

A Survey of Acute Transfusion Reactions in Thalassemic Patients in Pakistan: A Single Centre Experience

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ABSTRACT

Objective: To determine the frequency and types of transfusion reactions in thalassemic patients at Hamza Foundation Welfare Hospital and Blood Services, Peshawar.

Methodology: The current study was a descriptive cross-sectional study. The data was collected from 152 participants through a self-generated questionnaire for a period of 4 months (April to July 2022).

Results: The overall frequency of febrile non-hemolytic reactions (FNHTR), allergic transfusion reactions (ATR), and acute hemolytic transfusion reactions (AHTR) was 84%. Among the 152 participants, 91 (59.8%) were males, and 61 (40.2%) were females. Of the total males, 83 (55.6%) experienced transfusion reactions, while 46 (30%) of the females had transfusion reactions. Specifically, 56 males and 36 females experienced FNHTRs, 22 males and 4 females experienced ATRs, and 5 males and 6 females experienced AHTRs. Fever was observed as the predominant symptom 69.7% and 52.6% among FNHTR and AHTR, anxiety was predominantly observed in 34.8% in ATRs.

Conclusion: Among the transfusion reaction types, FNHTRs emerged as the most common, followed by ATRs and AHTRs.

Key words: Febrile Non-Hemolytic Reaction, Allergic Transfusion Reaction, Hemolytic Transfusion Reactions

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{3,4}Critical analysis and manuscript review; ^{5,6}Data analysis; Manuscript Editing.

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Introduction

Transfusion involves intravenously introducing either whole blood or its individual components into a person's bloodstream. ¹ Transfusing blood and its products are generally a safe and effective method for correcting hematological defects. However, adverse effects, commonly known as blood transfusion reactions, can occur during or after the transfusion process. The act of donating blood exemplifies humanity, and in an ideal world, offering blood without any personal gain or compensation

represents the pure essence of humanity.² Blood transfusion is a widely utilized life-saving therapeutic measure worldwide, but it has never been entirely devoid of risks and potential adverse effects, highlighting the need for careful consideration and vigilance during the process.³ The primary treatment for severe thalassemia continues to be life-long red blood cell (RBC) transfusion. It is advised to administer leucoreduced packed red cells containing a minimum of 40 grams of hemoglobin.⁴ Thalassemia is predominantly

prevalent among Asians globally, and due to significant population migrations, individuals of Asian descent form a substantial proportion of thalassemia patients in many Western countries' thalassemia centers.⁵ Patients afflicted with thalassemia experience irregularities in hemoglobin production. The World Health Organization reports that thalassemia is a significant health concern for children, both in developing countries and developed nations. In Pakistan, there are children affected by thalassemia who rely on blood transfusion therapy, with contributing factors such as consanguineous marriages, a rise in birth rates, and issues related to overpopulation. Despite the Government of Pakistan introducing a law that made thalassemia testing compulsory before marriage, the successful execution of this initiative encountered obstacles due to the high expenses of thalassemia diagnostic tests and the inadequacies in the country's management system.⁶ Thalassemia presents itself in different forms, such as minor disease, carriers of the disease, and major thalassemia, within Pakistan. The country currently harbors around 100,000 thalassemia patients, and this figure is steadily increasing over time. To maintain a healthy life, patients predominantly depend on blood transfusion therapy, opting for it over the costly chelation therapy. However, the expenses associated with this treatment impose substantial financial and psychological stress on both the patients and their families.⁷ Acute transfusion reactions frequently encountered encompass febrile non-hemolytic transfusion reaction (FNHTR), allergic transfusion reactions (ATR), acute hemolytic transfusion reactions (AHTR), isolated hypotension, bacterial contamination, and volume overload. These acute transfusion reactions vary in their causes, clinical manifestations, and seriousness. Nevertheless, the majority of these reactions are typically mild and of short duration. The incidence of acute transfusion reactions is estimated to range from 0.2% to 10% depending on multiple factors and these reactions are associated

with fatalities in approximately 1 out of every 250,000 cases.⁸ FNHTRs are commonly characterized by a temperature increase of at least 1° C during transfusion when no other apparent cause can be identified. Febrile reactions can be triggered by the transfusion of any blood product and are among the most prevalent types of transfusion reactions. These reactions are thought to be caused by an increase in cytokine production by leukocytes, which may arise due to storage-related changes. Additionally, they can occur when incompatible donor antibodies recognize recipient antigens as foreign. The accumulation of cytokines, especially in platelet units during storage, is believed to be the primary factor contributing to FNHTR symptoms.⁹ However, pre-storage leukodepletion has proven effective in reducing the risk by minimizing cytokine release from white cells. Complicated ATRs account for around 1% to 3% of all blood transfusions. These reactions are typically mild and often exhibit cutaneous manifestations like urticaria, rash, pruritus, and flushing.¹⁰ The root cause of these reactions can be linked to different factors, such as specific plasma proteins in the donor blood that the recipient's blood perceives as allergens, the presence of food allergens like peanut in the donor blood, or interactions between antibodies in the donor blood and the recipient's antibodies. AHTRs exhibit immediate signs and symptoms within 24 hours. ABO incompatibility is the primary cause of immediate AHTRs, rendering them the most dangerous type of transfusion reaction, but also highly preventable. These reactions often occur due to clerical or administrative errors.⁷

Methodology

The cross-sectional survey was conducted at Hamza Welfare Hospital and Blood Services. The duration of the study was 4 months (April to July 2022). The sampling method employed for this study was convenience sampling.

The current study was approved from the ethical committee of NCS University System, Department of Medical Laboratory Technology and the ethical committee of Hamza Foundation Welfare Hospital and Blood Services, Peshawar, Pakistan. The study involved data collection through a questionnaire from the participants (Annexure-I). Verbal and written consent (Annexure-II) was taken from each participant of the study before filling out the questionnaire. Each questionnaire was assigned a unique number for each participant.

The questionnaire was developed based on previous literature. The questionnaire was divided into 2 sections. The first section included demographic information and the second section included sign and symptoms for acute immunologic reactions to evaluate FNHTR, ATR, and AHTR.

152 patients suffering from Thalassemia and registered at Hamza Welfare Hospital and Blood Services for continuous transfusion were conveniently selected for the study. Following the description of the study's aims and objectives, patients or their parents completed the questionnaires on a visit to hospital for blood transfusion. The on-duty hematologist and staff members provided assistance in identifying the specific type of transfusion reaction. The type of transfusion reaction is classified according to American Association of Blood Banks¹¹.

Initially the data was incorporated in Microsoft Excel and exported into SPSS (Statistical Package for the Social Sciences Inc. Chicago, Illinois USA, version22) for the analysis of data. Frequencies and percentages were calculated for categorical variables.

Results

The current study included the most common acute transfusion reactions like FNHTR, ATR, and AHTR. The overall frequency of transfusion reactions was 84% (128) among all participants

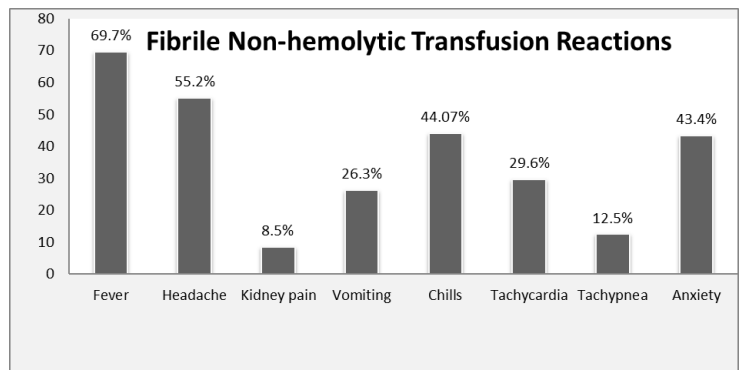


Figure 1: Frequency of sign and symptoms of FNHTRs

Figure 1 shows the frequency of signs and symptoms of FNHTRs among thalassemia patients. Fever 63 (69.7%) was the highest frequent symptom observed followed by headache 50 (55.2%), chills 40 (44.07%), anxiety 39 (43.4%), tachycardia 27 (29.6%), vomiting 24 (26.3%), tachypnea 11 (12.5%) and kidney pain 8 (8.5%).

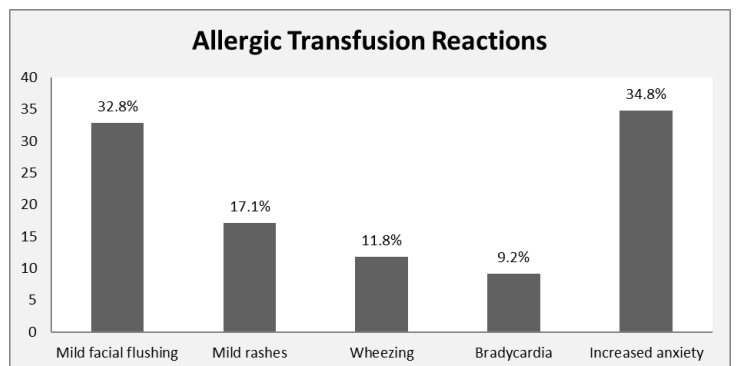


Figure 2: Frequency of sign and symptoms of allergic transfusion reactions

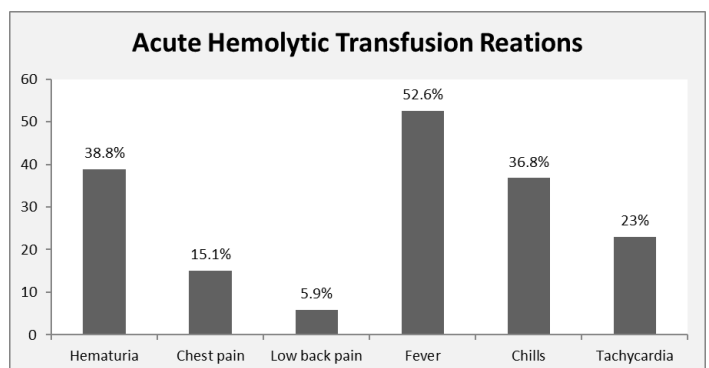


Figure 3: Frequency of sign and symptoms of AHTRs

Figure 2 shows the frequency of signs and symptoms of ATR among thalassemic patients. Among signs and symptoms, an increase in anxiety 9 (34.8%) was noted in the patients followed by mild facial flushing 9 (32.8%), mild rashes 4 (17.1%), wheezing 3 (11.8%) and bradycardia 2 (9.2%).

The figure 3 reveals frequency of sign and symptoms of ATRs among patients suffering from thalassemia. Fever 6 (52.6%) was noted most frequently among all ATRs followed by haematuria 4 (38.8%), chills 4 (36.8%), tachycardia 3 (23%), chest pain 2 (15.1%) and low back pain 1 (5.9%).

	FNHTR	ATR	AHTR
	91 (60%)	26 (17%)	11 (7%)
Male	56 (36%)	22 (14%)	5 (3%)
Female	36 (24%)	4 (3%)	6 (4%)

The table I provides an overview of the frequency of transfusion reactions in the study population, categorized by type and gender. Among the total participants, 91 (60%) experienced FNHTRs. Of these, 56 (36%) were male participants, and 36 (23%) were female participants. FNHTRs were the most common type of transfusion reaction observed in the study. A total of 26 (17%) participants had ATRs. Among these, 22 (14%) were male participants, and 4 (3%) were female participants. ATRs were the second most common type of transfusion reaction documented. AHTRs were observed in 11 (7%) participants. Of these, 5 (3%) were male participants, and 6 (4%) were female participants. AHTRs were the least frequent type of transfusion reaction in the study. FNHTRs were the most common, followed by ATRs, while AHTRs were the least frequent.

Discussion

The research was carried out at a blood services facility serving patients with thalassemia. Transfusion of blood is a common technique performed in different settings of health care facilities. Blood transfusion is the mainstay of care for individuals with thalassemia major and many with intermedia. Clinical reporting is the only source of information about the incidence of transfusion reactions. To the best of our knowledge, our study is the first study which is providing details of transfusion reactions in thalassemic patients in Pakistan, Khyber Pakhtunkhwa province. Reported rates of these reactions vary significantly across institutions due to a multitude of factors, including the use of premedication, blood product storage and preparation practices, and patient-specific characteristics. A recent study conducted in a hospital setting in Ethiopia found that the acute transfusion reactions were 5.2% of transfused patients.¹² In contrast, our study observed a higher incidence of acute transfusion reactions, with 73% of participants experiencing them. These disparities in reaction rates may be attributed to differences in healthcare practices, blood product preparation, and patient management among different regions and institutions.

Yong H.K et al. conducted a study in 2021 and reported clinical symptoms, including fever (54.9%), chills (21.9%), chest pain (6.0%), and bradycardia (2.1%).¹³ In comparison, our current study reported a higher prevalence of fever (69.7% and 52.6%), chills (44.07% and 36.8%), chest pain (15.2%), bradycardia (9.2%), hematuria (38.8%), rashes (17.1%), tachycardia (23%), and anxiety (43.4% and 34.8%). These variations can be attributed to differences in the study population, as well as the variability in patients' immune responses and individual sensitivities to blood components, which can lead to variations in symptom presentation.

A report by Eko P. et al. indicated that 56 cases (53.8%) of transfusion reactions occurred in males

and 48 cases (46.2%) in females.¹⁴ Our study findings align with this trend, as we observed acute transfusion reactions in 83 (55.6%) cases among males and 46 (30%) cases among females. These results support the consistency of transfusion reaction trends across both genders.

Transfusion Reaction	Current Study	U.Wahheed et al, 2016 (Pakistan)	S.Pahuja et al, 2017 (India)	L.Kasraian et al, 2015 (Iran)	R.Kumar et al, 2020 (United States)
FNHTR	59.9%	13%	58%	15%	56%
ATR	17.6%	9%	41%	66%	29%
AHTR	7.4%	—	1%	18%	1.4%

Table 2 presents a comparative analysis of FNHTR, ATR, and AHTR rates with studies conducted both nationally and internationally. Notably, FNHTR incidence was reported at 13% in the study by Waheed et al. (2016), which is significantly lower than the 59.9% reported in the current study, making it the highest among all studies referenced.¹⁵ This significant increase is indeed alarming and warrants further investigation. Such a rise may be attributed to a combination of environmental factors and potential issues related to transfusion management.

The present study reported ATR 17.6% which is lower from Pahuja et. al (2017) and Kasraian et, al (2015) revealing 41% and 66%.^{16,17} The variations in reports maybe due to genetic and demographic makeup of populations which can influence their susceptibility to allergic reactions. However, allergies or genetic predispositions to react to specific components of blood products could be a

possible cause of higher prevalence in certain populations.

We reported AHTR 7.4% which is lower than a report by Kasraian et, al (2015) revealing 18% and higher than Pahuja et. al (2017)¹⁶. Variability in healthcare provider education and training on blood transfusion safety and compatibility issues can contribute to differences in AHTR rates. The trend of FNHTR and AHTR reported by the current study is also supported by Kumar et. al (2020) revealing FNHTR (56.4%), ATR (29.2%) and AHTR (1.4%)¹⁸. ATR shows increased frequency, which may be due to environmental variations in geographic location.

Conclusion

The current study concluded that transfusion reactions are a significant concern in thalassemic patients, with an overall frequency of 84%. According to the current study, FNHTR is identified as the most prevalent transfusion reaction, with ATR and AHTR following closely behind. Additionally, there is a higher incidence of transfusion reactions in males compared to females. The study emphasizes the necessity for effective procedures to minimize transfusion reactions.

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