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Original Research Article

Associations between Alloantibodies and Multiple Red Cells Transfusion in Patients of Tertiary Hospital of Jharkhand with Sickle Cell Anaemia.

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Abstract:

Background: Sickle cell anemia (SCA) is a severe genetic disorder that necessitates frequent red blood cell (RBC) transfusions, potentially leading to alloimmunization. This study investigates the association between multiple RBC transfusions and the development of alloantibodies in SCA patients at a tertiary hospital in Jharkhand, aiming to enhance transfusion strategies and patient outcomes.

Methods: A retrospective cohort analysis was carried out on 62 SCA patients who received two or more RBC transfusions within the last year. Data on transfusion history, alloantibody presence, and clinical outcomes were collected from electronic health records. Logistic regression models, adjusted for age, gender, and comorbid conditions, were used to analyze the association between the number of transfusions and alloantibody development.

Results: Among the patients (54.8% male, mean age 29.4 years), 29.0% developed alloantibodies. A significant correlation was found among the number of transfusions and alloantibody development ($p < 0.01$), with patients receiving more than five transfusions showing a threefold increased risk. Alloantibody-positive patients were more likely to have a history of acute chest syndrome ($p = 0.03$) and frequent hospitalizations ($p = 0.05$). Logistic regression confirmed transfusion frequency as an independent predictor of alloantibody development (Odds Ratio = 3.2, $p = 0.005$).

Conclusion: The study highlights a significant link between multiple transfusions and alloantibody development in SCA patients, underscoring the need for careful transfusion management and monitoring.

Recommendations: Implementing antigen matching protocols and leukoreduced blood products could minimize the risk of alloimmunization. Further research is needed to develop targeted therapies for SCA patients at high risk of alloimmunization.

Keywords: Sickle Cell Anemia, Alloantibodies, Red Blood Cell Transfusion, Alloimmunization.

Introduction

A genetic blood disorder known as sickle cell anaemia (SCA) is characterised by the production of aberrant haemoglobin S, which causes red blood cells to resemble sickles. This condition can lead to a number of complications, such as increased susceptibility to infections, acute chest syndrome, and vaso-occlusive crises. Red blood cell (RBC) transfusions are a cornerstone in the management of SCA, providing symptomatic relief, preventing complications, and improving quality of life for patients. However, the repeated exposure to donor antigens through multiple transfusions raises the risk of alloimmunization, where the recipient's immune system develops antibodies (alloantibodies) against the foreign RBC antigens, leading to potential transfusion complications, including hemolytic transfusion reactions and difficulties in finding compatible blood units [1, 2].

The development of alloantibodies in SCA patients is affected by several factors, including the genetic background of the patient and the antigenic differences between donor and recipient blood. Studies have shown that the prevalence of alloimmunization in SCA patients varies widely, ranging from 5% to 36%, which can be attributed to differences in transfusion practices, the genetic diversity of the patient population, and the extent of antigen matching for transfusions [3, 4]. The clinical implications of alloimmunization are significant, as they can complicate the management of SCA by limiting the availability of compatible blood units, increasing the risk of delayed

hemolytic transfusion reactions, and contributing to iron overload due to ineffective transfusion [5].

Given the critical role of RBC transfusions in the management of SCA and the potential risks associated with alloimmunization, understanding the associations between multiple transfusions and the development of alloantibodies is essential for optimizing transfusion strategies and improving patient outcomes. This includes the implementation of antigen matching protocols, the use of leukoreduced blood products, and the development of targeted therapies to minimize the risk of alloimmunization [1, 2]. The current study aims to explore these associations in a cohort of SCA patients at a tertiary hospital in Jharkhand, providing valuable insights into the prevalence of alloantibodies and their impact on the management of SCA.

The aim of the study is to investigate the relationship between the presence of alloantibodies and the frequency of multiple red blood cell transfusions in patients with sickle cell anemia treated at a tertiary hospital in Jharkhand.

Methodology

Study Design: The study was designed as a retrospective cohort analysis.

Study Setting: The research wa carried out at M.G.M.M.C.H. Jamshedpur, between January 2023 to January 2024.

Participants: A total of 62 patients with confirmed sickle cell anaemia were included in the study.

Inclusion and Exclusion Criteria: Inclusion criteria were patients with a diagnosis of sickle cell anaemia who had received two or more red cell transfusions within the last year. Exclusion criteria included patients with other hemoglobinopathies, those who had received a bone marrow transplant, and patients with incomplete medical records.

Bias: To minimize selection bias, patients were consecutively selected based on their admission dates and transfusion history. Information bias was reduced through the standardized review of medical records by two independent researchers.

Variables: The primary independent variable was the presence of alloantibodies, identified through blood screening tests. The dependent variable was the number of red cell transfusions received. Covariates included age, gender, and the presence of any comorbid conditions.

Data Collection: Data were collected retrospectively from the hospital's electronic health records system. This included demographic information, clinical history, transfusion records, and laboratory results pertaining to alloantibody screening.

Procedure: Patients' medical records were reviewed to extract data on transfusion history and alloantibody presence. The review period covered up to two years prior to the study's initiation. Blood samples for alloantibody screening were collected as part of routine care during the study period.

Statistical Analysis: All statistical analyses were accomplished using SPSS software (version 25). The association between alloantibodies and the number of transfusions was analyzed using logistic regression models, adjusting for potential confounders. The significance level was set at $p<0.05$.

Ethical Considerations: The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Result

The study's analysis included 62 patients with sickle cell anemia who had undergone multiple red cell transfusions at a tertiary hospital in Jharkhand. The cohort comprised 34 males (54.8%) and 28 females (45.2%), with an age range of 6 to 58 years (mean age 29.4 years).

Table 1: Characteristics and Outcomes of Patients with Sickle Cell Anemia Based on Alloantibody Development

Variable	Alloantibody Positive (n=18)	Alloantibody Negative (n=44)	p-value
Demographics			
Age (years, mean ± SD)	31.2 ± 12.4	28.9 ± 15.6	0.56
Gender (male, %)	55.6%	54.5%	0.92
Clinical Characteristics			
Number of Transfusions (median)	7 (range: 3-15)	4 (range: 2-10)	<0.01
History of Acute Chest Syndrome (%)	44.4%	22.7%	0.03
Hospitalizations (median per year)	3 (range: 1-5)	1 (range: 0-3)	0.05
Outcomes			
Transfusion Reactions (%)	17%	5%	0.04

Out of the 62 patients, 18 (29.0%) developed alloantibodies following red cell transfusions. The majority of these alloantibodies were identified against common red cell antigens, including E, Kell, and C antigens.

Patients had received between 2 to 15 transfusions (median = 5) in the year preceding the study. A significant correlation was observed among the number of transfusions and the development of alloantibodies ($p < 0.01$). Specifically, patients who received more than 5 transfusions had a threefold increase in the risk of developing alloantibodies compared to those who received fewer transfusions.

No significant differences were found in the age or gender distribution between patients who developed alloantibodies and those who did not. However, patients with alloantibodies were more likely to have a history of acute chest syndrome ($p = 0.03$) and required hospitalization more frequently ($p = 0.05$) compared to their counterparts.

Logistic regression analysis, adjusting for age, gender, and the presence of comorbid conditions, confirmed that the number of transfusions was an independent predictor of alloantibody development (Odds Ratio = 3.2, 95% CI: 1.4 - 7.3, $p = 0.005$). Furthermore, the presence of alloantibodies was related with a higher rate of transfusion reactions (17% vs. 5%, $p = 0.04$).

Discussion

The study's findings reveal a significant correlation between the frequency of RBC transfusions and the development of alloantibodies in individuals with sickle cell anemia, with 29.0% of the cohort developing alloantibodies, predominantly against common red cell antigens.

Notably, patients undergoing more than five transfusions exhibited a threefold increased risk of alloantibody formation compared to those with fewer transfusions, underscoring the impact of transfusion frequency on alloimmunization risk. Despite no significant demographic differences between those with and without alloantibodies, the former group experienced higher rates of acute chest syndrome and hospitalizations, indicating a potential link between alloantibody development and severe clinical outcomes.

The logistic regression analysis further validated the number of transfusions as an independent predictor of alloantibody development, with alloimmunized patients also facing a significantly higher risk of transfusion reactions. These results highlight the critical need for careful transfusion management and monitoring in sickle cell anemia patients to mitigate the risks associated with alloimmunization.

In a study conducted in North Andaman, India, a 25-year-old female with SCA experienced a severe hemolytic transfusion reaction and hyperhemolysis after being treated with packed red cells, highlighting the challenges of managing sickle cell crises in remote locations but also demonstrating successful recovery with limited resources [6]. Another case in India focused on the utilization of automated RBC exchange for managing a sickle cell crisis, showing significant improvement in the patient's condition, with a reduction of HbS to 16% and maintenance of HCT at 21% post-procedure, underscoring the potential benefits of advanced therapeutic techniques in sickle cell disease management [7].

Additionally, a comprehensive review in the context of pediatric sickle cell anemia individuals identified multilevel barriers and facilitators to chronic RBC transfusion therapy, emphasizing the importance of understanding these factors to improve transfusion services and patient outcomes [8]. Research on the iron profile of pregnant women with sickle cell anemia in Odisha, India, revealed that most cases showed iron sufficiency, suggesting that iron status evaluation is crucial before initiating iron prophylaxis in pregnant women with sickle cell anemia, especially in regions with a high occurrence of the disease [9].

These studies collectively contribute to the understanding of transfusion-related challenges and management strategies in sickle cell anemia.

Conclusion

The findings suggest a significant association between the frequency of red cell transfusions and the development of alloantibodies in patients with sickle cell anemia. This relationship underscores the importance of judicious transfusion practices and the potential need for alloantibody screening protocols in this patient population to mitigate the risks associated with transfusion therapy. The study also highlights the need for further research into personalized transfusion strategies to improve outcomes for patients with sickle cell anemia.

Limitations: The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: Implementing antigen matching protocols and leukoreduced blood products could minimize the risk of alloimmunization. Further research is needed to develop targeted therapies for SCA patients at high risk of alloimmunization.

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