**Recipient Hemovigilance at a Tertiary Care Hospital in Southern India: A Cross-Sectional Study**

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**Abstract**

**Introduction:** Information on incidence of various transfusion reactions could help in early recognition as well as management and could also help to institute adequate measures to make blood transfusion as safe as possible. The primary objective of the present study was to determine the frequency and types of adverse transfusion reactions in patients who required blood component transfusion. **Methodology:** This was a cross-sectional, observational study conducted over a period of 22 months from September 2014 to June 2016 in the Department of Transfusion Medicine, JIPMER. All patients admitted to the wards of various specialty departments who were transfused with blood components and reported to have transfusion reaction during or after transfusion of blood components were included in the study. **Results:** A total of 90,758 components were issued during the study period, and 137 transfusion reactions were reported which accounted for 0.15% of total transfusions. Febrile nonhemolytic transfusion reaction (46.7%) was the most common reaction followed by allergic reaction (31.3%). Among different blood components, packed red blood cells (82%) were most commonly associated with transfusion reactions. **Conclusion:** Transfusion reactions unless serious are grossly underreported either due to lack of attributing the adverse event to transfusion or because the milder reactions are usually managed and unreported as the staff are too often used to having them, especially in chronically transfused patients.

**Keywords:** Blood components, hemovigilance, transfusion reaction

**Introduction**

Blood transfusion is a common and important component of medical therapeutics. Although blood transfusion can be a life-saving intervention, inappropriate use can endanger life because of infectious and noninfectious complications. It is, therefore, important that blood is administered with a clear understanding of risks and benefits.

The risks associated with blood transfusion were previously assumed to be predominantly due to infectious complications. However, over a period, infectious complications have reduced to all time low because of improvements in donor screening, advances in the infectious disease testing, introduction of pathogen reduction technology, etc.

On the other hand, risks of noninfectious complications of blood transfusion, especially transfusion-associated lung injury, transfusion-associated cardiac overload (TACO), and hemolytic transfusion reactions (HTRs), now account for significant morbidity and mortality. As a result of these, many countries have started hemovigilance systems (“hema” = blood and “vigilance” = paying particular attention to) to collect and assess the information on the incidence of these complications and to prevent occurrence and recurrence of this complications. In India, a centralized program, Haemovigilance Programme of India was started on December 10, 2012.

Data on incidence of various transfusion reactions could help in early recognition as well as management and could also help to institute adequate measures such as creating awareness among healthcare providers, introducing more sensitive immunohematological techniques, and use of modification in products such as leukoreduction and irradiation to make blood transfusion as safe as possible.

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Hence, the present study was undertaken with the primary objective of determining the frequency and types of adverse transfusion reactions occurring in patients who required blood component transfusion in our hospital located in South India and also to compare the data with other national and international studies.

Methodology

This was a cross-sectional study conducted over a period of 22 months from September 2014 to June 2016 in the Department of Transfusion Medicine, JIPMER, after obtaining the necessary approvals from the institutional research committees. The data were collected retrospectively from the reports and registers maintained in the department in real-time with no additional testing or change in the protocol for the purpose of the study. The institutional ethics committee approved the study under “less than minimal risk” category with waiver of consent from the included subjects, as it was a record-based study. All patients admitted to the wards of various specialty departments who were transfused with blood components issued by JIPMER blood bank and reported to have transfusion reaction during or after transfusion of blood components were included in this study. A sensitization for reporting adverse transfusion reactions was performed by conducting seminars and continuing medical education for the residents, interns, nursing staff, and regular inputs daily by calling each ward for the first 3 months. Feedback form along with compatibility form was issued with all components containing the various details of the intended patient including name, hospital number, ward, ABO, Rh group, type of blood component, blood bag number, cross-match details, and details regarding transfusion which included time of completion. Duly filled feedback forms for all transfusions were returned. In case of any reaction, the filled feedback form including details of signs and symptoms noticed, vitals of the patient prior, during and at the end of transfusion along with posttransfusion blood sample (2 ml EDTA and 5 ml clotted sample), first voided urine sample, and leftover blood bag with attached transfusion set was returned to the blood bank. After standard testing protocols, the type of reaction was ascertained in correlation with the signs and symptoms in the recipient. All noninfectious reactions (immediate and delayed) including both immunological such as hemolytic, febrile, and allergic and nonimmunological such as circulatory overload and dyspnea which had a temporal association with transfusion during the stay of the patient in the hospital as well those reported later, if any, were included in the study.

The transfusion reaction workup was done according to the Departmental Standard Operational Procedure based on the recommendations and guidelines from the Central Drugs Standard Control Organization and National AIDS Control Organization for blood safety. The protocol included checking into clerical errors, physical changes in the blood products and samples, immunohematological workup including regrouping and compatibility testing, Coombs test (both direct and indirect), biochemical tests, imaging, and microbial culture if applicable. These tests were correlated with the reported clinical profile of the patient to classify the transfusion reaction. The reactions were also reported to the National Hemovigilance Programme of India through their online portal.

The details were entered and analyzed using Microsoft Excel 2007.

Results

During the study period, 90,758 blood components were issued for transfusion from our department. The details of the various components transfused are given in Table 1. Of the total 90,758 component transfusions, a total of 137 transfusion reactions were reported. This comprised of 0.15% of total transfusions. Seventy of these reactions were noted in males and the remaining 67 were in the females. Twenty-two of these reactions were noted among pediatric age group patients. Fifty patients had a previous history of transfusion, 32 patients had a previous history of pregnancy, and 13 patients had a history of previous transfusion and pregnancy. In four cases, patients had a previous history of transfusion reaction (three had febrile non-HTR [FNHTR] and one had allergic reactions).

Overall, 49.6% of patients who had transfusion reactions had received transfusion for the hematological indications. In the next 30%, the transfusion was carried to correct perioperative anemia. Rest of them had received transfusion due to bleeding in emergency situations.

Distribution of transfusion reactions by different components

Among the 137 transfusion reactions reported, most of them were due to packed red blood cells (PRBCs) followed by random donor platelets (RDP) and fresh frozen plasma (FFP). In four cases, patients received multiple blood components (PRBC and FFP in 3 cases and PRBC, FFP, and RDP in one case) before developing a transfusion reaction.

In our study, no reaction was reported with cryoprecipitate and cryo-poor plasma transfusion.

Department-wise distribution of transfusion reactions

The incidence of transfusion reactions was more commonly seen in surgical departments, and most of the transfusions were
done for correction of preoperative and postoperative anemia and to control active bleeding. Table 2 shows the distribution of transfusion reactions among different departments.

Blood group-wise distribution of transfusion reactions

Among blood groups, B-negative and AB-positive patients had a higher incidence of transfusion reactions compared to others. Table 3 shows blood group-wise distribution of transfusion reactions.

Incidence of different types of transfusion reactions

FNHTR was the most common transfusion reaction in our study followed by allergic transfusion reaction. Signs/symptoms which could not be classified into any of the types of transfusion reaction occurred in six patients. Different types of transfusion reactions reported in our study are shown in Table 4.

Relative frequency of transfusion reactions by various products

A total of 112 (0.31%) transfusion reactions occurred out of 35,334 PRBC transfusions. The most common transfusion reaction reported was FNHTR followed by allergic reaction. All nonspecific reactions as mentioned previously occurred with PRBC transfusion.

A total of 10 (0.035%) transfusion reactions occurred out of 28,483 FFP transfusions. Allergic reaction \((n = 7)\) to the plasma protein was the most common followed by FNHTR \((n = 3)\). One severe anaphylactic reaction to the FFP was reported in a case of Guillain–Barre syndrome.

A total of 11 (0.04%) transfusion reactions occurred out of 24,476 platelet transfusions. Platelet transfusions include both whole-blood-derived and apheresis-derived platelets. Allergic reaction \((n = 8)\) to the plasma proteins was common with platelet transfusions. A case of HTR was reported with single donor platelet when group “O” unit was transfused to the group “B” patient. One case each of FNHTR and anaphylactic reaction was reported.

Table 4 shows estimated risk of transfusion reaction of individual blood component (number of transfusion reactions observed divided by total number of particular component issued).

Hemolytic transfusion reactions

The incidence of HTRs in our study population found to be 0.008% \((n = 8)\) and included four ABO-incompatible HTR, three non-ABO-incompatible HTR (due to anti-Fy\(^a\), anti-M, and anti-Le\(^b\)), and one case of nonimmune HTR due to mechanical lysis of blood due to improper storage.

Febrile nonhemolytic transfusion reactions

The incidence of FNHTR in our study was found to be 0.07%, and it constituted 46.7% \((n = 64)\) of total transfusion reactions. Thirty-five males and 29 females developed FNHTR and mean volume transfused was 107.83 ml.

Of 64 patients, 51 patients had a history of fever while remaining 13 patients developed chills and rigors without

Table 2: Department-wise distribution of adverse transfusion reactions

| Department                  | \(n\) (%) |
|-----------------------------|----------|
| Surgery                     | 30 (22.05) |
| Obstetrics and gynecology   | 28 (20.05) |
| Medicine                    | 22 (15.4)  |
| Pediatrics                  | 17 (12.5)  |
| Pediatric surgery           | 5 (3.6)    |
| Cardio thoracic vascular surgery | 4 (2.9)   |
| Medical oncology            | 4 (2.9)    |
| Radiotherapy                | 4 (2.9)    |
| Urology                     | 4 (2.9)    |
| Surgical oncology           | 3 (2.2)    |
| Surgical gastroenterology   | 3 (2.2)    |
| Orthopedics                 | 3 (2.2)    |
| Others                      | 10 (7.3)   |
| Total                       | 137 (100)  |

Table 3: Blood group-wise distribution of adverse transfusion reactions

| Blood group  | Number of components issued | \(n\) | Incidence (%) |
|--------------|-----------------------------|------|---------------|
| O positive   | 30,861                      | 52   | 0.17          |
| B positive   | 26,762                      | 43   | 0.16          |
| A1 positive  | 13,873                      | 23   | 0.16          |
| AB positive  | 4975                        | 11   | 0.22          |
| B negative   | 1632                        | 5    | 0.30          |
| O negative   | 2400                        | 2    | 0.08          |
| A1 negative  | 860                         | 1    | 0.11          |
| Others       | 9395                        | -    | -             |
| Total        | 90,758                      | 137  | 100           |

Table 4: Different categories of transfusion reactions and product-wise estimated risk

| Type                        | Transfusion reactions, \(n\) (%) | Product implicated and ER of transfusion reactions by product |
|-----------------------------|---------------------------------|---------------------------------------------------------------|
| FNHTR                       | 64* (46.7)                      | PRBC, \(n\) (ER) | FFP, \(n\) (ER) | Platelets, \(n\) (ER) |
| Allergic reactions          | 43** (31.3)                     | 60 (1.69) | 7 (0.24) | 1 (0.04) |
| HTR                         | 8 (5.83)                        | 26 (0.70) | 1 (0.04) |
| Nonspecific reactions       | 8 (5.83)                        | 9 (0.19) | - | - |
| Anaphylactic reactions      | 6 (4.3)                         | 4 (0.11) | 1 (0.03) | 1 (0.04) |
| TACO                        | 4 (2.9)                         | 4 (0.11) | - | - |
| TRALI/TAD                   | 3 (2.18)                        | 3 (0.08) | - | - |
| Total                       | 137                             | - | - | - |

*One of the patients had received multiple components, **Two of the patients had received multiple components. HTR=Hemolytic transfusion reaction, FNHTR=Febrile non-HTR, TACO=Transfusion-associated cardiac overload, TRALI=Transfusion-associated lung injury, TAD=Transfusion associated dyspnea, ER=Estimated risk, PRBC=Packed red blood cell, FFP=Fresh frozen plasma.
any history of fever. Eighty-five percent of the FNHTR to the red cells occurred with bags which are more than 7 days old. Table 5 shows details of febrile transfusion reactions in relation to the age of PRBC. 65.25% of patients with FNHTR had a history of previous transfusion or pregnancy.

**Allergic transfusion reactions**

Incidence of allergic transfusion reactions in our study was 0.047% and constituted 31.3% (n = 43) of total transfusion reactions. Twenty-two males and 21 females developed allergic transfusion reaction and mean volume transfused was 99.4 ml. Among the 43 patients, 35 patients had rashes all over the body with itching, seven patients developed periorbital edema, and one patient developed wheal below the eye. On analysis of the allergic reactions with the age of RBCs transfused, it was seen that 75% of the allergic reactions occurred with bags which were more than 7 days old as shown in Table 5.

As in the case of FNHTR, most of the patients (72%) with allergic reaction had a history of previous history of sensitization. One of the patients had a history of allergy to other substances. Immunohematological workup of these patients was unremarkable. All the patients of allergic reaction received antihistamines and hydrocortisone and recovered without any clinical sequelae.

**Mixed allergic and febrile reactions**

Three patients (2.18%) had signs and symptoms of both febrile and allergic transfusion reactions. All these reactions were due to the PRBC transfusion. All three patients had fever with rigors and itching and rash. Two of the patients had a prior history of sensitization in the form of transfusion or pregnancy. Bacterial culture and immunohematological workup were unremarkable in these cases. All three patients recovered without any clinical sequelae.

**Anaphylactic transfusion reaction**

The incidence of anaphylactic transfusion reactions in our study was found to be 0.006% and constituted 4.3% (n = 6) of total transfusion reactions. Among six patients, three were males and three were females. Rash and hypotension were the most common sign/symptom of anaphylactic reactions occurred with bags which were more than 7 days old as shown in Table 5.

Of the 90,758 components transfused, the incidence of transfusion reactions in our study was found to be 0.15%. When compared to the other studies, much lower incidence was reported in hemato-oncology patients in our study, which can be probably due to the underreporting of mild transfusion reactions. Narvios et al., in their study on oncology patients observed that underreporting of mild transfusion reactions such as FNHTR and allergic reactions in oncology patients is more common compared to nononcology patients. They attributed it to the expertise of the nursing and medical personnel in the oncology setups in the handling of minor transfusion reactions and not reporting them. In our study, majority of transfusion reactions are due to PRBC transfusions. Reaction to the FFP and platelets transfusion was found to be much less compared to the other studies by Kumar et al. and Sharma et al. It can be due to attributing the signs and symptoms to the prevailing disease condition rather than to a transfusion reaction is more common with platelets and FFP compared to the PRBC. In the case of patients receiving multiple transfusions, transfusion reaction is usually attributed to PRBC compared to other components by our physicians and health caregivers. Incidence is similar to studies done in other parts of Asia, but much lesser incidence is reported in study done by AIIMS, New Delhi (0.018%), probably because of usage of leukoreduced blood components at their center.

In our study, FNHTR and allergic reactions were the common adverse reactions to blood transfusion, which is similar to the other studies. Leukocytes and inflammatory mediators responsible for FNHTR are present in the plasma, which comprises 30%–40% of PRBC, but it is the main component in case of platelets, so higher incidence is expected with platelets compared to PRBC. In our study, it was found that incidence was more with PRBC compared to the platelets. This could be due to more amount of leftover plasma during component preparation in products collected with no additive.

### Table 5: Incidence of transfusion reactions (all) and febrile nonhemolytic transfusion reaction in relation to the expiry of packed red blood cells

| Age of PRBC | Number of reactions (%) | Number of FNHTR (%) |
|-------------|-------------------------|---------------------|
| 0-7 days    | 9 (15)                  | 5 (25)              |
| 8-14 days   | 21 (35)                 | 12 (48)             |
| 15-21 days  | 18 (30)                 | 4 (16)              |
| >21 days    | 12 (20)                 | 4 (16)              |
| Total       | 60                      | 100                 |

HTR=Hemolytic transfusion reaction, FNHTR=Febrile non-HTR, PRBC=Packed red blood cell

**Transfusion-associated cardiac overload**

The incidence of TACO in our study was found to be 0.004% and constituted 2.9% (n = 4) of total transfusion reactions. Three out of four patients had a history of the preexisting cardiac disease.

**Discussion**

Blood transfusion is a double-edged sword in the sense that though it is life-saving, transfusion reactions which are sometimes fatal can occur. The present study was conducted with the primary objective of estimating the incidence of transfusion reactions in blood transfusion recipients of JIPMER. JIPMER is a multispecialty tertiary care hospital and teaching institute. Incidence of transfusion reactions to the blood components varies widely among different centers which can be due to type of reporting system, population included, local policies on premedication, modification of blood products, and monitoring and reporting or even defining the transfusion reaction itself.

Of the 90,758 components transfused, the incidence of transfusion reactions in our study was found to be 0.15%.
solution. This is also the case with allergic reactions wherein the plasma components are the ones commonly implicated due to the presence of immunological proteins in them.\[^{[10]}\] Hence, standardization in the component preparation will help in reducing the incidence of FNHTR to PRBC. Seventy-five percent of the patients who developed FNHTR in the present study had a history of prior sensitization in the form of transfusion or pregnancy. It is known that these events lead to the formation of anti-HLA antibodies which are responsible for the occurrence of FNHTR. Similar results were also reported by Vasudev et al. in their study where most of the patients (68%) had a previous history of sensitization.\[^{[5]}\]

In our study, no case of transfusion-associated sepsis, delayed HTR, and hypotensive transfusion reaction was reported. The reason for absence of septic transfusion reaction probably could be due to attributing fever after transfusion to the patient disease condition or negative culture results, as most of the patients will be on antibiotic therapy or can be due to the low sensitivity of culture techniques.\[^{[12]}\] All patients who had developed signs/symptoms of TACO did so with a single unit of transfusions, probably because of three out of four patients had a history of preexisting cardiac disease. Similarly, Popovsky and Taswell reported that in around 20% of the cases single unit of PRBC was sufficient to cause the reaction, and each of the cases had underlying cardiac or pulmonary disease.\[^{[14]}\]

The limitations of the study were that the study was dependent on reporting transfusion reactions by the resident and nursing staff, so there would be underreporting and mild transfusion reactions may be missed. Some of the workup of the transfusion reactions could not be completed either because of death of the patients or complete transfusion of the component, especially platelet and FFP leaving no component behind for completing the testing. Confirmatory diagnosis of reactions such as anaphylactic can be made only after measuring serum IgE levels,\[^{[12]}\] but no such investigations were available at our setting.

**Conclusion**

Hemovigilance gives insight into the current ongoing practices and helps in identifying areas for improvement and standardization. Obtaining previous history of transfusion reactions will help in providing appropriate component such as washed blood components or antigen-negative PRBC to reduce the further reactions. Better preparation techniques leading to lesser residual alternate components such as plasma in PRBC shall also reduce few of the reactions. Similarly, better immunohematological techniques can reduce immune-mediated transfusion reactions. Education of nursing staff, resident doctors, and interns in the handling, administration, and storage of blood components and also signs and symptoms of transfusion reactions will help in diagnosing and reporting of more transfusion reactions. Strict adherence to the blood bank standard operating procedure by technical staff will be helpful in reducing never events such as ABO-incompatible HTR.

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**Conflicts of interest**

There are no conflicts of interest.

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