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True incidence of acute transfusion reactions using active surveillance versus passive reporting among pediatric thalassemia patients at a tertiary care children's hospital

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Abstract:

BACKGROUND: Blood transfusion therapy is the main therapy for thalassemia patients. Active reporting of acute reactions during blood transfusions can play a pivotal role in the prevention of under-reporting of these events.

OBJECTIVE: The objective of the study was to evaluate the true incidence of acute transfusion reactions in pediatric thalassemia patients using active surveillance in comparison with the data obtained from passive reporting for the same duration of time.

MATERIALS AND METHODS: This cross-sectional cohort study comprised both prospective (active surveillance) and retrospective (passive reporting) components, including 248 and 292 thalassemia patients, respectively, aged 1–16 years, who underwent regular blood transfusions. Information collected included patient demographics and details of present and previous transfusion reactions. The data were analyzed using IBM-SPSS Statistics 16.0.

RESULTS: A total of 300 transfusion episodes were directly observed among 248 thalassemia patients, all receiving red blood cell concentrates. During 4 months of active surveillance, the incidence of acute transfusion reactions was 6.3% (19 out of 300), including 11 (3.7%) febrile nonhemolytic transfusion reactions (FNHTRs) and eight urticarial reactions (2.6%). In the retrospective data from passive reporting, 320 transfusion episodes occurred among 292 patients, with only 2 reactions (0.62%), FNHTRs and acute hemolytic transfusion reactions reported.

CONCLUSION: Active surveillance revealed a significant difference between the acute reactions identified during active surveillance in comparison with the data obtained from passive reporting for the same duration of time in pediatric thalassemia patients. In this regard, increased awareness related to transfusion reactions and importance of their reporting will be helpful to design a preventive framework for patients' safety.

Keywords:

Active surveillance, hemovigilance, transfusion reaction

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Introduction

Thalassemia is a monogenic disorder with considerable diversity and a global distribution.[1] The estimated prevalence of thalassemia is 1 in 100,000 individuals.[2] Blood transfusion and iron chelation are the primary treatments for managing thalassemia, though these interventions come with risks of adverse events.[3,4] A transfusion reaction is an unintended response in a patient during or after the transfusion of blood or blood components, which can lead to extended

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hospitalization. These reactions are categorized by their timing: acute (occurring within 24 h of transfusion) or delayed (manifesting after 24 h), and by their pathophysiology as immune or nonimmune.[5] The true incidence of acute reactions is likely underestimated due to several factors, including a lack of awareness or reluctance to report among clinical staff, errors in patient identification, and symptoms that overlap with the patient's existing condition.[6]

Acute reactions can be classified by their common etiology and the presenting signs and symptoms during transfusion. The most frequently reported transfusion reactions include acute hemolytic transfusion reactions (AHTRs), typically occurring in patients with multiple transfusions due to ABO-incompatible blood transfusions, often caused by bedside blood bag mix-ups, analytical errors, or the heavy workload in clinical settings,[5] febrile nonhemolytic transfusion reactions (FNHTRs) are the most common acute complications, characterized by a 1°F increase in body temperature during or up to 4 h following a transfusion,[7] urticarial or allergic transfusion reactions (ALTRs) are another common hypersensitivity reaction, presenting with symptoms such as urticaria, hives, itching, rash, skin redness, wheezing, and respiratory difficulty.[8] Minor ALTRs usually present within 24 h, while more serious conditions such as transfusion-associated circulatory overload and transfusion-associated lung injury are often overlooked.[9]

To enhance safety for both donors and patients, it is crucial to report, track, and monitor adverse transfusion reactions. Despite the absence of a comprehensive hemovigilance program in the Children's Hospital, Lahore, tracking these reactions is vital for patient safety.[10] When undesired reactions occur in conjunction with a transfusion, the certainty that the reaction is due to the transfusion may not always be clear to healthcare personnel at the bedside. Reporting suspected transfusion reactions is essential to ensure the prevention of similar events.[11] Multiple transfusion reactions in thalassemia patients have been observed in our clinical settings, often overlooked for various reasons. Active hemovigilance would provide better insight into the true incidence of these reactions and improve awareness regarding their reporting.[11] It will also be helpful in preventing future acute reactions. Therefore, we conducted active transfusion surveillance in pediatric thalassemia patients to determine the true prevalence of acute transfusion reactions.

Materials and Methods

This cross-sectional study was conducted at the Department of Hematology and Transfusion Medicine at the University of Child Health Sciences, The Children's Hospital, Lahore, Pakistan. Ethical approval was obtained before the study under IRB Letter No. 1248/SAHS. For active reporting, diagnosed cases of pediatric thalassemia patients, aged 1–16 years, which were confirmed using high-performance liquid chromatography technique (*Ion Exchange Bio-Rad HPLC system*) from August 2023 to November 2023 were included using purposive sampling method approach. For active reporting, a designated investigator visited the thalassemia patient units daily. A thorough history was taken from all patients, with a special focus on blood transfusions, including the frequency of transfusions, the type of blood components received, and any history of previous transfusion reactions (type and severity). A self-designed pro forma was used for this purpose. For the passive reporting, data from April 2023 to July 2023 were collected from the blood bank records. Data collected included patient demographics and transfusion details including transfusion adverse reactions.

During active reporting, where a transfusion reaction was detected, additional data were collected, including whether the reaction was reported to the transfusion service or not, the type and severity of reaction, and the details of the transfused component. Severity was defined according to the International Society of Blood Transfusion (ISBT) guidelines (www.isbtweb.org): Grade 1 (nonsevere): The recipient may have required symptomatic treatment, but the absence of treatment would not have resulted in any harm. Grade 2 (severe): The adverse event required medical or surgical intervention to prevent damage or impairment of bodily functions, or the recipient needed hospitalization directly related to the event, and/or the event resulted in persistent or significant disability or incapacity. Grade 3 (life-threatening): To avoid mortality, the recipient required significant intervention following the transfusion, such as admission to the intensive care unit or the administration of vasopressors. Grade 4 (death): The patient died due to an adverse event that was likely or directly related to the transfusion.

Data were entered and analyzed using IBM-SPSS Statistics 16.0 (SPSS Inc., Chicago, USA). Categorical variables, such as age and gender, were presented as frequencies and percentages. Prevalence was calculated by dividing the total number of transfusion reactions by the total number of transfusion episodes.

Results

During active reporting, a total of 300 transfusion episodes were analyzed in 248 patients diagnosed with thalassemia who were undergoing red cell concentrates' transfusions. Of all the patients who

were recruited for the study, 96.3% (239/248) were diagnosed with beta-thalassemia major (β-TM), while 3.6% (9/248) were diagnosed with beta-thalassemia intermedia (β-TI). Out of these, 161/248 (64.9%) were male while 87/248 (35.0%) were females. There were two major sub-ethnic groups identified, i.e. Punjabi (241/248, 97.1%) and Pashtun (7/248, 2.9%). The incidence rate of acute transfusion reactions actively identified was 6.3% (19/300). The reactions observed were either FNHTR 11/19 (57.8%) or ALTR 8/19 (42.1%). The severity of these reactions was either of Grade 1 or 2 [Table 1].

Contrary to active surveillance, the incident rate of passively reported data was 0.62% (2 out of 320) which is 10 times lower than the rate observed during active surveillance. The two reactions found through passive reporting were FNHTR and AHTR. The severity of both these transfusion reactions was of Grade 2 [Table 1].

Out of 19 transfusion reactions, which were identified during active surveillance, 52.7% (10/19) occurred in males and 47.3% (9/19) occurred in females. The incidence rate of transfusion reaction was not associated with gender. After interviewing patient attendants/parents and clinical staff, we got to know that the transfusion reactions that occurred in thalassemia patients had a previous history of transfusion reactions. In case of passively reported reactions unfortunately, most of the cases were reported with incomplete clinical details.

When the information obtained from the active surveillance was analyzed, it was found that the mean age at the initiation of transfusion therapy was 7 months. The frequency of transfusion in most cases was one or two times per month while a few were getting transfusion therapy three or four times per month [Table 2]. In active surveillance, patients who showed FNHTR had varying symptoms: 8/11 patients (72.3%) developed fever (100.4–102.2°F) within 1 h of transfusion while 3/11 (27.8%) developed a fever after the completion of transfusion. Other symptoms observed were shivering 9/11 (81.8%) and tachypnea 6/11 (54.5%). Among the patients who experienced posttransfusion urticarial reactions, 6/8 (75.0%) presented with rash, 7/8 (87.5%) with hives and only 2/8 (25%) developed fever (100.4–102.2°F). Passive reporting for FNHTR showed presentation with fever and rigors and patients with AHTR developed fever, tachycardia, tachypnea, lower back pain, and hemoglobinuria.

In case where transfusion reactions were observed in patients, the first action taken by the clinical team was to immediately stop the transfusion and give antihistamine medication. In almost all of the cases after giving the treatment, the condition of the patient started getting stable and transfusion was resumed except for AHTR.

Table 1: Frequency distribution of transfusion reactions in percentages and grade of severity identified during active surveillance

Type of reaction	Frequency (%)	Maximum number of transfusions (monthly)	Grade of severity
Active surveillance (*n*=19)			
Urticarial reaction	8 (42.10)	1	Grade 1 and 2
FNHTR	11 (57.90)	1	Grade 2
Passive reporting (*n*=2)			
FNHTR	1 (50)	1	Grade 2
AHTR	1 (50)	1	Grade 2

FNHTR=Febrile nonhemolytic transfusion reaction, AHTR=Acute hemolytic transfusion reaction

Table 2: Monthly frequency of number of transfusions during active surveillance

Number of transfusions	Frequency (%)
1	148 (49.3)
2	132 (44.0)
3	13 (4.3)
4	7 (2.3)
Total	300

Discussion

Blood transfusions for thalassemia patients can be cumbersome, requiring one to four transfusions per month depending on their condition.[12] These transfusions can become life-threatening if reactions are not properly monitored. Taking proactive steps to prevent transfusion reactions would not only contribute to a stronger hemovigilance system but also provide relief to patients. Our study revealed a significant difference between actively monitored transfusion reactions and those reported passively.

Similar to our findings, where there lies a difference between true incidence of transfusion reactions among actively reported and passively reported reactions among pediatric thalassemia patients, a university medical center in the US reported under-estimation of transfusion reactions by passive reporting in the adult patient population.[13] Recently, another study in Brazil found significant under-reporting of acute adverse transfusion events in a hospital system[14] where the actual transfusion reaction rate found was 16.3/1000 (0.016%), while the notification rate was 3.83/1000 (0.003%). A study carried out at a tertiary care hospital in Saudi Arabia found an actual transfusion reaction rate of 0.79% through active surveillance which was higher than that reported passively (0.17%–0.26%) by the same hospital during the same months in the previous years.[11] The incidence of acute transfusion reactions reported from different regions of the world, however, varies with the highest incidence reported at

KSA (0.79%),[11] followed by Pakistan (0.06%, this study) and Brazil (0.016%).[14]

Studies have shown that FNHTR and ALTR are the most common reactions among thalassemia adults[15-17] as well as pediatric patients.[18] A study on acute transfusion reactions in thalassemia patients from Egypt reports that 21.6% of thalassemia patients presented with fever and rigors while 3.9% showed allergic reactions.[19] Similarly, another study from Saudi Arabia reports urticaria as the most common reaction comprising 21% of the reported ones.[20] Similar to the reports from most of the regions of the world, our study also had FNHTR as the most prevalent transfusion reaction type (11/300, 3.7%) followed by urticarial reactions (8/300, 2.6%) during active reporting among pediatric thalassemia patients.

The possible causes of underreporting of these reactions are the heavy workload of healthcare professionals in our clinical setting, lack of culture of encouraging the reporting of transfusion reactions, and/or no proper training in this regard. So far, there is no centralized system of hemovigilance in Pakistan.[21] Hemovigilance is a concept which is at its beginning in transfusion-related practices in our country.[22] Execution of an automated or semi-automated electronic system to report these reactions and having a patient history will be beneficial for future prevention of such reactions. In another study in Iran, documentation and reporting after the establishment of proper hemovigilance system has resulted in reporting of severe and life-threatening reactions more frequently compared to pre-implementation.[23] Active surveillance with proper education of transfusion chain members regarding transfusion reactions and significance of their reporting, proper communication with patients' family members can lower the burden of healthcare professionals. This study is a small effort to highlight the importance of hemovigilance program in our clinical setting, particularly for thalassemia patients exposed to multiple transfusions. The transfusion reactions which remain unrecognized or are not reported at the right time which may sometimes lead to fatal consequences.

Limitations of study

Some of the limitations of this study were that it was time-bound with selection bias as the patients enrolled had already undergone multiple transfusions, which may have resulted in a higher rate of transfusion reactions and so a higher incidence of missed reactions.

Conclusion

A significant difference was found between the number of transfusion reactions identified through active surveillance and passive reporting among the thalassemia patients. The observed differences suggest that minor transfusion reactions, although clinically identified, were often not reported to transfusion services. Raising awareness about transfusion reactions and the importance of reporting them will aid in developing preventive frameworks for future safety.

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Conflicts of interest

There are no conflicts of interest.

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