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Adverse Blood Transfusion Reaction in Tertiary Care Hospitals an Initiative Towards Improvement: A Multi Center Study

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ABSTRACT

Introduction: Blood and blood components transfusion is a life-saving procedure, but it carries the risk of adverse outcomes. Hemo-vigilance is a surveillance system that includes reporting and analysis of adverse events related to blood transfusion and taking steps to prevent their occurrence or recurrence

Aims & Objectives: This study is to determine the incidence and type of adverse transfusion reactions and type of blood products associated, in patients had undergone blood transfusion.

Place and duration of study: A retrospective descriptive cross-sectional study Blood bank, Pathology department, University College of Medicine / University of Lahore Teaching Hospital, Lahore and Blood bank, Mansoorah Teaching Hospital, Lahore. The study was conducted over a period of 04 years (1st January 2018 to 31st December 2021).

Material & Methods: All the adverse blood transfusion reactions reported to Blood Bank during the 4 years were analyzed according to institution's protocol.

Results: Out of 9597 units transfused, 72 (0.75%) adverse transfusion reactions were reported. Febrile non hemolytic transfusion reactions (0.36%) were the most frequent type of reaction followed by Allergic reactions (0.33%). ATRs were mostly associated with whole blood followed by Pack Cell Volume (PCVs).

Conclusion: For an accurate estimation of ATR incidence, proper transfusion monitoring and reporting of all such responses will be required. To enhance the quality, safety, efficacy, and cost-effectiveness of blood and its components and as well as the donation process, an effective hemo-vigilance system must be established

Key words: Adverse transfusion reactions(ATRs), Hemo-vigilance, febrile non-hemolytic transfusion reactions, Allergic reactions

INTRODUCTION

Blood transfusion is a life-saving intervention that helps save many lives each year worldwide. Along with its many advantages, it is not free from complications. These complications involve transfusion-transmitted infections as well as non-infectious transfusion reactions. Transfusion-transmissible infections (TTIs) screening is a very essential step to ensure safe transfusion[1]. With advances and the use of specialized techniques like enzyme-linked immunoassay (ELISA) and Chemiluminescence immunoassay (CLIA), the risk of Transfusion-transmissible infections (TTIs) can be reduced. But the risk of non-infectious complications becomes more evident.[2]

Non-infectious transfusions reactions are also called adverse blood transfusion reactions.[3] The time frame between blood transfusion and the onset of signs and symptoms is used to categorize adverse transfusion reactions.[4] Acute transfusion reactions take place within 24 hours after the transfusion, while delayed transfusion reactions occur after 24 hours.[4]

Acute transfusion reactions include acute hemolytic transfusion reaction (AHTR),transfusion associated sepsis(TAS),febrile non-hemolytic transfusion reaction (FNHTR), allergic transfusion reactions (ALTR), transfusion related acute lung injury (TRALI), transfusion associated circulatory overload (TACO) and transfusion associated dyspnea (TAD).[4] Delayed transfusion reactions (DTR) include delayed hemolytic transfusion reactions (DHTR), transfusion associated graft versus host disease (TA-GVHD) and Post-transfusion Purpura (PTP).[4]

According to WHO, in Pakistan with an estimated population of 220 million, 1.5 million donations are collected each year.[5] Out of these only 25% are from voluntary donors, 65% from replacement donors, and about 10% from professional donors.[5] The reported frequency of adverse blood transfusion reactions spans from 0.2% to 10% and these are responsible for 1 in 25000 deaths.[6]

Hemovigilance is defined as "the systematic monitoring of transfusion-related adverse events."[7] The purpose of hemovigilance is to have a system of surveillance and reduction of the risks associated with transfusion.[2,8] There is no developed hemovigilance system is present in Pakistan.[4] Due to underreporting of adverse transfusion reactions by medical staff, unattended minor adverse reactions, and poor hemovigilance system, the actual incidence of adverse transfusion reactions is often underestimated.[9,10]

The purpose of this study is to investigate the frequency and types of adverse transfusion responses, as well as the blood products associated with them, in patients requiring blood transfusions at two tertiary care hospitals in Lahore, Pakistan. The rationale of this study is to collect comprehensive information regarding the adverse effects of blood transfusion so that steps must be established to avoid these adverse events at any stage and improve patient transfusion safety.

MATERIAL AND METHODS

It was a multi-center, retrospective descriptive cross-sectional study performed at the Blood bank, Pathology department, University College of Medicine / University of Lahore Teaching Hospital, Lahore, and Mansoorah Hospital, Lahore. Ethical approval was taken from the institutional Ethical Review Committee (ERC) under the registration no. **ERC/91/22/01**The study included patients who had undergone blood transfusion over 04 years (1st January 2018 to 31st December 2021). This study covered all patients who experienced adverse transfusion responses (ATRs), both acute (within 24 hours of transfusion) and delayed (beyond 24 hours after transfusion). All the adverse transfusion reactions (ATRs) were identified and labeled according to the American Association of Blood Banks (AABB) guidelines.[11] .

The medical staff had filled up an adverse reaction form and reported it to the blood bank. Data included patient medical record number, blood bag number, the patient's ABO and Rh blood groups, as well as the donor's, type of blood product, patient's vital signs, date of transfusion, the timing of starting and stopping transfusion, volume of blood product transfused, post-reaction signs and symptoms of the patient, post-reaction vital signs of the patient along with post-transfusion sample of patient and blood bag.

Blood bank assessment of adverse reaction included clerical check, re-checking of ABO and Rh blood groups of pre-transfusion and post-transfusion samples of the patient, ABO and Rh blood groups of the donor, direct anti-globulin test (DAT), and Indirect anti-globulin test (IAT) of post-transfusion sample, re-cross match of pre-transfusion and post-transfusion samples of the patient, Hemoglobin and serum bilirubin levels and urine complete examination of the patient as hemolysis screen. Type of reaction was noted and documented as per hospital policy.

Statistical Package for Social Sciences (SPSS) v20.0 was used to collect and analyze data for variables like age, gender, frequency and type of adverse transfusion reaction, type of associated blood product, and blood group.

RESULTS

During the four-year period from January 01, 2018, to December 31, 2021, 9597 blood bags were issued to indoor patients of ULTH and Mansoorah Hospital. Out of these 9597 units transfused, 72 (0.75%) adverse transfusion reactions were reported. The mean age of patients was 35 years with a range between 15 to 69 years. Gender distribution is shown in Fig-1.

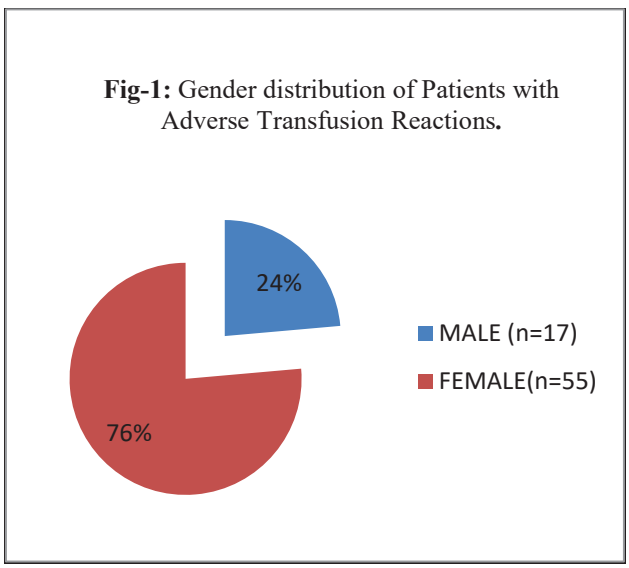

Fig-1: Gender distribution of Patients with Adverse Transfusion Reactions**.**

Of the 72 adverse transfusion reactions reported, febrile non-hemolytic transfusion reactions (FNHTR) were the most common, followed by

allergic reactions, shown in Fig-2.There were three cases of transfusion-associated circulatory overload (TACO), one event of transfusion-associated sepsis (TAS), and one case of delayed hemolytic transfusion reaction (DHTR). FNHTRs were found in 0.36 percent of cases, allergic responses in 0.33 percent, TACO in 0.03 percent, and DHTRs in 0.01 percent of cases.

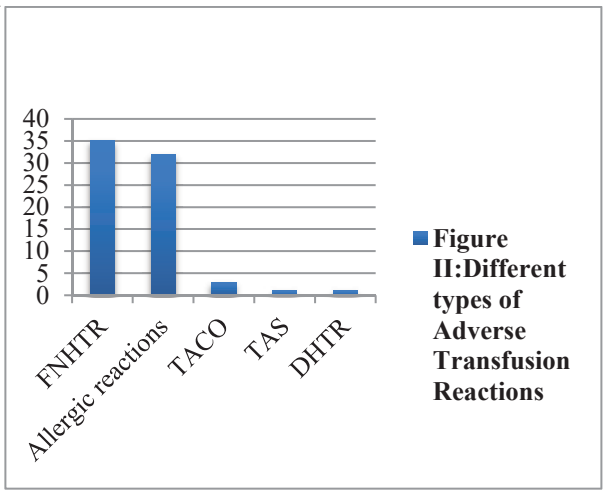

Figure II:Different types of Adverse Transfusion Reactions

FNHTR-febrile non-hemolytic transfusion reaction, TACO-transfusion associated circulatory overload, DHTR-delayed hemolytic transfusion reaction

The most commonly presented signs and symptoms of patients with ATRs include rigors and chills, fever, itching, anxiety, and headache as shown in Fig-3.

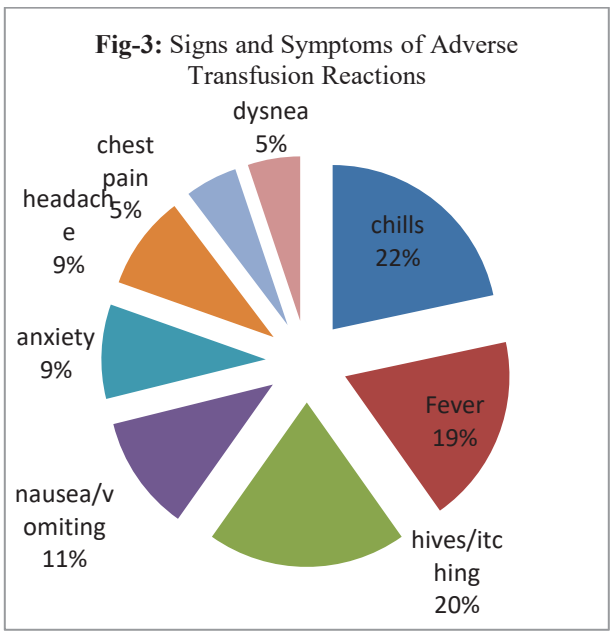

Fig-3: Signs and Symptoms of Adverse Transfusion Reactions

The type of components associated with ATRs was mostly whole blood followed by Pack Cell Volume (PCVs) and Fresh Frozen Plasma (FFPs), while no adverse reaction was observed with Platelet concentrate and Cryoprecipitate transfusion as depicted in Table-1.

No.	Type of components	Number	Percentage
1	Whole blood	48	66.7%
2	Pack Cell Volume(PCVs)	22	30.5%
3	Fresh Frozen Plasma (FFPs)	02	2.8%
4	Platelet concentrate	0	0
5	Cryoprecipitate	0	0

Table-1: Different types of blood Components associated with adverse transfusion reactions (ATRs)

The blood groups of patients who had adverse transfusion reactions (ATRs) were mostly,B-positive, O-positive, and A- positive. The frequency of different blood groups is demonstrated in Table-3.

No.	Blood groups	Number	Percentage
1	B-positive	33	45.6%
2	O-positive	10	13.7%
3	A- positive	10	13.7%
4	AB- positive	07	9.0%
5	B-negative	03	4.5%
6	A- negative	03	4.5%
7	O- negative	03	4.5%
8	AB-negative	03	4.5%

Table-2: Different types of blood groups related to adverse transfusion reactions (ATRs)

DISCUSSION

Adverse transfusion reactions (ATRs) are unfavorable occasions related with the transfusion of whole blood or one of its components.[11]They range in seriousness from mild to life threatening and can happen during transfusion or within 24 hours of transfusion are named as Acute transfusion reactions or days to weeks after the transfusion, named as Delayed transfusion reactions. This study was led to assess the comprehensive evaluation of adverse transfusion reactions reported to blood transfusion services at 2 tertiary care hospitals in Pakistan.

The approximated incidence of ATRs is 0.5 to 2.9 per 1,000 blood units.[10]In our study, 72 adverse transfusion reactions reported during the period of 4 years with frequency of 0.75%. It was slightly higher than reported incidence in various studies in Pakistan. A study in Karachi by Rashid et al reported the frequency of 0.34%. Other studies in Multan and Karachi by Akhtar et al and Khalid et al

reported the incidence as 0.38% and 0.082% respectively.[2,3,10] Our finding was quite lower than reported frequency in many different countries of the world when compared to various studies in India, Japan, Ethiopia and Taiwan.[12,13,14,15] But it was higher as compared to other studies in India by Pahuja et al and Saha S et al respectively.[16,17]
Comparison between current study and other national and international studies is shown in the Table-3.

No	Author	Place of study	Frequency of ATRs (%)	Most common type of reaction	Most common blood component involved
1	**Current Study**	Lahore, Pakistan	0.75	FNHTR	WB
2	**Khalid S et al[2]**	Karachi, Pakistan	0.082	FNHTR	PCVs
3	**Akhtar N et al[3]**	Multan, Pakistan	0.38	FNHTR	WB
4	**Rashid A et al[10]**	Karachi, Pakistan	0.34	Allergic TRs	PCVs
5	**Kato H[12]**	Japan	1.5	Allergic TRs	PC
6	**Gelaw Y[13]**	Ethiopia	5.2	Allergic TRs	WB
7	**Yao C[14]**	Taiwan	3.5	FNHTR	
8	**Sahu A[15]**	India	1.8	TACO	LD-RBCs
9	**PahujaS et al[16]**	Delhi, India	0.19	FNHTR	PCVs
10	**Saha S[17]**	India	0.13	Allergic TRs	FFPs

Table-3: Comparison with national and international studies

The reason of low reported frequency of adverse transfusion reactions is often underreporting.[10] It may involves many factors like absence of mindfulness about existing ATRs detailing frameworks among medical staff, ignoring minor transfusion reactions, an absence of easy availability of ATRs forms in various clinic units, unused blood bags not returned to the blood bank or discarded and unreasonable utilization of bonding premedication (allergy medicines and NSAIDs) without knowing the patient's past history of TR.[2,3,10] Reporting can be improved by improving the hemovigilance system, increasing awareness and better understanding of ATRs among medical professionals as well as proper functioning of Hospital Transfusion Committee (HTC).[18]
The most frequent type of ATRs encountered in our study was febrile non-hemolytic transfusion reaction (FNHTR) with reported incidence of 0.36% followed by Allergic reactions. This was not completely unusual, and the current findings were in line with data that other studies had documented. The febrile non-hemolytic transfusion reaction (FNHTR) is an acute transfusion complication that includes a 1°C increase in body temperature, as well as chills, nausea or vomiting, tachycardia, and a blood pressure spike.[20] The most common presenting symptoms in our patients with FNHTR were chills and fever followed by nausea and vomiting. FNHTR is caused by immunological factors such as the existence of preformed antibodies against WBCs in blood components, which causes the release of pyrogens, or the generation and release of biologically active cytokines by white cells during storage.[19].
FNHTR are mostly encountered ATRs in many local and foreign studies.[2,3,14,16]The common component associated with FNHTR in our study was whole blood. The most effective way to prevent FNHTR is Pre-storage Leucocyte depletion (LD), causing removal of WBCs before the release of cytokines. The incidence of FNHTR was shown to be reduced in Leucocyte reduced blood components (0.19%) than in non- Leucocyte reduced blood components (0.37%) in a comparative research[20]. In another comparative study the FNHTRs reduced from 0.24%with non-Leucocyte reduced RBCs to 0.05% in pre-storage Leucocyte reduced RBCs.[21]
Leucocyte depletion not only decreases the incidence of FNHTRs but also prevents transmission of CMV and reduces platelet refractoriness.[22]As part of the blood transfusion safety programs, many nations have introduced universal leukocyte reduction (ULR). The main reason for the lack of implementation of universal leukocyte reduction is financial constraints. However, current global evidence strongly suggests that ULR is a technique that enhances the safety of allogeneic blood components.[22]
Allergic transfusion reactions (ALTR) are transfusion-related immunological complications that manifest as a spectrum of symptoms that differ in severity. ALTR is induced by antibodies in the recipient reacting to an allergen in the blood component.[19]In current study 32 patients presented with milder allergic reaction with incidence of 0.33%. Itching,± hives, anxiety and headache were the most frequent symptoms observed. No case of anaphylaxis was observed. Incidence of Mild reactions is 0.03 - 0.61% with RBC transfusions, 0.3 - 6% with platelet transfusions and 1 - 3% with plasma transfusions and Anaphylaxis is 1/20,000 - 1/47,000 of transfusions.[23]Allergic reactions can be prevented by using washed PLTs and RBCs

especially in patients with previous history of serious allergic reactions.

In our study, 3 cases of Transfusion Associated Circulatory Overload were observed. The most common signs and symptoms in these patients were hypertension, dyspnea and anxiety. There were no cases of TRALI (Transfusion-Related Acute Lung Injury). Studies shows that this complication is rarely reported in Pakistan.[2] The less awareness among medical professionals and confusion other circulatory complications like TACO could be the reason behind reduced reporting of this complication here in Pakistan. In contrast to that TACO was the most common ATRs in transfused patients in study by Sahu A et al.[17]

The overall risks for acute HTR have been found to range from 0.02–0.07% to 3-5% per 1000 red cell unit transfusion in various investigations.[24]There was no acute hemolytic transfusion reactions or ABO incompatibility reported as well as no clerical error was noted. One case of delayed hemolytic reaction was observed in a patient known case of beta thalassemia Major with previous history of multiple transfusions. Delayed hemolytic transfusion reaction (DHTR) is a side effect of a blood transfusion due to recipient RBC auto antibodies or allo-antibodies. Allo-immunization is common in patients with transfusion dependent anemias. In our patient a drop in Hb was reported 2 days after transfusion, DAT was positive and Antibodies screening and identification revealed multiple auto and allo-antibodies. DHTRs can be avoided by identifying and recording clinically relevant red cell allo-antibodies. Some patient population on chronic blood transfusions, using partially or totally phenol typically matched red cell units may reduce the likelihood of allo-immunization and consequently DSHTR.[20]

Adverse transfusion reaction can be reduced by effective hemovigilance system which includes proper identification of patients, maintaining blood component quality control, rationale use of blood and its products, pre-storage leucocyte depletion, monitoring of patients during transfusion and active reporting of ATRs to the transfusion services.

CONCLUSION

For an accurate estimation of ATR incidence, proper transfusion monitoring and reporting of all such responses will be required. Awareness and understanding of ATRs among the clinical staff must be improved. Leucocyte depletion of blood components can reduce the incidence of Febrile hemolytic Transfusion reaction. To enhance the quality, safety, efficacy, and cost-effectiveness of blood and its components and as well as the donation process, an effective hemovigilance system must be established.

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