Section: Transfusion Medicine

Original Research Article

PHENOTYPE FREQUENCIES OF RH AND KELL BLOOD GROUP SYSTEM IN BLOOD DONORS: A RETROSPECTIVE ANALYSIS FROM TERTIARY CARE HOSPITAL IN WESTERN INDIA

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ABSTRACT

Background: Alloimmunization is a complication that can occur after red blood cell transfusion and worsens with increasing antigenic differences between donor and recipient. Rh and Kell antigen phenotypes are crucial in preventing the adverse event and alloimmunization in patients who have received multiple transfusions. The aim is to determine the frequency of Rh and Kell antigens in blood donor population of western India. Settings and Design Retrospective observational study. **Materials and Methods:** A retrospective observational study over a period of two year (i.e., August 2023 - August 2025) was done after the approval of Institutional Ethics Committee. The data of blood donors typed for Rh and Kell antigens was analysed for the study. Statistical analysis was performed using Microsoft Excel Software. Appropriate statistical methods were used for the final analysis. Antigen frequencies were expressed as percentages. **Result:** A total of 9307 blood donors were typed for Rh and Kell phenotyping. Out of 9307 donors, 7910 were male (85%) and only 1397 were females (15%). The mean age of the donors was 34 years. The frequencies of Rh antigens i.e., D, C, E, c and e were 94%, 89%, 17%, 53% and 99%, respectively. In our study, the most common phenotypes in D antigen positive and D antigen-negative donors were R1R1 and rr, respectively. K antigen was found in only 1% of the donors. **Conclusion:** Data on antigen frequency of various blood group antigens in the local donors will help in providing antigen-negative compatible blood units to patients with alloimmunization.

INTRODUCTION

As of November 2023, there are currently 45 blood group systems with 362 red blood cell antigens. The 45 systems are genetically determined by 50 genes.[1] The discovery of ABO and Rh blood group system marked the beginning of the concept of safe blood.[1] In 1946, the Kell blood group system was discovered.[1] For transfusion and transplantation, the ABO and Rh (mostly D) blood group systems are given the highest significance among these antigens.[2] Since the Kell antibodies can result in HTR and HDFN, the Kell blood group system is the second most significant protein-bound blood group system in transfusion medicine, after Rh. The Kell antigen is much less prevalent but highly immunogenic.[1] Antibodies to Rh system are most implicated and anti-kell antibodies are lethal and cause alloimmunization.

Red blood cell transfusion-related complications such alloimmunization get worse with increased exposure to allogeneic transfusion and donor-recipient antigen discrepancy.[3] Patients who require multiple transfusions, such as those with thalassaemia, sickle cell anaemia, aplastic anaemia, and haematological malignancies, are particularly at risk for alloimmunisation.[4] Anti-E, anti-c, and anti-K antibodies were frequently found in these patients due to their prevalence and immunogenicity.[3,5]

The use of antigen-matched red blood cells (RBCs) can reduce alloimmunisation in patient who received multiple transfusion, also it improves RBC survival and reduces the frequency of transfusion.[6] Alloimmunization incidences have been documented in a number of papers from throughout the world, emphasizing the need for phenotyping and provision of antigen-matched blood.[3] As a result, a partial method of matching the antigens (D, C, c, E, e, and K) that are primarily causing alloimmunization is taken into consideration.[3]

The primary goal of the blood transfusion service is to provide blood which is free from transfusion

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transmitted infections and compatible with the recipient, to minimize the transfusion reactions.[3] Thus, this study aims to determine the frequency of Rh and Kell antigens and phenotype the donors to propose the importance of providing Rh and Kell phenotype matched Packed RBC (PRBC) units to minimize the alloimmunization and transfusion reactions. Since India is a large country with various diverse population groups, it is necessary to assess phenotypic frequencies in different parts of India.[7]

The exiting practice in India is still based on random cross-matching of available units in the inventory. Knowledge on antigen frequency in blood donor population can help the blood centres to manage the blood inventory accordingly and to overcome the challenges associated with the incompatible cross-matching. Several studies have been conducted till now on antigenic frequency of various blood group antigens from different parts of India. However, there is limited literature available on antigenic frequencies of two of the most important blood group system such as Rh and Kell system in western Indian blood donor population. Thus, this present study is aimed to determine the frequencies of Rh antigens (D, C, c, E and e) and Kell (K) antigens and their phenotype in blood donors in Western India.

MATERIALS AND METHODS

A retrospective observational study was initiated after the approval of Institutional Ethics Committee. The data of 9307 voluntary blood donors tested between August 2023 to August 2025 was collected for analysis.

All whole blood donors who fulfilled the eligibility criteria of blood donation and who donated Whole blood at our institute were included in this study and the donors who did not qualify the eligibility criteria were excluded from the study.

Methodology: Voluntary blood donors were selected based on donor selection criteria as per the Drugs and cosmetics Act, 1945 and rules therein.

a. Sample collection: As a routine procedure, at the time of blood donation, 3 ml of the blood sample were collected from each donor from the diversion pouch into a sample tube containing ethylenediaminetetraacetic acid anticoagulant.
b. Routine immunohematology testing: At our blood centre, each donor unit is subjected for tests such as blood grouping, antibody screening, Rh and Kell antigen phenotyping (C, c, E, e and K).
c. Phenotyping: The phenotyping of the donors was performed using fully automated platform DIAGAST QWALYS® 3 EVO (Method: Erythrocyte Magnetized Technology). Test procedure for antigen phenotyping were performed as per the manufacturer's instructions.

Statistical analysis: Statistical analysis was performed using Microsoft Excel Software (Microsoft Redmond, Washington, USA).

The total number of donors who tested positive for a particular antigen or phenotype divided by number of donors tested yielded the frequencies of that particular antigen or phenotype. Results are expressed as percentage. Descriptive variables are analysed using mean, median, standard deviation, range wherever required.

RESULTS

Donor demographic details: During study period, a total 9307 donors were phenotyped for Rh and Kell blood group systems. Out of 9307 donors, 7910 were male (85%) and only 1397 were females (15%). Mean age of the donor was 34 years.

Frequency of ABO and D antigens: Among 9307 donors 33% of donors were 'O' blood group followed by 'B' blood group (31%), 'A' blood group (27%) and 'AB' blood group (9%). The 'D' antigen was present in 94% (8761) donors and absent in 6% (546) donors [Figure 1].

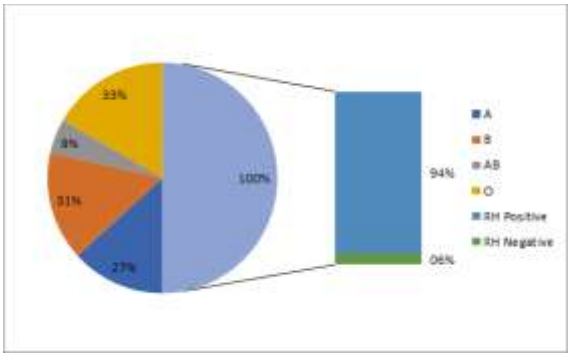

Figure 1: Frequency of ABO and Rh antigen

Frequency of 5 Rh antigens: The prevalence of 5 Rh antigens tested in the donors population is shown in [Table 1].

The frequency of D antigen was 94 %. The frequencies of C and e antigens are high i.e., 89 and 99%, while the frequencies of c and E antigens are lower i.e., 53 and 17, respectively [Table 1]. The most frequent antigen in the donor was homozygous e (E-e+) followed by homozygous C (C+c-). The least frequent antigen was homozygous E (E+e-) [Table 2].

Table 1: Prevalence of 5 Rh antigens

Sr. No	Antigen	Percentage	Number of donors
1	D	94	8761
2	C	89	8247
3	c	53	4945
4	E	17	1533
5	e	99	9233

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Table 2: Frequency of Homozygous and Heterozygous Rh antigens

Sr. No	Rh antigen frequency	Number of donors	Percentage
1	Homozygous C(C+c-)	4362	47
2	Homozygous c(C-c+)	1060	11
3	Heterozygous (C+c+)	3885	42
4	Homozygous E(E+e-)	74	1
5	Homozygous e (E-e+)	7774	83
6	Heterozygous (E+e+)	1459	16

Frequency of Kell antigen

The frequency of Kell antigen (K) was 1% (59 donors), while 99% (9248) of the donors were Kell negative [Figure 2].

Distribution of Rh (C, c, E, e) and Kell (K) phenotype: The distribution of Rh and phenotype among 9307 Indian donors is shown in the [Table 3]. R1R1 was the most prevalent Rh phenotype, accounting for 50% of the research group, whereas R1Rz was the rarest.

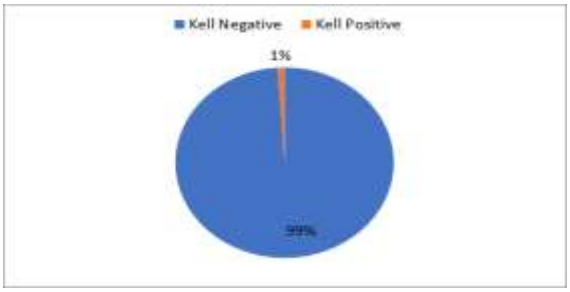

Figure 2: Kell antigen frequency

Table 3: Distribution of the Rh phenotype in blood donor population.

Sr. No	Fisher-race	Weiner	Number of donors	Percentage
1	Dce/DCe	R1R1	4336	46.58
2	DCe/dce	R1r	2769	29.75
3	DCe/DcE	R1R2	1077	11.57
4	DcE/DcE	R2R2	71	0.76
5	Dce/dce	R0r	133	1.42
6	DcE/dce	R2r	351	3.77
7	DCe/dCE	R1ry	22	0.02
8	DcE/dCE	R2ry	1	0.01
9	DcE/dCE	RzRz	1	0.01
10	dce/dce	rr	496	5.32
11	dCe/dce	r'r	37	0.39
12	Dce/dcE	rr''	8	0.08
13	dCe/dCe	r'r'	3	0.03
14	dcE/dcE	r''r''	1	0.01
15	dCE/dce	ryr	1	0.01

DISCUSSION

Although blood transfusion save lives, it is often associated with adverse effects such as alloimmunization. The antigenic variations in red blood cells between the mother and the fetus or between the donor and the recipient contributes to alloimmunization. After the ABO system, the Rh system has the most important antigens in transfusion, followed by the Kell blood group system antigen. The Rh and Kell antibodies are immunogenic, whereas the ABO system's antibodies are found naturally. Blood lacking these antigens should be given to patients who have Rh and Kell alloantibodies. These antibodies are also known to cause severe haemolytic disease in the fetus and newborn. These antibodies are also associated with reduced survival of red blood cells in vivo.

The present study was a retrospective study conducted over a period of 2 year. It is important to know the frequencies of different blood group antigens and their different phenotypes in the population and this information plays pivotal role in areas such as paternity testing, antenatal serology and for selecting compatible red cells in difficult transfusions. Thus, this study aimed to determine the frequencies of Rh antigens (D, C, c, E and e) and Kell (K) antigens and their phenotype in blood donors in Western India.

Frequency of ABO antigens: In this study, the ABO blood group antigens frequencies showed the prevalence as O > B > A > AB, similar to study by Sai Prasad et al. While in other studies the ABO blood group frequencies showed prevalence as B > O > A > AB.

Table 4: Comparison of ABO antigen frequency (%) among the donors in the study to previously published studies.

Antigen	Present study (n=9,307) (%)	Sai Prasad et al. (n= 43,839) (%).[8]	Chandra et al. (n=23,320) (%).[9]	Pathak et al. (n=10,000) (%).[3]	Basu et al. (n=1528) (%).[10]	Raja et al. (n=40,732) (%).[11]
A	27 (n=2475)	6.9	21.50	22	25	24.35
B	31 (n=2917)	42.61	34.84	37	34	34.43
AB	9 (n=883)	4.8	13.91	9	9	8.94
O	33 (n=3032)	45.59	29.75	32	32	32.26

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Frequency of 5 Rh antigens: "D" is the most common Rh antigen worldwide, as indicated by various studies and its frequency in this study was 94 % which was similar to those studies.[12-15] The frequency of "e" antigen was found to be 99% which was comparable to that of other studies as shown in [Table 5].

Table 5: Comparison of Rh antigen frequencies with other studies.

Antigen	Present study (n=9,307) (%)	Thakral et al. (n= 1,240) (%).[12]	Setya et al. (n=6,678) (%).[13]	Makroo et al. (n= 3,073) (%).[14]	Ranjan et al. (n=10,032) (%).[6]	Pathak et al. (n=10,000) (%).[3]	Philip et al. (n=10,133) (%).[15]
D	94 (n= 8761)	93.4	93.8	93.6	95.7	94.5	92.2
C	89 (n= 8247)	84.7	88.25	87	90.5	86.6	87.5
c	53 (n= 4945)	52.8	52.62	58	50.5	57.5	51.1
E	17 (n= 1533)	17.9	19.77	20	15.9	18.8	26.5
e	99 (n= 9233)	98.3	98.38	98	99.16	98.5	98.4

Frequency of Kell antigen: K antigen has been described as highly immunogenic apart from Rh antigens, followed by 'c" and "E".[6] In present study, the frequency of "K" antigen positive was 1% and Kell antigen negative in 99%, which was similar to that determined in other studies by Agarwal N et al and Gargand Singh et al. In other studies the frequency of K antigen was 2-9% as shown in [Table 6].

Table 6: Comparison of frequencies of Kell antigen among different studies.

Antigen	Present study (n=9, 307) (%)	Agarwal N et al [16]	Gargand Singh et al.[17]	Thakral et al. (n= 1,240) (%).[12]	Setya et al. (n=6,678) (%).[13]	Makroo et al. (n= 3,073) (%)	Ranjan et al. (n=10,032) (%)	Kahar MA et al. (n=115) (%).[18]
Kell Positive	99(n= 9258)							
Kell negative	1 (n= 59)	1.97	1.60	5.56	5.14	3.5	2.67	6.09

Frequencies of RH phenotype: In the present study, the commonest Rh phenotype was R1R1 constituting 46% of the study population. The frequencies of Rh phenotypes among 9,307 blood donors were compared with other studies [Table 7].

Table 7: comparison of Rh phenotype frequencies among different studies.

Sr No.	Rh phenotype	Present study (%)	Makroo et al. (%).[19]	Kahar MA et al. (%).[18]	Thakral et al. (%).[12]	Gundrajukuppam et al. (%).[20]	Pathak et al. (%).[3]
1	R1R1	46.58	40.95	40.87	43.8	43.4	46.73
2	R1r	29.75	30.91	23.48	30	31.2	27.93
3	R1R2	11.57	14.54	13.91	8.22	10.7	12.58
4	R2R2	0.76	0.78	-	1.45	0.7	1.03
5	R0r	1.42	1.15	0.87	0.97	1.2	1.48
6	R2r	3.77	3.69	4.35	8.95	0.5	3.70
7	R1ry	0.02	-	-	-	-	-
8	R2ry	0.01	-	-	-	-	-
9	RzRz	0.01	0.002	-	-	0.4	0.40
10	rr	5.32	4.76	11.3	5.81	4.7	0.13
11	r'r	0.39	2.32	-	0.56	0.6	0.03
12	rr''	0.08	-	1.74	-	-	-
13	r'r'	0.03	0.05	1.74	-	0.1	3.45
14	r"r"	0.01	0.004	-	-	-	0.08
15	ryr	0.01	0.075	-	-	-	-

CONCLUSION

1. Knowledge of red cell antigen frequencies is helpful in providing antigen – negative compatible blood to patient with alloimmunization.
2. In resource constrained country like India, the practice of providing at least Rh and Kell antigen matched red cells can lead to great decrease in alloimmunization rates and increase the red cell survival leading to decreased frequency of transfusion and better clinical outcome.
3. Though the sample size of study was relatively small compared to huge population of the country, it still gives an estimate of the frequencies of blood group antigens.

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