Section: Transfusion Medicine

Original Research Article

A STUDY OF TRANSFUSION RELATED ADVERSE EVENTS AT A TERTIARY CARE CENTER IN SOUTHERN INDIA

Anitha M[1], Sindhuja K[2]

[1]Assistant Professor, Department of Transfusion Medicine, Anam Chenna Subba Reddy (ACSR) Government Medical College, Nellore, Andhra Pradesh, India
[2]Associate Professor, Department of Transfusion Medicine, Anam Chenna Subba Reddy (ACSR) Government Medical College, Nellore, Andhra Pradesh, India.

Received : 09/08/2023
Received in revised form : 12/08/2023
Accepted : 14/08/2023

Keywords:
Adverse Transfusion Reactions, allergic reactions, Whole blood transfusion.

Corresponding Author:
Dr. Sindhuja K,
Email: drksindhuja@gmail.com

DOI: 10.47009/jamp.2023.5.4.400

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (4); 1996-2000

Abstract

Background: Blood transfusion plays an important role in improving the health and saves lives. However, it is also inherently embedded with adverse reactions ranging in severity from minor to life-threatening. An identification of Adverse Transfusion Reactions (ATRs) will help to take appropriate steps to reduce their incidence and make blood transfusion safe. This study was aimed to assess the frequency and type of ATR s in blood recipients. **Materials and Methods:** During the period of 36 months (January 2020 to December 2022) all the adverse events related to transfusion of blood and blood products admitted in our hospital were recorded. They were analyzed and classified using standard definitions, based on their clinical features and laboratory tests. The present prospective study was conducted in the department of transfusion medicine, ACSR Government medical college Nellore. **Result:** During the study period, a total of 2898 whole blood and blood components were issued from our blood bank to 2890 patients. Among them 14 (0.48%) adverse reactions were noted. The most common type of reaction observed was allergic (n = 9; 64.2%), followed by Febrile Non Haemolytic Transfusion Reactions (FNHTRs) (n=3, 21.04%), Transfusion Associated Circulatory Overload (TACO) (n = 1, 7.2%), and Transfusion Related Acute Lung Injury (TRALI) (n = 1, 7.2%). The ATRs were seen mostly with Whole Blood (64.2%). **Conclusion:** The frequency of transfusion reactions in our study was found to be 0.48%. This could be an underestimation of the true incidence because of under reporting as well as due to the management of few cases by the treating clinician itself. Rational use of blood, improving storage conditions, bedside monitoring of transfusion and documentation of adverse events will help in improving transfusion safety.

INTRODUCTION

Blood has no substitutes. Every year millions of blood components are transfused across the globe. Transfusion of blood and its products are lifesaving and relatively safe procedure. However, it is a double-edged sword, which should be used judiciously as it is also inherently embedded with adverse reactions ranging in severity from minor to life-threatening. An adverse transfusion reaction (ATR) is an unfavourable reaction to the transfused blood unit. Knowledge of these ATRs helps not only in their easy identification and management but also it alerts us to prevent its occurrence by taking precautionary and adequate measures. The lack of proper and strict hemovigilance systems throughout the country makes it difficult to assess the true and actual incidence of these reactions.[1]

Continuous monitoring of transfusion-related complications can promote understanding of factors contributing to transfusion reactions and help to formulate necessary remedial Measures.[2] In addition, it can promote patientcare and safety. Hence the present study was done with the primary objective to determine the frequency and types of adverse TRs occurring in hospitalized patients who required blood product transfusion at a tertiary care hospital in South India.

MATERIALS AND METHODS

The study was conducted in the Department of Transfusion Medicine of a tertiary care teaching hospital of South India. This was a prospective, observational study in which all ATRs observed among patients admitted in various clinical departments over a periodof 36 months (January 2020 to December 2022) were analyzed.

Consent for blood transfusion was obtained by patients or their attenders before every transfusion

ISSN (O): 2687-5365; ISSN (P): 2753-6556

episode. Patients were monitored at ward from the start of each transfusion till the end. As per the SOP for blood issue, every unit of blood component was issued along with a transfusion reaction/evaluation form to record the details of transfusion including patient details, component details, date and time of transfusion, vital parameters, and record of transfusion reaction if any. If the transfusion procedure was uneventful, the transfusion form had to be completely filled providing the date and time of starting and completion of the transfusion, patient's pre and post -transfusion vital signs, and returned to the blood bank with the empty blood bag. This helped us to trace the fate of every blood unit. To the extent possible, efforts have been made to monitor the recipient personally. Instructions were given to the healthcare personnel to monitor for any signs of reaction and to report to the blood bank. In case of ATR, the form had to be completely filled with details of reaction (time of onset of reaction) and sent to blood bank along with the left-over blood product bag with the attached transfusion set and patient postreaction blood samples – ethylenediaminetetraacetic acid (EDTA) and plain vacutainer. These cases were worked up by the transfusion medicine physician according to a standard protocol. As part of the routine transfusion reaction evaluation the patients blood sample and blood components were checked for clerical errors. Relevant clinical history regarding indications of blood transfusion, history of any previous similar episodes of adverse events, any previous history of transfusions and in the case of female patients, history of pregnancy were collected. Donor unit was checked for any abnormal mass or clot, any peculiar odour coming from the blood bag to rule out any abnormal delay in transfusion and improper storage after release of the unit from the blood bank, any leakage / breakage, number of ports broken from the blood bag and the condition of transfusion set filter was observed. The serum or plasma in a post-reaction blood sample was inspected for any evidence of hemolysis and compared with a pre-reaction sample. Urine examination was carried out for every case of transfusion reaction. The tests performed after the occurrence of transfusion reaction were patient's ABO and Rh group on pre- and post-reaction samples, donor's ABO and Rh group, patient and donor re-crossmatching on pre- and post-reaction samples (minor and major cross matching), direct antiglobulin test on patient's pre- and post-reaction samples.. Blood bag transfusion set and the patient's blood samples were sent for culture. Recipient blood sample was analysed for post transfusion complete blood counts, peripheral blood smears for schistocytes and spherocytes, reticulocyte count, serum bilirubin, plasma haemoglobin, liver function tests (LFT), renal function tests (RFT) and lactate dehydrogenase (LDH) levels. Fresh urine sample was collected to test for the presence of haemoglobinuria and urobilinogen and blood samples from the bag and the recipient were subjected for bacterial culture If there is suspicion of TRALI, X-ray Chest AP view was requested. Based on the clinical features experienced by the recipient and laboratory parameters, these reactions were classified by standards and recognized definitions defined by American Association of Blood Banks.[3]

RESULTS

During the period of study, a total of 2,898 units of whole blood and blood components were transfused to 2,890 patients, admitted at our hospital. Out of 2,898 units issued during the study period 1404 (48.5%) were of whole blood, 1331 (45.9%) packed red blood cells, 163 (5.6%) fresh frozen plasma (FFPs), respectively [Table 1].

Table 1: Type of blood/blood components transfused.

Type of components	No. of units transfused	Percentage
Whole blood	1404	48.5%
Packed re cells	1331	45.9%
Fresh frozen plasma	163	5.6%
Total	2898	100%

Table 2: Sex distribution of all type of transfusion reactions.

SEX	Allergy	FNHTR	TRALI	TACO	TOTAL (%)
FEMALES	7	3	1	1	12 (85.7%)
MALES	2	0	-	-	2 (14.3%)
Total	9	3	1	1	14 (100%)

There were 12 (85.7%) females and 2 (14.3%) males who had experienced a transfusion reaction. [Table 2]

Table 3: Distribution of ATRs according to age, blood group and clinical diagnosis.

Age/Sex M= male F=female	Blood group	Clinical diagnosis	Department
28/F	A Positive	anemia	Obstetrics
25/F	O Positive	Antenatal	Obstetrics
38/M	A Positive	Stab injury	surgery
24/F	A Positive	Anaemia	Obstetrics
18/M	B Positive	Anaemia	Obstetrics
21/F	O Positive	Anaemia	Obstetrics
28/F	B Positive	Anaemia	Obstetrics

ISSN (O): 2687-5365; ISSN (P): 2753-6556

31/F	O Positive	Anaemia	Obstetrics
19/F	O Positive	Anaemia	Obstetrics
24/F	O Positive	antenatal	Obstetrics
32/M	B Positive	Anaemia	Medicine
20/F	O Negatove	Missed abortion	Obstetrics
22/F	A Positive	antenatal	Obstetrics
19/F	O Positive	Anaemia	Obstetrics

A total of 14(0.48%) transfusion reactions were observed during the study period. Among them 2 (14.3%) were seen in males and 12(85.7%) in females. Majority of the patients belonged to blood group O Positive. The age range of all these ATR s spanned between 18 to 38 years. [Table 3]

Table 4: Relative frequency & over all incidence of transfusion reactions in the present study.

Type of reaction	Number (n=14)	Frequency	Over all incidence (%)
Allergic reactions	9	64.2%	0.3%
FNHTR	3	21.4%	0.10%
TRALI	1	7.2%	0.034%
TACO	1	7.2%	0.034%
Total	14	0.48%	0.48%

FNHTR-febrile non haemolytic transfusion reaction, TRALI-Transfusion related Acute Lung injury, TACO-Transfusion associated circulatory over load.

Most common reaction reported was allergic reaction (n=9; 64.2%) followed by FNHTR (n= 3;21.4%). In the present study 9 allergic reactions were noted and their overall incidence is 0.3%. Each of 1 case of TRALI and TACO were noted and their overall incidence is 0.034 respectively [Table 4].

Table 5: Categorization of transfusion reactions according to the type of Whole blood/blood component transfused.

S. No	Transfusion Reactions	Frequency n (%)	Whole blood n (%)	Packed red blood cells n (%)
1	Allergic reactions	9(64.2)	6(66.7)	3(33.3)
2	FNHTR	3(21.4)	1(33.3)	2(66.7)
3	TRALI	1(7.2)	1(100)	-
4	TACO	1(7.2)	1(100)	
	Total	14(100)	9	5

Table 6: Signs and symptoms of transfusion reactions.

Signs and symptoms	Number	Percentage
Rashes	06	42.84
Urticaria	-	-
Itching	01	7.14
Fever	04	28.56
Rigors	03	21.42
Tachycardia	02	14.28
Vomitings	-	-
Dyspnoea	02	14.28
Myalgia	01	7.14
Sweating	01	7.14
Chest tightness	01	7.14
Hypertension	01	7.14
Hypotension	01	7.14
Chills	05	35.7

Present Study rashes are most common followed by chills and fever(Table-6)

Table 7: Comparative study of overall frequency of adverse reactions in different studies.

S.no	Author	Place of study	Year	Overall frequency
1	Callera et al,[21]	Sau Paulo, Brazil	2004	0.54%
2	Shil et al,[22]	Dhaka, Bangladesh	2005	7.90%
3	Khalid et al,[23]	Karachi, Pakistan	5010	0.082%
4	Bhattacharya eta al,[5]	PGIMER, Chandigarh	2011	0.18%
5	Venkatachalapathy et al,[24]	IGGGH&PGI Pondicherry	2012	3.30%
6	Praveen Kumar et al,[1]	AIIMS, New Delhi	2012	0.05%
7	Meena Sidhu et al,[8]	Shri Maharaja Gulab Singh Hospital, Jammu.	2015	0.27%
8	Dhruva Kumar Sharma et al,[2]	Sikkim	2015	0.92%
9	Gupta et al,[25]	Ludhiana, Punjab	2015	0.42%
10	Present study	ACSR Govt.Hospital, Nellore.	2023	0.48%

Majority of the reactions were due to transfusion of Whole Blood (n=9;64.3%), followed by Packed cells(n=5;35.7%). Overall, 0.6%(9/1404X100) of whole blood, 0.3% (5/1331X100) of PRBCs, issued from the blood bank during the study period were implicated in causing transfusion reactions (Table 5). A single case of TRALI was reported and the recipient was 28-year-old female who developed fever, hypotension, dyspnea, chest tightness and tachycardia following whole blood transfusion.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

A single case of TACO was seen in 32 years female admitted with severe anemia. She received multiple transfusions. She developed dyspnea, myalgia, sweating and tachycardia. The symptoms were relieved after diuretic therapy.

DISCUSSION

The overall frequency of adverse reactions during the present study period was 0.48 % [Table 4]. The reported incidence of ATRs in the literature varied widely from 0.5% to 3% of all transfusion episodes.[4] In our study, the frequency of ATRs was observed to be 0.48%, which is comparable to that of a study carried out in Chandigarh by Bhattacharya et al., where the incidence of ATRs was 0.18%.[5] Similarly, lower incidence of 0.05% was reported in a study conducted in New Delhi by Kumar et al.[6] A study done by Chakravarthy-Vartak U et al showed a frequency of transfusion reactions of 0.16%.[7]

In our present study, females were more affected than males [Table 2] which is similar to the study by Sidhu et al.[8] However, Kumar et al. in their study found males to be more affected than females.[1]

In our study highest number of Transfusion reactions were found in blood group O followed by blood group A [Table 3]. However, in kanthi Sinha et al study the highest number of ATR were found in blood group A followed by B.[9]

Majority of the reactions were due to Whole Blood(64.3%) transfusion followed by packed red blood cells(35.7%), transfusions [Table 5]. A study done by Negi et al. at blood bank of a tertiary care center of Northern India showed that 92% of reactions were due to whole blood and packed RBC transfusion followed by FFP.[10]

In the present study most common reaction reported was allergic reaction (64.2%) and its overall incidence was 0.3% [Table 4]. Whole Blood (66.7%) is the most commonly implicated in causing allergic reaction followed by packed red cells (33.3%) [Table 5]. According to a recent study carried out at AIIMS, New Delhi also the majority of the type of reactions observed were allergic and its overall incidence was 0.028%,[1] which is lower than the incidence of allergic reactions in our study. The blood component most commonly implicated in allergic reactions in their study was platelet rich plasma (PRP) (0.053%) followed by packed red blood cells (PRBC). Another report from North India also states that allergic reactions was the commonest form of transfusion reactions.[8]

Febrile reactions usually occur in about 1% of transfusions. It is defined as a 1°C temperature rise associated with transfusion and having no medical explanation otherthan blood/component transfusion.[10] Rigors and other symptoms in the absence of fever are also included as FNHTR. Data on the incidence of FNHTR vary greatly in the literature. Possible reasons for this variation include differences in recording of symptoms by the bedside staff, case ascertainment,and use of pretransfusion medications to control fever.

The frequency of FNHTR in the present study was 21.4% [Table 4] which was lower than the study by Praveen Kumar et al. where he reported 35.7%.[1] They are reported to be more common with platelet transfusions than PRBCs because platelets require storage temperature of between 20°C –24°C, which results in donor leukocyte activation and pro-inflammatory cytokine accumulation. However, in the present study FNHTRs were found to be more with Whole Blood. The higher rate of FNHTRs in our study could be due to lack of leukoreduction facility at our hospital. A comparative study on incidence of FNHTR in leukoreduced and nonleukoreduced blood components showed that the incidence is 0.12% in nonleukoreduced and 0.08% in presto rage leukoreduced blood.[11] Hence, introduction of leukoreduction at our institution could possibly enable us to reduce the febrile reactions.

In the present study allergic reactions (64.2%) is the most common ATR followed by FNHTR (21.4%). Chavan sk, et al. reported that allergic (55.6%) is common than FNHTR (33.3%).[1] Kumar p et al also reported allergic reaction (55.1%) as commonest followed by FNHTR (35.7%).[1] Pahuja et al,[13] Mukherjee, et al,[14] in their study showed FNHTR were most common transfusion reaction followed by allergic. Ramanathan, et al.[15] Study shows FNHTR (53%) as a most common ATR followed by allergic TR (39%).

There was a single case of suspected TRALI. Thus, the overall incidencefor TRALI appeared to be 0.034%. The incidence of TRALI israre in the Indian subcontinent where most donors are male. The incidence of TRALI reported in variousstudies from Western literature ranged from 0.014% to 0.08%,[16] per units transfused. However, it is generally agreed that TRALI is underdiagnosed. This is likely because of poor awareness, lack of recognition of the condition, and/or because TRALI is easily confused with other conditions, e.g., adult respiratory distress syndrome (ARDS), hypervolemia, and congestive heart failure. The frequency of TRALI in the present study was low (7.2%) (Table 4). It has been reported that TRALI probably occurs about 1 in 2500 to 4000 units of female donor plasma transfused. In our blood bank the female donors are much less (3% during the study period) particularly the donors for component preparation. This could be one of the reasons for the decreased frequency of TRALI observed. However, the donor sample could not be evaluated for anti-HLA or anti-HNA antibodies which suggest susceptible host factors. Careful selection of donors can decrease incidence of TRALI.

TACO mainly occurred due to inappropriate request and administration of blood components. Patients with severe anemia are at increased risk of TACO because of already being in hyperkinetic state, with heart being intolerant to slight increase in blood volume.[17] Rapid infusion of blood products should be avoided and AABB recommends an infusion rate

ISSN (O): 2687-5365; ISSN (P): 2753-6556

of 2-4 ml per minute for RBC s and faster rates for plasma.[18] In the present study a single case of TACO was observed which has occurred following the isolated transfusion of RBC that too only 30 ml. Agnihotri et al. reported a case of TACO following single blood unit transfusion.[19] Here, it occurred with only one episode of RBC transfusion showing that it can occur even with small volume of the RBC transfusion of 1 unit or less as reported by Li G et al.[20] The rationale of transfusion and rate of transfusion were not appropriate in this recipient in spite of the diuretic cover.

Rashes (42.84%) followed by chills (35.7%) were the predominant signs and symptoms of allergic reactions in the present study [Table 6]. Bhattacharaya et al also observed rash as the most frequent sign in 76% of their allergic reactions.[5] Other reported symptoms like peri orbital oedema, vomiting were not observed in the present study.

The most common signs and symptoms of FNHTR were fever chills and rigors. Study by Meena siddhu et al,[8] also reported chills and rigors (100%) as common symptoms followed by fever (35.1%).

CONCLUSION

To conclude, frequency of transfusion reactions in present study was 0.48%, majority of these were due to transfusion of Whole Blood. This can be an underestimation of the true incidence because of underreporting which can be improved by hemovigilance system. This study shows the importance of rational use of blood and its components, improving storage conditions, bedside monitoring of transfusion and documentation of adverse events and implementation of the hemovigilance system, thus helping to improve transfusion safety. Emphasis should be given to adoptnewer technologies with improvement in existing ones so thatblood transfusion can be towards zero risk transfusion. Adequate skilled and dedicated manpower, reporting of all adverse events, fully functioning hospital transfusion committee with continuousmedical education to medical and paramedical staff will definitely reduces the incidence of adverse TRs to minimum.

REFERENCES

1. Kumar P, Thapliyal R, Coshic P, 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; 7:109-15.
2. Sharma DK, Datta S, Gupta A. Study of acute transfusion reactions in a teaching hospital of sikkim: A hemovigilance initiative. Indian J Pharmacol 2015; 47:370-4.
3. Narvios AB, Lichtiger B, Neumann JL. Underreporting of minor transfusion reactions in cancer patients. MedGenMed 2004;6:17.
4. Cho J, Choi SJ, Kim S, Alghamdi E, Kim HO. Frequency and pattern of non-infectious adverse transfusion reactions at a tertiary care hospital in Korea. Ann Lab Med 2016; 36:36-41.
5. Bhattacharya P, Marwaha N, Dhawan H, Roy P, Sharma R Transfusion related adverse events at the tertiary care centre in North India: An Institutional hemovigilance effort. Asian J Transfuse Sci.2011; 5:164-70.
6. Kumar R, Gupta M, Gupta V, Kaur A, Gupta S. Acute Transfusion Reactions (ATRs) in Intensive Care Unit (ICU): A retrospective study. J Clin Diagn Res 2014; 8:127-9.
7. Chakravarthy-Vartak U, Shewale R,Vartak S,Faizal F,Majethia N. Adverse reactions of blood transfusion: A study in a tertiary care hospital. Int J Sci Study 2016;4(2):90-94.
8. Sidhu M, Meenia R, Yasmeen I, Akhtar N. A study of transfusion related adverse events at a tertiary care centre in North India: An initiative towards hemovigilance. Int J Adv Med. 2015; 2:206-10
9. Sinha RTK, Rai P, Dey A. A Study of Transfusion Related Adverse Events at a Tertiary Care Center in Central India: A Retrospective Evaluation. Journal of Medical Sciences and Health.Sep-Dec 2016;2(3):6-12.
10. Negi G, Gaur DS, Kaur R. Blood transfusion safety: A study of adverse reactions at the blood bank of a tertiary care center. Adv Biomed Res 2015; 4:237.
11. Uhlmann EJ, Isgriggs E, Wallhermfechtel M, Goodnough LT. Prestorage universal WBC reduction of RBC units does not affect the incidence of transfusion reactions.
12. Chavan SK, Patil G, Rajopadhye P. Adverse blood transfusion reactions at a tertiary Care hospital. Int J Res Med Sci 2016;4(6):2402-07.
13. Pahuja S, Puri V, Mahajan G, Gupta P, Jain M. Reporting adverse transfusion reactions: A retrospective study from tertiary Care hospital from New Delhi, India.Asian J Transfus Sci 2017;11(1):6-12.
14. Mukherjee S, Sahoo D, Ramnath A, Maiti R.A pilot study analysis of transfusion related adverse events at the tertiary care hospital in Eastern India: Encourages the establishment of institutional hemovigilance program. Glob J Transfus Med 2018;3(1):76-7.
15. Ramanathan, Meena, Sushama. Reporting adverse Transfusion Reactions Section in a Tertiary Care centre, Kerala, India. National Journal of Laboratory Medicine 2019;8(3):8-10.
16. Kathryn E, Webert, Blajchman MA. Transfusion-related acute lung injury. Transfus Med Rev 2003; 17:252-62.
17. StackG, PomperGJ.Rossi's Principles of Transfusion Medicine,3rd edi. Philedelphia, PA: Lippincott Williams & Wilkins:2002, Febrile, allergic and non-immune transfusion reactions;831.
18. mazzai CA, Popov sky MA, Kopko PM. Technical Manual.16th edition. Maryland: American Association of Blood Banks; 2008.Non-infectious complications of blood transfusion;715-751.
19. Agnihotri N, AgnihotriA. Transfusion associated circulatory overload. Indian J Crit Care Med.2014:18;396-8.
20. Li G, Rach male S, Kojicic M, Shahjahan K, Malinchoc M, Kor DJ et al. Incidence and transfusion risk factors for transfusion-associated circulatory overload among medical intensive care unit patients. Transfusion. 2011; 51:338–43
21. Callera F, Silva ACO, Moura AF, Melo DB, Melo CMT. Descriptions of acute transfusion reactions in a Brazilian Transfusion Service. Rev bras. hematol. hemoter.2004;26:78-3.
22. Shil N, Biswas J, Islam A, Khatun A. Day care transfusion therapy—One year experience in a day care transfusion unit of Transfusion Medicine department in a tertiary care hospital. Bangladesh J Med 2005; 16:83–6
23. Khalid S, Usman M, Khurshid M. Acute transfusion reactions encountered in patients at a tertiary care center. J Pak Med Assoc2010; 60:832-6.
24. Venkata Chalapathy TS. A Prospective audit of blood transfusion reactions in tertiary care hospital for the use of Blood and Blood Components. J Blood Disord Transfus 2012; 3:118.
25. Gupta M, Kumar R, Gupta S, Kaur A. Acute transfusion reactions encountered in patients at a tertiary care centre in Punjab. Natl Med J India.2015:28:8-11

ISSN (O): 2687-5365; ISSN (P): 2753-6556