services is given in Table 1.

**Table 1: Type of blood product issued during 1 year study period.**

Type of Product	Whole Blood	PRBCs	Fresh frozen plasma (FFP)	Platelet
Total (33,852)	5274 (15.5%)	17875 (52.7%)	8232 (24.3%)	2471 (7.2%)



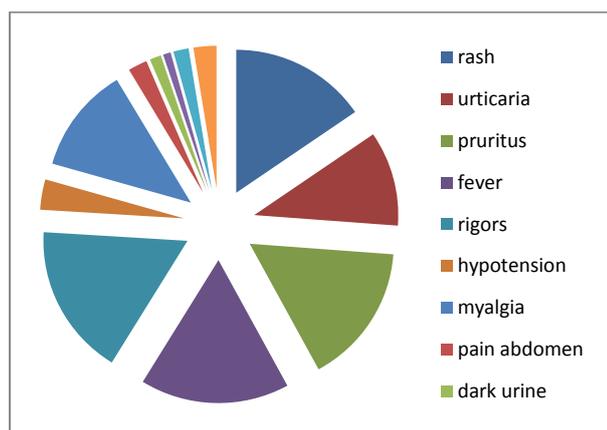
**Figure 1: The number of blood products issued to clinical department.**

The total number of transfusion reactions reported to blood bank were 94 i.e. (0.27%), of which 45(47.8%) were seen in males and 49(52.1%) in females. Age of the patients ranged from 5 days to 72 years with the mean of 32.1 years. Of all the transfusion reactions reported 95.7% were acute reactions and 4.3% were delayed transfusion reactions. Whole blood was implicated in 47.8% of transfusions, packed red blood cells in 36%, platelet concentrate in 10.8% and FFP in 6.3% of all the transfusion reaction (Table 2).

**Table 2: Different type of transfusion reactions according to the type of blood component used.**

Type of Reaction	Whole Blood No=45 (47%)	PRBCs no=34 (36.1%)	FFP no=6 (6.3%)	PC no=10 (10.6%)
Allergic Reac no=38(41.5%)	21 (55.2%)	10 (26.3%)	0	7 (18.4%)
FNHTR no=33(35.1%)	19 (57.5%)	8 (24%)	2 (6%)	5 (15%)
AcHR no=11(11.7%)	1 (9.09%)	10 (90.9%)	0	0
DHTR no=4(4.2%)	0	4 (100%)	0	0
TACO no=4(4.2%)	3 (75%)	0	1 (25%)	0
Bact sepsis no=2(2.1%)	2 (100%)	0	0	0
TRALI no=1(1.06%)	0	0	0	1

Rigors, fever, rash, pruritus and urticaria were the most common symptoms reported in transfusion reactions (Figure 2).



**Figure 2: Sign and symptoms of transfusion reaction.**

Allergic transfusion reactions were the commonest acute reactions reported and comprised of 41.5% (38/94) of all reactions. The most common sign and symptoms were rash (94.7%), pruritus (97.3%) and urticarial (65%). Whole blood was implicated in 55%, packed red blood cells (PBRCs) in 26.3% and Platelet concentrate in 18.4% patients.

FNHTR were found in 35.1% (33/94) patients. The most common sign and symptoms were fever (90.9%), chills and rigors (100%), hypotension (15.1%) and myalgia (84.8%) patients. Whole blood transfusions were implicated in 57.5%, PBRCs in 24%, platelets in 15% and FFP in 6% patients

Acute hemolytic reactions (AcHR): Nine patients developed acute hemolytic transfusion reactions 6 females and 5 males. Seven were reported from medical specialities, two from orthopedics and two from labor

room of obstetrics department. Seven of these were ABO incompatible hemolytic reactions and 4 were related to storage and transportation errors. Out of seven ABO incompatible reactions two were due to wrong issuance of blood, two were due to labeling errors, one were due to transposition of blood at bedside (patient with O+ve was transfused B+ve, whereas patient with B+ve transfused O+ve, one was due to analytical error i.e. incorrect crossmatching and one due to transfusing Oneg whole blood to neonate for exchange transfusion. The most common sign and symptoms were pain abdomen 45.4%, fever 63%, chills with rigors 63% and dark urine 27% patients. Direct antiglobulin was reactive in 5/11(45.4%) patients in post transfusion sample. Indirect anti globulin was non reactive in all cases. Mild to moderate reactions developed in 9 patients and severe in 2 patients requiring intensive care. All the patients recovered.

Delayed hemolytic transfusion reactions developed in 4 thalassemic patients 48 hrs after transfusion. There was history of yellowish discoloration of skin and urine, fall in post transfusion hemoglobin and vomiting. Antibody screening was positive in both pre and transfusion samples. In all these patients, best matched units were transfused. Antibodies identified later on these patients were Anti E in two patients, Anti N in one and Anti K in one patient.

Anaphylactoid reactions developed in one patient within 10 minutes of administration of whole blood. Patient developed dysnoea and marked hypotension. Patient shifted to ICU and recovered after 2 days.

A suspected case of TRALI was reported from radiotherapy/ oncology department where patient developed respiratory distress, tachycardia and hypotension following random donor platelet transfusions. X-ray chest showed bilateral infiltrates. However pretransfusion X-ray was not done. Patient did not recover. All the donors implicated in random donor platelet were males.

TACO was observed in 4 patients. Three patients of severe anemia (Hb<4gm/dl) on hemodialysis were transfused with 2-3 units of whole blood in a day developed marked dysnoea and periorbital odema. Both were relieved with diuretics. One neonate 5 days old transfused two units of FFPs developed acute respiratory distress and cyanosis. Responded to diuretics and recovered.

Two cases of suspected bacterial contamination were reported as patients developed high grade fever, hypotension and vomiting after more than 150 ml of PRBCs were transfused. Remaining blood in the bag was sent for bacterial culture one of which was reported pseudomonas spp and other coagulase positive staphylococcus aureus. Laboratory investigations ruled out hemolytic reactions in them and blood culture was negative in these patients. Patients recovered with antibiotics.

Table 3 shows frequency of transfusion reactions. No of blood components transfused was taken as denominator.

**Table 3: Frequency of transfusion reactions.**

Type of reaction	Frequency per 1000
Allergic reactions	1.1 per 1000 transfusions
FNHTR	0.97 per 1000 transfusions
Ac HR	0.32 per 1000 transfusions
DHTR	0.11 per 1000 transfusions
TACO	0.11 per 1000 transfusions
TRALI	0.02 per 1000 transfusions
Bacterial sepsis	0.05 per 1000 transfusions

## DISCUSSION

Allogenic blood transfusion is associated with risks of adverse events. An informed decision about transfusion has to be made based on the risks to benefit ratio associated with blood transfusion to a particular patient. Only cases reported to the blood bank were included in the study. There may be under reporting of adverse events as some reactions like allergic or FNHTR may have been managed without informing blood bank. In present study frequency of adverse reactions was found to be 0.28% whereas a study from Chandigarh (PGIMER)<sup>5</sup> reported it to be 0.18% and Delhi (AIIMS) 0.05%.<sup>6</sup>

The overall incidence of allergic and anaphylactoid reactions is 0.11% in present study. Whole blood transfusions were most commonly implicated in allergic reactions. Kumar et al reported 0.028% and 0.003%, Domen et al. also reported 0.02% and 0.003% incidence for allergic reactions and anaphylactoid reactions.<sup>7</sup> In a concise review done by Moore et al at Mayo's clinic, the rate of mild allergic reaction was estimated to be 3%.<sup>8</sup>

The frequency of FNHTR in present study was 0.09% and is associated most frequently with Whole blood transfusions. Kumar et al<sup>6</sup> and Bhattacharya et al.<sup>5</sup> reported FNHTR due to PRBC 0.04% and 0.114% respectively. With the concept of universal leucoreduction, there is dramatic decrease in the FNHTR. A comparative study on incidence of FNHTR in leucoreduced and nonleucoreduced blood components showed that the incidence is 0.12% in nonleucoreduced and 0.08% in leucoreduced blood components.<sup>9</sup>

Risk factors associated with Acute ABO incompatible hemolytic reactions were mainly non technical or clerical errors. Baele et al. reported bedside transfusion errors occur in 12.4/ 1000 transfusions.<sup>10</sup> Goodnough estimated that the administrative errors were the most serious risks leading to Acute ABO incompatible hemolytic reactions.<sup>11</sup> Overall risk of acute hemolytic reactions in present study was 0.32 per thousand transfusions.

Bhattacharya et al<sup>5</sup> reported it to be 0.23/1000 transfusions and Kumar et al reported it to be 0.03/1000 PRBCs transfusions.<sup>6</sup> Other studies also reported the frequency from 0.02-0.07/1000 PRBCs.<sup>12-14</sup>

Delayed hemolytic reactions were found in multi transfused thalassemic patients. The incidence of DHTR in present study was 0.11 per 1000 transfusions. The overall risk estimates of DHTR in various studies vary from 0.007-0.69/1000 red cell transfusions.<sup>4,12</sup> Alloantibodies implicated were anti E, anti K and anti N. As respective anti sera was not available, so best matched unit were transfused which led to DHTR in these patients and reported after 2 days post transfusion.

The incidence of TACO was 0.11 per 1000 transfusions in present study. This mainly occurred due to inappropriate request and administration of blood components. Patients with severe anemia (Hb < 4-5gm/dl) are at increased risk of TACO because of already being in hyper kinetic state, with heart being intolerant to slight increase in blood volume.<sup>15</sup> Rapid infusion of blood products should be avoided and AABB recommends an infusion rate of 2-4ml/minute for RBCs and faster rates for plasma.<sup>4</sup>

The overall risk of TRALI in various studies from western literature ranged from 0.014%-0.08%.<sup>16</sup> however, TRALI is generally due to lack of recognition of the condition and /or TRALI is easily confused with other conditions like adult respiratory distress syndrome, hypervolemia and congestive cardiac failure.<sup>17</sup> There was no confirmed case of TRALI in present study. One suspected case of TRALI was reported following platelet transfusions, deteriorated fast and died within two days and the donor of the implicated unit was however, male. Careful selection of donors can decrease incidence of TRALI.

Despite vigorous screening of donors, bacterial contamination still remains an important cause of morbidity and mortality. In various studies, incidence ranged from 0.0002-0.003 for PRBC and 0.01-0.02 for platelets per thousand units of blood components transfused.<sup>18</sup> The sources of bacteria are usually bacteria from venepuncture site or breach in aseptic technique during component preparation. In present study, incidence for bacterial contamination was 0.05 per 1000. Bhattacharya et al reported 0.08 for PRBCs and 0.20 for platelets per 1000 components transfused.<sup>6</sup>

The whole blood was implicated in most of the adverse transfusion reactions (47%). Hemovigilance data in present study is highly valuable in initiating changes to improve transfusion safety such as shifting to 100% component preparation and discontinue the use of whole blood transfusions formulating guidelines for rational use of blood for clinicians and getting them implemented through hospital transfusion committee.

To conclude, frequency of transfusion reactions in present study was 0.27% majority of these were due to

whole blood transfusions. This reaction rate can be underestimation of true incidence, because of underreporting which can be improved by hemovigilance system. Fully functional hospital transfusion committee with refresher trainings to medical and paramedical staff will help in improving hemovigilance system and reducing the incidence of transfusion reactions.

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