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Is There any Relationship with Multiple Transfusion and Development of Alloantibodies - An Observational Study

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Introduction

All over the world, blood transfusion is the most common procedure performed during a hospitalization. Transfusions, while often life-saving, are not without risk. Alloantibodies are one type of sequela that arises in a subset of Red Blood Cell (RBC) transfusion patients. Given alloantibody induction and evanescence patterns, missed opportunities for alloantibody detection, and record fragmentation, it is expected that only 30% of induced RBC alloantibodies are recognised. Various antigens in blood groups and their genes have been identified, and their physiological activities have been established, and they have been found to be important factors in transfusion therapy. There are approximately 400 Red Blood Cell (RBC) antigens discovered. These RBC antigens and alloantibodies differ greatly amongst human populations and ethnic groupings. After being exposed to RBC antigens, red blood cells (RBCs) can develop alloantibodies. Alloimmunization to RBC antigens is a significant complication of transfusion therapy, and alloantibodies cause a variety of clinical issues, including blood transfusion-related adverse reactions.

Alloantibodies could be clinically significant in future transfusion scenarios, causing acute or delayed hemolytic transfusion reactions or making it difficult to find suitable RBC units for future transfusion. Alloantibodies can also be clinically significant in future pregnancies, potentially leading in foetal and infant hemolytic syndrome. Accordingly, allo-immunization after exposure to red cell alloantigens depends on genetic and acquired patient-related factors, dosage, and antigen immunogenicity [1,2]. The exact kinetics of allo-immunization are not clear [3,4]. The formation of alloantibodies can significantly complicate transfusion therapy and lead to difficulties in cross-matching the blood. RBC products for transfusion [5]. Antibod-

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ies that may cause hemolysis include those specific to most of the major and the minor blood groups [3,5-9]. One report on autoantibodies to red cells in thalassemia patients in Kelantan has been published [10]. It is well-known that alloimmunization to RBC antigens resulting from the genetic disparities between donor and recipient is one of the risks of blood transfusion. The risk depends on the recipient's exposure to the foreign antigen and its immunogenicity. Immunization may also be influenced by the number and frequency of the transfusions as well as the recipient's sex, age, and underlying disease. In terms of frequency of occurrence, the most common irregular RBC alloantibodies in everyday transfusion practice are directed at RH (anti-D, -C, -E, -c, and -e), Kell (anti-K), FY (anti-Fya and -Fyb), JK (anti-Jka and -Jkb), and MNS (anti-M, -S, and -s) blood group systems. The D-antigen is the most immunogenic of these, with more than 80% of immunocompetent D-negative people becoming alloimmunized after receiving D-positive erythrocytes. Clinically substantial antibodies have been linked to transfusion responses and neonatal hemolytic syndrome. The antibody screening cells are used to detect unexpected antibodies: If antibody screening is positive, additional tests are carried out to specifically identify antibody using the antibody identification panel and RBC antigen typing. Screening cells are prepared from cells from two or three individual donors. These cells are procured from Group O blood donor and to be licensed by the Food and Drug Administration and must contain the following antigens: D, C, E, c, e, M, N, S, s, P_1, Le ^{a}, Le ^{b}, K, k, Fy ^{a}, Fy ^{b}, Jk ^{a}, and Jk ^{b}. The most common clinically significant antigens must be present to detect the clinically significant antibodies. The presence of homozygous antigens on the RBCs is preferred to have a double dose of the antigen resulting in stronger reactions and ability to detect weaker antibodies. Antibody screening with a 2-3 cell panel is not an obligatory pretransfusion test in India, however it is commonly conducted in a few blood clinics. In India, very few research on the prevalence of antibodies in multi-transfused patients have been conducted. As a result, there is a scarcity of data on the prevalence of RBC alloantibodies in a population that accounts for 17% of the world's population. This bicentric study (one regional blood transfusion centre in North India and one in South India) looked at the prevalence of antibodies in multi-transfused patients with higher risks of alloimmunization, such as thalassemia, other haematological disorders, renal failure patients on dialysis, and females with a poor obstetric history.Hence, the objectives of this study was to study the prevalence of RBC alloantibodies in multiply transfused patients and to detect the to detect the most common alloantibody in multiply transfused patients.

Materials and Methods

An observational study was conducted at Department of Transfusion Medicine, The Tamil Nadu Dr.M.G.R.Medical University, and Chennai for a period of one year. Study participants. Multiple transfused patients attending hospitals were enrolled in this study .Purposive sampling was used. Patient data like history of transfusion, medical history, gender, age and history pregnancy was collected using a structured questionnaire.

Laboratory investigations The serum samples from fifty patients who had received more than four units of blood during a period of atleast 3 months with mean transfusion period of 21 days was tested by 3 cell panel and 11 cell panel. Antibody was detected by in house screening cell panel.

Ethical consideration

The proposal for this study was approved by Ethics committee of the TN Dr.M.G.R.Medical University Approval was also obtained from respective hospitals. Informed consent was obtained from the subjects before they were enrolled into study. The study was conducted in accordance with the declaration of Helsinki.

Statistical analysis

Data entry was done by using Epi data 3.1 version and analysis was done using SPSS package. The entered data was cleaned and validated for consistency. Descriptive statistics was expressed in frequency and percentage. For comparison among categorical variables Chi-square test was used. A p value of < 0.05 was considered to be significant.

Results

A total of 50 patients were enrolled in this study. Table-1 depicts the distribution of blood group among participants.

Table 1: Blood group distribution.

Blood group	Frequency	Percent
A	16	32.0
AB	1	2.0
B	10	20.0
O	23	46.0
Total	50	100.0

Among the multiple transfused cases, 50% of them were O group patients.

Table 2: Gender distribution.

Gender	Frequency	Percent
Female	21	42.0
Male	29	58.0
	50	100.0

In this study around 58% were male and 42% were female **(Table-2 and Figure-1)**.

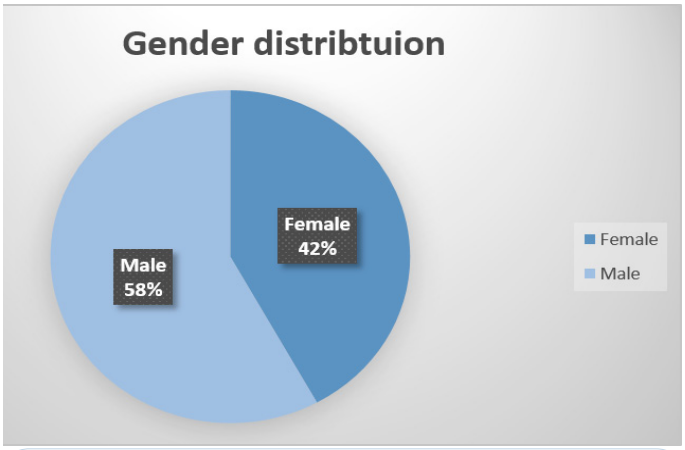

Figure 1: Distribution of gender.

Table 3: Age distribution.

Age group	Frequency	Percent
20-30	2	4.0
31-40	18	36.0
41-50	17	34.0
51-60	9	18.0
61 and above	4	8.0
Total	50	100.0

Among the total cases 31-40 age groups are higher in range than the other age groups. And mean age of the patients was 44.22 with SD of 10.473.

Table 4: Previous history of Number of transfusion.

H/o No of transfusion	Frequency	Percent
4	22	44.0
5	20	40.0
6	8	16.0
Total	50	100.0
		S

Majority of transfused cases transfused four times that is 44% followed which 5 times.

Table 5: Reason for multiple transfusion.

	Frequency	Percent
Oral cancer	1	2.0
Prostat cancer with anemia	1	2.0
Aml with anemia	1	2.0
Anemia	2	4.0
Anemia with necrotising fasiculitis	3	6.0
Aplastic anemia	2	4.0
Breast cancer	3	6.0
Cancer breast with anemia	2	4.0
CABG	6	12.0
Cancer cervix with anemia	1	2.0
Cancer in cervix	1	2.0
Cancer ovary and anemia	1	2.0
Cancer breast with anemia	1	2.0
Chronic renal failure	2	4.0
Chronic renal failure	2	4.0
Endometrial cancer	1	2.0
Fracture	1	2.0
Fracture in femur	1	2.0
GI bleeding	1	2.0
Hemophilia	1	2.0
Hip replacement	1	2.0
Lung cancer	2	4.0
Oral cancer	1	2.0
Postpartum hemorrhage	5	10.0
Sickle cell anemia	1	2.0
Stomach cancer	1	2.0
Thalassemia major	5	10.0
Total	50	100.0

In this study thalassemia cases and CABG cases more in number compare to other patients.

Table 6: Distribution of associated medical condition among multiple transfused patients.

Medical conditions	Frequency	Percent
Nil	44	88.0
DM	3	6.0
DM+HTN	1	2.0
HTN	2	4.0
Total	50	100.0

Around 6% had diabetes and 4% had Hypertension and 2% had both DM and HTN.

Table 7: Distribution of Alloantibody types.

Type of alloantibody	Frequency	Percent
Nil	48	96.0
AntiE	2	4.0
Total	50	100.0

Correlation

Table 8: Correlation of multiple transfusion and alloantibody status.

		Alloantibody status		Total	p-value
		Negative	Positive		
No of previous transfusion	4	22	0	22	0.290
	5	19	1	20	
	6	7	1	8	
Total		48	2	50	

According to this study, there is no association with multiple transfusion and alloantibody positivity (Table 8).

Table 9: Correlation of multiple transfusion and type of alloantibody.

		Type of alloantibody		Total	p-value
		No antibody	AntiE		
No of previous transfusion	4	22	0	22	0.290
	5	19	1	20	
	6	7	1	8	
Total		48	2	50	

Also in this study, antiE antibody was found in multiple transfused cases (Table-9).

Table 10: Comparison of Gender with multiple transfusion.

		Gender		Total	p-value
		Female	Male		
No of previous transfusion	4	10	12	22	**0.045**
	5	5	15	20	
	6	6	2	8	
Total		21	29	50	

There is statistically strong association with number of transfusion and gender (p-value 0.045) (Table 10).

Table 11: Comparison of blood group and multiple transfusion.

		Blood group				Total	p-value
		A	AB	B	O		
No of previous transfusion	4	6	1	5	10	22	0.454
	5	9	0	4	7	20	
	6	1	0	1	6	8	
Total		16	1	10	23	50	

There is no significant association with number of transfusion and blood group (Table 11).

Table 12: Comparison of medical conditions and multiple transfusion.

History of multiple transfusion		Associated medical condition				Total	p-value
			DM	DM+HTN	HTN		
No of previous transfusion	4	19	1	1	1	22	0.830
	5	17	2	0	1	20	
	6	8	0	0	0	8	
Total		44	3	1	2	50	

The above table-12 shows that there was no significant association noted while comparing medical conditions and multiple transfusion.

Discussion

The prevalence of alloimmunization against RBC antigens depends on the demography of the population being studied. Previous data from a number of communities describe alloimmunization following transfusions for indications such as anemia, thalassemia, and end-stage renal failure (ESRF) [11]. Similar findings was obtained in this study also.

The overall prevalence of alloimmunization among blood recipients in this work is comparable with rates previously reported on patients receiving transfusion. This study shows that the majority of the study subjects have single antibody than multiple alloantibodies, of which anti-E was the most common alloantibody found, which may be determined genetically. The anti-E was detected in almost all available studies at relatively high levels. Furthermore, it implies that the E antigen and the Lewis (a and b) antigens are highly immunogenic and that they are expressed differentially among individuals of one community. In other words, the absence of antigen E may render a recipient prone to sensitization by the E antigen that comes from an E-positive donor [12]. This explanation marks the necessity for RBC phenotyping to stop unnecessary sensitization to RBC antigens, and to aid in avoiding unwanted clinical consequences. In a study carried by Habibi and Lecolier, 7 (1.27%) out of 405 patients developed RBC alloantibodies. According to the study from India Shukla and Chaudhary, there is 1.3% risk of alloimmunization in chronic renal failure patients.

In this study, as in most other studies, the incidence of alloimmunization among females is more predominant than in male patients, possibly because most of the blood recipients are females, especially those with histories of eventful pregnancies. Hence, immunization through pregnancy could be one main reason for the high incidence of RBC alloimmunization among female patients. However, female patients were reported not to be a majority once. Also expected, patients who had experienced blood transfusions were found to be more liable to developing alloantibodies than those who never experienced a blood transfusion. Similar findings have been indicated in other works. However, the statistical association between the development of alloantibodies with blood group A was not clear. No such remark has been reported.

Nevertheless, this work represents a pilot study, which attempted to show some light into the blood groups that have the potential for alloantibody formation. Hence, two things are recommended, knowledge of prevalent RBC antigens in a community and routine investigation for alloantibodies in blood donors.

Conclusion

Since, the patients of chronic renal failure and thalassemia who have received blood transfusions is at risk of alloimmunization. We recommend including antibody screening test in routine pretransfusion testing protocol at least for the patients who are at higher risk of alloimmunization and require long-term transfusion dependence. This test may not be cost-effective for all the patients currently in our country. We also recommend obtaining an RBC antigen phenotype on all thalassemia patients and other patients at high risk of alloimmunization before the start of transfusion support and if feasible, providing leukodepleted blood.

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