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BURDEN AND CHARACTERISTICS OF ACUTE TRANSFUSION REACTIONS IN TRANSFUSION-DEPENDENT THALASSEMIA MAJOR PATIENTS

Abid Ur Rehman[1], Habib U Rahman[2], Aqib Marwat[3], Inayat Ullah[4], Amir Hussain[5], Jamal Ahmad[6], Muhammad Asif Zeb[*7]

[*1]*Department of MLT, Ahmad Medical Institute, Peshawar*
[2,3,6,7]*Institute of Paramedical Sciences, Khyber Medical University, Peshawar*
[4]*Department of MLT, NCS University System, Peshawar*

[*7]muhammadasif.ipms@kmu.edu.pk

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Corresponding Author: *
Muhammad Asif Zeb

Abstract

Background: *Patients with transfusion-dependent beta-thalassemia major (β-TM) are at significant risk of acute transfusion reactions (ATRs) due to lifelong exposure to blood products. This study aimed to determine the frequency and types of ATRs among multi-transfused thalassemic patients in Khyber Pakhtunkhwa (KPK), Pakistan.*

Materials and Methods: *A descriptive cross-sectional study was conducted at the Hamza Foundation Welfare Hospital and Thalassemia Center, Peshawar. Data were collected from the medical records of 294 registered β-TM patients using a pre-designed questionnaire. All patients were transfusion-dependent and had received multiple packed red cells concentrate (RCC) transfusions, cross-matched via the Jell card method. Statistical analysis was performed using SPSS version 20.0.*

Results: *The mean age of participants was 12.52 years (range: 2–35 years), with 158 (53.7%) males and 136 (46.3%) females. The most common blood group was B+ (32.7%). Febrile non-hemolytic transfusion reactions (FNHTRs) were observed in 71 patients (24.1%), with fever (19.4%), chills (2.7%), headache (1.4%), vomiting (0.3%), and tachycardia (0.3%) being reported. Allergic reactions occurred in 8 patients (2.7%), manifesting as facial flushing (1.7%), hives/rashes (0.7%), and severe wheezing (0.3%). No hemolytic reactions, tachypnea, anxiety, bradycardia, chest pain, or hematuria were documented.*

Conclusion: *FNHTRs and mild-to-moderate allergic reactions are the most common acute transfusion complications in multi-transfused thalassemia major patients. Immediate recognition and evidence-based management of these reactions are essential to improve patient safety. The implementation of standardized transfusion protocols, leukoreduction, and vigilant monitoring is recommended to mitigate these adverse events.*

INTRODUCTION

Thalassemia represents one of the most prevalent inherited hemoglobinopathies globally, characterized by defective synthesis of alpha or beta globin chains, leading to ineffective erythropoiesis, hemolytic anemia, and a variable clinical spectrum. (1,2) Beta-thalassemia major (β-TM), the most severe form, manifests early childhood and necessitates lifelong, regular packed red blood cell (RBC) transfusions to sustain life and suppress complications of marrow expansion. (3,4) In Pakistan, the burden of thalassemia is substantial, fueled by a high carrier rate (estimated at 5-7%) and consanguineous marriages, with over 60,000 affected children and approximately 4,000 new cases added annually. (5,6)

While transfusion therapy is life-sustaining, it exposes patients to a cumulative risk of acute and delayed adverse events. Acute transfusion reactions (ATRs), defined as unfavorable events occurring during or within 24 hours of transfusion, constitute a significant cause of morbidity and, rarely, mortality in this vulnerable population. (7,8) These reactions are broadly classified as infectious or non-infectious. Non-infectious complications, which are more frequently reported with modern donor screening, are further categorized into immunologic and non-immunologic types. (9) For multi-transfused patients with thalassemia, immunologic reactions, particularly febrile non-hemolytic transfusion reactions (FNHTRs) and allergic reactions, are the most encountered. (10)

FNHTRs are clinically defined as a temperature increase of ≥1°C occurring during or shortly after transfusion, often accompanied by chills or rigors, in the absence of hemolysis or other causes. (11) Their pathogenesis is multifactorial, primarily attributed to the recipient's anti-leukocyte antibodies reacting against donor white blood cells or to the transfusion of pro-inflammatory cytokines (e.g., IL-1, IL-6, TNF-α) that accumulate in cellular blood products during storage. (12) Allergic reactions range from mild localized urticaria and flushing to systemic anaphylaxis. They are typically mediated by recipient IgE antibodies directed against soluble proteins in donor plasma, such as IgA, haptoglobin, or other allergens. (10) The clinical and economic impact of these reactions is considerable, as they cause patient distress, may lead to transfusion delays or discontinuation, and necessitate additional medical interventions. (13)

Given the lifelong transfusion dependence of β-TM patients, understanding the local epidemiology and pattern of ATRs is crucial for strengthening hemovigilance systems, informing preventive strategies, and optimizing clinical management protocols. Data on the frequency of these complications in the specific context of Khyber Pakhtunkhwa, Pakistan, remain limited. Therefore, this study aimed to determine the frequency and clinical spectrum of common acute transfusion reactions, specifically FNHTRs and allergic reactions, among multi-transfused thalassemia major patients at a major thalassemia care center in Peshawar, KPK.

Materials and Methods

A descriptive cross-sectional study was conducted at the Hamza Foundation Welfare Hospital and Thalassemia Center in Peshawar, KPK, Pakistan. The study population comprised all registered patients with transfusion-dependent beta-thalassemia major. The sample size was calculated as 294 using the formula $n = p(1-p)(Z/e)^2$, assuming a prevalence (p) of 26% for transfusion reactions from prior literature, a 95% confidence level (Z=1.96), and a 5% margin of error. A non-probability (convenience) sampling technique was employed.

Inclusion criteria were patients diagnosed with β-TM who were dependent on regular blood transfusions. Patients who had received only a single transfusion were excluded. After obtaining approval from the institutional research ethics committee and necessary administrative permissions, data were collected retrospectively from the patients' medical record books using a pre-designed, structured questionnaire. The collected data included demographic details (age, sex), blood group, transfusion history, and documented evidence of any acute transfusion reactions, including febrile, allergic, and hemolytic types.

All patients at the center received leuko-depleted packed red cell concentrate (RCC) transfusions, cross-matched with the recipient using the Jell card method and were transfused with the first-choice compatible donor blood group. Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20.0 and Microsoft Excel.

Descriptive statistics were computed, with frequencies and percentages used for categorical variables, and mean, median, and mode for continuous variables like age. Results were presented in tables and figures.

Results

A total of 294 transfusion-dependent β-TM patients were studied. The demographic characteristics are presented in Table 1. The cohort had a mean age of 12.52 years (median=12, mode=12), with an age range from 2 to 35 years. There were 158 males (53.7%) and 136 females (46.3%). The distribution of blood groups among the participants is detailed in Table 2. The most common blood group among recipients was B positive (96 patients, 32.7%), followed by O positive (76, 25.9%), A positive (71, 24.1%), and AB positive (37, 12.6%). Minor blood groups (A-, B-, AB-, O-) collectively accounted for 6.8% of patients.

Regarding acute transfusion reactions, 71 patients (24.1%) experienced febrile non-hemolytic reactions (FNHTRs). The specific manifestations among these are summarized in Table 3. Fever was documented in 57 patients (19.4% of total), chills in 8 (2.7%), headache in 4 (1.4%), vomiting in 1 (0.3%), and tachycardia in 1 (0.3%). No cases of tachypnea or anxiety related to FNHTR were recorded.

Allergic reactions were less frequent, observed in 8 patients (2.7%). The types of allergic reactions documented are shown in Table 4. These included mild facial flushing in 5 (1.7%), mild hives or rashes in 2 (0.7%), and severe wheezing in 1 patient (0.3%). No incidents of bradycardia or increased anxiety as part of an allergic response were noted.

Importantly, no hemolytic transfusion reactions were identified in this cohort, as evidenced by the absence of documented hematuria, chest pain, or low back pain in all 294 patients.

Table 1: Demographic Characteristics of Study Participants (N=294)

Characteristic	Frequency (n)	Percentage (%)
Male	158	53.7%
Female	136	46.3%

Table 2: Distribution of Blood Groups among Thalassemia Major Patients

Blood Group	Frequency (n)	Percentage (%)
A+	71	24.1%
B+	96	32.7%
AB+	37	12.6%
O+	76	25.9%
A-	4	1.4%
B-	4	1.4%
AB-	3	1.0%

Blood Group	Frequency (n)	Percentage (%)
O-	3	1.0%
Total	294	100.0%

Table 3: Frequency and Types of Febrile Non-Hemolytic Transfusion Reactions (FNHTRs)

Type of Reaction	Frequency (n)	Percentage (%)
Fever	57	19.4%
Chills	8	2.7%
Headache	4	1.4%
Vomiting	1	0.3%
Tachycardia	1	0.3%
Total with FNHTR	71	24.1%

Table 4: Frequency and Types of Allergic Transfusion Reactions

Type of Reaction	Frequency (n)	Percentage (%)
Facial Flushing	5	1.7%
Hives/Rashes	2	0.7%
Severe Wheezing	1	0.3%
Total with Allergy	8	2.7%

Discussion

The findings of this cross-sectional study indicate that acute transfusion reactions, although predominantly non-hemolytic, are common among multi-transfused thalassemia major patients in our setting. Specifically, FNHTRs were documented in 71 patients (24.1%), with isolated fever being the predominant manifestation (57 patients, 19.4%). Allergic reactions were less frequent, occurring in 8 patients (2.7%), and were and were generally mild.

The observed prevalence of FNHTRs in our study (24.1%) is noteworthy. It is lower than the rates reported in some earlier studies from Pakistan, such as the one by Sardar et al, which recorded fever in 59.8% and rigors in 43.5% of thalassemia patients.

(5) This discrepancy may be positively attributed to the routine use of leuko-reduced (leuko-depleted) blood products at our study center. Universal leukoreduction is a well-established intervention that significantly reduces the incidence of FNHTRs by removing donor white blood cells and the cytokines they release during storage, which are key mediators of these reactions. (9,12) Our lower rate suggests that this preventive measure is having a beneficial impact. However, the persistence of a 24% reaction rate indicates that other factors, such as platelet-derived mediators or recipient-specific immune responses, may still be contributory. (10)

The spectrum and frequency of allergic reactions (2.7%) in our study also appear lower than rates sometimes reported in the literature, which can range from 1-5% and higher for mild urticarial reactions. (8,10) This could be due to several factors. First, our data collection relied on retrospective record review, which is susceptible to under-documentation of mild, transient symptoms like localized itching or rash that may not have been reported by the patient or recorded by staff. Second, variations in donor population genetics and plasma protein profiles can influence the allergen load in transfused units. The absence of severe anaphylactic reactions in our cohort is reassuring and aligns with its rarity, often associated with IgA deficiency in the recipient, which was not screened for in this study.

A critical and positive finding was the complete absence of documented acute hemolytic transfusion reactions (AHTRs). This underscores the efficacy of the standard pre-transfusion practices employed at the center, including rigorous ABO/Rh typing and cross-matching using the Jell card method. It highlights success in preventing the most dangerous type of immunologic reaction, which is often the result of clerical errors. (14) However, continuous vigilance is required, as human error remains a persistent risk in transfusion chains worldwide.

When compared to studies from other regions, such as the work by Waheed et al, which reported a different profile of reactions including dyspnea and abdominal pain, our findings highlight the variability in reaction patterns. (6) This variability may be influenced by differences in transfusion protocols, the type of blood components used (e.g., degree of leukoreduction, use of washed RBCs), genetic differences in donor and recipient populations, and local reporting practices.

The clinical implications of our findings are significant. Even mild to moderate FNHTRs and allergic reactions contribute to transfusion-related anxiety, reduce the quality of life for patients undergoing frequent procedures, and may lead to unnecessary investigations and treatments. (13) They underscore the importance of pre-transfusion counseling, close monitoring during transfusion, and having clear institutional protocols for the management of such events. (7) For patients with recurrent reactions, preventive strategies such as pre-medication with antipyretics/antihistamines or, in selected cases, the use of washed RBCs for those with severe allergic histories, should be considered. (10)

Conclusion and Recommendations

In conclusion, this study confirms that febrile non-hemolytic and mild allergic reactions are the predominant acute transfusion complications among multi-transfused thalassemia major patients in KPK, Pakistan. The absence of hemolytic reactions is a testament to effective cross-matching practices. However, the significant frequency of FNHTRs indicates an area for potential further improvement.

Based on the findings, the following recommendations are made to enhance transfusion safety and patient care:

Sustain and Universalize Leukoreduction: Continue and ensure the consistent use of pre-storage leuko-reduced blood products for all thalassemia patients to further mitigate FNHTRs.

Strengthen Prospective Hemovigilance: Implement a standardized, active surveillance system to prospectively document all transfusion reactions, including mild symptoms, to capture true incidence more accurately.

Regular Antibody Screening: Maintain a protocol for regular (e.g., annual) screening for the development of new red cell alloantibodies to prevent delayed hemolytic reactions.

Consideration for Special Products: For patients with severe, recurrent allergic reactions unresponsive to pre-medication, consider consultation for the use of washed red cell components.

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