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ORIGINAL ARTICLE

Surveillance of Transfusion Related Adverse Reactions in a Tertiary Care Centre in Bangalore: A 4-Year Hemovigilance Initiative

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Abstract Even though blood transfusion is a life saving measure, it is nonetheless associated with a number of risks and hazards. The adverse reactions that can be potentially expected range anywhere in severity from mild to life threatening. The hemovigilance program deals with the systematic surveillance of these reactions as and when they occur in a hospital setting with an explicit aim of improving the quality and safety standards of the entire transfusion process. The current study was undertaken in the blood bank of a tertiary care centre in Bangalore to ascertain frequency of the blood transfusion related adverse reactions and to make a systematic profile assessment. Data was collected over a period of 4 years and 3 months. All adverse reactions caused by transfusion of blood and its products during the study period were included in the study. A total of 6910 units of blood and its components were issued to patients during the study period. Transfusion reactions accounted for 0.5% of transfusions. Febrile non-hemolytic transfusion reactions were the most common reactions (51.4%) followed by allergic reactions (40%), fluid overload (5.7%) and anaphylactic reactions (2.9%). Majority of these reactions were seen with PRBC transfusions (74.3%) followed by platelet transfusions (25.7%). The use of leukoreduced PRBCs will help in reducing the frequency of these reactions. The hemovigilance program of our institution helps in assessing the diversity of adverse reactions associated with transfusion of blood and its various components. It is also an efficient scheme for minimizing their occurrence by ensuring safety standards.

Keywords Transfusion reactions · Hemovigilance program · Febrile non-hemolytic transfusion reactions · Allergic reactions

Introduction

Blood transfusion has become an integral part of modern medical practice [1]. Though a lifesaving and relatively safe procedure, it is not entirely free of risks and hazards. The potential adverse reactions associated with any blood transfusion can range from mild to life threatening. Hemovigilance is the systematic surveillance of these type of reactions in a hospital setting [2]. It is done with the aim of improving both the quality and the safety standards of the transfusion process. The practice was initiated in France in the early 1990s and later gained popularity in the international health community. It was soon followed by the Serious Hazards of Transfusion program (SHOT) launched in the United Kingdom in 1996. Nearly 366 deaths were reported as a part of this initiative, 52% of which were due to transfusion of incompatible blood to the recipient [3]. The hemovigilance program of India was launched on 10th of December 2012. Its prime objective was to ascertain the frequency of adverse reactions that occur during blood transfusions and to provide appropriate interventions in view of patient safety and care [4]. Despite the fact that the available advanced testing modalities have reduced the overall frequency of these adverse reactions, their incidence due to human error, alloimmunization, immunomodulation and bacterial contamination still remain a cause for concern [5, 6]. The

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current study was undertaken to ascertain the frequency of the blood transfusion related adverse reactions and to profile them.

Materials and Methods

The current retrospective study was conducted in the blood bank of a tertiary care centre in Bangalore. Data was collected over a period of 4 years and 3 months starting from October 2015 up to December 2019. Informed consent was obtained from the donors and recipients as per the institutional requisites and international ethical guidelines. All the adverse reactions caused due to transfusion of blood and its products were recorded in transfusion reaction forms and were reported in the blood bank. These transfusion reaction forms were formulated on par with the guidelines provided by Director General of Health Services Technical Manual, Ministry of Health and Family Welfare, Government of India.

Details of the investigations done for transfusion related adverse reactions:

1. Patient's name, age, gender, in-patient number, blood group were rechecked on the request forms, pretransfusion samples and transfusion reaction forms to rule out any clerical error and wrong sampling.
2. The indications for blood transfusion, past history of transfusions, pregnancy history in case of female patient and similar adverse reactions related to transfusion of blood or its products in the past were noted.
3. The adverse transfusion reactions were recorded in detail like fever, chills, rigors, urticaria, rashes, pain abdomen, hypotension, change in urine colour, jaundice, respiratory discomfort and any other clinical features associated to transfusion reactions.
4. The causative blood component bag was examined for any clots, discolouration, foul smell or leakage.
5. Post transfusion blood samples collected in EDTA tube were sent to the blood bank for relevant investigations.
6. Post centrifugation plasma was examined for any colour change. A pink or red tinge was taken to indicate the presence of hemolysis.
7. ABO and Rh typing (cell and serum grouping) on patient's samples and implicated blood component was done.
8. Compatibility testing was done by gel card method.
9. Screening of antibodies was done.
10. Direct antiglobulin test was done.
11. Blood bag and the patient's sample was sent to microbiology laboratory for culture. [Usually if the growth of microorganisms is same in the patient as well as in the transfused component then bacterial contamination of the blood unit is confirmed.]
12. Patient's urine was tested for hemoglobinuria.
13. Relevant blood tests like complete blood count, reticulocyte count, peripheral blood smear for schistocytes and spherocytes, serum bilirubin (direct and indirect), blood urea, serum creatinine, prothrombin time and activated partial thromboplastin time were done.
14. Chest X-ray, ECG and other relevant investigations were carried out.

The data collected during the study period was analysed for percentage, frequency, mean and standard deviation. Statistical software used was Microsoft Office Excel 2019 and IBM SPSS Statistics version 20 (Statistical Package for the Social Sciences IBM Corporation).

Results

A total of 6910 units of blood and its components were issued to patients during the 4 years and 3 months study period. Out of them, 35 patients developed adverse transfusion reactions accounting for 0.5%. Table 1 depicts the demographic characteristics of the transfusion reaction patients. The age of the patients ranged from 17 to 68 years with mean age of 40.9 years. There was female preponderance (65.7%) compared to males (34.3%). The mean age of female patients was 40.9 years with a standard deviation of 13.7 and that of males 41.2 years with standard deviation of 14.3. Transfusion reactions were more commonly seen in 3rd, 4th and 5th decade [9 cases each (25.7%)] and were least commonly seen in 2nd decade [1 case (2.9%)] (Table 2).

The most common blood group among patients was O positive [17 cases (48.6%)] followed by B positive [11 cases (31.4%)] and A positive [6 cases (17.1%)]. One patient (2.9%) was of B negative blood group (Table 1). Figure 1 shows the total number of transfusion reactions that occurred during our study period. All the transfusion reactions in the present study were acute reactions. We did not encounter any delayed reactions. Adverse transfusion reactions were more common with transfusion of PRBCs [26 reactions out of 2833 transfusions (74.3%)] as compared to that of platelets [9 reactions out of 1113 transfusions (25.7%)]. There were no reactions observed with the transfusion of the whole blood or that of fresh frozen plasma.

Table 1 Demographic characteristics of the transfusion reaction patients (n = 35)

Variable	Values
Gender	
Males	12 (34.3%)
Females	23 (65.7%)
Age (years)	
Range	17–68
Mean age	40.9
Range males	22–65
Mean age males	41.2 ± 14.3
Range females	17–68
Mean age females	40.9 ± 13.7
Blood group	
A+	6 (17.1%)
B+	11 (31.4%)
O+	17 (48.6%)
B−	1 (2.9%)

Table 2 The distribution of age and gender in the transfusion reaction patients

Age (years)	Males	%	Females	%	Total	%
0–10	0	0	0	0	0	0
11–20	0	0	1	4.4	1	2.9
21–30	5	41.6	4	17.4	9	25.7
31–40	2	16.7	7	30.4	9	25.7
41–50	2	16.7	7	30.4	9	25.7
51–60	1	8.3	2	8.7	3	8.6
61–70	2	16.7	2	8.7	4	11.4
> 70	0	0	0	0	0	0
Total	12	100	23	100	35	100

Most of the transfusion reactions occurred in medicine wards or in Medical intensive care unit [19 cases (54.3%)] followed by Obstetrics and gynaecology (OBG) [10 cases (28.6%)] and Surgery [5 cases (14.3%)] departments. Orthopaedic department reported a single case of transfusion reaction (2.8%) (Fig. 2). When signs and symptoms of transfusion reactions were studied, it was found that fever was the most common reaction (27%) followed by chills (26%) and urticaria (17%) (Fig. 3).

Categorization of Transfusion Reactions

Adverse transfusion reactions were classified according to the time of their onset [7].

1. Acute transfusion reactions (onset within 24 h)—Febrile non-hemolytic transfusion reaction (FNHTR), allergic reactions, anaphylactic and anaphylactoid reactions, acute haemolytic transfusion reactions, transfusion related lung injury, bacterial contamination, fluid overload, physical and chemical hemolysis, hypothermia and hyperkalemia.
2. Delayed transfusion reactions (onset after 24 h)—Transfusion-associated Graft-Versus-Host disease, Post transfusion purpura and Iron overload.

Febrile Non-hemolytic Transfusion Reactions (FNHTR)

Altogether 18 patients (51.4%) developed FNHTR, out of which 12 (66.7%) were females and 6 (33.3%) were males. Most of the patients were in 41–50 years age group [5 cases (27.8%)] followed by 31–40 years age group [4 cases (22.2%)]. Age groups 51–60 and 61–70 had 3 cases (16.7%) each. Two cases (11.1%) fell in 21–30 years age group and one case (5.5%) in 11–20 years. Out of the 18

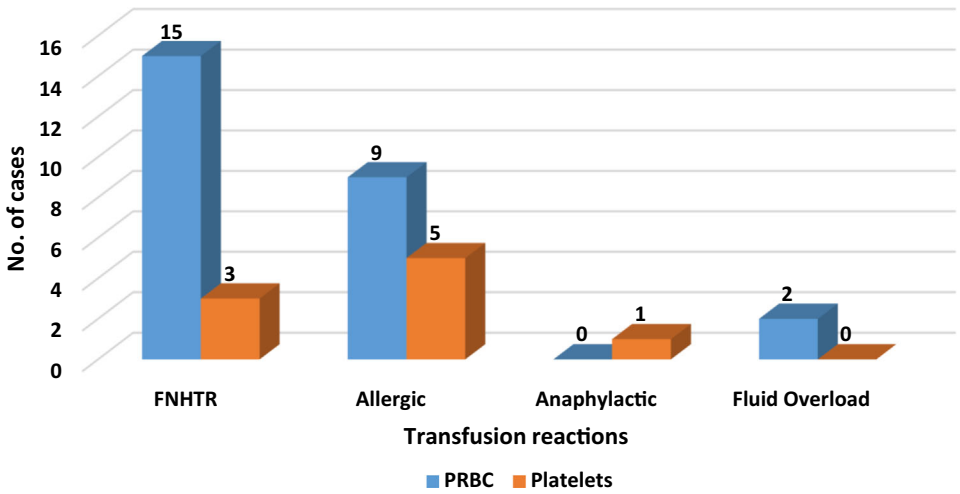

Fig. 1 Different type of transfusion reactions according to the type of blood component used

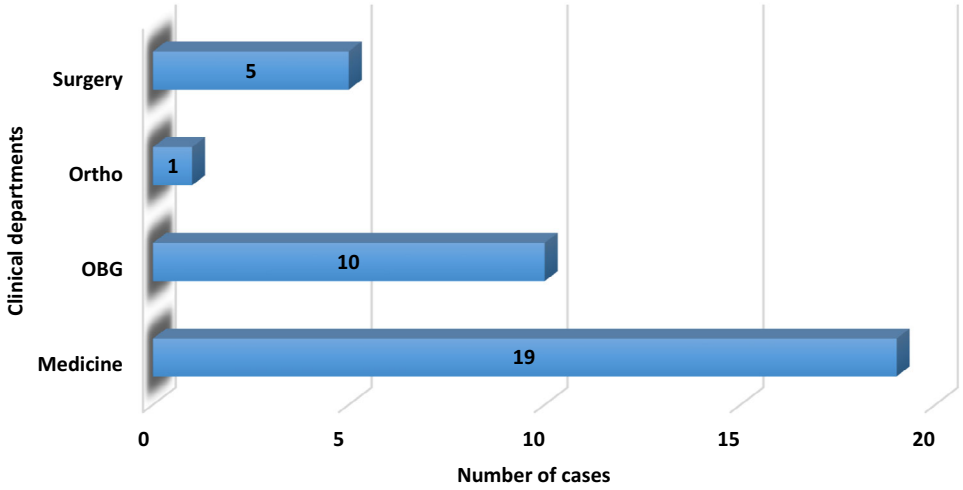

Fig. 2 Transfusion reactions in various clinical departments

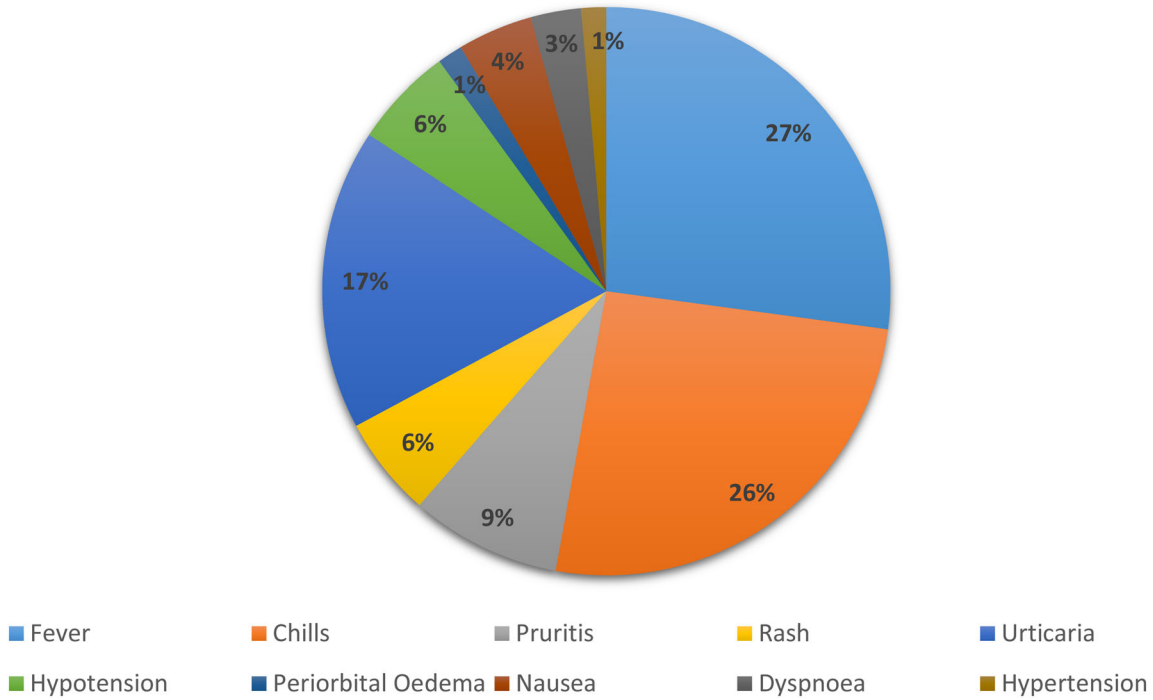

Fig. 3 Signs and symptoms of transfusion reactions

cases of FNHTR, 10 (55.6%) were reported from Medicine department, OBG department reported 4 cases (22.2%), Surgery department reported 3 cases (16.7%) and Orthopaedic department reported a single case (5.5%) of FNHTR. Clinical signs and symptoms observed in decreasing order of frequency were fever (18 cases), chills (13 cases), hypotension (3 cases), nausea (3 cases) and hypertension (1 case). Eight patients (44.5%) were of O positive blood group, 6 patients (33.3%) were B positive and 4 patients (22.2%) were A positive. PRBC transfusion was implicated in 15 cases (83.3%) and platelet transfusion in 3 cases (16.7%).

Allergic Reactions

Allergic transfusion reactions were seen in 14 cases (40%). Out of them 9 (64.3%) were females and 5 (35.7%) were males. Six patients (42.9%) were in 21–30 years age group, 5 patients (35.7%) in 31–40 years and 3 (21.4%) in 41–50 years age group. Medicine department reported 7 cases (50%), OBG department 6 cases (42.9%) and Surgery department 1 case (7.1%). Patients presented with the following signs and symptoms in decreasing order of frequency, Urticaria (11 cases), chills (5 cases), fever (1 case) and hypotension (1 case). When their blood groups were

analysed it was found that eight (57.2%) were of O positive blood group, four (28.6%) were B positive and one (7.1%) each of A positive and B negative blood group. PRBC transfusions were implicated in 9 cases (64.3%) and platelet transfusions in 5 cases (35.7%).

Anaphylactic Reaction

Anaphylactic reaction was seen in one patient (2.9%). He was a 26-year-old male with B positive blood group admitted in the medicine department. He developed urticaria and anaphylactic symptoms during the transfusion of a platelet unit, so transfusion was stopped immediately. Relevant investigations were done and he was given antihistaminic (Injection Avil) and hydrocortisone injections after which his symptoms subsided.

Fluid Overload

Symptoms of fluid overload were observed in 2 patients (5.7%). Both were females aged 50 and 64 years with blood group of O positive and A positive respectively. They were admitted in surgery and medicine departments respectively. PRBC transfusion was implicated in both the cases. They developed symptoms of fluid overload and dyspnoea following which transfusion was stopped and injection Lasix (Furosemide) was administered. They recovered following the treatment.

Discussion

The concept of hemovigilance had its inception in the 1990s as mentioned earlier. From then onwards, it is an ever-growing field and is currently recognized as an imperative component of the quality management of blood transfusion programs worldwide. Ideally it is designed to detect and analyse any untoward events associated with the blood transfusion. The adverse reactions may be acute or delayed depending on the stipulated time of 24 h. They are further sub classified as immunologic or non-immunologic reactions. The estimated frequency of these adverse transfusion reactions ranges from 0.2 to 10%, and their mortality is approximately, 1 in 250,000 [8, 9].

In the present study, the incidence of transfusion reactions was 0.5% which was similar to the study done by Yulu et al. who reported 0.4% incidence [10]. Studies done in Sikkim and Punjab reported higher incidence of transfusion reactions of 0.92% and 1.09% respectively [11, 12]. However, several studies documented lower incidence of transfusion reactions like that of Chandigarh, New Delhi, Switzerland and Quebec hemovigilance system (0.18%, 0.05%, 0.042% and 0.035% respectively) [13–16].

Adverse transfusion reactions were more commonly seen in females (65.7%) in our study compared to males (34.3%). Female preponderance was also noted in studies done in Sikkim (59.4%), Saudi Arabia (54.3%) and Zimbabwe (61.6%) [11, 17, 18]. However, other studies showed low incidence of reactions among female patients like that of Bhattacharya et al. and Kumar et al. (34.2% and 45.7%, respectively) [13, 14].

The most common age group in which transfusion reactions occurred in the Prathima et al. study was the 3rd decade followed by the 4th decade [19]. However, in our study we found that transfusion reactions occurred with uniform frequency from the 3rd to the 5th decade, with 9 cases in each decade.

The most common adverse transfusion reaction observed in our study was febrile non-haemolytic transfusion reaction [51.4% (18 cases)]. It is caused when HLA (Human Leucocyte Antigen) class I antigens or leucocyte antigens on the white blood cells of the donor react with the recipient's antibodies leading to the activation of the complement system and the release of cytokines [7]. Criteria of temperature rise of at least 1 °C during the transfusion or shortly after that was used to diagnose this reaction [13]. It presented more commonly with fever and chills in the present study. Nausea and hypotension were also seen in few cases. They were more commonly observed with PRBC transfusion (0.53% of all PRBC transfusions) in our study. Similar finding was noted in studies conducted by Sharma et al. and Kumar et al. (0.57% and 0.88%, respectively) [11, 12]. A study conducted in AIIMS, Delhi however reported a much lower incidence of FNHTRs with PRBC transfusions (0.04%). The reason could be attributed to a very low observance of incidence of FNHTRs in their study to begin with [14].

Allergic transfusion reactions were second most common reactions observed in our study accounting for 40% (14 cases) similar to study done by Sidhu et al. (41.5%) [20]. However other studies such as done in Iran, Delhi and Sikkim documented much higher frequency (49.2%, 55.1% and 65.6% respectively) [11, 14, 21]. Allergic reactions can occur in about 2% of transfusions due to interactions between donor antigens and recipient IgE resulting in release of histamine and denovo synthesis of platelet activating factor and leukotrienes [22]. Clinically these reactions presented in our study mainly as urticaria and rashes. Few cases also showed symptoms like chills and fever.

Anaphylactoid reaction was observed in one patient in the current study accounting for 2.86% of all transfusion reactions and 0.14 per 1000 units of transfusion of all blood components whereas Pineda et al. observed a much lower incidence in their study (0.0021 per 1000 units) [23]. However, Bhattacharya et al. noted a higher incidence of these reactions amounting to 1.02 per 1000 transfusion

units [13]. Anaphylactoid reactions are generally found to occur in patients with IgA deficiency, with the presence of anti-IgA antibodies in their plasma following exposure [7]. However, in our study the plasma anti-IgA antibodies were found to be negative.

Fluid overload is a transfusion reaction that can occur if transfusion is excessive or too rapid. It generally tends to happen in patients who are already having underlying conditions such as impaired renal function, chronic severe anemia or cardiovascular diseases [7]. In the present study, this was observed in two female patients who had history of chronic anemia. PRBC transfusion was implicated in both the cases though it occurs more commonly with whole blood transfusions. Few studies documented fluid overload as a transfusion reaction and its frequency varied from 0.31 to 0.42 per 1000 transfusion recipients which is similar to our study (0.29 per 1000 transfusion recipients) [24, 25].

Conclusion

Blood transfusion process is a noble and lifesaving procedure. Having said that, it is also true that it is not completely free from complications which include adverse transfusion reactions. In our study, adverse reactions accounted for 0.5% of all transfusions. Majority of these reactions were seen with PRBC transfusions followed by platelet transfusions. Febrile non-hemolytic transfusion reactions and allergic reactions were the most common reactions. The use of leukoreduced PRBCs will help in reducing the frequency of these reactions. The hemovigilance program in our institution is extremely useful as it not only helps to assess diverse adverse reactions associated with transfusion of blood and its various components but also helps to minimize them. This ensures quality and safety of the blood transfusion process.

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