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A CLINICOHAEMATOLOGICAL PROFILE OF ADVERSE TRANSFUSION REACTIONS AND ITS ASSOCIATION WITH BLOOD COMPONENTS

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ABSTRACT

Different blood components are associated with various types of adverse transfusion reactions and are linked to several factors including the number, rate and volume of transfusions. The given study was conducted to study the relationship between various transfusion reactions and its causative factors. This study was a prospective study carried out over eighteen months on all patients who received a blood transfusion and blood components including various adverse reactions and events related to transfusion. These were correlated with tests for compatibility including general blood picture ,tests for haemolysis ,hematuria and haemoglobinuria, Coombs Test (Direct and Indirect), culture along with relevant clinical details of the patient. Out of a total of 31451 units of blood issued, 47 adverse transfusion reactions were noted with a maximum number in the age group of > 18 years (87.3%) with M: F being 1.6: 1 .0.24% of adverse transfusion reactions were by Packed red blood cell transfusion and mostly were immediate transfusion with a mean volume of 100 ml and mean time of 20 minutes. Febrile Non Hemolytic Transfusion Reaction (FNHTR) was the most common Adverse Transfusion Reaction (ATR)(0.128%) with 2 cases positive for Direct Coombs Test. A thorough serological and immunological examination and the addition of methods like buffy coat reduction and leucocyte filtration help in reducing the incidences of hemolytic transfusion reactions and transmitted infections and establishing a hemovigilance system help in the attainment of the goal of safe transfusion.

KEYWORDS: Adverse transfusion reaction, Blood components, FNHTR, DCT, Incompability..

INTRODUCTION

Any undesirable response which occurs in patients during or after a transfusion of blood or a blood component is defined as an adverse transfusion reaction (1). With the recent testing facilities,the occurrence of transfusion-transmitted infections has lowered, however, the incidence of adverse events due to ABO incompatibility, human error, bacterial contamination ,alloimmunisation, and immunomodulation phenomenon remains worrisome (2). Adverse transfusion reactions can either be immune-mediated or non-immune mediated. The most commonly encountered immune-mediated transfusion reactions unclude the delayed hemolytic transfusion reactions, acute hemolytic transfusion reactions, , febrile non-hemolytic transfusion reactions etc. The most common non-immune mediated transfusion reactions are transfusion-associated volume overload and iron overload (3). An adverse transfusion event is thus linked not only to immune differences between the donor and the recipient rather also to the number, rate and volume of transfusions. Different blood components are associated with different types of adverse reactions depending on the pathophysiology of adverse reactions (4). Since the process of adverse event identification, its documentation and reporting are variable and inadequate, this study was undertaken to study the the various reactions associated with transfusion reactions and their relationship with different blood components, number and volume of transfusions leading to adverse transfusion reaction(4).

MATERIALS AND METHODS

This study was a prospective study carried out over eighteen months in the Blood bank, Department of Pathology, Shri Guru Ram Rai Institute Of Medical &Health Sciences on all patients who received a transfusion of blood and blood components. Patients with a prior history of any transfusion or those receiving more than one unit of blood or blood components were taken as multiple transfusions recepients. All transfusion related adverse events were recorded and followed up to study any transfusion-related reactions. All relevant clinical details of the

patient including (name, age, sex, hospital no., ward, unit) along with patients records and blood unit transfused was rechecked both on the vial and compatibility card to rule out any possibility of wrong sampling, besides transposition or any clerical error. Returned blood bags were inspected for any discolouration, clot, hemolysis or foul smell. The pre and post transfusion samples and their reconfirmation was done for ABO and Rh blood group and also compatibility testing was done on these samples. Other investigations like haemolysis, serum bilirubin (direct & indirect), hematuria, hemoglobinuria, DCT and ICT, peripheral smear examination were done on patients pre & post-transfusion samples. Additionally the blood sample was sent for culture testing in microbiology department.The transfusion reaction form was filled according to haemovigilance guidelines and the form was uploaded to the hemovigilance site. Ethical Clearance was taken from the Institutional Ethical Committee.

OBSERVATIONS

A total of 31451 unit of blood was transfused to the patients who were admitted at Shri Mahesh Indresh hospital, Dehradun along with the outsourced units to the hospitals in the vicinity of the city out of which 47 (0.14%) adverse transfusion reactions were reported from different type of blood component. The maximum number of adverse transfusion reactions were seen in adults (>18 years)(n= 41, 87.3%),followed by Adolescent age group (n= 4, 8.5 %).In the pediatric age group, only 2 adverse transfusion reactions (4.2%)were noted, which was the minimum among all the age groups (Fig.1).Transfusion-related events showed a male predominance with 29 cases (61.7%) as compared to females with 18 cases (38.3 %).The M: F ratio was 1.6:1.Of all the components issued (31452), Packed red blood cells(PRBC) accounted for a maximum number of blood components (n=16935,53%), followed by Fresh Frozen Plasma (FFP) 12914 (41.1%). Platelets accounted for only 1461 units (4.6%) issued during this period (Table 1).The maximum number of adverse transfusion reactions was 40 (0.2361%) of transfused Packed Red blood cells followed by Fresh frozen Plasma (FFP) which accounted for 6 ATRs (0.0464 %)(Fig.2)The maximum number of cases (31.9%) had an adverse transfusion reaction after transfusion of 101-150 ml of the blood component (Fig.3).Maximum adverse transfusion reactions (23 cases, 48.9 %) were noted in the initial 0 to 20 minutes of initiation of transfusion. Only 4 transfusion reactions (8.6 %) were noted after 60 minutes following initiation of transfusion (Table 2).The maximum number of adverse transfusion reactions were noted from first time recipients of blood or blood product (n= 37,78%) with a minimum number of adverse transfusion reactions noted following massive blood transfusions (n=2, 4.2%) amongst all transfusion reactions (Fig.4).The adverse transfusion reactions showed a frequency as Febrile Non Hemolytic Transfusion Reaction > Allergic reaction > Anaphylactoid reactions > Transfusion Related Acute Lung Injury (TRALI) >Transfusion Associated Circulatory Overload (TACO). Febrile Non Hemolytic Transfusion Reaction (FNHTR) was the most common type of adverse transfusion reaction 40(85.2%). No hemolytic transfusion reactions, bacterial contamination, anaphylaxis and other adverse transfusion reaction were noted in the study (Table 3).The maximum number of adverse transfusion reactions was 40/47(85.1%) due to Packed RBC transfusions of all the reactions. Maximum patients presented with Febrile Non Hemolytic Transfusion Reaction - 34(85.0%). There were 6/47 (12.7%) adverse transfusion reactions due to Fresh Frozen Plasma transfusions and all the patients presented with Febrile Non-Hemolytic Transfusion Reaction. Only one case (2.5%) of allergic reaction was noted after platelet transfusion (Table 4).The maximum number of blood transfusions was in the Medicine department (n=13522, 43%) while the maximum number of adverse transfusion reactions was in the department of Medicine and Obstetrics and gynaecology 14 cases (29.8%). Maximum adverse transfusion reactions were found in Chronic Kideny Disease patients accounting for 7 cases (14.9%) in Medicine department (Table 5,6).Only 2 cases (4.2%) were noted as Direct Coombs Test positive amongst all adverse transfusion reactions while not a single case of Indirect Coombs Test positive was identified in all types of adverse transfusion reactions (Table 7).Blood group O+ve (29.8%) & B+ve (29.8%) showed the maximum no of adverse transfusion reactions followed by A+ve (27.7 %),minimum transfusion reactions from blood group A-ve and B-ve (2.1%) each (Fig.5).

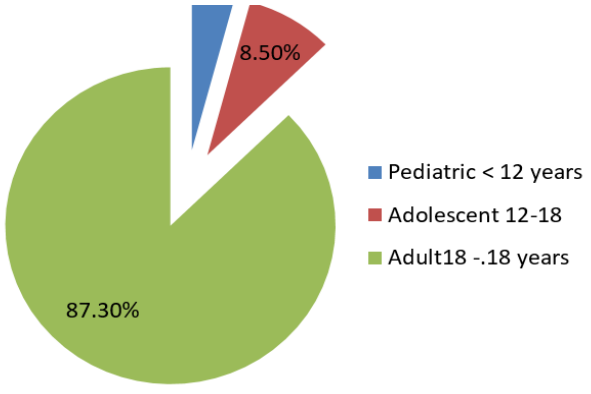

Fig. 1: Age-wise distribution of all types of transfusion reactions.

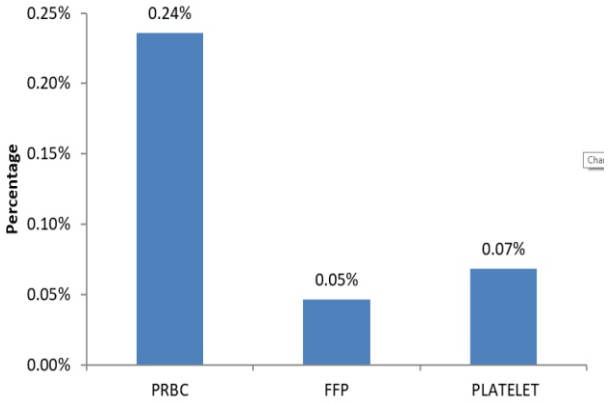

Fig. 2: Number of transfusion reactions according to the Blood components

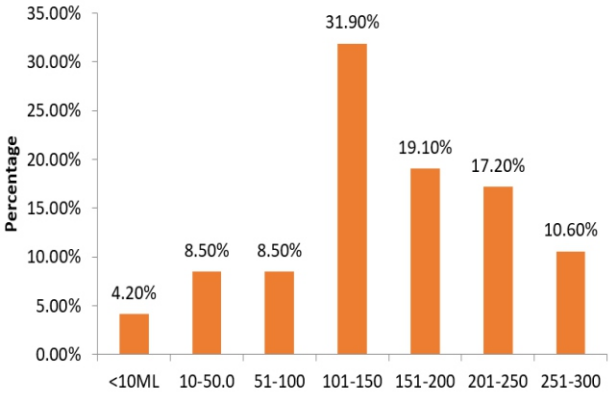

Fig. 3: Number of Adverse Transfusion Reactions According to the Volume of Blood Component Transfused

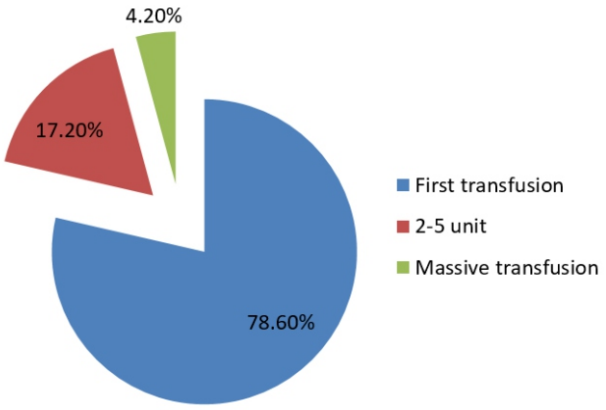

Fig. 4: Distribution of total cases according to the history of BCG Immunization

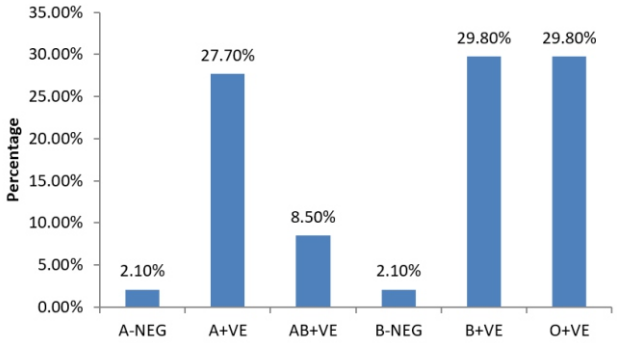

Fig. 5: Distribution of Adverse transfusion reactions according to different blood groups

BLOOD PRODUCTS	NO OF UNITS	PERCENTAGE
Whole blood	141	0.4%
PRBC	16935	53.8%
FFP	12914	41.1%
PLATELETS	1461	4.6%
TOTAL	31451	100.0%

Table I: Type of Blood Products Transfused during the Study Period

Duration of ATR	Number of Cases	Percentage
0 – 20 min	23	48.9 %
21- 40 min	11	23.4 %
41- 60 min	9	19.1 %
>60 min	4	8.6 %

Table II: Detail of time Association of Adverse Transfusion Reactions

ATR	NO OF ATR	PERCENTAGE
FNHTR	40	85.2%
ALLERGIC REACTION	3	6.4 %
ANAPHYLACTOID	2	4.2 %
TACO	1	2.1%
TRALI	1	2.1%
Total	47	100.0%

***Table III:* Types of Transfusion Reactions**

	RBC	FFP	PLATELET
Transfusion reaction	**No. of cases(%)**	**No. of cases(%)**	**No. of cases(%)**
ANAPHYLACTOID	2 (0.012%)	6(0.046%)	0(0.000%)
FNHTR	34(0.020%)	0(0.000%)	0(0.000%)
ALLERGIC REACTION	2(0.012%)	0(0.000%)	1(0.068%)
TACO	1(0.006%)	0(0.000%)	0(0.000%)
TRALI	1(0.006%)	0(0.000%)	0(0.000%)
Total	40(0.236%)	6(0.046%%)	1(0.046%)

Table IV: Profile of Adverse Transfusion Reaction by PRBC, FFP and Platelets

Department	Diagnosis	Reaction	Percentage
Medicine (29.8%)	GI bleed	4	8.6 %
	CKD	7	14.9 %
	Severe Anemia	3	6.3 %
Surgery (25.5%)	Trauma	6	12.7 %
	Carcinoma	4	8.6 %
	Haemorrhoids	2	4.2 %
Orthopedic (8.6%)	RTA, Fracture	4	8.6 %
Obs & Gynecology (29.8%)	ANC	5	10.7 %
	Anaemia	2	4.2 %
	Carcinoma	4	8.6 %
	AUB	3	6.3 %
Paediatrics (4.2%)	Thalassemia	1	2.1 %
	Anaemia	1	2.1 %
Emergency (2.1%)	Trauma	1	2.1 %
Total		47	100%

***Table VI:* Distribution of Adverse Transfusion Reactions According to Clinical Diagnosis**

Department	Indication(%)	Number of adverse reaction(%)
Medicine	13522 (43%)	14 (29.7%)
Surgery &	13209(42%)	16 (34.3%)
Orthopedic Obs & Gyn	3775(12%)	7(14.8%)
Pead	631(2%)	5(10.6%)
EMR	314(1%)	5(10.6%)
Total	31451(100%)	47(100 %)

Table V: Department wise distribution of blood transfusion and adverse transfusion reaction.

Coombs Test	Direct	Indirect
	No. of cases (%)	No. of cases (%)
Negative	45 (95.8%)	47(100%)
Postive	2 (4.2%)	0(0%)
Total	47(100%)	47(100%)

Table VII: Distribution of Transfusion Reactions According to Coombs Test

RESULTS

A total of 31541 units comprising Packed red blood cells, Fresh Frozen Plasma, Platelets(apheresis and random donor) cryoprecipitate were issued and transfused during the study period.Out of these total units of blood issued, 47 adverse transfusion reactions were noted. The frequency of adverse transfusion reactions in our study was 0.149%.Maximum number of adverse transfusion reaction were in the age group of > 18 years accounting

87.3% of adverse transfusion reactions.The M: F ratio of Adverse Transverse Reactions in our study was 1.6: 1 thus exhibiting a male preponderance.Packed Red Blood Cell accounted for maximum number of blood component issued (n=16935, 53%).Overall 0.24% of adverse transfusion reactions were noted by Packed red blood cell transfusion during study period.All the Advrese Transfusion Reactions in our study were immediate transfusion reactions and were recorded when a mean volume 100 ml was transfused. The mean time at which reactions were noted was 20 minutes from the start of transfusion (range 5-250 min.)Maximum incidence of adverse Transfusion reactions was Febrile Non-hemolytic Transfusion Reaction(FNHTR) accounting 40 cases (0.128%) in the present study. Of these 40 cases of FNHTR, 34 ATRs were following Packed red blood cell transfusion and 6 due to Fresh frozen plasma transfusion.Allergic adverse transfusions reaction accounted 3 cases (0.009%) of all Adverse Transfusion Reactions. Of all the allergic adverse Transfusion Reactions, 2 cases (0.012 %) were following Packed Red blood cell transfusion and one case (0.068 %) was noted following platelet transfusion.There were 2 cases (0.12%) of Anaphylactoid/ Anaphylactic reactions following transfusion of Packed RBC.Single case each of Transfusion Related Acute Lung Injury (TRALI) and Transfusion Associated Circulatory Overload (TACO) accounting 0.003% (1/31451) was reported in our study. Both the pulmonary events occurred following PRBC administration.Department wise maximum blood transfusions were in the Department of Medicine (n=13522, 43%) during study period however maximum adverse transfusion reactions were reported from the Department of Surgery 16(34.3%) , where 13209 (42%) blood and blood components were transfused.On work up of adverse transfusion reaction 2 cases were Direct Coomb's test (DCT) positive following transfusion. Despite being DCT positive, the patient did not presented with Immune mediated hemolysis. On analysis of these patient ,pretransfusion sample were tested and were found to be DCT positive, although the units issued were compatible. In our study, the highest number of Adverse transfusion Reaction was observed in blood Group B and O each accounting 14 cases (29.8 %). During the study period 2 near miss events were documented. Preventive and corrective actions were taken to avoid repetition of such events in future.

DISCUSSION

Various adverse reactions are known to occur after blood transfusion despite adopting all the precautions and preventive measures, which sometimes turn serious (1).Reporting of an adverse transfusion reaction not only requires a close collaboration between the blood bank and the clinicians but also relies on transfusion procedures detail, their timely identification, maleffects ssociated with the use of blood along with its further investigations and management (2). The frequency of adverse transfusion reactions in the present study was 0.149%, similar to the study conducted by Bhattacharya et al., who reported 0.18% adverse transfusion reaction in their study which was slightly higher in comparison to our study (6), which may be due to higher number of denominator i.e., recipients requiring transfusions and possible underreporting during the covid period. Adverse transfusion reactions are found to be more common among adults > 18 years (7). A male preponderance is found in most of the studies while studies by Sidhu et al., reported an increased frequency of Adverse Transfusion Reactions amongst females in contrast to males (7) (8). Various studies reported maximum Transfusion Reactions were caused by Packed RBC. The transfusion reaction was further reduced with the use of a buffy coat and leucodepleted Packed RBC. However, in contrast to these studies, our study had a relatively low frequency of Adverse transfusion reactions with platelets. This may be due to the relatively low frequency of platelets issued during this period at our institute. A relatively higher number of Adverse Transfusion Reactions were due to Fresh Frozen Plasma transfusion in our Blood Bank when compared with studies by other authors. This finding may be due to the enormous frequency of Fresh frozen Plasma issued and transfused from our Blood bank in contrast to other studies. All the Adverse Transfusion Reactions in our study were immediate transfusion reactions and were recorded when a mean volume of 100ml was transfused. The mean time at which reactions were noted was 20 minutes from the start of transfusion (range 5-250 min.). Similar findings were observed by Pahuja et al.,(5). In this study maximum incidence of Adverse Transfusion Reactions was Febrile Non-hemolytic Transfusion Reaction (FNHTR) accounting for 40 cases (0.128%). FNHTR is an immune-mediated reaction caused by the antibodies against white cell in the recipient's plasma. The frequency of Febrile Non-hemolytic Transfusion Reactions (FNHTRs) with PRBC in our study was 0.20%, followed by FFP which was 0.046%. Rates of FNHTR by red cells in most studies ranged from 0.5 % to 1 %, (9). Studies by other authors have suggested that with the wider use of leukoreduced blood products, the incidence of FNHTRs decreases (10). However in our blood bank leukoreduced PRBC and filters are being used exclusively for Thalassemic patients and is not used routinely, which may a cause of large number of Febrile Non-hemolytic

Transfusion Reaction (NHTRs).The overall incidence of allergic reactions in different studies varies from 0.2% to 3%.(11). In our study, we noted 2 cases of anaphylactoid/ anaphylactic reactions following transfusion of Packed RBC accounting for an overall 0.012%. However, since IgE estimation was not avalaible in our centre,further differentiation between anaphylactic reactions and anaphylactoid reactions was not done.Transfusion Related Acute Lung Injury (TRALI) presents with sign and symptoms similar to other medical conditions causing lung injury and is often misdiagnosed (12). Department wise maximum blood transfusions were in the Department of Medicine (n=13522, 43%) while maximum adverse transfusion reactions were reported from both the Department of Medicine and Obstetrics and Gynecology 14 cases (29.8%).This may be due to multiple units being transfused to one patient and/ or underreporting of minor events by these departments. On workup of adverse transfusion reaction, 2 cases were Direct Coomb's test positive following transfusion. These patients were from the Department of Medicine who have received repeated transfusions as they were undergoing treatment for leukaemia. Despite being Direct Coombs Test positive, the patient did not present with Immune-mediated hemolysis. Pretransfusion samples were tested and were found to be Direct Coobs Test positive, although the units issued were compatible. The highest number of Adverse Transfusion Reaction was found in blood Group B 14(29.8 %) and O, 14(29.8 %) followed by blood group A 13 (27.7%), least number of adverse transfusion reactions were from blood group A and B Negative 1(2.1%) respectively. However, Sinha, et al., in their study found the highest number of adverse transfusion reactions was from blood group A followed by blood group B (13). Risk factors associated with acute ABO-incompatible hemolytic reactions were mainly technical or clerical errors. Clerical errors include misidentification of the patient or the recipient. Technical errors included errors in blood grouping of donor or patient's blood or errors in cross-matching. Baele et al., reported bedside transfusion errors to occur in 12.4/1000 transfusions (14). Not a single ABO-incompatible induced hemolytic reaction was found in our study.No infectious complications were noted in this study.All collection as well as handling and storage were done under strict aseptic measures. The quality control is ensured by checking 1% of the collected Platelet Rich Plasmas by the Bac-Alert system to check any bacterial contamination.Near miss events are more frequent and result from human action and thus are preventable (15). During the study period, 2 near-miss events were noted one of them was the wrong sample sent to the blood bank from emergency and the other one was due to the wrong bag being picked up and issued to the attendant but the error was realized before administration due to vigilance of Blood bank staff. Preventive and corrective actions were taken at the time of events to avoid repetition of such events in future.

CONCLUSION

Febrile Non Hemolytic Transfusion Reaction is one of the most commonly reported adverse Transfusion Reactions and is usually associated with Packed RBC transfusion. These ATRs could be reduced if buffy coat methods Packed RBC preparation or inline leucocyte filter is used. Allergic and anaphylactoid reactions are another common type of ATRs and show association with transfusion of plasma containing blood components. Fresh Frozen Plasma (FFP) is mostly been issued to patients admitted to the medicine ward (predominately patient with cirrhosis). Usage of albumin along with recombinant factor VIIa can limit the transfusion of FFP in such patients, however, cost constraints lead to the prescription of FFP in these patients. A robust check is undertaken for the clerical error before the blood component issue and transfusion helps in minimizing the haemolytic reaction as in this study. Thus it can be concluded that though serological and immunological advances have reduced the incidences of hemolytic transfusion reactions and transfusion-transmitted infections, still other ATRs like FNHTRs are very common and demand the introduction of methods like Buffy coat reduction and leucocyte filtration in preparation of Packed RBCs. The goal of safe transfusion can be achieved only by establishing a hemovigilance system and is the joint responsibility of blood transfusion consultants and their clinical counterparts to create awareness about safe transfusion services.

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