ORIGINAL ARTICLE

Prevalence of Kell Blood Group Antigens among Blood Donors & Impact of its Alloimmunization in Multi-transfused Thalassemia & Sickle Cell Disease Patients with Recommendation of Transfusion Protocol—Need of the Hour

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ABSTRACT

Background: The aim of the study was to analyze the prevalence of Kell antigen and its correlation to major blood groups, ABO & Rh system in Eastern India. There was simultaneous retrospective analysis of Kell alloimmunization to find out the implication and recommendation of transfusion protocols in multi-transfused thalassemia and sickle cell patients. **Methods**: The study was a prospective observational conducted on 3000 donors for KELL and ABO grouping. Retrospective analysis was made to identify common alloantibodies in multi-transfused patients. **Results**: The overall prevalence of Kell antigen was 2.6% (80) in 3000 donors. Among male, it was highly prevalent i.e. 2.77% and in females 0.65%. Kell antigen was highly prevalent among AB donors, i.e. 5.1%. It was 2.5% in A, 2.9% in B, 1.9% in Blood Donors. Kell prevalence was high in Rh D positive donors, i.e. 2.72% and was 1.72% among Rh D negative donors. Anti-K was the 3rd most common alloantibody detected in 638 cases of multi-transfused thalassemia and sickle cell (SCD) patients (9.25%). Anti-E (42.6%)was most common entity followed by anti-c (24.0%). **Conclusion**: The higher incidence of Kell prevalence in AB & Rh D Positive Blood groups and also in male persons indicate that there should be a donor database and knowledge of red cell antigen prevalence in a population. This will help blood centers in providing antigen negative compatible blood units to patients with corresponding alloantibodies. Hemolytic transfusion reactions due to Kell alloimmunization are of a significant severity. Prevalence of Kell alloantibody is high among multi-transfused patients and is next to anti E & anti c. Kell sensitized mothers may also cause serious consequences like hemolytic disease of fetus and newborn. Therefore, it is suggested that extended phenotyping including Kell blood group antigen should be implemented in cases of multi-transfused patients.

KEY WORDS: Blood donors, Extended phenotyping, Kell, Multitransfused thalassemia patients, Multitransfused sickle cell disease patients.

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Introduction

Safe and adequate blood supply with minimal transfusion reactions is the main goal of Transfusion Medicine. International Society for Blood Transfusion has identified several blood groups based on the presence of antigens on the surface of RBCs. In addition to routine blood grouping, extended phenotyping of other clinically significant blood groups is very important in multi-transfused patients. Knowledge on the frequency of red blood cell

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antigens in a population is of much importance for the creation of donor data base to minimize the development of alloantibodies and subsequent transfusion reactions.

Kell antigen is one of the important clinically significant antigens as it may cause blood transfusion reactions such as Hemolytic transfusion reactions and Hemolytic disease of the newborn[1]. Rh and Kell matching of blood has been recommended in multi-transfused and antenatal patients[2].

The phenotyping of Rh and Kell can play a major role in preventing the alloimmunization and avoiding adverse events in subsequent transfusions in multi-transfused cases. Phenotyping of all clinically significant antigens is ideal in these cases, however, manpower and financial burden restrains blood centers from performing such extensive work up.

Kell might also play role in regulating vascular tone, though further studies needed to establish evidence[3]. The aim of study was to find out the prevalence of Kell Antigen (KEL1/K) among whole blood donors in Eastern India. Simultaneously retrospective analysis of Kell alloimmunization was done to understand the effect on multi-transfused patients.

Materials and methods

The study was a prospective observational study which was conducted on 3000 donors over a period of 3 months (June 2021 to August 2021) in the Department of Transfusion Medicine, SCB Medical College, Cuttack. About 6 ml of blood was collected in the pilot tube of which about 3 ml in red top vial and 3 ml in purple top vial (K_3EDTA). All samples were processed for antigen typing within 48 hours of collection. Samples were antigen (ABO and Rh "D") typed by conventional tube technique using monoclonal anti seras from Ortho-Clinical Diagnostics. Kell phenotyping was done using anti Kell 1 antisera by Indirect Agglutination Test method using conventional tube technique. The procedures were done in accordance with technical manual (AABB) and our Institutional Standard Operating Procedure[3].

Alloimmunization among multi transfused thalassemia and sickle cell patients with transfusion reactions were evaluated referred from all over Eastern India. The individuals for donation and who were patients giving consent were included in the study. It was found by performing antibody screening and identification using Ortho Biovue System, Surgiscreen, Resolve panel. Frequency of Kell alloantibody was compared with other clinically significant alloantibodies. The data was analyzed with the help of computer Software SPSS for Windows version 17.0. The data was presented as percentage in tabular and appropriate diagrammatic forms.

Results

Total 3000 donors were eligible for whole blood donation during the above 3-month period. Among them 153 (5.1%) were female donors and 2847 (94.7%) were male donors. The overall prevalence of Kell antigen was 2.6% (80) in our study (Figure 1).

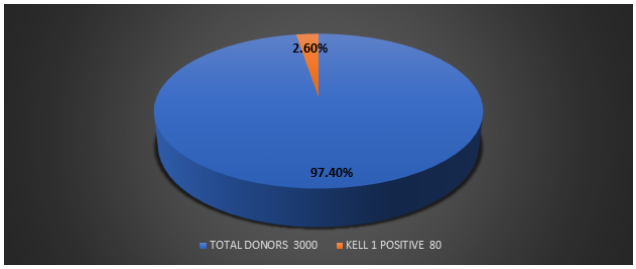

Figure 1: Prevalence of K antigen among blood donors

Among males the prevalence was 2.77% and in females, 0.65% (Table 1).

Table 1: Gender distribution of K antigen

Gender	No of donors	K antigen	Percentage
Male	2847	79	2.77%
Female	153	1	0.65%

Kell antigen was comparatively higher in prevalence among AB donors, i.e. 5.1%. It was 2.5% in A, 2.9% in B, 1.9% in O blood group donors (Figure 2).

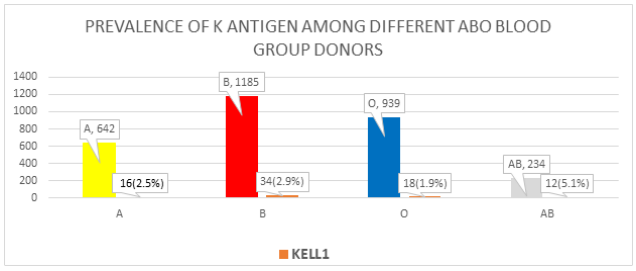

Figure 2: Prevalence of K antigen among different ABO blood group donors

Prevalence was 1.72% among D negative donors. It was 2.72% among D positive donors (Table 2).

Table 2: Distribution of K antigen among Rh D type donor

Rh type	No of donors	K antigen	Percentage
Rh D +ve	2826	77	2.72%
Rh D -ve	174	3	1.72%

Total 54 alloantibodies were identified from 638 Thalassemia & Sickle Cell Disease (SCD) patients with transfusion reactions. These 54 patients had hemolytic transfusion reactions. 33 alloantibodies were from 221 SCD patients and 21 were from 417 Thalassemia patients. Anti-K alloantibody was the 3rd most common entity after anti-E and anti-c among the multi-transfused patients (Table 3). Anti-K was encountered in 5 instances out of 54, whereas anti-E and anti-c were found in 23 and 13 instances respectively. Among multi-transfused Thalassemia patients, anti-K was found in 2 cases out of 21 (9.5%). Similarly, among multi-transfused SCD patients, anti-K was present in 3 instances out of 33 (9.09%). However, anti-E and anti-c were most common alloantibodies in both thalassemia and SCD (Figures 3 and 4).

Table 3: Common alloantibodies encountered in multitransfused patients

Allo-antibodies	Number (n)	Percentage (%)
Anti E	23	42.60%
Anti c	13	24.00%
Anti K	5	9.25%
Anti M	3	5.55%
Anti S	2	3.70%
Anti e	2	3.70%
Anti s	1	1.85%
Anti C	1	1.85%
Anti Jka	1	1.85%
Anti Jkb	1	1.85%
Anti Fya	1	1.85%
Anti Fyb	1	1.85%

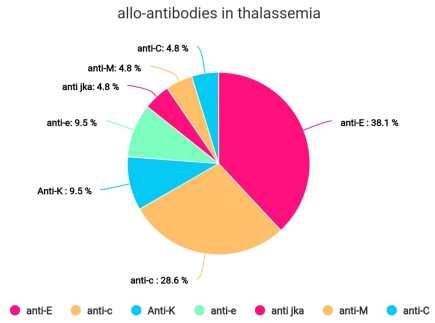

Figure 3: Alloantibodies in thalassemia patients

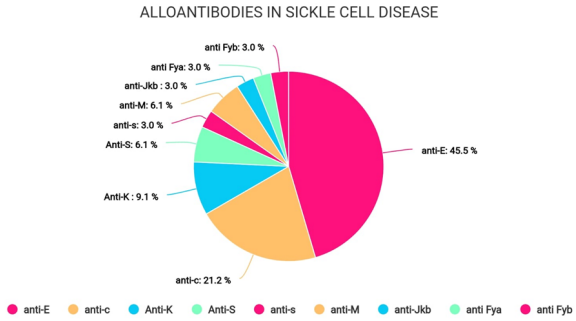

Figure 4: Alloantibodies in SCD patients

Discussion

The overall prevalence of Kell antigen was 2.6% (80) in our study. It was similar to that was reported in Agarwal N et al., (1.97%); Yasmin N et al. (2.6%); Garg N et al., (1.6%)[4–6]. But this study results are lower than the studies conducted by Kahar MA et al., which shows the frequency of 6.09% of K positive antigen and 93.91% of K negative antigen[7]. Thakral B et al., found higher prevalence of Kell (5.68%)[8]. The prevalence of Kell antigen is 2% among black population and 8.8% among whites[3].

In our study, 5.1% of AB blood group donors were K positive (highest) and 1.9 % of O blood group donors were K positive (lowest). In one study by Prinja N, Narain R et al.[9], K was higher in frequency among AB blood group donors i.e. 5.2% and lower in frequency among O blood group donors i.e. 1.9 %. In present study, K was more frequent among Rh D positive blood donors i.e. 2.72 % in comparison to Rh D negative blood donors (1.72%).

In this study K was less frequent among females i.e. 0.65% in comparison to males i.e. 2.77%. If Kell positive blood will be exposed to the Kell negative population, there is risk of antibody formation. This makes the female population more susceptible towards alloimmunisation due to transfusions. In this population, additional risk of alloimmunisation is present due to possibilities of Kell positive pregnancies.

Analysis of alloantibodies detected in our institute for multi-transfused thalassemia and sickle cell patients having transfusion reactions referred from different hospitals from all over the Eastern India was done. It revealed that anti-K is the 3rd most common alloantibody found in multi-transfused thalassemia and sickle cell disease patients. Anti-K constituted about 9.25% of total number of allo-antibodies. However, the most common antibody was anti-E followed by anti-c. It's well-known that alloimmunization is more common in sickle cell disease. In our analysis among SCD patients, anti-K was 3rd most common antibody. Nevertheless, among multitransfused thalassemia patients, anti-K was also more common after anti-E and anti-c.

In the study by Anjali Handa et. al, anti-K was most common allo-antibody (42.8%) followed by anti E (28.57%)[10]. Dhawan et al. and Roopam et al. also found similar results, where anti-K was more frequent[11,12]. Similar to our study, Sood et al., Gupta et al. and Philip et al. found anti-E to be more common entity[13–15]. It's well-established that alloimmunization is more common in multi-transfused sickle cell disease. In our analysis, anti-E, anti-c and anti-K were most common allo-antibodies in sickle cell disease patients. Similar trends were also observed in multi-transfused thalassemia patients. Therefore, it's recommended to transfuse Rh and Kell matched units to multi-transfused patients at minimum.

The Kell system is much importance due to the strong immunogenicity of K antigen. It is the most immunogenic system after the Rh system. The knowledge of antigen prevalence in a given population is clinically important as one can predict the common alloantibodies that could be formed in patients who had received multiple transfusions such as in patients with thalassemia, dialysis patients, cancer patients etc. and also helps in selection of antigen negative blood units for these patients who had developed the alloantibodies. It may also reduce the reported RBC antigens alloimmunization along with their possible complications such as hemolytic transfusion reactions (HTRs) and hemolytic disease of fetus and newborn (HDFN).

Conclusion

This study will be helpful in the transfusion management of multiparous women and multi-transfused patients especially the Thalassemia and SCD patients. This will also be helpful in creating donor database for Kell blood group. Transfusing K antigen negative blood units will be beneficial for all the multi-transfused patients. In the cases of Kell positive blood units, the same can be transfused to the Kell positive recipients. Therefore, Kell group typing should be considered both in the donors and recipients to minimize wastage of Kell positive units, though this will be very less in number. Extended blood grouping which includes Kell blood group system is the need of future to ensure safe blood transfusion practices.

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