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ORIGINAL ARTICLE

FREQUENCY AND NATURE OF TRANSFUSION RELATED ADVERSE REACTIONS IN PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL

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Abstract:

Background:*Transfusion of blood and blood products if employed safely, with intensive care can save manyvaluable lives. But a number of transfusion reactions may develop that are sometimesmore serious and life threatening.So this study was done to find out the most frequent and life threatening reactions that develop during transfusion.* ***Methods:*** *A Cross sectional descriptive observational study was performed at a tertiary care centre. Patients of 18 years and older irrespective of sexes who received blood and blood products due to different reasons between April 2020 to September 2020 were included in this study. A total of 96 patients were included in the study.* ***Results:****In thisstudy 11(11.5%) out of 96 patients had transfusion reactions of different types .Febrile non haemolytic reaction was the highest with 8 patients (8.33%),followed by Allergic reaction in 2 patients(2.08%) and Acute haemolytic transfusion reaction in 1 patient (1.04%).Among them 7(63.6%) reactions occurred with whole blood , 2(18.2%) reactions occurred with red cell concentrate and 1 reaction occurred with Apheresis platelet (9.1%) and fresh frozen plasma(9.1%).Statistically significant association was found between duration of storage of blood and transfusion reaction.* ***Conclusion:*** *Febrile non haemolytic reaction was the commonest type of transfusion reaction found in this study and there was also statistically significant association between duration of storage of blood and transfusion reaction.*

Keywords: *Transfusion reaction, febrile non haemolytic, duration of storage of blood and blood products*

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Introduction:

Having a safe blood transfusion facilities is integral to any basic health care delivery infrastructure. They can often saves life in critically ill patients. Inversely, blood transfusions are also embedded with risks ranging in severity from minor to life threatening.[1]

An adverse reaction or event is an undesirable response or effect in a patient, temporally associated with the transfusion of blood or blood component.[2] The incidence of acute blood transfusion reactions is estimated to be 0.2-10% and is responsible for mortality in 1 per 250,000.[3] Now-a-days, even in developed countries, the greatest risk to the patient lies in non-infectious complications of transfusions that account for significant morbidity and mortality.[4] The commonly encountered blood transfusion reactions include acute hemolytic reactions, allergic reactions, anaphylactic reactions, febrile nonhemolytic transfusion reaction (FNHTR) also rare but fatal reactions like Transfusion related acute lung injury (TRALI), sepsis etc.[2]

Knowledge about various features of acute and delayed transfusion reactions will aid to assess the serious reactions on time leading to a better prognosis.[1]Observation and monitoring throughout the transfusion episode, more within first 15 min ,are required.[1] So ,a standard operating procedure containing the details for documentation, reporting, evaluation of severity, and follow-up of all adverse reactions should be established.Complete documentation and reporting of a transfusion reaction is important to identifying the problem and the risk to blood recipients in the transfusion chain. This provides the basis for a successful investigation of transfusion reactions, which may, in turn, lead to an improvement in the safety of subsequent transfusions.

In many countries there is reporting scheme for blood transfusion reactions[5]. But we even do not have enough data to find out the frequency and type of adverse reactions related to transfusion.

In a study in DMCH, Bangladesh in 2008 by Chowdhury F. S. Et al. They found an overall incidence of transfusion reactions was 6.66% among them 62.5% were febrile reactions.[7] In one study done by Rahman (1977)[8] total transfusion reactions were 10%. In another study done at BSMMU(2005)[9] reactions were 8%. But no recent study was found to know the actual incidence of transfusion related adverse events in our country. We also do not have any national programme in our country for monitoring and prompt reporting of any blood transfusion reactions like other developing countries. Judicious patient selection with realistic pretransfusion assessments of risk versus benefit to the potential recipient combined with tough quality control is an effective mode of reducing transfusion related adverse events.[9] In addition, continuous monitoring of transfusion related complications can promote patient care and safety.

The main aim of this study is to find out the actual situation of transfusion related adverse events in our country which will eventually help us in developing a strong survellience system for safe transfusion and reduce the serious and life threatening reactions related to transfusion of blood and blood products.

Methods:

A hospital based cross sectional descriptive observational study was performed in indoor patients of Sir Salimullah Medical College Mitford hospital. Patients of 18 years and older irrespective of sexes who received blood and blood products between April 2020 to September 2020 due to different reasons were the study population .History, clinical features, Investigation and treatment given was collected from the records and face to face interview.The time of storage of blood products was determined based on the difference of time between collection and transfusion of blood products. Patients with life threatening medical conditions(like acute massive stroke, recent Myocardial Infarction, hepatic encephalopathy, end stage renal disease,respiratory failure, diabetic ketoacidosis etc), patients with temperature > 39!and with history of anaphylaxiswere excluded from the study.

A total of 96 patients were included in the study.The sample size is calculated by using statistical formula: $n= z^2\text{-}pq / d^{2\cdot}$ Where n= the desired sample size.P= P means prevalence = 0.5(50%), [In unknown prevalence, it can be regarded as 50%],q = (1-p) = (1-0.5)=0.5,z = 5% level of significance or 95% confidence level, z=1.96,d = degree of accuracy or acceptable error usually set as 5% (0.05), but it should not exceed more than 20%. Here d is 10% (0.1) to keep the sample size desired with time.

$$n = \frac{(1.96)^2 \times 0.5 \times 0.5}{(0.1)^2} = 96$$

Type of transfusion reactions were determined by analyzing all the data and statistical analysis was done.

Statistical analysis:

Results were expressed as percentages and mean. Chi square test for discrete variables were used to test significance. The p value of less than 0.05 was

considered statistically significant. The SPSS 25 software was used for statistical analysis.

Results:

In this study, there were 96 participants who satisfied the selection criteria. Out of them 48(50%) were male.Out of the patients one- fourth (25.0%) of the patients were between 18 to 24 years of age followed by 20.8% between 25 to 34 years, 19.8% between 35-44 years, 17.7% between 45-54 years and remaining 16.7% above 55 years old. The mean age of patient was 37.67 years.Among the study population 5 types of blood group were seen, B+ being the highest in number with 35% followed by A+(28%) then O+(23%) then AB+(12%) and O- is the lowest covering 2% of the patients .There was variety of indications for transfusion which are presented in Table I.

Table I

Distribution of patients by diseases requiring transfusion (n = 96):

Disease	Number	Percentage
Anaemia(Iron Deficiency, Aplastic, Anaemia of chronic disease , Anaemia due to bleeding, Undiagnosed)	34	35.4
Thalassaemia	11	11.5
Haematological Malignancy	23	24
Clotting factor deficiency	9	9.4
Other Malignancy	13	13.5
Gynaecological	6	6.2
Total	96	100

Patients received various blood products ,which are shown in Figure 1

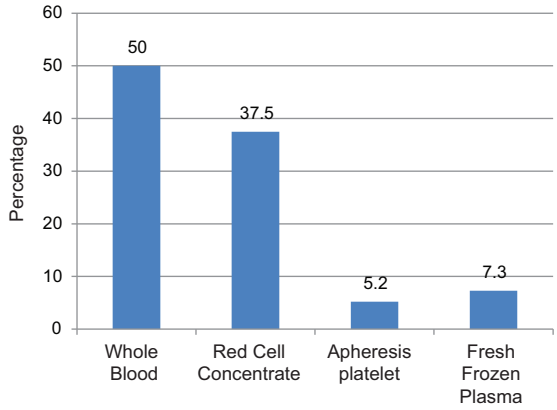

Fig.-1: *Distribution of patients by received Blood products (n =96)*

All the patients received blood products within 1 to 4 units,87.5% received 1-2 units anr 12.5% received 3-4 units. Storage duration of blood and blood products were documented which is presented in Table II.

Table II

Distribution of patients by duration of storage of blood products (n =96):

Storage Duration	Number	Percantage
<1 Hour	15	15.6
1-4 Hour	55	57.3
4-6 Hour	15	15.6
6-8 Hour	5	5.2
8+ Hour	6	6.3
Total	96	100

Among the patients 68.8% had no history of transfusion previously,15.6% had d"10 transfusions and 15.6% had >10 transfusions before. Transfusion reaction occurred in 11(11.5%) patients out of 96,among them 8(8.33%) Reactions were Febrile non-haemolyticreactions ,2(2.08%) were allergic reaction and 1(1.04%)reaction was Acute Haemolytic Transfusion reaction. Only 1(1%)patient had history of previous transfusion reaction.

Transfusion reactions occurred with different blood component are demonstrated in Figure 2.

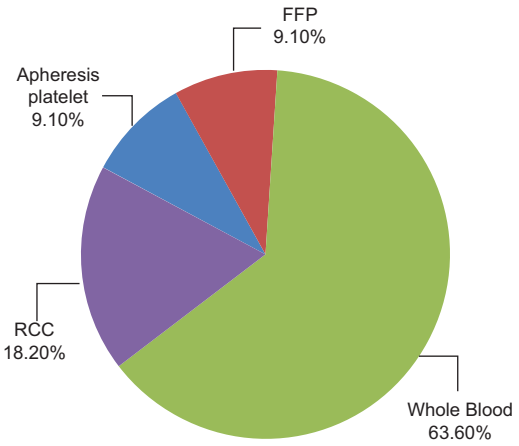

Fig.-2 : *Distribution of transfusion reaction by blood component (n=96)*

The relationship of transfusion reaction with different charachteristics of patient using p-value‡ is shown in Table III. Significant p-value‡ is seen in terms of storage duration of blood products and history of previous transfusion reaction

Table III

Transfusion reaction by characteristics of the study population, (n=96)

Characteristics	Transfusion Reaction		P-Value‡
	Yes% (n)	No% (n)	
Age			0.544
18-24 Years	45.5 (5)	22.4 (19)	
25-34 Years	18.2(2)	21.2 (18)	
35-44 Years	18.2(2)	20.0 (17)	
45-54 Years	9.1 (1)	18.8 (16)	
≥55 Years	9.1 (1)	17.7 (15)	
Gender			0.749
Female	45.4 (5)	50.6 (43)	
Male	54.6 (6)	49.4 (42)	
Blood Group			0.706
A+	18.2 (2)	29.4 (25)	
B+	54.6 (6)	32.9 (28)	
AB+	9.1 (1)	11.8 (10)	
O+	18.2 (2)	23.5 (20)	
O-	0.0 (0)	2.4 (2)	
Storage Duration			<0.001
<1 Hour	0.0 (0)	17.7 (15)	
1-4 Hour	9.1 (1)	63.5 (54)	
4-6 Hour	27.3 (3)	14.1 (12)	
6-8 Hour	27.3 (3)	2.4 (2)	
8+ Hour	36.4 (4)	2.4 (2)	
History of Blood Transfusion			
0.927			
No	63.6 (7)	69.4 (59)	
Yes (d”10)	18.2 (2)	15.3 (13)	
Yes (>10)	18.2 (2)	15.3 (13)	
History of Transfusion Reaction			
0.005			
No	90.9 (10)	100.0 (84)	
Yes	9.1 (1)	0.0 (0)	
Total	100.0 (11)	100.0 (85)	

‡p-Values was obtained from chi-square tests

Discussion:

Transfusion of blood and blood products is the most commonly encountered procedure in different health care settings in our country and an integral part of healthcare system.[10] Reactions to transfusion ranges from minor to life threatening.[2,9]

The concept of hemovigilance had its inception in the early 1990s.The French blood agency had initially developed it as a national system of surveillance and alert, from blood collection to the follow-up of recipients.[11]

This programmeincludes the monitoring, reporting, investigation and analysis of adverse events related to the donation, processing and transfusion of blood, and taking action to prevent their occurrence or recurrence. The reporting systems play a fundamental role in enhancing patient safety by learning from failures and then putting in place system changes to prevent them in future.[12] It is now encountered in many countries of the world.[13]

As a primitive step to develop a National programme for ensuring safe blood transfusion this study is done to assess the frequency and nature of transfusion reaction and to see the relationship among different characteristics of study population with transfusion reactions.The main aim of this study was to find out the most frequent and life threatening reactions that develop during transfusion.

Study population were patients admitted in Medicine Department of Sir Salimullah Medical College Mitford Hospital and they were selected randomly irrespective of age ,sex and indication of transfusion.96 patients were included in this study ranging from 18 to 68 years . 25% of them were between 18-25 years with mean age of 37.67 years .48 patients were male and 48 were female.

Total 5 types of blood groups were found in this study ,B+ being the most common covering 35 % of total patients which represents the most common blood group in our country also seen in Chowdhury’s study[6].The other blood groups are A+ (28%), O+ (23%), AB+ (12%) and O- (2%).

Most common indication for transfusion was anaemia due to different reasons (35.4%) including Aplasticanaemia, Iron deficiency anaemia , Chronic Kidney disease, SLE, bleedinpudetc;some causes were unknown also. In a study to see the pattern of day care transfusion service[14] they also found anaemia being the most common cause for transfusion. In our study11.5% patients were Thalassaemia of different types like Hb E âthalassaemia, bthalassaemia major etc. Other resons behind transfusion were Haematological malignancy (24%) namely AML,ALL,CML,NHL ; other malignancies(13.5%) like carcinoma of colon, carcinoma of breast, carcinoma of cervix, carcinoma

of stomach; Clotting factor deficiency (9.4%) both congenital and acquired due to Chronic liver disease and Gynaecological(6.2%). In Chowdhury's study[6] they found Thalassaemia was the major indication for transfusion which is different from this study.

In this study majority of the patients received whole blood (50%) followed by Red cell concentrate (37.5%), Fresh frozen plasma (7.3%) ,Apheresis platelet (5.2%) .As red cell concentrate requires some time and expertise to prepare, so in this centre still whole blood is the preferred component to be given in emergency situation but in Chowdhury's study[6] red cell concentrate was the highest to be transfused.In a study at central India[15] they found whole blood were the most to be transfused (68.15%) which is consistent with this study.In a Japanese study[16] red cell concentrate was the highest to be transfused. So we can say that it varies from centre to centre.

All the patients received blood and blood products between 1 to 4 units. 66 (68.7%) patients received 1 unit of transfusion, 18 (18.8%) patients received 2 units, only 5 (5.2%) and 7(7.3%)pateints received 3 and 4 units respectively. This shows the impact of current pandemic situation in overall hospital stay of the patients. Most of the transfusion of the patients were for emergency condition only. In Chowdhury's study[6] the found positive relationship between transfusion reaction and number of transfusion but this is not significant in this study.

In this study reaction to transfusion occurred in 11(11.5%) out of 96 patients. In Chowdhury's study[6]done in 2008, transfusion reaction was 6.66%. Similar International studies like Sinha's[15] study, Sharma's study[9], it was only 0.27% &0.92% respectively. But in one Japanese study [16] transfusion reaction was 5.7%.So the rate of transfusion reaction is sometimes unpredictable and can be related to factors like underreporting as reported in a study by Narvios*et al*[17]. Large scale study is needed to find out the exact situation. Also one thing to note that in Indian studies the transfusion reaction was low as they follow strict haemovigilance system but still more studies are required to make any concrete comment regarding that.

Eight (72.7%)out of 11 transfusion reactions were Febrile non haemolytic reactions which is consistent with Chowdhury's study[6] where 62.5 % were febrile non haemolytic reactions. Fever occurred in the middle half of transfusion with chills and rigor in half of the cases. 5 patients showed 2! rise in temperature and 3 patients had 1! rise in temperature which was managed by temporarily stopping the transfusion, giving Paracetamol and steroid. 3 patients had nausea and chest pain but no shortness of breath were present; 2 patients had nausea with fever and 3 patients had only fever.All were improved after few hours.No other cause of fever was found and no clinical or biochemical evidence of haemolysis was seen.Among these 8 patients 6 received Whole blood transfusion and 2 received Red cell concentrate .

Differing from our study,in Indian study like Sharma's[9] study, allergic reaction was the most to occur comprising 65.6% followed by febrile reaction 28.1%.Also in Sinha's[15] study and Hatayama's[16] study allergic reaction was highest followed by febrile reaction . This variation in the results among different studied can be attributed to variations in reporting all the sign symptoms therapeutic intervention and use of leukodepleted blood in some centres.[9,15,16]

In this study allergic reaction occurred in 2(18.2%) out of 11 patients. One of them received Apheresis platelet and the other fresh frozen plasma. They had some pruritus and redness at the end of transfusion which was relieved by anti histamine. No signs of anaphylaxis or airway compromise were seen.

Acute haemolytic transfusion reaction occurred in 1 (9.1%) patient who received whole blood. The patient developed fever with 1! rise in temperature as well as chills and rigor and back pain. Laboratory findings showed some features of haemolysis like raised LDH and positive direct Coomb's test. Patient had history of previous blood transfusion (³10 unit) and also history of previous transfusion reaction (type unknown); p value is 0.005 which is statistically significant. Febrile haemolytic transfusin reaction was not found in Sinha's study.[15] In our study as the patient had previous history of repeated blood transfusion so there is a possibility of previous mismatched transfusion, hence this reaction occurred.

In this study 4(36.4%) out of 8 transfusion reaction occurred when given blood was stored for more than 8 hours, 3(27.3%) reactions occurred with 6-8 hours stored blood, 3(27.3%) reactions occurred with 4-6 hours stored blood, 1(9.1%) reaction occurred with 1-4 hours stored blood and no reaction occurred with < 1 hour stored blood.Statistical analysis showed significant difference (p <0.001) in occurrence of transfusion reaction while giving blood that were stored for a longer period of time. A study by Sosnoski M, et al.[17] done in 2019 at Brazil also showed that storage duration increase the risk of Transfusion

reaction but no National study is there to support this.

Conclusion:

Febrile reactions constituted the majority of adverse transfusion reactions encountered in this study . Significant association were found between the duration of storage of blood products and transfusion reactions. This study is a small step towards development of coordinate national haemovigilance programme.

Limitation of the Study:

However, like any other study, the present study is not without limitations, the following limitations deserve to mentions. The present study was conducted on small sample size as such the findings cannot be generalized to reference population. Rare but fatal transfusion reactions were not observed, large sample study will help to find out their frequencies in our country. Delayed transfusion reactions couldn't be observed due to loss of follow up. Longer duration study is needed to combat that.

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Declaration of interest:

The authors report no conflict of interest.

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Ethical consideration:

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained.

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