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STUDY OF ALLOIMMUNIZATION AMONG TRANSFUSION DEPENDENT THALASSEMIA PATIENTS

KEYWORDS: Thalassemia, Autoantibodies, Alloantibodies, Alloimmunization, Anti-C ^{w}, Anti Kell

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ABSTRACT *Thalassemia is a congenital hemolytic disorder, caused by a partial or complete defect in α or β globin chain synthesis and requires lifelong blood transfusions which may provoke the patient's immune system and produces anti-erythrocyte antibodies (alloantibodies and/or autoantibodies) mainly against ABO, Rhesus, Kell, Duffy etc. Study was carried out on 100 multiply transfused patients with thalassemia. Clinical and transfusion records of all the patients were examined for age of patients, age at initiation of transfusion therapy, total number of blood units transfused, transfusion interval, status of spleen. Alloantibody screening and identification was done using three cell panel (Erythrocyte magnetized technology, Diagast) and 11 cell panel (Diapanel, Bio-rad, Switzerland) respectively. Out of total 100 patients (2%) developed alloantibodies. 1% belonged to Rh blood group system (Anti-C ^{w}), 1% belonged to Kell blood group system.*

INTRODUCTION

Thalassemia is a major health problem in India, more commonly occurring in Punjabis, Sindhis, Bengalis, and Gujaratis[1]. It is a congenital hemolytic disorder, caused by a partial or complete defect in α or β globin chain synthesis and is treated by life-long red blood cell (RBC) transfusion [2] to keep the hemoglobin (Hb) level between 9 and 11.5 g/dl. The development of red cell alloantibodies occurs in a variable number of multi-transfused thalassemia major patients, in majority it is non hemolytic but can lead to hemolysis. Due to alloimmunization, transfusion becomes significantly complicated.[3] Reported alloimmunization rates ranged from 4% to 50% in thalassemia patients.[2,4,5,7] Alloantibodies in order of frequency are towards the Rh (D, C, E, c and e) and Kell (K) antigens, followed by other blood group antigens of the Duffy, Kidd, MNS and other minor blood group systems[6] which may lead to delayed hemolytic reactions.[3] The homogeneity of the donor - recipient population, RBC phenotype matching policy and age at transfusion initiation are major factors contributing to alloimmunization. This paper reports the result of study conducted in our department to determine the prevalence of alloimmunization and possible contributory factors for its development.

MATERIAL & METHOD

This study was conducted from January 2015 to January 2016 in the department of Transfusion Medicine. In this study 2 ml blood sample was collected from 100 thalassemia patients and allowed to clot, the serum was separated to screen for alloantibodies using Erythrocyte Magnetic Technology for the presence of irregular antibodies using 3 cell panel pack and those sample coming positive were analyzed for the type of antibody using extended 11 cell panel pack to identify the antibody.

Statistical Analysis

Chi square statistical test was performed and p value of less than 0.05 is considered significant. The results were analyzed using SPSS statistical software version 17.0.

RESULTS & OBSERVATIONS

The study included 100 transfusion dependent patients with 69 males and 31 females. Majority of patients were in age group1-10 yrs age group (48%) followed by 11-20yrs (44 %) 3 % patients in this study are below 1 year age and 5% above 20 year .

10% patients had undergone splenectomy and none of them developed alloantibodies. 64 % of the patients were started with blood transfusion before 1 yr age. Most common blood group identified is B + 61 % patients followed by O + in 20 %, A+ 15 %, A- 2%, AB +2%. In our study maximum number of patients (60 %) has received above 100 units of blood, 36 % patients received between 11-100 units & 4 % patients below 10 units.

In our study the duration between transfusions is 11 to 20 days for 64 patients, between 21 to 30 days for 34 patients. Only 2 patients need transfusion within 10 days. The number of packed cells transfused to the patient is less than 10 units in 4 % patients, 11 to 100 units in 36 % patients and more than 100 units in 60% patients.

Significant association is found between age & frequency of transfusion with alloimmunization (p value=0.025) & (p value less than 0.001). Rate of Alloimmunization is 2 %. Alloantibodies identified are Anti C^{w} & Anti K.

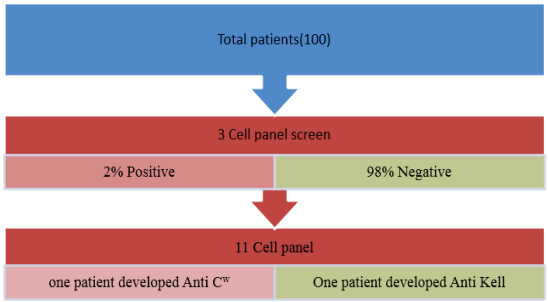

Chart 1- Frequency of red cell alloimmunization in thalassemia

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DISCUSSION

To the best of our knowledge this is the first report on the prevalence of alloimmunization among transfusion dependent thalassemia patients in Punjab. In our study alloimmunization rate is 2 % with positive results for Anti K and Anti C^{w} alloantibodies. In thalassemia major, red cell alloantibody production usually occurs after the age of 6 years after multiple transfusions. Perhaps this is due to immune tolerance developed by periodic blood transfusion started in early age.[7] Similar finding is seen in our study where low alloimmunization rate could be due to early start of transfusion 64% patients were transfused before 1 year age.

Table 1: Data of the patient with alloantibody development

	Patient1	Patient 2
Diagnosis	β Thalassemia Major	β thalassemia Intermedia
Age	18 Years	34 Years
Sex	Male	Female
Age at diagnosis	2 Years	20 Years
ABO blood group	B+	B+
Splenectomy	Not done	Not done
Packed cells transfused	380 Units	130 Units
Frequency of transfusion	10 Days	30 Days
Alloantibody development	Yes	Yes
Type of Alloantibody	Anti C^{w}	Anti K

A policy of transfusing better matched blood to prevent the development of alloantibodies has been repeatedly proposed.[8,6] The recommendations are to type for at least Rh (C,c,D,E,e) and Kell antigens as these account for majority of alloantibodies among Asians.

In a study by Pahuja et al, the frequency of alloimmunization among 211 multitransfused thalassemics of Indian origin. All the patients have been receiving blood matched for ABO and Rh(D) antigens only. The frequency of alloimmunization was 3.79%. The alloantibodies identified were anti-E, anti-K, anti-D, anti-Kp(a), anti-C(w), anti-c and anti-Jk(a)[4]

Our results showed that there was no association between alloimmunization and gender as among the positive patients one is a male while the other is an adult female in whom, alloimmunization could be due to previous pregnancy or blood transfusion. Clinically significant alloantibodies have been reported to occur twice as often in women compared to men.[9]

There's significant association between alloimmunization and age of the patient in this study, this is also supported by a study conducted by Elhence et al.[10]

In the present study 66 % of the patients were started with blood transfusion before 1 yr age. This is similar to a study by Dutcher et al in which alloimmunization rate was related to the age of first transfusion.[11] This implies that the age of the first blood transfusion is a risk factor for alloimmunization. Transfusion at early age may offer some protection against red cell alloimmunization because of immune tolerance in young children.

CONCLUSION

Our data showed low alloimmunization rate in multiply transfused thalassemia patients possibly due to availability of phenotypically matched blood, leucodepleted blood transfusion, homogenous population and early transfusion.

Table 2: Rate of Alloimmunization in different studies.

Study	Year	No. of Patients	Rate of Alloimmunization (%)	Comments
Karimi et al[12]	2007	711	5.3	Anti K, anti D, anti E
Pahuja et al[4]	2010	211	3.8	Anti E, anti K, anti D
Gupta R et al[13]	2010	116	9.48	Anti E followed by anti K
Chaudhari CN et al[14]	2011	32	18.8	Anti E followed by anti c
Guirat-Dhouib N et al[15]	2011	130	7.7	Anti Rh system
Chao YH et al[16]	2013	64	9.4	Anti E, Anti Mia & Anti C
Datta et al[17]	2015	500	5.6	Anti c, Anti E
Present study	2015	100	2	Anti C^{w} & Anti Kell

In our study we observed that anti K and Anti C ^{w} was the most frequent antibody formed by the patient. We recommend routinely performing RBC antigen phenotyping for all transfusion dependent thalassemia patients before starting the transfusion and early diagnosis and transfusion in the patients. The knowledge of the distribution of red cell antigens can help to prevent alloimmunization and hemolytic transfusion reactions among transfusion dependent patients.

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