Journal of
Kerman University of Medical Sciences

https://jkmu.kmu.ac.ir
10.34172/jkmu.2023.38
Vol. 30, No. 4, 2023, 229-232

Original Article



# Prevalence of Acute Complications of Transfusion in Children with β-thalassemia Major in Southeast Iran: A Prospective Study

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**Abstract**

**Background:** Acute complications of transfusion are among the leading causes of morbidity and mortality in chronically transfused patients. One of the main goals of blood transfusion is to reduce complications and improve blood safety and patient health care worldwide. The present study aimed to investigate the prevalence of acute complications of transfusion beta-thalassemia major (TM) patients in Southeast Iran.

**Methods:** In a prospective study, 23 882 transfusions were evaluated in TM patients of a thalassemia clinic for acute reactions during a two-year period. Data were collected by forms to record the information related to blood transfusion at the time of reaction occurrence.

**Results:** The assessment of the data revealed that 228 TM patients (0.95%) had acute complications of transfusion. Among 23882 TM patients undergoing transfusion, 211 (0.87%) developed allergic reactions, 11 (0.04%) were diagnosed with febrile non-hemolytic reaction, and one patient (0.004%) had experienced acute hemolytic transfusion reaction.

**Conclusion:** The results of the current study support preventive measures for the reduction of these complications to improve patients' health. Acute complications occurred may be due to insufficient ability to perform blood bank tests, lack of standard operating instructions, and lack of necessary monitoring during the transfusion process. The best way to reduce the risk of blood transfusion reactions is to provide special care to the patients during the first 24 hours after transfusion. Creating a consistent and continuous education system with standard operating instructions and establishing an error reporting system leads to improve knowledge about transfusion guidelines and best practices.

**Keywords:** Thalassemia major, Transfusion reactions, Children

**Citation:** Miri-Aliabad G, Asgarzadeh L, Dorgalaleh A, Bahraini M. Prevalence of acute complications of transfusion in children with β-thalassemia major in Southeast Iran: a prospective study. *Journal of Kerman University of Medical Sciences*. 2023;30(4):229-232. doi:10.34172/jkmu.2023.38

**Received**: August 27, 2022, **Accepted**: October 5, 2022, **ePublished**: August 20, 2023

## Introduction

Thalassemia is a hereditary disorder caused by mutations in the globin genes. Hemoglobinopathies are distributed around the world with the highest incidence in an extensive area called the thalassemia belt including the middle-eastern areas such as Iran, Southeast Asia, and the shores of the Caspian Sea (1,2). It is estimated that 5% of the world's population is affected by hemoglobinopathies, 1.7% of whom are thalassemia carriers. About 4.4 newborns per 10 000 births around the world develop thalassemia (3). The prevalence of β-thalassemia is variable in different areas of Iran, mainly found around the Caspian Sea and the Persian Gulf. With 74 cases per 100 000 individuals, Sistan and Baluchestan province has the highest incidence of the disease nationwide (4,5). With about three million carriers, thalassemia is the most common inherited blood disorder in Iran. According to defects in globin genes, thalassemia is classified into two major types including α-thalassemia which is mainly due to the deletion of α-globin gene fragments, and β-thalassemia known by reduced production of beta chain (6-8). So far, about 200 different mutations have been identified in beta-thalassemia resulting in clinical symptoms ranging from asymptomatic to severe anemia (9). In Sistan and Baluchestan province, south-east of Iran, the frequency of beta-thalassemia carriers is about 10%. Also, there are about 3100 thalassemia major (TM) patients, of whom 780 are under follow-up and treatment in the thalassemia ward at Aliasghar children's hospital, Zahedan (10). Based on blood transfusion, thalassemia is classified into transfusion-dependent thalassemia and non-transfusion-dependent thalassemia (11). Regular blood transfusion and the use of iron chelators can transform thalassemia from severe fatal anemia into a

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chronic illness and increase lifespan, but transfusion complications have significant effects on patients' life (12,13). Transfusion reactions are classified as acute (during or within 24 hours of transfusion) and delayed transfusion reactions (after 24 hours of transfusion). Delayed transfusion reactions include graft-versus-host disease, alloimmunization, post-transfusion purpura, and hemosiderosis. Acute transfusion reactions include acute hemolytic transfusion reaction, transfusion-related acute lung injury, allergic reactions, anaphylactic transfusion-associated circulatory overload, and febrile non-hemolytic transfusion reactions (FNHTR) (14). Due to the high prevalence of acute blood transfusion complications, and the high prevalence of the disorder in Southeast Iran, further studies are required to assess the prevalence of these complications in this area. Thus, the present study prospectively evaluated the prevalence of acute complications of transfusion in children with β-thalassemia major referred to the Ali Asghar hospital in Zahedan, Iran, and appropriate preventive measures to reduce serious complications and subsequently improve the overall health of these patients.

## Material and Methods

In this cross-sectional prospective study 23 882 transfusions in patients with β-thalassemia major referred to the Ali Asghar children's hospital in Zahedan during a two-year period were evaluated. Patients with fever, skin rash, or urticaria before the transfusion were excluded from the study. All patients were interviewed by an expert staff to obtain demographic data. The patients' medical records also were reviewed by the staff to collect the required data. All patients were followed-up during the course of transfusion, and 24 hours after transfusion, and required data were recorded during this period. Collected data included age at transfusion complication development, gender, transfusion reactions, type of red blood cell (RBC) units, blood group, therapeutic measures after the incidence of transfusion complications, and clinical status of recipients after receiving supportive care. The SPSS software version 16 (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis.

## Results

Among 23 882 thalassemia patients undergoing transfusions, 228 (0.95%) patients had acute transfusion complications. The range of their age was five months to 34 years. The most frequent acute complications of transfusion were in the age group of 11 to 20 years. One hundred and sixteen patients (50.9%) were male and 112 (49.1%) were female. Two hundred and eleven patients (0.87%) with acute transfusion complications had experienced only allergic reaction, 11 cases (0.04%) had FNHTR, one case (0.004%) had hemolytic transfusion reaction, two cases (0.008%) had the combination of non-hemolytic febrile reaction plus allergic reaction, one case (0.004%) was found with allergic reaction and hypotension simultaneously, and two patients had other complications (Table 1). Patients with blood group O (85%) had the highest rate of complications (Table 1). Leukocyte-reduced RBC was the most frequent product, which was transfused to 91.2% of the thalassemia patients (21 790 patients) (Table 2) and 95.2% of the cases who experienced acute complications of transfusion later (217 patients) (Table 1). Supportive care included discontinuation of transfusion and treatment with antihistamines and steroids. Two hundred and eighteen patients (95.6%) had completely recovered after treatment. None of these complications resulted in death or severe disability during the study period (Table 3).

## Discussion

Although by chelation therapies the life expectancy of patients with thalassemia has increased dramatically in recent years, consequent complications of frequent transfusions remain a major concern for thalassemia treatment centers (1). Estimation of the blood transfusion reactions is not accurate enough due to some hidden side effects and symptoms mimicry with other clinical conditions. In this study, only acute reactions during the blood transfusion were evaluated, and the study population was thalassemia patients referred to Ali Asghar children's hospital in Zahedan city. Our cross-sectional study provided epidemiologic data to assess the prevalence of acute reactions in this region. Identifying these reactions and examining the relationship between their incidence and different variables can help to provide accurate management and preventive measures (15). It was found that 0.95% of thalassemia patients had experienced acute complications. The most common acute complications in these patients were allergic reactions and FNHTR. Treatments with antihistamines and steroids and discontinuation of the transfusion were the most frequent supportive measures after the occurrence of the transfusion reactions. In a study by Oshvandi et al, it was found that 6% of thalassemia patients had FNHTR (16). Another study by Geiger and Howard revealed that allergic reactions with platelets and red blood cells have an incidence rate of 3.7% and 0.15%, respectively, and according to Bodaghkhan et al the reported incidence was 0.033% (17,18). In the present study, the incidence rate of FNHTR in transfused patients was 0.04% which is lower than other reports. Fever usually develops following the transfusion of cellular products such as packed red blood cells, whole blood, and platelets but rarely occurs after the transfusion of plasma products. According to a study by Sazama, the highest rate of FNHTR occurs following platelet transfusion (30%) (19). However, despite being the most transfused product, packed red blood cells account for 0.5% of FNHTR cases (20).

**Table 1.** Prevalence of the acute transfusion reactions in thalassemia patients.

| | | Type of the complication | | | | | | Total | % |
|---|---|---|---|---|---|---|---|---|---|
| | | FNHTR | Allergy | FNHTR + Allergy | Allergy + TAD + hypotension | HTR | Other | | |
| Gender | Male | 3 | 108 | 2 | 1 | 1 | 1 | 116 | 50.9 |
| | Female | 8 | 103 | 0 | 0 | 0 | 1 | 112 | 49.1 |
| Age (years) | 1-10 | 3 | 51 | 1 | 0 | 0 | 0 | 55 | 24 |
| | 11-20 | 1 | 91 | 1 | 1 | 1 | 0 | 95 | 42 |
| | 21-30 | 6 | 66 | 0 | 0 | 0 | 0 | 72 | 31 |
| | >30 | 1 | 3 | 0 | 0 | 0 | 2 | 6 | 3 |
| Type of blood component | Leukocyte-reduced PRBC | 11 | 202 | 1 | 1 | 1 | 1 | 217 | 95.2 |
| | Washed PRBC | 0 | 9 | 0 | 1 | 1 | 0 | 11 | 4.8 |
| Type of blood group | A | 2 | 48 | 0 | 0 | 0 | 0 | 50 | 21.9 |
| | B | 2 | 74 | 1 | 2 | 0 | 1 | 80 | 35.1 |
| | AB | 1 | 12 | 0 | 0 | 0 | 0 | 13 | 5.7 |
| | O | 6 | 77 | 0 | 0 | 2 | 0 | 85 | 37.3 |

FNHTR, Febrile non-hemolytic transfusion reactions; HTR, Hemolytic transfusion reaction; TAD, Transfusion associated dyspnea; RBC, packed red blood cell.

**Table 2.** Total number of transfused thalassemia patients and different blood components.

| Type of blood component | Number of transfusions | Number of blood components |
|---|---|---|
| Washed PRBCs | 2092 | 3555 |
| Leukocyte-reduced PRBCs | 21790 | 33004 |
| Total | 23882 | 36833 |

RBCs, packed red blood cells.

**Table 3.** Supportive measures and their clinical outcomes after acute transfusion reactions in thalassemia patients

| | Number of patients |
|---|---|
| Supportive care | |
| Antihistamines | 211 |
| Stop transfusion | 201 |
| Hydrocortisone | 197 |
| Continuation of transfusion | 22 |
| Treatment with antipyretics | 7 |
| Supplemental oxygen | 3 |
| Diuretics | 1 |
| Vasopressor | 1 |
| Clinical outcomes | |
| Complete recovery | 218 |
| Minor disability | 10 |
| Severe disability | 0 |
| Death | 0 |

The frequency of allergic reactions in thalassemia patients was 0.87% which seems lower than the reported risk in a general population of approximately 1%. In the study performed by Oshvandi et al, none of the patients had allergic reactions (16). The prevalence of allergic reactions is reported between 0.02% and 6.1% in other studies (17,18,20). Allergic reactions usually occur following the transfusion of plasma products. In our study, allergies occurred following the transfusion of packed red blood cells.

The number of allergic reactions has decreased in recent years due to the use of leukoreduction filters to remove leukocytes. The incidence rate of acute hemolytic reactions in the present study was 0.008%. Teimuri et al reported one patient with a severe hemolytic reaction that was caused by the wrong blood transfusion (20). In another study, Oshvandi et al reported no acute hemolytic complications (16). The significant decrease in acute hemolytic reactions in recent years has been associated with careful control of blood donors, profiling of recipients' blood groups, and performing cross-match. Applying diagnostic techniques that are sensitive and specific enough can also help patients screen and identify complications. The incidence rates of acute complications of transfusions in both genders are proximate to each other, so it can be concluded that gender has no significant relationship with the incidence of these reactions. Most of the complications occurred in patients with O and B blood groups, which may be related to the higher frequency of these two blood groups in the population.

This survey has some limitations that should be taken into consideration. First, since the present study was conducted only in one of the thalassemia centers, it is not a good representative to show the epidemiology of acute complications of transfusion in thalassemia patients in Sistan and Baluchestan province. Second, this study has concentrated on acute but not all complications that occurred in this population which highlights the need for more comprehensive studies to determine the extent of complications in these patients.

## Conclusion

In summary, the findings of this study indicate that blood transfusions are not a completely safe treatment and can be associated with early complications. The best way to reduce the incidence of transfusion morbidity is to keep patients under surveillance during the first 24 hours of transfusion. Acute complications should be promptly identified, and precautions should be taken. Establishing a coherent and continuous education system in the field of transfusion medicine, having standard practice guidelines, and establishing error reporting and hemovigilance systems at medical centers can be effective in the reduction of these complications.

**Acknowledgments**

The authors would like to thank the patients who participated in this study.

**Authors' Contribution**

**Conceptualization:** Ghasem Miri-Aliabad.
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**Competing Interests**

The authors declare that they have no conflict of interest.

**Ethical Approval**

The study was approved by the Ethical Committee of Zahedan University of Medical Sciences (Ethics No. IR.ZAUMS.REC.1394.362), and informed consent forms were obtained from all participants.

**Funding**

None.

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