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Study of the incidence and profile of acute transfusion reactions in children

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ABSTRACT

Background: Blood is a vital human tissue and a precious health resource. Use of these components may be associated with adverse events, which compromise the efficiency and safety of blood transfusion. The incidence of adverse transfusion reactions has declined with modern facilities like improved screening and transfusion practices, but some are still observed due to alloimmunization, bacterial contamination, immunomodulation, etc. **Aims and Objectives:** To study the incidence and profile of acute blood transfusion reactions (ATR) in pediatric patients at our center. **Materials and Methods:** We monitored ATRs in patients receiving blood components among the age group of 1 month–18 years, during September 2021–August 2022. A detailed proforma was used to collect data from patients developing ATR. **Results:** ATRs were observed among 329 patients (3.9%) out of 9501 transfusions. In decreasing order of frequency, febrile nonhemolytic transfusion reactions (3.3%), allergies (0.5%), hemolytic reactions (0.1%) were observed. ATRs were most commonly observed with red cell concentrate transfusions (90.6%) followed by platelets (7%) and then plasma (2.2%) ($P=0.059$). Most of the reactions occurred within 1st 2 h (82.4%) of transfusion and the most common symptom recorded was fever (61.5%) followed by chills and rigors (20.9%). We found a significant association between ATRs and previous history of blood transfusion (81.8%) ($P<0.00001$) and also with storage of blood components for more than 3 days (88.8%) ($P=0.019$). **Conclusion:** The prevalence of ATR was 3.9% among pediatric patients in our setup. Knowledge of risk factors associated with transfusion reaction will help in improving transfusion practices.

Key words: Acute transfusion reactions; Acute transfusion reactions incidence; Incidence risk factors; Risk factors; Febrile non hemolytic transfusion reactions; Allergic reactions; Hemolytic reactions

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INTRODUCTION

Blood is a vital human tissue and a precious health resource, required to be adequately available, safe and rationally used. However, the use of these components may be associated with adverse events, ranging from minor chills and rigors to life-threatening anaphylaxis. Transfusion reaction is defined as any adverse event that occurs as a result of blood product transfusion, during or after its administration. The incidence of transfusion reactions reported in studies from different parts of India varies between 0.05% and 11.6%.[1,2] Transfusion reactions can be acute or delayed.[3] Acute transfusion reactions occur during or within 24 h of blood transfusion.[3] It includes febrile nonhemolytic transfusion reactions (FNHTRs), allergic reactions, hemolytic transfusion reactions, bacterial contamination, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), adverse metabolic effects such as citrate toxicity and hyperkalemia.[3]

Delayed transfusion reactions occur beyond 24 h of transfusion up to many years even. It includes delayed hemolytic transfusion reactions, delayed serologic transfusion reactions, transfusion-transmitted infections, iron overload, alloimmunization, post transfusion immunosuppression, posttransfusion purpura, immunomodulation, Graft Versus

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Host Disease[3] Adverse transfusion reactions compromise the efficiency and safety of blood transfusion particularly in settings burdened by financial inaccessibility to advanced transfusion reaction prophylaxis. Although the incidence of blood transfusion reactions has declined substantially with facilities like improved screening and transfusion practices, use of leukofilters, and modified blood components; a significant number of cases are still observed due to human errors, alloimmunization, bacterial contamination, etc.

In our Department, yearly, approximately 10,000 blood transfusions take place. However relatively less amount of data is available about acute blood transfusion reactions (ATRs) in pediatric patients. Hence with this study, we want to find out the incidence of ATR, improve our knowledge on the same and laying down standard operating procedures for transfusion practices, monitoring, and management of the same.

Aims and objectives

Primary objective:

- To estimate the incidence and study profile of acute transfusion reactions in pediatric patients at our centre.

Secondary objective:

- To determine risk factors associated with increased frequency of transfusion reactions.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Pediatrics CNBC and MY Hospital from September 2021–August 2022. All patients between age group 1 month–18 years who got admitted in ward, intensive care unit (ICU) and Thalassemia Day Care Centre for blood transfusion and developed ATR following transfusion of blood components (whole blood, red cell concentrate [RCC], platelets or plasma) were enrolled for the study after taking informed written consent. In our center, we followed national AIDS control organization guidelines for blood banking. Each unit of blood component transfused was considered separate transfusion. Patient with previous history of transfusion or those receiving more than one unit of blood components was considered as having multiple transfusions. Transfusion reactions were defined according to the World Health Organisation guidelines for the clinical use of blood.[3] In case an ATR occurred, patient's name and identification number, both on the bag and requisition form was rechecked to rule out the possibility of wrong sampling or bedside transposition. Verification of the patient's clinical records and his/her red cell ABO and Rh type was done to look for any error during the issue of blood components from the blood bank. The blood bag and transfusion set were sent to the blood bank with notification. Relevant clinical history of the patient regarding the indications of blood component transfusion and past history of ATR was recorded. In the case of Category 3 Transfusion reaction, samples were collected depending on the nature of reactions; like CBC with Peripheral blood smear, urine routine microscopy, cross matching, blood culture from the blood bag and patient's blood, Chest X-ray, arterial blood gas in TRALI, serum calcium in suspected hypocalcemia, Serum electrolytes in suspected hyperkalemia. We studied the association between occurrences of ATRs with various factors.

Statistical analysis

Data were entered into Microsoft Excel sheet and analyzed using SPSS 20. Appropriate tests of significance, like Chi-square test, were applied to look for any significant association between ATR and variables like age of the patient, type of blood component, etc. and $P<0.05$ was considered statistically significant.

RESULTS

During the study period, a total of 9501 units of blood were transfused at our center, out of which 371 (3.9%) ATRs were observed. The most common ATR observed was FNHTR (n=319, 85.9%) followed by allergic reactions (n=44, 11.8%) and then hemolytic reactions (n=8, 2.3%) (Table 1). ATRs were most commonly observed with RCC transfusions (n=336, 90.6%), followed by platelets (n=26, 7%) and then plasma (n=8, 2.2%) (P=0.059) (Table 2). FNHTRs was the most common ATR with all types of blood products (100% ATRs with whole blood [n=1] and Platelets [n=8] followed by 92.3% ATRs with platelet [n=24] and 84.9% ATRs with RCC [n=286]). The rate of ATRs was higher among children in 12–18 years of age (n=106/1071, 6.2%) followed by 1–6 years (n=140/2804, 5%) and least among 1 month–12 months age (n=25/1877, 1.3%) (P<0.00001) (Table 3). Similarly, rate of ATRs was higher among females (n=161/2601, 6.2%) as compared to males (n=210/6900, 3%) (P<0.00001). We observed most ATRs within 1st 2 h of transfusion (83.3%) (n=135 in 1st h and n=174 in the next 1 h), followed by 10%

Table 1: Incidence of ATR

WHO category of ATR	Type of ATR	No. of ATR	% of total ATR
Category 1	Allergic reactions	44	11.8
Category 2	FNHTR	319	85.9
Category 3	Hemolytic reactions	08	2.3

ATR: Acute blood transfusion reactions, FNHTR: Febrile non hemolytic transfusion reactions

Table 2: Risk factors for ATR

Risk factors	No. of ATR	% of ATR	P-value
Blood component transfused			
RCC	336	90.6	0.053439
Platelet	26	7	
Plasma	08	2.2	
Whole blood	1	0.3	
History of blood transfusion			
Previous transfusion	289	77.9	<0.00001
Previous ATR	254	68.5	
Storage duration of blood components prior to transfusion			
Within 3 days	46	12.3	0.019616
After 3 days	325	87.7	

RCC: Red cell concentrate, ATR: Acute blood transfusion reactions

Table 3: Other risk factors for ATR

Risk factors	No. of ATR	Total transfusion	%	P-value
Different pediatric comorbid groups				
Hemoglobinopathies	247	5155	4.8	<0.00001
Hematological malignancy	19	620	3.1	
Undergone BMT	3	432	0.7	
Patient admitted in PICU	91	2823	3.2	
Age				
1–12 month	25	1877	1.3	<0.00001
1–6 years	140	2804	5	
6–12 years	110	3119	3.5	
12–18 years	106	1701	6.2	
Blood group				
A	105	2568	4.1	0.472648
B	121	2773	4.4	
AB	39	1006	3.9	
O	114	3154	3.6	

PICU: Pediatric intensive care unit, ATR: Acute blood transfusion reactions

ATR (n=37) between 2 and 4 h of transfusion and least commonly beyond 4 h of transfusion, i.e.; n=25, 6.7% ATRs. The most common symptoms of ATRs were fever (n=319, 61.5%), chills and rigors (n=105, 20.9%), and itching (n=30, 5.7%). The most common signs of ATRs were rise in temperature (n=319, 48.5%), tachycardia (n=325, 49.4%), rashes (n=30, 6.5%), hematuria and hemoglobinuria (n=8, 1.2%) and then icterus (n=5, 0.9%). ATRs were observed in almost same proportion with different ABO blood groups (approx.4%) (Table 3). ATRs were more frequent with blood components stored beyond 3 days (n=325, 87.7%) (P=0.019616) (Table 2). ATRs were most commonly observed in patients with hemoglobinopathies (n=247/5155, 4.8%) followed by patients admitted to pediatric ICU (PICU) (n=91/2823, 3.2%) and then hematological malignancy (n=19/620, 3.1%) (Table 3). Of all 371 ATRs, 77.9% (n=289) had a previous history of transfusion and 254 had a previous history of ATR (68.5%) (P<0.05) (Table 2). 8 blood recipients were suspected of having hemolytic reactions. There was rise in serum bilirubin, and hematuria/hemoglobinuria post transfusion in those who developed hemolytic reactions. Direct coombs test (DCT) was positive in three cases. There was no blood group incompatibility in any of these cases. None of them had renal or liver dysfunction before ATR.

DISCUSSION

This study was conducted to describe the incidence and risk factors of ATR among pediatric blood recipients at a tertiary-level hospital. We studied pediatric patients who developed ATR during the period of 1 year. We assessed the profile and severity of each ATR, and management done was recorded.

During the study period, a total of 9501 blood components were transfused to pediatric patients in our center. Of these, 371 transfusions were associated with ATR (3.9%). Transfusion reactions were observed in 11.6% of cases from a study in Gujarat[2] to 3.3% reported in studies from Bali, Kano and Brazil[4-6] to as low as 0.95% in a study in USA[7] among pediatric patients. This wide variation in the frequency of ATR can be attributed to various factors like differences in the profile of patients, hemovigilance pattern, etc. RCC was the most frequently transfused blood component (n=3638, 38.3% transfusions) in our study. This appears to be due to the high incidence of hemoglobinopathies[8] and nutritional anemia in our study population. ATRs were seen most frequently associated with RCC transfusions (n=336, 90.6%), followed by platelets (n=26, 7%) and then plasma (n=8, 2.2%). A study by Oakley et al.,[9] showed highest rate of ATR with platelet transfusion but ATRs most commonly occurred with RCC transfusions in studies from Sikkim[10] (risk 0.76%, P=0.42) and Gujarat[2] (82.8%). This difference can be because of difference in methods of preparation of blood components, patient comorbidities, or other immunological mechanisms. Studies have shown platelet production by apheresis to decrease transfusion reactions.[11]

FNHTR (n=319, 85.9%) was the most common ATR in our study, followed by allergic reactions (n=44, 11.8%) and then hemolytic reactions (n=8, 2.3%). Other category 3 reactions, like TRALI, TACO, etc., were not observed during the study period. FNHTR was the most common transfusion reaction in studies reported from Uganda[12] (49%) and Kano[6] (3.3%). Some other studies showed allergic reactions as the most common transfusion reactions, as reported from Sikkim[10] (65.6%) and Brazil[5] (77.2%). FNHTR depends on various factors like leukocyte reduction, storage time, medications, patient and donor characteristics, monitoring practices, etc. We had a large proportion of

multitransfused patients in our study. It is advised to use leukoreduced bloods to decrease the chances of ATR for patients at risk for repeated transfusions.

On analyzing the age distribution, ATR rates were higher in the children above 12 year age group (n=106/1701, 6.2%) followed by 1–6 year age group (n=140/2804, 5%) least among children below 1 year (n=25/1877, 1.3%) (P<0.00001). This may be due to a large number of patients with hemoglobinopathies who required multiple transfusions, and each subsequent blood transfusion increased the risk of alloimmunization in the recipient. In a study from Bali[4] on pediatric blood recipients, more than 12 months of age group was found as a possible risk factor for ATR (odds ratio2.8, P<0.05). In our study, males received 72.6% (n=6900) transfusions and females 27.4%(n=2601). However, ATRs were observed most frequently in females (n=161, 6.2%), and 3% (n=210) transfusions in males developed ATR (P<0.00001). Based on patterns observed in a previous study from Bali[4] and USA,[9] males had a higher percentage of ATR.

ATRs were observed most frequently in patients with hemoglobinopathies (n=247/5155, 4.8%), and patient admitted to PICUs (n=91/2823, 3.2%) (P<0.05). It can be seen that the aforementioned comorbidities itself predispose the patient to multiple transfusions, which by itself is a risk factor for ATR. ATRs were seen in very few patients undergoing Bone marrow transplants (n=3/432, 0.7%). This was because of the use of leukoreduced blood products, premedication with antihistamines and steroids in patients with a history of ATR in BMT unit. Furthermore, a history of previous blood transfusion was significantly associated with ATR (n=289, 77.9%; P<0.00001). There was also a statistically significant association between the history of an ATR and the occurrence of subsequent ATR in our study population (n=254, 68.5%; P<0.00001). A study done in Kano[6] found a statistically significant relation between ATR and previous transfusion (8/78 vs. 3/102). The study by Kennedy et al.,[13] showed that there is a lower incidence of transfusion reactions in patients receiving premedication compared to placebo.

On analyzing the clinical features of ATR, the most common symptom observed in our study was fever (n=319) which is consistent with our observation that the most common ATR was FNHTR. Also, more than 2/3rd of ATR occurred within the 1st 2 h of initiating transfusion (n=309, 83.3%). A study in Bali[4] showed that most of the transfusion reactions were observed in 1st h (63.55%) and 2nd h of transfusion (28.97%).

The study by Apriastini and Ariawati[4] showed the highest prevalence of transfusion reactions with type O blood products. However, in our study, there was no increased frequency of ATRs with any particular ABO blood group.

More than 2/3rd of ATR occurred in patients who received blood products stored for more than 3 days (n=325, 87.7%, P=0.019616). Similar findings were reported in a study done in Kano.[6]

In this study, eight blood recipients were suspected of having hemolytic transfusion reactions (n=8, 2.3%). They had a fever, chills, hematuria, and icterus. Among them, 3 had immune hemolytic reactions (DCT positive) while other 5 were hemolysis due to probable non-immune causes like human or machine error, extended storage of red cells, improper storage temperatures, improper use of blood warmers, administration though a narrow-gauge needle or use of a rapid infuser. Many hemolytic reactions can be prevented by strict adherence to proper blood infusion techniques. There was no ABO and Rh blood group incompatibility in this study. Hence, the immune hemolysis was attributed to the development of some other alloantibodies to an RBC antigen through transfusion. All patients with hemolytic reactions had a normal baseline creatinine, liver enzymes which ruled out any underlying comorbidity in the patient predisposing to hemolysis like burns. Prevention and treatment of hemolytic reactions can be done by limiting RBC transfusions to evidence-based indications, developing international and national RBC alloantibody databases and developing prophylactic and treatment approaches.

All transfusion reactions were reported to the blood bank, and supportive management was given based on standard guidelines. Most cases of transfusions complicated by FNHTR and allergic reactions could be completed by antipyretics or antihistaminic coverage and other symptomatic management. In cases of ATR suggestive of hemolysis, blood transfusion was stopped.

Limitations of the study

In our study, half of study population was from patients with hemoglobinopathies which makes this study difficult to be generalized to pediatric population. Hence studies among large groups are needed to derive meaningful conclusions on acute transfusion reactions in children.

CONCLUSION

The present study analysed the incidence and risk factors for ATRs in pediatric population. ATR constituted 3.9% of all blood transfusions, of which majority were FNHTRs and allergic reactions. ATRs were highest with RCC transfusions. ATR rates are comparable to early

hemovigilance reporting from other countries. Fever and chills were most frequently reported symptoms suggesting any increase in temperature during transfusion should be taken seriously.

We found a statistically significant relation of ATR with previous transfusion and also with age of stored blood. Use of premedications, avoiding old blood components can decrease ATRs. Many ATRs can be prevented by strict adherence to proper blood transfusion techniques like right sized infusion set, slow infusion, using fresh blood components, maintaining proper storage temperatures, transfusing blood components within the stipulated time period.

This study helped us in analyzing risk factors associated with increased frequency of ATR. Thereby we could establish a proper hemovigilance pattern and adopt appropriate preventive measures. Appropriate use of blood products as well as safe blood transfusion practices will help in saving patient lives.

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REFERENCES

1. Kumar P, Thapliyal R, Coshic P and Chatterjee K. Retrospective evaluation of adverse transfusion reactions following blood product transfusion from a tertiary care hospital: A preliminary step towards hemovigilance. Asian J Transfus Sci. 2013;7(2):109-115. https://doi.org/10.4103/0973-6247.115564
2. Ghataliya KJ, Kapadia JD, Desai MK, Mehariya KM, Rathod GH, Bhatnagar N, et al. Transfusion-related adverse reactions in pediatric and surgical patients at a tertiary care teaching hospital in India. Asian J Transfusion Sci. 2017;11(2):180-187. https://doi.org/10.4103/0973-6247.214348
3. WHO. Manual on Clinical Use of Blood. WHO: Switzerland. Chapter 7- Adverse effects of transfusion Available from: https://apps.who.int/iris/bitstream/ handle/10665/42397/a72894.pdf
4. Apriastini NK and Ariawati K. Risk factors of acute blood transfusion reactions in pediatric patients in Sanglah General Hospital, Bali-Indonesia. Bali Med J. 2017;6(3): 534-538. https://doi.org/6.534.10.15562/bmj.v6i3.630
5. Pedrosa AK, Pinto FJ, Lins LD and Deus GM. Blood transfusion reactions in children: Associated factors. J Pediatr (Rio J). 2013;89(4):400-406. https://doi.org/10.1016/j.jped.2012.12.009
6. Gwaram BA, Borodo MM, Dutse AI and Kuliya-Gwarzo A. Pattern of acute blood transfusion reactions in Kano, North-Western Nigeria. Niger J Basic Clin Sci. 2012;9(1):27-32. https://doi.org/10.4103/0331-8540.102110
7. Harvey AR, Basavaraju SV, Chung KW and Kuehnert MJ. Transfusion-related adverse reactions reported to the National healthcare safety network hemovigilance module, United States, 2010 to 2012. Transfusion. 2015;55(4):709-718. https://doi.org/10.1111/trf.12918
8. Colah RB, Mukherjee MB, Martin S and Ghosh K. Sickle cell disease in tribal populations in India. Indian J Med Res. 2015;141(5):509-515. https://doi.org/10.4103/0971-5916.159492
9. Oakley FD, Woods M, Arnold S and Young PP. Transfusion reactions in pediatric compared with adult patients: A look at rate, reaction type, and associated products. Transfusion. 2015;55(3):563-570. https://doi.org/10.1111/trf.12827
10. Sharma DK, Datta S and Gupta A. Study of acute transfusion reactions in a teaching hospital of Sikkim: A hemovigilance initiative. Indian J Pharmacol. 2015;47(4);370-374. https://doi.org/10.4103/0253-7613.161257
11. Tobian AA, Savage WJ, Tisch DJ, Thoman S, King KE and Ness PM. Prevention of allergic transfusion reactions to platelets and red blood cells through plasma reduction. Transfusion. 2011;51(8):1676-1683. https://doi.org/10.1111/j.1537-2995.2010.03008.x.
12. Waiswa MK, Moses A, Seremba E, Ddungu H and Hume HA. Acute transfusion reactions at a national referral hospital in Uganda: A prospective study. Transfusion. 2014; 54(11):2804-2810. https://doi.org/10.1111/trf.12684
13. Kennedy LD, Case LD, Hurd DD, Cruz JM and Pomper GJ. A prospective, randomized, double-blind controlled trial of acetaminophen and diphenhydramine pretransfusion medication versus placebo for the prevention of transfusion reactions. Transfusion. 2008;48(11):2285-2291. https://doi.org/10.1111/j.1537-2995.2008.01858.x

Authors Contribution:
SS - Literature survey, Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **UC** - Literature survey, Concept, design, clinical protocol, statistical Analysis and Interpretation, manuscript preparation, editing, and Coordination and manuscript revision; **PM** - Concept, design and clinical protocol of study, statistical Analysis and Interpretation; Review Manuscript; Coordination and Manuscript revision

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