Originbal Research

ANALYSIS OF RED CELL ALLOIMMUNIZATION IN MULTITRANSFUSED B-THALASSEMIA PATIENTS AT A TERTIARY CARE CENTRE

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ABSTRACT

Background: β-thalassemia major patients require lifelong repeated red blood cell transfusions, which predispose them to alloimmunization against foreign erythrocyte antigens. Development of alloantibodies complicates transfusion therapy and may lead to delayed hemolytic transfusion reactions and difficulty in obtaining compatible blood. This study was undertaken to evaluate the frequency and specificity of red blood cell alloantibodies in multitransfused β-thalassemia patients.

Materials and Methods: This cross-sectional study was conducted at Dr. D. Y. Patil Medical College, Hospital and Research Centre, Kolhapur, over a period of three years. A total of 84 β-thalassemia patients who had received more than 10 packed cell transfusions were included. ABO and RhD blood grouping was performed using standard methods. Antibody screening was carried out using a commercial three-cell reagent panel, and positive samples were further evaluated with 11-cell antibody identification panel using the gel card method.

Results: Among the 84 multitransfused β-thalassemia patients, 10 patients were positive for red cell alloantibodies, giving an overall alloimmunization prevalence of 11.90%. The majority of alloantibodies belonged to the Kell blood group system, with Anti-K being the most frequently detected antibody (40%), followed by Anti-e (20%). Other antibodies identified included Anti-k, Anti-D, antibodies against Js^b,Kp^b,Lu^b and MNS system antibodies. No statistically significant association was observed between alloimmunization age and gender.

Conclusion: Red cell alloimmunization remains a significant complication in transfusion-dependent β-thalassemia patients. The predominance of Kell and Rh alloantibodies highlights the importance of extended antigen phenotyping and provision of phenotype-matched blood from the initiation of transfusion therapy. Early screening and preventive transfusion strategies can substantially reduce alloimmunization and improve transfusion safety in β-thalassemia patients.

Keywords: B-Thalassemia Major, Alloimmunization, Red Blood Cell Antibodies, Kell System,Transfusion, Phenotype Matching.

INTRODUCTION

β-thalassemia major is a severe hereditary hemoglobinopathy characterized by the deficient or absent synthesis of β-globin chains, requiring lifelong and regular red blood cell transfusions[1]. Though chronic transfusion therapy prevents the complications of severe anaemia and suppresses ineffective erythropoiesis, it remains a double-edged sword[2]. Repeated exposure to foreign erythrocytic antigens triggers an immune response in the recipient, leading to the development of RBC

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alloantibodies-a phenomenon known as alloimmunization[3].

The prevalence of alloimmunization among multi-transfused β-thalassemia patients is highly variable, with reported rates ranging from 2.9% to 42.5% globally[4]. This variability is often attributed to the degree of antigenic disparity between donor and recipient populations, the recipient's immune status and specific transfusion protocols employed by different hospitals[5]. Clinical data indicate that the majority of these alloantibodies are directed against the Rh (particularly E, D, and c antigens) and Kell systems which are known for their high immunogenicity[6].

The clinical consequences of alloimmunization are profound and multifaceted. The presence of alloantibodies can significantly shorten the lifespan of transfused red cells, causing increased frequency of transfusions and the resulting iron overload[7]. Furthermore, it complicates pre-transfusion cross-matching, leading to life-threatening delays in securing compatible blood units. In severe cases, it can culminate in delayed haemolytic transfusion reactions (DHTR) or hyperhaemolysis syndrome, which are associated with significant morbidity and mortality[8].

Recent literature underscores that standard ABO and RhD matching is no longer sufficient for managing transfusion-dependent patients. There is a growing clinical consensus that extended phenotyping for minor antigens should be performed at the time of diagnosis, prior to the first transfusion event[9]. Studies have shown that implementing such phenotype-matched transfusion protocols can reduce the risk of alloimmunization by up to 80-90%[10].

Given the increasing life expectancy of thalassemia patients due to improved chelation therapies, the long-term management of transfusion related immunological complications such as alloimmunization has become a priority. This study aims to evaluate the frequency and type of RBC alloantibodies in multitransfused β-thalassemia patients, emphasizing the critical importance of early screening and identification protocols to ensure transfusion safety and improve overall clinical outcomes[9].

MATERIALS AND METHODS

This was a cross-sectional study conducted at Dr. D.Y. Patil Medical College Hospital and Research Centre, Kolhapur over a 3 year period. A total of 84 patients diagnosed with β-thalassemia, who had received more than 10 PCV transfusions, were enrolled following informed consent. Peripheral venous blood samples were collected in EDTA tubes for immunohematological analysis. ABO and RhD grouping were performed using standard forward and reverse grouping techniques. Antibody screening was executed using a commercially available three-cell reagent panel. Samples with a positive screen were further processed for antibody identification using 11-cell identification panel to determine the specificity of the alloantibodies. The testing was conducted using gel card method.

RESULTS

A total of 84 patients with β-thalassemia major were included in the study. All patients were receiving regular blood transfusions.They received ABO- and RhD-matched packed red blood cells (PRBCs). 5 patients underwent splenectomy. 10 patients were found positive for RBC alloantibodies.The prevalence of alloimmunization was 11.90% (10/84). A total of 58 (69.05%) study subjects were male while 26 (30.95%) were female, amongst them 12.06% (7/58) male and 11.53% (3/26) females were alloimmunized.There was no significant association between sex and alloimmunization status (Fisher's exact test, $p > 0.05$). The age of study subjects ranged from 1 to 23 years.The mean age of alloimmunized patients was 11 years. Age distribution of all antibody positive β-thalassemia subjects is presented in Table 1. ABO blood group distribution (Table 2) revealed that 23 (27.38%), 29(46.42%), 23 (27.38%) and 9 (10.71%) subjects were of O, A, B and AB blood group respectively; amongst them 3 (30%), 3 (30%), 3 (30%) and 1(10%) subjects of O, A, B and AB blood group respectively were alloimmunized.Only six subjects were RhD negative of which one was alloimmunized. The transfusion history revealed that all the patients received >10 transfusions.5 patients out of 84 had undergone splenectomy of which one was alloimmunized.

The most detected antibody was 4 cases of Kell[anti-K(40%)] followed by 2 cases of Rhesus [Anti e (20%)] and one case each (10%) of Kell [Anti k(10%)], Kell[Anti k, Js^b, kp^b, Lu^b(10%)], Rhesus [Anti D (10%)] and MNS (10%). (Table 3)

Table 1: Age Distribution of Alloimmunized patients

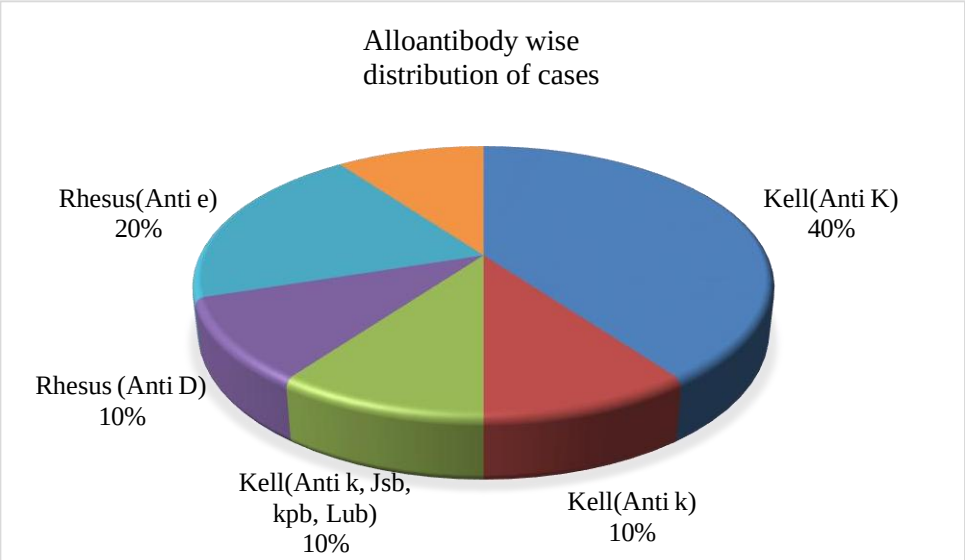
Age Group(Years)	No. of Cases	Percentage (%)
<10	4	40
10-20	4	40
≥21	2	20
Total	10	100

Table 2. ABO and Rh Blood Group Distribution of Total Number of Cases and Alloimmunized Patients

Blood Group	Total No. of Cases	No. of Alloimmunized Cases
A+	28	2
A-	1	1
B+	18	3
B-	5	0
AB+	9	1
AB-	0	0
O+	23	3
O -	0	0
Total	84	10

Table 3: Prevalence of Alloantibodies in the study group

Sr. No.	Antibodies	No. of Cases	Percentage (%)
1	Kell (Anti K)	4	40
2	Kell (Anti k)	1	10
3	Kell(Anti k, Js^b, kp^b, Lu^b)	1	10
4	Rhesus (Anti D)	1	10
5	Rhesus(Anti e)	2	20
6	MNS	1	10
	Total	10	100



DISCUSSION

Red cell alloimmunization is an immune response directed against foreign red blood cell antigens which is usually stimulated by the transfusion of blood products and is one of the complications of RBC transfusions. Other than RBC Alloimmunization other immunological complications of repeated RBC transfusions include: Difficulties in obtaining compatible blood, development of autoantibodies, acute or delayed haemolytic transfusion reactions and haemolytic disease of the newborn.

The factors for alloimmunization are complex and involve at least three main contributing elements: (1) the RBC antigenic difference between the blood donor and the recipient; (2) the recipient's immune status; (3) the immune modulatory effect of the allogeneic blood transfusions on the recipient's immune system.

Overall rate of alloimmunization was 11.90% in our study. Similar incidence was noted in studies by Azarkeivan et al, Dogra et al, Ahmed AM et al and Gupta R et al. Other studies reported prevalence ranging from 5-18%.

Table 4. Rate of Alloimmunization in Various Studies

Study	Prevalence of alloimmunization
Present study	11.90%
Azarkeivan A et al[11]	11.3%
Ahmed AM et al.[12]	11.3%

Gupta R et al[13]	9.48%
Dogra A et al[14]	8.5%
Arainezad A et al[15]	5.8%
Chaudhari CN[16]	18.8%

In our study, the most frequently detected alloantibodies belonged to Kell blood grouping system (60%). Individually, most frequent alloantibody detected was anti-K (40%). This finding is in concordance with the studies by Arainezad et al, Dogra A et al., Dhawan HK et.al., Ameen R et al and Singer ST et.al.

Table 5. Frequency of Anti K Alloantibody in Thalassemia Patients

Study	Anti K Antibody
Present study	40%
Arainezad et al[15]	39.6%
Dogra A et al[14]	33.34%
Dhawan HK et al[5]	35%
Ameen R et al[17]	72%
Singer ST et al[10]	30%

We did not find any association of age and gender (male/female) with rate of alloimmunization (p=0.93). In literature, the studies of Dhawan et al., Dogra *et al*. and Chaudhari CN showed that age and gender was not a significant factor in the development of alloimmunization.

In our study splenectomy was performed in 5 (6%) of the β-thalassemia patients out of which one was alloimmunized. Thus, no significant association(p=0.404) was observed between splenectomy and alloimmunization status. This finding is in concordance with the studies by Arianezhad A et al., Keikhaei B et al[18]. and Gupta R et al.

CONCLUSION

The rate of RBC alloimmunization was found to be 11.90% in β-thalassemia patients receiving regular transfusions. Of these Kell and Rh antibodies accounted for 90% of cases. Blood transfusion is the principal and life-saving management for thalassemia patients. Thus, early institution minor antigen phenotyping in pretransfusion testing and issuing antigen matched blood could be instrumental in prevention of alloimmunization among transfusion-dependent β-thalassemia patients.

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