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Prevalence and Factors Associated with Acute Blood Transfusion Reactions: A Cross-sectional Study in Southwest of Iran

Mahin Behzadifard [1,*], Fatemeh Shajari [2], Kosar Ghasemi [2], Roqaye Karimi [3], Somayeh Jafrasteh [4], Alireza Momeni [4]

[1] Department of Laboratory Sciences, School of Allied Medical Sciences, Dezful University of Medical Sciences, Dezful, Iran
[2] Student Research Committee, Dezful University of Medical Sciences, Dezful, Iran
[3] Department of Hematology and Cell Therapy, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
[4] The Clinical Research Development Unit of Ganjavian Hospital, Dezful University of Medical Sciences, Dezful, Iran

[*] ***Corresponding Author:*** Department of Laboratory Sciences, School of Allied Medical Sciences, Dezful University of Medical Sciences, Dezful, Iran. Email: mahinbehzadi2020@gmail.com

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Abstract

Background: Blood transfusion may lead to adverse events ranging in severity from minor to life-threatening. These events can occur during a transfusion, termed acute transfusion reactions (ATRs), or days to months later, and termed delayed transfusion reactions. Understanding the prevalence and factors associated with ATRs is essential for enhancing patient safety and optimizing transfusion practices.

Objectives: The present study aimed to assess the prevalence of ATRs and identify associated factors among transfused patients in a teaching hospital over a two-year period.

Methods: This retrospective cross-sectional study was designed based on the medical records of 36,595 transfused patients in a teaching hospital in southwestern Iran from 2020 to 2021. Inclusion criteria were patients who experienced ATRs, while exclusion criteria involved patients with ATRs but incomplete records. Demographic and clinical data were extracted from complication reporting forms. Data were analyzed using GraphPad Prism software version 8.3. The chi-square test was used to compare the correlation between reactions with or without a previous history of blood transfusion ($P < 0.05$).

Results: In the total number of transfusions, the reaction rate was 0.3% (100 cases); 57% were men and 43% were women. The age range was 9 days to 89 years (mean age, 43.1 ± 20.8 years). The most common reaction was allergic (80%), followed by non-hemolytic febrile reactions (15%), anaphylaxis (2%), acute lung injury related to blood transfusion (2%), and volumetric overload (1%). A history of blood transfusion was noted in 52% of cases. No statistically significant relation was observed between the history of transfusion and transfusion reactions ($P = 0.7$).

Conclusions: Allergic and febrile non-hemolytic reactions (FNHRs) were the most prevalent complications related to transfusions. The study indicated that the history of blood transfusions did not significantly trigger these reactions. Nurses should closely monitor patients for ATRs and ensure timely reporting of any reactions. The hemovigilance center of the hospital should analyze the prevalence of reactions and the frequency of each type of reaction to identify the sources of errors that may induce reactions and develop potential strategies for minimizing errors in future transfusions.

Keywords: Blood Transfusion, Acute Transfusion Reactions (ATRs), Allergic Reactions, Febrile Non-hemolytic Reactions (Fnhrs), Anaphylactic Reactions, Transfusion Related Acute Long Injury (TRALI), Transfusion Associated Circulatory Overload (TACO), Hemolytic Reactions

1. Background

After the creation of the ABO classification of blood groups in the twentieth century, the transfer of blood products has become one of the most important medical measures to save the lives of patients (1). The primary purpose of transfusing blood products is the treatment of chronic anemia, coagulation disorders,

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and fatal bleeding. However, there are other objectives, such as the treatment of von Willebrand disease, hemophilia A, factor XIII deficiency, and fibrinogen deficiency (2). Fibrinogen can also be used in surgeries such as organ transplants, cardiovascular surgeries, large tumor resections, and pregnancy-related complications (3).

Blood transfusion complications range from mild to life-threatening in terms of severity and are divided into acute and delayed types based on the time of occurrence: The acute type occurs during the transfusion or within the first 24 hours thereafter, and the delayed type occurs days or weeks after receiving the blood products (4). Acute transfusion reactions (ATRs) occur in 0.5% to 3% of transfusions globally. The incidence rates of ATRs include hemolytic reactions (1:30,000 to 1:76,000; 1:1.8 million fatal rate), febrile non-hemolytic reactions (FNHR) (0.1% to 1%), allergic reactions (1% to 2%), anaphylaxis (1:20,000 to 1:50,000; fatality rate 0.6 to 1.6 per 100,000 packed cell transfusions), septic reactions (platelet 1:25,000, packed cell 1:2.5), transfusion-related acute lung injury (TRALI) (0.04% to 0.1%; mortality rate 5% to 15% despite supportive care), and transfusion-associated circulatory overload (TACO) (1% up to 6% in critically ill patients). Delayed complications include alloimmunization of platelets and erythrocytes, delayed hemolytic complications, post-transfusion purpura, graft-versus-host disease (GVHD), transfusion-transmitted infections (TTIs), and iron overload (1-5).

The ATRs are a significant concern in blood transfusion safety, with varying incidences reported globally. Packed red cells, anaphylactic reactions, TRALI, and sepsis related to transfusion may cause a notable proportion of moderate to severe reactions (6). Transfusion-related errors were reported in a substantial number of cases occurring during blood sample collection and handling, and misidentification of the patient at the time of injection, leading to adverse reactions and blood product wastage (7, 8). These findings emphasize the necessity of robust hemovigilance systems to enhance transfusion safety and prevent adverse events.

2. Objectives

The present study was conducted to determine the prevalence of ATRs and the relation of these reactions with demographic factors, previous blood transfusion history, and underlying diseases in a teaching hospital in southwestern Iran over a period of two years.

3. Methods

This cross-sectional study, conducted after receiving ethical approval from the Ethics Committee of Dezful University of Medical Sciences (IR.DUMS.REC.1401.096), recorded information on blood-transfused patients with ATRs from Ganjavian Hospital, a teaching hospital in southwestern Iran (2020 - 2021). Data were manually extracted by trained staff. Underlying diseases were categorized according to clinician diagnosis. Inclusion criteria encompassed patients who experienced ATRs, while exclusion criteria involved ATR cases with incomplete records. Data collection involved manual review of medical records, utilizing standardized forms for data extraction. Variables collected included demographic characteristics (age, gender), type of blood product consumed, history of underlying diseases, and transfusion history. Underlying diseases were categorized based on clinical diagnosis.

3.1. Data Analysis

Statistical analysis was performed using GraphPad Prism software version 8.3. Descriptive statistics included frequency, percentage, mean, and standard deviation. The chi-square test was employed to compare patients with or without transfusion reactions, with $P < 0.05$ considered statistically significant.

4. Results

Among 36,959 transfusions, 100 patients experienced ATRs (57% men and 43% women). The youngest and oldest patients were 9 days and 89 years old, respectively, with an average age of 43.1 ± 20.86 years. Among patients with ATRs, 23% showed no history of disease, while 77% had a history of underlying diseases. The highest frequencies were related to patients with thalassemia major (24.1%), high blood pressure (22.2%), and heart diseases (18.2%), followed by other diseases (16.1%), kidney disease (8.0%), diabetes (6.2%), and liver disease (5.2%) (Figure 1). Among the blood products, packed RBCs had the highest consumption share, and the highest number of acute reactions was also related to this product. Cryoprecipitate and washed red blood cells had the lowest consumption and the lowest incidence of ATRs (Table 1). The findings showed that 48% of patients had no history of blood transfusion, 39% had a transfusion in less than three months, and 13% of patients had a history of transfusion more than three months ago. Patients with a history of blood transfusion had a higher frequency of ATRs compared to patients without a history of blood transfusion (52% vs. 48%). Statistical analysis also showed no significant difference between the group with and without a history of blood transfusion ($P = 0.7$).

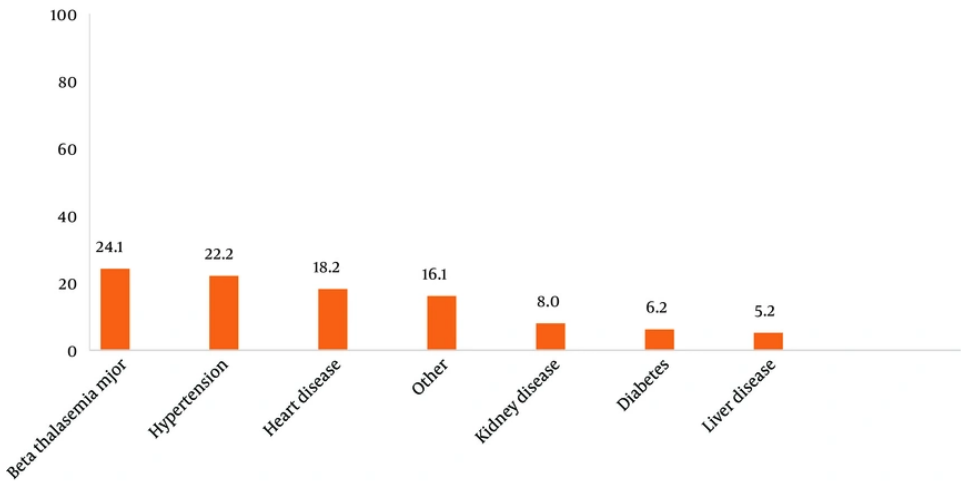

Figure 1. Disease frequencies in all transfused patients. Among the transfused patients beta thalassemia major has the most rate. Other diseases included celiac disease, esophageal cancer, premature infant, pneumonia, ichthyosis, gastrointestinal bleeding, colon cancer, esophageal varices, intestinal obstruction, ovarian cancer, anemia, diabetic foot ulcer (each 1%). This graph shows the most recipients had no history of disease and then were major thalassemia.

Table 1. Details of Blood Products Usage in Ganjavian Hospital in 2020 and 2021 [Packed RBCs Caused Most Reactions (%)]

Products	Number (Units)	Frequency/Percentage	Number of Acute Reactions	Frequency Percentage of Acute Reactions
Blood products consumed in 2020				
Packed red blood cells	6209	35.54	16	0.25
Fresh frozen plasma	2689	15.39	1	0.037
Platelets	4604	26.35	1	0.0217
Cryoprecipitate	668	3.82	0	0
Leukoreduced red blood cells	3062	17.52	1	0.032
Washed red blood cells	238	1.36	0	0
Total	17470	99.98	19	0.34
Blood products consumed at in 2021				
Packed red blood cells	7165	37.46	53	0.73
Fresh frozen plasma	1942	10.15	2	0.1
Platelets	5676	29.67	6	0.1
Cryoprecipitate	1138	5.95	2	0.17
Leukoreduced red blood cells	2905	15.19	18	0.61
Washed red blood cells	299	1.56	0	0
Total	19125	99.98	81	0.42

According to the findings, allergic reactions were the most common ATRs observed among blood and blood product recipients (80%) (Figure 2).

5. Discussion

Our findings confirm that allergic reactions and FNHRs are the most prevalent ATRs. The lack of significant relationships among underlying diseases suggests that other factors may contribute to triggering ATRs. For instance, allergic reactions may be influenced by genetic predispositions, plasma protein susceptibility, and the presence of IgE in recipients against these proteins. FNHRs are usually attributed to cytokines released from donor leukocytes during storage of blood components or recipient antibodies reacting against human leukocyte antigens (HLA) on

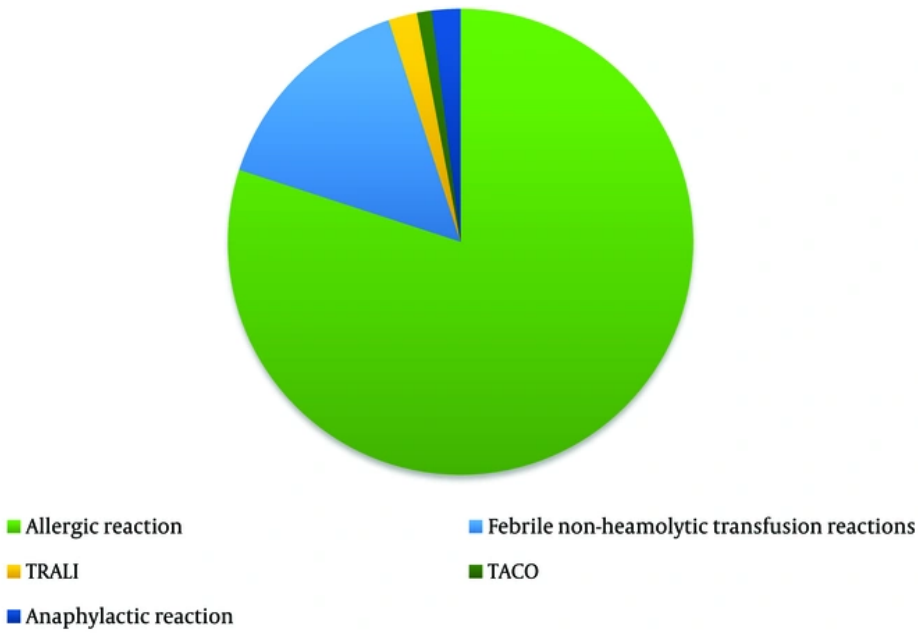

Figure 2. Percentage frequency of acute reactions caused by product transfusion in patients; Allergic reactions have the most proportion.

donor leukocytes, especially in patients with a history of previous transfusion or pregnancy, or contamination of blood products with bacteria or certain medications in the recipient's system (1-4).

In this study, a total of 36,959 transfused units resulted in 100 ATR cases. The age range of transfused patients was 9 days to 89 years. The most consumed blood product was packed cells, and the most common diseases among them were thalassemia major (24.1%) and hypertension (22.2%). Although the presence of anemia was significant in the two groups with and without acute transfusion complications ($P = 0.006$), no significant relationship was reported between other recorded underlying diseases (hypertension, diabetes, thyroid disorder, heart disease, kidney failure, malignancy, and liver disorder) in the two groups with and without acute complications ($P < 0.05$). No association between transfusion history and ATRs was observed ($P = 0.7$).

In a study by Azizi et al. at the Heart Center in Sari, out of a total of 9,193 blood products transferred, the product with the highest consumption was packed cells (69.4%). However, no definitive relationship between the type of product and the reactions was reported in their study (9). According to the results of our study, allergic reactions (80%) were the most common acute reactions due to blood transfusion, followed by FNHRs (15%), TRALI (2%), anaphylactic reactions (2%), and TACO (1%).

In the study by Bodaghkhan et al. conducted at Namazi Hospital in Shiraz, out of 57,902 blood recipients, 52 patients (0.1%) experienced acute transfusion complications, with FNHRs (48%) being the most common acute reaction, and allergic reactions ranking second (15%) (10). The study by Payandeh et al. showed that the most common acute reaction was allergic reactions (49.2%), which were accompanied by various skin manifestations such as itching, rash, and pruritus. An increase in body temperature 1°C above baseline was considered an FNHR, which was the second most common reaction (11).

In another study by Salimi et al. conducted at the Urmia Blood Transfusion Center, out of 261 cases of ATRs, the most common reactions were allergic reactions, FNHRs, and acute hemolytic reactions, respectively (12). This study aligns with our findings. A study in a tertiary care hospital in Bangladesh showed that transfusion reactions occurred in 11.5% of the 96 patients who received blood and blood products, with FNHRs (72.7%), allergic reactions (18.2%), and acute hemolytic transfusion reactions (9.1%) being the most common reactions, respectively (13).

According to reports at Methodist Hospital, Wenchi-Ghana, from January 2021 to December 2022, a total of 5,857 units of blood were used during the study period, with an incidence of 0.5 ATRs per 30 units of blood transfused. Factors such as previous history of transfusion, abortion, and longer storage of transfused blood were associated with an increased likelihood of ATRs. The number of transfused blood units also influenced the odds of developing ATRs (14). Contrary to the Wenchi-Ghana study, in our study, prior transfusions did not elevate the risk of ATRs (P = 0.7).

The study by Subair et al. monitored ATRs in pediatric patients, observing 329 ATRs out of 9,501 transfusions, supporting the incidence rate that showed the majority of reactions occurred within the first 2 hours of transfusion, with fever being the most frequently recorded symptom (61.5%) (15). Healthcare providers should be trained to recognize early signs of ATRs and implement strategies to mitigate risks.

5.1. Conclusions

This study showed a high prevalence of allergic and FNHR in blood transfusions. By recording and not neglecting blood reactions that occur immediately or within 24 hours of transfusion, and then analyzing the collected data by the hemovigilance department, errors can be identified and reduced to enhance patient safety and optimize transfusion protocols in future transfusions.

5.2. Study Limitation

This study has certain limitations, including its retrospective design and single-center data.

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Footnotes

Authors' Contribution: S. J., M. B., and A. M. participated in the design of the study. F. S., K. G., and R. K. collected and analyzed the data. All authors participated in the manuscript writing and approved the final revision.

Conflict of Interests Statement: The authors declare no conflict of interests.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: This study was approved by the Research Ethics Committee of Dezful University of Medical Sciences (IR.DUMS.REC.1401.096).

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Informed Consent: Informed consent was obtained from all participants.

References

1. Obeta M, Obeta K, Lugus M. Current Trend in Blood Transfusion Science, Where are we? *Haematol Int J.* 2020;**4**(2). https://doi.org/10.23880/hij-16000159.
2. Quintana-Diaz M, Andres-Esteban EM, Sanchez-Serrano J, Martinez-Virto A, Juarez-Vela R, Garcia-Erce JA. Transfusions in the Emergency department: More than a blood transfusion. *Rev Clin Esp (Barc).* 2020;**220**(7):393-9. [PubMed ID: 31744619]. https://doi.org/10.1016/j.rce.2019.10.002.
3. Lassila R, Weisel JW. Role of red blood cells in clinically relevant bleeding tendencies and complications. *J Thromb Haemost.* 2023;**21**(11):3024-32. [PubMed ID: 37210074]. [PubMed Central ID: PMC10949759]. https://doi.org/10.1016/j.jtha.2023.05.009.
4. Ajmani PS. Transfusion Reactions. In: Ajmani PS, editor. *Immunohematology and Blood banking: Principles and Practice*. Singapore: Springer Singapore; 2020. p. 175-95. https://doi.org/10.1007/978-981-15-8435-0_15.
5. Hong H, Duque MA, Mana AF, Wu Y. Noninfectious transfusion-associated adverse events. *Ann Blood.* 2022;**7**:19. https://doi.org/10.21037/aob-21-83.
6. Wahidiyat PA, Marpaung E, Iskandar SD, Pratanata AM, Sitompul NE. Acute transfusion reaction and its associating factors: An insight from Indonesian National Referral Hospital. *Asian J Transfusion Sci.* 2024;**10**:10.4103/ajts.AJTS_62_19. [PubMed ID: 01376746-990000000-00031]. https://doi.org/10.4103/ajts.AJTS_62_19.
7. Chavez Ortiz JL, Griffin I, Kazakova SV, Stewart PB, Kracalik I, Basavaraju SV. Transfusion-related errors and associated adverse reactions and blood product wastage as reported to the National Healthcare Safety Network Hemovigilance Module, 2014-2022. *Transfusion.* 2024;**64**(4):627-37. [PubMed ID: 38476028]. [PubMed Central ID: PMC11299550]. https://doi.org/10.1111/trf.17775.
8. White SK, Walker BS, Schmidt RL, Metcalf RA. The incidence of transfusion-related acute lung injury using active surveillance: A systematic review and meta-analysis. *Transfusion.* 2024;**64**(2):289-300. [PubMed ID: 38116828]. https://doi.org/10.1111/trf.17688.
9. Azizi S, Tabary SZ, Soleimani A. Prevalence of acute blood transfusion reactions in Mazandaran Heart Center, Sari, Iran, 2010-2012. *Med Arch.* 2014;**68**(2):137-9. [PubMed ID: 24937941]. [PubMed Central ID: PMC4272498]. https://doi.org/10.5455/medarh.2014.68.137-139.
10. Bodaghkhan F, Ramzi M, Vazirian SR, Ahmadi M, Hajebi Rajabi M, Kohan N, et al. [The prevalence of acute blood transfusion reactions in Nemazee Hospital]. *J Iran Blood Transf.* 2014;**11**(3):247-51. FA.

11. Payandeh M, Zare ME, Kansestani Nasir A, Pakdel Falah S, Jahanpour F, Yousefi H, et al. Descriptions of acute transfusion reactions in the teaching hospitals of Kermanshah University of Medical Sciences, Iran. *Int J Hematol-Oncol Stem Cell Res*. 1970;**7**(2).
12. Salimi S, Feizi A, Vanabadi N. Incidence rate of acute reactions in transfusion of blood and its products prepared by Urumia Blood Refinery Center. *Adv Nurs Midwifery*. 2010;**19**(66):8-13. https://doi.org/10.22037/anm.v19i66.1476.
13. Islam N, Uddin Khan ME, Chakrabarty A, Arifuzzaman M, Hossain MS; Amiruzzaman, et al. Frequency and Nature of Transfusion Related Adverse Reactions in Patients Admitted in A Tertiary Care Hospital. *Bangladesh J Med*. 2021;**33**(1):27-33. https://doi.org/10.3329/bjm.v33i1.56786.
14. Muche Y, Gelaw Y, Atnaf A, Getaneh Z. Blood Transfusion Complications and Associated Factors Among Blood-Transfused Adult Patients at Debre Markos Comprehensive Specialized Hospital, Ethiopia: A Cross Sectional Study. *J Blood Med*. 2023;**14**:389-98. [PubMed ID: 37313438]. [PubMed Central ID: PMC10259606]. https://doi.org/10.2147/JBM.S412002.
15. Subair S, Malpani P, Channa U. Study of the incidence and profile of acute transfusion reactions in children. *Asian J Med Sci*. 2023;**14**(8):193-7.