

# Patterns of Adverse Transfusion Reactions related to Blood and Blood Components in a Tertiary Care Centre: A Step towards Hemovigilance

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## 1. Introduction

Transfusion of blood products is a double edged sword, because it is lifesaving as well as hazardous. Although the incidence has declined substantially with modern facilities such as improved screening and transfusion practices, use of leukofilters and modified blood components, a significant number of cases are still observed due to human errors, alloimmunization, bacterial contamination and immunomodulation<sup>1</sup>.

Blood transfusion typically uses sources of someone else's (allogenes or homologous transfusion) or one's own (autologous transfusion). Before transfusion ABO compatibility and Rh compatibility is tested. Donated blood is then separated to components like RBC, plasma, Platelets, Albumin, clotting factor concentrate cryoprecipitate etc.<sup>2</sup>

Prior to discovery of blood group antigens, approximately one third of human transfusion resulted in adverse outcome, often death. With the discovery of blood group antigens in 1901, by KARL LANDSTEINER, transfusion therapy changed from a hazardous proposition to a relatively safe procedure. Though blood transfusion services have undergone major advancements in the last decade, the system of recording and reporting of adverse events related to blood transfusion is lagging.<sup>3</sup>

Transfusion reaction is any untoward effect occurring in a patient during or after receiving blood and blood products. This can be categorized as acute transfusion reactions occurring within 24 hours of transfusion and delayed transfusion reactions occurring within days or months. Acute and delayed reactions are further categorized as immune mediated and non-immune mediated

Infectious adverse transfusion reactions have decreased by approximately 1000 folds because of strict donor screening, however incidence of non-infectious transfusion reaction still remain high. Majority of these reactions such as febrile non-haemolytic transfusion reactions and allergic reactions are short term and reversible. A few of these reactions can cause significant morbidities such as transfusion related acute lung injury and transfusion related dyspnoea and mortality. The incidence of acute blood transfusion reactions is estimated to be 0.2-10% and is responsible for mortality in 1 per 250,000.

Hemovigilance is a set of surveillance procedures covering the entire transfusion chain from collection of blood and its components to follow up of its recipients, intended to collect

and assess information on unexpected or undesirable effects resulting from therapeutic use of labile blood products and to prevent its occurrence and recurrence. It includes monitoring identifying reporting investigating and analyzing adverse events associated with transfusion of blood and blood components. Information gathered from such monitoring is useful for Early detection and identification.<sup>4</sup>

The concept of hemovigilance emerged from an already existing system of pharmacovigilance. Many countries in the developed world have established national hemovigilance systems, a few developing countries are setting it up.<sup>2</sup>

In India hemovigilance system is included in NATIONAL BLOOD POLICY, but is yet to be implemented.<sup>1</sup>The software development started on 15th November 2012. Hemovigilance software was uplinked on national institute of biology on 24th January. There are about 2545 licensed blood banks out of which 981 are in public sector and remaining 1564 are in private hospital or managed by charitable organizations.<sup>2</sup>

Since adverse event identification, recording and reporting are grossly inadequate, this study is being undertaken to study the acute transfusion reactions in a tertiary care centre.

## 2. Review of Literature

**Sidhu Meena et al.** (2015) conducted a retrospective study for a period of 1 year on adverse reactions reporting and found it to be poor and hence recommended the need for improvement.<sup>3</sup>

**Bassi R, et al** (2016) studied the Patterns of Adverse Transfusion Reactions for period of 1 year and concluded that the majority of ATRs were FNHTRs and found that leucodepleted PRBCs help in reduction of FNHTR.<sup>5</sup>

**Jooyoung cho et al.** (January 2016) analyzed two-year transfusion data from electronic medical records retrospectively and observed that Leukocyte-reduction was associated with a lower rate of FNHTRs, but not with allergic reactions.<sup>9</sup>

**Chavan SK et al.**(April 2016) conducted A retrospective review of all TRs reported to the blood for a period of 2 years and observed that there was Not a single case of anaphylactic reactions, TRALI, acute immune hemolytic transfusion reaction, and sepsis.<sup>6</sup>

**Urmi chakravarthy et al.** (may 2016) conducted a Retrospective review of all the transfusion reactions reported to the blood bank during a period of 2 year and observed that the Most common adverse reaction following blood transfusion is fever with chills.<sup>7</sup>

**Asha Latha Mappu et al.**(September 2016) :conducted a study on Transfusion reactions over a period of 3 months and analysed that The overall incidence of ATRs in this hospital was low. Though there were no leucoreduction facilities, the ATRs were less due strict aseptic compatability testing.<sup>2</sup>

**Sinha RTK et al.**(October 2016) conducted A retrospective review of all transfusion reactions reported to the Blood Bank during 1 year period and observed that The most common type of transfusion reaction among all the ATRs was allergic followed by febrile nonhemolytic transfusion reactions.<sup>1</sup>

**Vidya shree M.,et al.**(November 2016) conducted a study to know the extent, incidence and severity of transfusion reaction and also report the suspected transfusion reactions in a timely manner to facilitate effective risk management and to assess the causality of transfusion reaction for a period of 9 months and observed that the most common type of reaction encountered was FNHTR.<sup>8</sup>

**Kunal J. Ghataliya, et al** (2017)studied Patients receiving transfusion of blood or its components in a randomly elected unit each from Departments of Pediatrics, including thalassemia OPD and surgery, who were monitored intensively for a period of 6 months and observed that Transfusion reactions in children and surgical patients are commonly observed with cellular blood components. Majority of reactions are acute and nonserious, FNHTRs and allergic reactions.<sup>4</sup>

### 3. Aims and Objectives

- 1) To determine the pattern of acute adverse reactions associated with transfusion of blood and its components in patients receiving transfusion at a tertiary care teaching hospital.
- 2) To describe the demographic profile of these subjects. (patients suffering acute transfusion reactions)

### 4. Methods and Materials

This observational descriptive study was conducted in a tertiary care teaching hospital over a period of 2 months that is July 2018 to September 2018. Ethical clearance was obtained from the Institutional Ethical Review board.

The transfusion reactions were worked up as outlined in the departments' standard operation procedures prepared in accordance with the guidelines laid down by the Directorate General of Health Sevices (DGHS) Technical manual, Ministry of Health, Government of India.<sup>5</sup>

The study was conducted in patients receiving transfusion of blood and blood components in the selected units. Each unit of blood or blood component was considered a separate

transfusion. Patients with a previous history of transfusion or those receiving more than one unit of blood or blood components were considered as having received multiple transfusions. An informed written consent was obtained from the patients or guardians before enrollment<sup>4</sup>. Detailed information of enrolled patients including age, gender, department under which admitted, hemoglobin percentage before transfusion, indication for transfusion, number of transfusions, time of onset of transfusion since issue of blood component from the blood bank, duration of transfusion, nature of the component transfused and type transfusion reactions like fever, chills, rigors, blood pressure, pulse, rashes, abdominal pain, vomiting, giddiness, sweating, shortness of breath, unconsciousness, evidence of jaundice, high colored urine, epilepsy, volume of blood transfused before reaction, previous history of any general allergic reaction, previous history of transfusion/s, previous history of reaction to blood transfusion/s and other necessary relevant data was collected by direct observation, interrogation with the patient, from treating consultant, attending ward staff nurse as well as from the transfusion reaction cards returned to the blood bank and case records of the patients.

Instructions to the clinical residents and nursing staffs in the wards were given regarding reporting of adverse events related to transfusion.<sup>3</sup>

Each patient was followed up till discharge to monitor transfusion related adverse reactions.

### 5. 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.
- 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.
- 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: 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 post transfusion 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.
- 7) Laboratory investigations in the Department of Transfusion Medicine.

## Gross examination:

\*Blood bag and transfusion set were examined for any abnormal findings namely discoloration, clot, and hemolysis or foul smell.

\*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.

\*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 was also done.

\*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.

## 8) Other supportive laboratory investigations of hemolytic reaction:

\*Quantitative estimation of plasma hemoglobin by the peroxidase method. Here every effort was made to prevent hemolysis during collection of the blood sample.

\*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.

\*Peripheral blood smears examination for the presence of schistocytes and spherocytes.

## 9) In non-hemolytic transfusion reactions investigations were done according to their clinical presentations namely in:

In suspected Transfusion-related acute lung injury (TRALI): Chest X-ray

Estimation of serum calcium in suspected hypocalcemia

Skin biopsy in suspected transfusion associated graft vs. host disease (TAGvHD).

\*Serological testing on pre and post transfusion samples was done

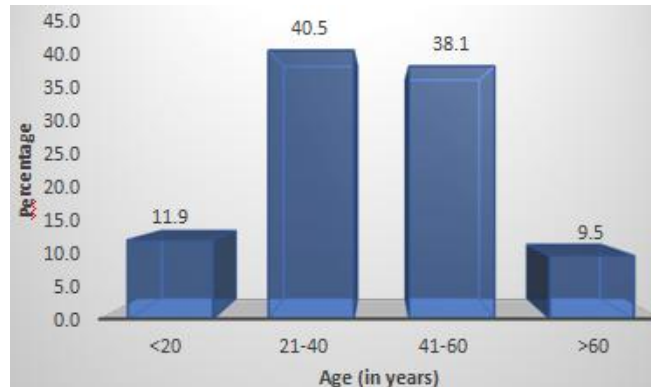
Febrile nonhemolytic transfusion reaction (FNHTR) and allergic and anaphylactoid reactions were diagnosed by their clinical features namely fever, rigors, chills, and rashes which had no primary causes for their manifestation.

Definition of FNHTR as given in American Association of Blood Banks technical Manual 16th ed. "A body temperature rise of  $>1^{\circ}\text{C}$  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.<sup>6</sup>

## 6. Observation and Results

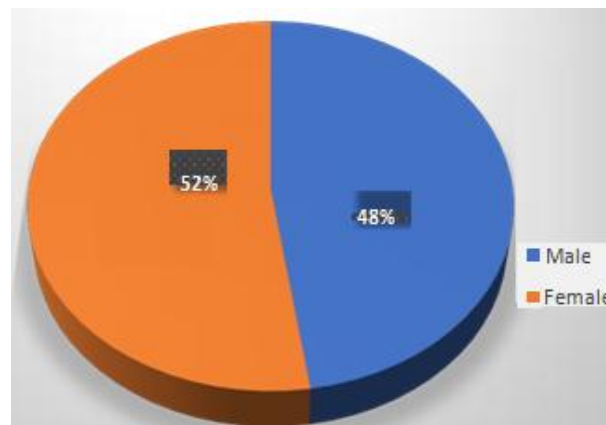
A total of 1640 units of whole blood and component transfusions were carried out in the study duration, out of which a total of 42(2.56%) ATRs were encountered.

Demographic characteristics of the recipients reported with transfusion reactions were recorded.



Bar diagram 1: Age distribution of patients with transfusion reactions

The age of the recipients with transfusion reactions ranged from  $< 20$  years to  $>60$  years. Maximum reactions were seen between 21-40 years of age.



Bar diagram 2: Distribution of patients with transfusion reaction according to department

There was a female preponderance (52.4%) in the frequency of transfusion reactions, over males (47.6%). However, this difference was not significant ( $P>0.05$ )

Maximum 16 (38.1%) cases were seen with patients admitted to the department of General Medicine, followed by department of General Surgery (26.2%) and OBG(19%).

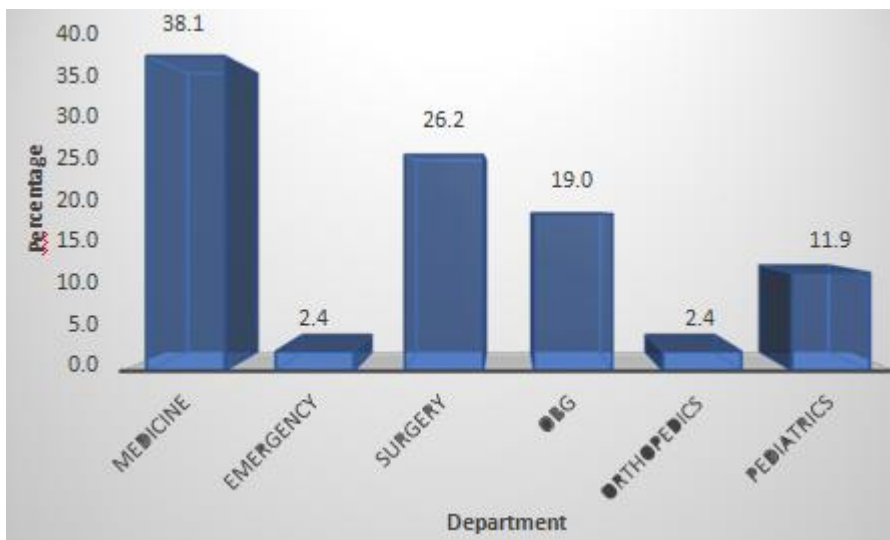
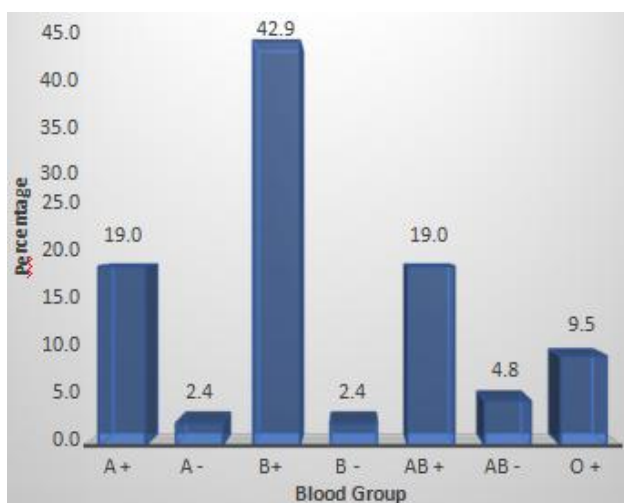


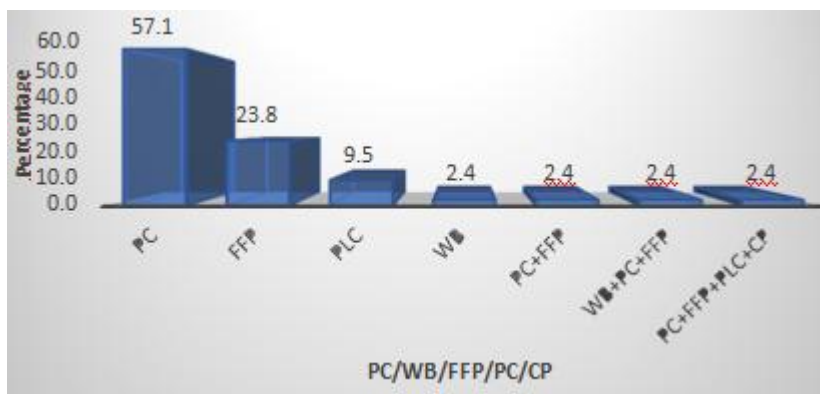
Chart 1: Gender distribution of patients with transfusion reaction



Bar diagram 3: Blood group wise distribution of patients with transfusion reaction

Maximum adverse transfusion reactions were seen in patients with blood group B positive (42.9%) followed by A positive (19%) and AB positive (19%)

Transfusion with packed cells (PC) was most commonly associated with adverse reactions (24 reactions out of a total of 42 transfusions=57.1%), followed by fresh frozen plasma (FFP) transfusions (10 reactions out of a total of 42 transfusions=23.8%)



Bar Diagram 4:

**Table 1:** Febrile reaction was the most frequently encountered transfusion reaction (69%). This was followed by Grade

Transfusion Reaction Encountered	Frequency	Percent
Febrile	29	69.0
Grade 1	8	19.0
Grade 2	5	11.9
Total	42	100.0

1(19%) and Grade 2(11.9%) reactions. No hemolytic reactions were encountered in the study period. FEBRILE reaction is defined as: During or within 3 hours of transfusion

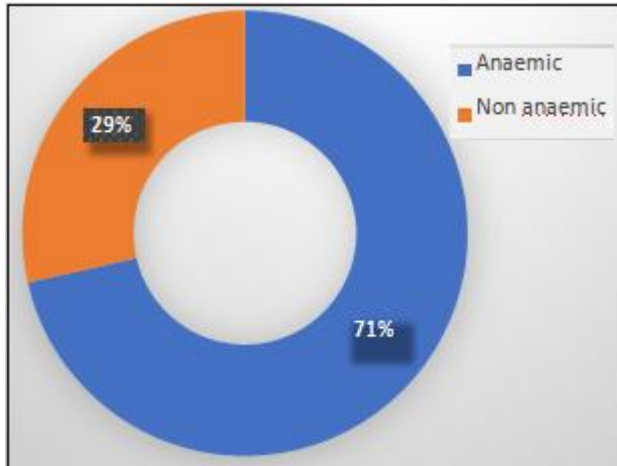
Grade 1 as: Rise of temperature upto 2 degree F

Grade 2 as: Rise of temperature to more than 2 degree F + feeling cold

**Table 2:** Various reasons for transfusion reaction

Reason For Reaction	Frequency	Percent
Repeated blood transfusion	30	71.4
Febrile non haemolytic reaction	12	28.6
Total	42	100.0

Patients undergoing multiple transfusion reactions encountered the maximum adverse events considering it to be the probable cause.



**Chart no. 2:** Relation between levels of hemoglobin of patient and occurrence of adverse transfusion reactions.

Considering levels of normal Hemoglobin in males to be 14-16gm/dl and females to be 12-15gm/dl, patients less than haemoglobin levels 14gm/dl and 12gm/dl respectively were taken as anaemics.

Majority of cases of adverse transfusion reactions were seen in Anaemics(71.4%) than Non Anaemics(28.6%).

## 7. Discussion

Hemovigilance is a standard tool to advance the quality of the blood transfusion chain primarily focusing on safety. Hemovigilance is required for every health institution to have an inclusive approach to address the adverse events following transfusion of blood and blood products. The present observational descriptive study was carried out for a period of 2 months, from July 2018 to September 2018 at a tertiary care centre.

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.<sup>5</sup>

The information obtained is intended to bring about required changes in transfusion policies, improve transfusion standards, assist in the formulation of transfusion guidelines, and thus improve safety and quality of the transfusion process. It is thus not only an avenue to analyze blood transfusion incidents, but also a tool to measure the effects of new processes or corrective actions implemented to remedy their causes and prevent their recurrence.<sup>1</sup>

In this study, the frequency of ATRs was observed to be 2.56%, which was comparable to that of a study carried out in Punjab, where the incidence of ATRs was 1.09%. Two larger studies done in New Delhi and Chandigarh, however, showed a relatively lower frequency of transfusion reactions (0.05% and 0.18%, respectively). A study in Switzerland and the Quebec hemovigilance system reported transfusion reaction rates of 0.042% and 0.035%, respectively. The incidence of transfusion reactions at our center was thus higher than that observed at some national and international centers.

Studies	Females		Males	
	Frequency	Percentage	Frequency	Percentage
Dhruva Kumar et al. (2015)	72	59.4%	28	40.6%
Sinha RTK et al. (2016)	11	73.3%	04	26.7%
Praveen kumar et al. (2013)	76	45.5%	120	54.3%
Chavan SK. et al. (2016)	32	71.1%	13	28.9%
Present study		52.4%		47.6%

In the present study there is a female preponderance with 52.4% which is comparable to the study conducted by Dhruva Kumar et al. (59.4%)

Various studies	Department with maximum cases of adverse transfusion reactions
Chavan SK. Et al.(2016)	Department of Medicine
Praveen Kumar et al.(2013)	Department of General surgery
Dhruva Kumar et al.(2015)	Department of General Medicine
Present Study (2018)	Department of General Medicine

In the present study the maximum cases are seen with department of medicine with is similar to the study by Chavan SK and Dhruva Kumar.

	Febrile reactions		Allergic reactions		Tachycardia		Anaphylactoid reactions	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Chakravarty- Vartak, <i>et al.</i> (2016)	19	38%	12	24%	9	18%	1	0.08%
Sinha RTK <i>et al.</i> (2016)	2	13.33%	5	33.33%	2	13.33%	2	12.50%
Asha Latha <i>et al.</i> (2016)	6	37.50%	8	50%	NIL	NIL	4	3.80%
Sidhu Meena <i>et al.</i> (2015)	43	41%	36	34%	NIL	NIL	NIL	NIL
Praveen kumar <i>et al.</i> (2013)	70	35.70%	108	55.10%	NIL	NIL	NIL	NIL
Dhruva kumar <i>et al.</i> (2015)	9	0.26%	21	0.60%	NIL	NIL	NIL	NIL
Chavan SK <i>et al.</i> (2016)	15	33.30%	25	55.60%	NIL	NIL	NIL	NIL
Present study(2018)	29	69%	NIL	NIL	NIL	NIL	NIL	NIL

The percentage of febrile reactions occurring in present study is 69% which is comparable to the study conducted by Sidhu Meena *et al.*(41%)

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.

## 8. Conclusion

Febrile and Grade 1 reactions constituted the majority of adverse transfusion reactions encountered, with maximum cases belonging to the department of General Medicine, repeated blood transfusions being the probable cause. The overall incidence of transfusion reactions in this hospital is slightly higher than those having more advanced transfusion facilities in India. There was no significant difference among the overall incidence of ATRs based on the type of component transfused. The use of leuko reduced WB and PRBCs could possibly reduce the incidence of ATRs in general and FNHTRs in particular.

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.<sup>6</sup>

## 9. Summary

- 1) The age of the recipients with transfusion reactions ranged from < 20 years to >60 years. Maximum reactions were seen between 21-40 years of age
- 2) There was a female preponderance (52.4%) in the frequency of transfusion reactions, over males (47.6%).
- 3) Maximum Adverse transfusion reactions were seen with patients admitted to the department of General Medicine(38.1%).
- 4) Maximum adverse transfusion reactions were seen in patients with blood group B positive (42.9%).
- 5) Transfusion with packed cells (PC) was most commonly associated with adverse reactions (24 reactions out of a total of 42 transfusions).

- 6) Febrile reaction was the most frequently encountered transfusion reaction (69%).
- 7) Patients undergoing multiple transfusion reactions encountered the maximum adverse events.

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