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Original Research Article

Correlation between blood group and autoantibodies formation in multi-transfused thalassaemia patients

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ABSTRACT

Background: Thalassemia is a prevalent genetic disorder of hemoglobin synthesis, characterized by reduced production or absence of one or more globin chains, requiring frequent blood transfusions that can lead to complications such as autoantibody formation. The purpose of this study was to assess the correlation between blood group and the formation of autoantibodies in thalassemia patients who have received multiple blood transfusions.
Methods: This cross-sectional study at the Department of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, conducted from October 2017 to September 2018, included 384 thalassemia patients who received at least 10 units of red cell concentrate. Participants were selected based on specific inclusion and exclusion criteria, with informed consent obtained. Data collection involved patient interviews, clinical examinations, and hematological tests. Statistical analysis using SPSS version 23.0 included Chi-square, Fisher's exact, and t-tests, with significance set at $p<0.05$.
Results: Among 384 patients, the most common blood group was B+ (46.2%). Coombs' test results showed DCT positivity in 3.1% of 384 patients, ICT positivity in 7.5%, and both DCT and ICT in 4.2%. Most patients (92.3%) had their first transfusion after age 2, with 84.6% receiving transfusions every 2-4 weeks.
Conclusions: In conclusion, B positive blood group thalassemia patients receiving frequent transfusions are at a higher risk of autoantibody formation, and Rhesus phenotype-matched blood with pre-storage leukodepletion is recommended to mitigate this risk.

Keywords: Alloimmunization, Autoantibodies, Blood transfusion, Blood group, Thalassemia

INTRODUCTION

Thalassemia is a prevalent genetic disorder of hemoglobin synthesis, characterized by reduced production or absence of one or more globin chains, commonly found in the Mediterranean region and Southeast Asia.[1,2] It is the predominant type of inherited anemia globally, marked by reduced or absent production of either the alpha-like (alpha-thalassemia) or beta-like (beta-thalassemia) globin chains crucial for hemoglobin tetramer formation in fetal and postnatal stages.[3] Thalassemia was initially identified in 1925, with severe (Cooley's anemia) and milder (La Malattia di Rietti-Greppi-Micheli) forms recognized independently in the US and Italy. These are now termed thalassemia major (TM) and thalassemia intermedia (TI). It has since been

acknowledged that thalassemia due to alpha and beta globin chain production defects extends beyond the Mediterranean, affecting populations across Africa, the Middle East, Southeast Asia, and the Western Pacific.[4-6] Current treatment involves monthly blood transfusions to sustain a mean hemoglobin level of 10-11 g/dL, which continues to be the primary approach for managing severe thalassemia.

The thalassaemia are a group of congenital anaemias that have in common deficient synthesis of one or more of the globin sub units of the normal human haemoglobin. The primary defect is usually quantitative consisting of the reduced or absent synthesis of normal globin chain. Thalassaemia sub groups have in common an imbalanced globin synthesis, with the consequences that the globin produced in excess in responsible for ineffective erythropoiesis and haemolysis.[7] Life-long red blood cell (RBC) transfusions are the mainstay of treatment for severe thalassemia. A complication of blood transfusions is the recipient's production of antibodies against RBCs. These risks are particularly relevant for patients who have undergone multiple transfusions. It is essential to systematically identify these antibodies in the recipient's serum before each transfusion to ensure compatible blood is provided. Failure to do so can lead to serious, potentially life-threatening issues.[8] However, the emergence of anti-RBC antibodies, including alloantibodies and autoantibodies, can greatly complicate transfusion therapy. While erythrocyte autoantibodies are less common, they can still cause clinical hemolysis and create difficulties in blood cross-matching.

Previous studies have documented the formation of autoantibodies against RBCs.[9-11] Patients with these autoantibodies may need more frequent transfusions and often require immunosuppressive medications, splenectomy, or other treatments.[12-14] Despite acknowledging autoantibodies as transfusion-related risks, there is limited understanding of the prevalence and causes of these issues in thalassemia patients or the best prevention strategies. Therefore, the purpose of this study was to evaluate the correlation between blood group and autoantibody formation in patients with thalassemia who have undergone multiple transfusions. The aim of this study was to evaluate the correlation between blood group and autoantibody formation in patients with thalassemia who have undergone multiple transfusions.

METHODS

This cross-sectional study was conducted at the Department of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, over a 12-month period from October 2017 to September 2018. The study population comprised 384 consecutive patients with thalassemia who had received at least 10 units of red cell concentrate.

Inclusion criteria

Age >1 year to <40 years, both sexes, diagnosed with thalassemia via Hb-electrophoresis, received at least 10 units of blood transfusion, Bangladeshi nationality, able to provide written informed consent, capable of understanding questions and communicating effectively were included.

Exclusion criteria

Age <1 year and >40 years, presence of any autoimmune or connective tissue disease, individuals refusing to participate or unable to comprehend the study for any reason were excluded.

Institutional approval was obtained from the IRB of BSMMU, with ethical considerations addressed per the Helsinki Declaration. Informed written consent was obtained from participants, ensuring privacy and confidentiality. Patients were initially interviewed, clinically examined, and underwent routine hematological investigations, blood grouping, DAT, and IAT using a spin-tube technique. Research instruments included pre-tested questionnaires, reagents (Anti-Human Globulin, Anti-A, Anti-B, Anti-D), test tubes, glass slides, pipettes, normal saline, a centrifuge machine, and a microscope. Statistical analysis was performed using SPSS version 23.0, with qualitative variables expressed as frequencies and percentages, and quantitative variables as mean ± standard deviation. Associations were assessed using Chi-square, Fisher's exact, and unpaired t-tests, with OR and 95% CI calculated. A p-value <0.05 was significant. Ethical clearance was obtained, and participants' rights and health were safeguarded with the assurance of confidentiality and freedom to withdraw at any time.

RESULTS

Table 1 shows the distribution of the study population by blood group. Among the 384 patients, 59 (15.4%) had A positive, 177 (46.2%) had B positive, 118 (30.8%) had O positive, and 30 (7.7%) had O negative blood types.

Figure 1 shows the distribution of the study population by Coombs' test results. It was observed that DCT was positive in 12 patients (3.1%), ICT in 30 patients (7.5%), and both DCT and ICT in 16 patients (4.2%).

Table 2 shows the age at which patients received their first blood transfusion. Among the 384 patients, 354 (92.3%) received their first transfusion after the age of 2 years, while 30 (7.7%) received their first transfusion before 2 years of age.

Table 1: Distribution of the study patients by blood group (n=384).

Blood group	Frequency	Percentage
A+	59	15.40
B+	177	46.20
O+	118	30.80
O-	30	7.70
Total	384	100.00

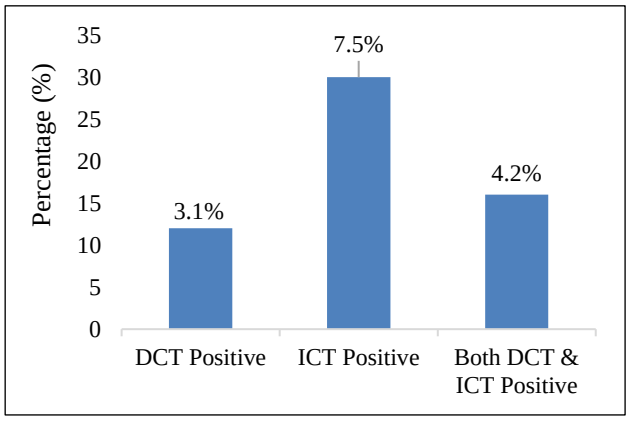

Figure 1: Distribution of the study respondents by coombs' test (n=384).

Table 2: Distribution of the study patients at the 1st time transfusion (n=384).

1st time of transfusion (years)	Number of patients	Percentage
>2	354	92.30
<2	30	7.70
Total	384	100

Table 3: Distribution of the study patients by interval of blood transfusion (n=384).

Interval of blood transfusion	Number of patients	Percentage
2-4	325	84.60
4-6	59	15.40
Total	384	100

Table 3 shows the interval of blood transfusions among the study population. Most patients (325, 84.6%) received transfusions at intervals of 2 to 4 weeks, while 59 patients (15.4%) received transfusions every 4 to 6 weeks.

DISCUSSION

Thalassemia is a genetic disorder characterized by impaired globin chain synthesis, leading to ineffective erythropoiesis and shortened red blood cell lifespan. Standard treatment involves regular blood transfusions, often on a monthly basis, to maintain hemoglobin levels between 10-11 g/dL. However, one of the major complications of repeated transfusions is the development of alloantibodies and autoantibodies against red blood cells, increasing the risk of hemolytic reactions and complicating further transfusions.

In this study, we evaluated the correlation between blood group and the formation of autoantibodies in a cohort of 384 thalassemia patients who had received more than 10 units of blood transfusions at Bangabandhu Sheikh Mujib Medical University. Our findings revealed that 12 patients (3.1%) tested positive for the direct Coombs' test (DCT), 30 (7.8%) tested positive for the indirect Coombs' test (ICT), and 16 patients (4.2%) were positive for both tests. These results suggest a relatively higher rate of immunization in our patient population, particularly when compared to reports from neighboring countries such as India (0.47%) and Pakistan (1.87%). The variation in Coombs' positivity across different regions could be attributed to differences in transfusion practices, the use of leukodepletion filters, or the availability of phenotype-matched blood, which is not widely practiced in Bangladesh.

Our study found that the blood group distribution among thalassemia patients was as follows: B+ was the most common blood group (46.2%), followed by O+ (30.8%) and A+ (15.4%). Notably, patients with blood group B had the highest incidence of positive direct Coombs' tests. This suggests that blood group B may be more susceptible to alloimmunization, possibly due to antigenic variability between donor and recipient blood. This finding is consistent with another study suggesting a possible association between certain blood groups and a higher risk of alloantibody formation.[15] The role of antigenic differences between donor and recipient blood groups in increasing alloimmunization risk needs further exploration in larger studies.

A significant observation from our study is that patients who started transfusions before the age of 2 years had a lower rate of Coombs' positivity. Among the 384 patients, only 30 (7.7%) received their first transfusion before the age of 2 years, and this group exhibited fewer positive DCT results. This supports the hypothesis that early initiation of transfusions in thalassemia patients may induce immune tolerance and reduce the risk of alloimmunization. Another study suggests that younger patients, due to their relatively immature immune systems, may develop a form of immune tolerance to donor red cell antigens, lowering the likelihood of autoantibody formation later in life.[16]

The storage duration of transfused blood may also play a role in the higher rate of immunization observed in our study. Most of our patients received blood that had been stored for more than five days. Prolonged storage of red blood cells is known to cause cytokine release from apoptotic leukocytes, which may increase the risk of immune sensitization. In low-resource settings like ours,

the absence of leukodepletion filters further exacerbates this risk, as these filters help to minimize residual leukocytes in transfused blood and thus reduce the likelihood of alloimmunization.

In our study, none of the patients received phenotype-matched blood, a practice that has been shown to significantly reduce the risk of alloimmunization in multi-transfused patients. The lack of phenotype-matched blood is a particular challenge in low-resource settings like Bangladesh, where donor pools are limited, and infrastructure for advanced blood matching is underdeveloped. This likely contributed to the relatively high rate of Coombs' positivity observed in our cohort.[9,17]

In conclusion, this study identifies several key factors influencing autoantibody formation in multi-transfused thalassemia patients, with a specific focus on the correlation between blood group and alloantibody development. These results underscore the importance of personalized transfusion practices, such as early initiation of transfusions and the use of leukodepleted, phenotype-matched blood, to minimize the risk of alloimmunization. Further research is needed to optimize transfusion protocols and improve outcomes for thalassemia patients in resource-limited settings.

This study has few limitations. The study population was selected exclusively from patients at BSMMU, limiting the generalizability of the results to the broader population. A larger sample size would provide more robust data and a more accurate representation of the autoimmunization status in multi-transfused thalassemia patients. The study did not differentiate between autoantibodies mediated by IgG and those mediated by complement. The specific antigens responsible for producing these autoantibodies were not identified.

CONCLUSION

In conclusion, our study found that regular blood transfusion is a significant cause of autoimmunization in thalassemia patients. Autoantibody formation was most common in patients with the B positive blood group, comprising 46.2% of the study population. Most patients received their first blood transfusion after the age of 2 years and had transfusion intervals of 2-4 weeks. To prevent autoantibody formation in multi-transfused thalassemia patients, it is recommended to use Rhesus phenotype-matched blood and implement pre-storage leukodepletion. This approach can help minimize the risk of alloimmunization and improve patient outcomes.

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