Clin. Lab. 2021;67:XXX-XXX

ORIGINAL ARTICLE

ABO, RH, and KEL1 Antigens, Phenotypes and Haplotypes in Southwestern Saudi Arabia

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SUMMARY

Background: **Over the past years, the vast majority of blood grouping research in Saudi Arabia has been noted to be mainly focusing on ABO and D antigens. Consequently, knowledge on other clinically significant antigens regarding the RH and KEL blood group systems is required. Therefore, an experimental study using serotyping of ABO antigens, five main antigens (D, C, c, E and e) of the RH blood group system and the KEL1 antigen of the KEL blood group system will be carried out.**
Methods: **A total number of 3,563 blood samples obtained from Saudi volunteer blood donors in Jazan Province were investigated. The following antigens were included in this study: A, B, AB, O, and D type (D VI) and C, c, E, e, and KEL1 antigens. Moreover, RH phenotypes and haplotypes were also determined. Serological analysis was performed using ID System gel cards. DiaClon ABO/D + Reverse grouping and DiaClon Rh subgroups + K were used. Statistical analysis was used to determine the frequency of all antigens, phenotypes, and RH haplotypes.**
Results: **Regarding the ABO blood group system, observations were as follows: A, 29.44%; B, 10.44%; AB, 1.15%; and O, 58.97%. Antigens of RH blood group systems demonstrated as follows: D, 93.32%; C, 70.97%; E, 18.91%; c, 75.38% and e, 97.95%. The frequency of KEL1 antigen is 4.54%. The frequencies of RH haplotypes are as follows: Dce, 0.0078; DCe, 0.4723; DcE, 0.2736; DCE, 0.0051; dce, 0.2410; dCe, 0; dcE, 0.0001; and dCE, 0.**
Conclusions: **We established the frequencies of ABO, RH, and KEL1 antigens in Jazan Province of Saudi Arabia. In addition, RH phenotypes and haplotypes were determined. This blood donor screening may help provide compatible blood units for transfusion and patient safety. Therefore, this might be recommended to other provinces of Saudi Arabia to investigate the prevalence of these antigens for better transfusion practice.**
(Clin. Lab. 2021;67:xx-xx. DOI: 10.7754/Clin.Lab.2020.200633)

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Manuscript accepted July 11, 2020

KEY WORDS

blood groups, RH haplotypes, blood donors, Saudi Arabia, immunohematology

INTRODUCTION

Blood transfusion is a crucial treatment for patients with blood loss. Matching the red cell antigens is a safer blood transfusion practice. Recently, 38 blood group systems were identified according to the International Society of Blood Transfusion [1]. Four antigens of the ABO blood group system were identified by Karl Landsteiner [2].

A total of 55 antigens were identified based on the RH blood group system. Five main antigens may be involved in hemolytic transfusion reaction (HTR) and hemolytic disease of the fetus and newborn (HDFN), i.e., D, C, E, c, and e [3]. Furthermore, the antibody for KEL1 antigen was reported to be involved in HTR and HDFN [4].

Matching the antigens in the ABO, RH, and KEL systems paved the way for a safer practice of blood transfusion. Incompatibilities of these antigens between donor red cells and recipient may result in alloimmunization in particular for transfusion-dependent patients, such as those with sickle cell disease (SCD) [5].

Serotyping remains the gold standard approach for matching the blood group antigens [6]. It is a simple and rapid procedure and possesses an appropriate sensitivity. Furthermore, it assists in the reduction of alloimmunization events. Matching these antigens to these systems is very important for patients who have undergone multiple transfusions, such as those with SCD and thalassemia [7].

Establishing a database on the prevalence of blood group antigens in a certain population is crucial and worthwhile. Indeed, clinically significant antigens, which were reportedly involved in HTR and HDFN, should also be investigated to help prevent further occurrence of alloimmunization following the transfusion procedures [8].

A majority of studies conducted in the Kingdom of Saudi Arabia mainly reported the incidences of ABO and D antigens [9-13]. Therefore, this study aimed to demonstrate the frequencies of the following antigens: A, B, AB, O, and D type (D VI) and C, c, E, e, and KEL1 antigens among the Saudi blood donors in Jazan Province. The frequencies of these antigens accompanied by their antigenicity may determine the incidence rates of the corresponding antibodies. Moreover, the frequencies of RH phenotypes and haplotypes were also determined.

MATERIALS AND METHODS

Blood samples

Ethical approval was obtained from Jazan Hospital IRB (No. 1846), Ministry of Health, Kingdom of Saudi Arabia. Blood units were received at the Blood Bank of Prince Mohammed Bin Nasser Hospital from various hospitals from anonymous unpaid volunteer healthy Saudi blood donors who live exclusively in Jazan Province. These hospitals include Jazan General Hospital, King Fahad Central Hospital, Samtah Hospital, Baish General Hospital, Sabya General Hospital, Al Aridhah Hospital, and Abu Arish General Hospital. All donor data and donation details were kept confidential with only coded samples used in this study without any link to the donors' identities. All donors were healthy and aged 18 - 55 years from both genders. All participants were tested for infectious diseases. Donors were provided with an informed consent and signed a letter after filling out the questionnaire before the blood donation procedure.

Immunohematology

A total of 3,563 samples from Saudi blood donors were investigated for the following antigens: A, B, AB, O, and D type (D VI) and C, c, E, e, and KEL1 antigens using ID System gel cards (Biorad, Dreieich, Germany). DiaClon ABO/D + Reverse Grouping and DiaClon Rh Subgroups + K were used.

Statistical analysis

Frequencies of ABO, RH, and KEL1 antigens and phenotypes were determined by summing the number of donors possessing the specific antigen/phenotype and dividing by the whole number of donors. Outcomes were expressed as percentages. In addition, RH haplotypes were calculated using formulas proposed by Mourant et al. [14]. p-values were calculated using chi-square test of independence in order to compare the frequencies in this study with that in other ethnic groups.

RESULTS

Frequencies of ABO, RH, and KEL1 antigens determined are shown in Table 1. Regarding the ABO blood group system, observations were as follows: A, 1,049 (29.44%); B, 372 (10.44%); AB, 41 (1.15%); and O, 2,101 (58.97%). Antigens of the RH blood group systems demonstrated as follows: D, 3,325 (93.32%); C, 2,529 (70.97%); E, 647 (18.91%); c, 2,686 (75.38%); and e, 3,490 (97.95%). A total of 162 samples were positive for the KEL1 antigen, which is considered to be 4.54% among Saudi blood donors in Jazan area. Table 2 demonstrates the frequencies of RH phenotypes. The eight common RH haplotypes were determined using specific formulas and calculated as mentioned above and data are presented in Table 3.

DISCUSSION

This study helps determine the prevalence of blood group antigens among the Saudi blood donors in Jazan Province. Establishing a database on the prevalence of blood group antigens is extremely crucial and beneficial, especially in this region, with endemic transfusion-dependent patients including those with SCD and thalassemia [15]. In addition, knowledge on the frequency of these antigens and their importance is worthy to be obtained and implemented for the clinical practice. This will help reduce the incidence of alloimmunization events due to multiple blood unit transfusion.

In this study, frequencies of ABO, RH, and KEL1 antigens and phenotypes were determined. The frequency of the ABO blood group system was as follows: A (29.44%), B (10.44%), AB (1.15%), and O (58.97%).

Table 1. Frequencies of ABO, RH, and KEL1 antigens in Saudi blood donors in Jazan Province.

System	Phenotype	Observation (n)	Frequency (%)
ABO	A	1,049	29.44
	B	372	10.44
	AB	41	1.15
	O	2,101	58.97
RH	D	3,325	93.32
	C	2,529	70.97
	E	674	18.91
	c	2,686	75.38
	e	3,490	97.95
KEL	KEL1 (K)	162	4.54

Table 2. Frequencies of RH phenotypes. Chi-square value was calculated at 5 degrees of freedom (d. f.) at 5% level of significance.

D	C	c	E	e	Phenotype	Rh-Hr	Observation (n)	Frequency %	Frequency % in Riyadh [16]
+	−	+	−	+	Dce/dce	R_0r	452	12.69	8
+	+	+	−	+	DCe/dce	R_1r	1,352	37.95	28.7
+	+	−	−	+	DCe/DCe	R_1R_1	854	23.96	24.5
+	+	+	+	+	DCe/DcE	R_1R_2	301	8.45	6.8
+	+	−	+	+	DCe/DCE	R_1R_z	11	0.31	0.3
+	−	+	+	+	DcE/dce	R_2r	283	7.94	11.5
+	−	+	+	−	DcE/DcE	R_2R_2	71	2	4
+	+	−	+	−	DCE/DCE	R_zR_z	1	0.03	0.5
−	−	+	+	−	dcE/dce	r''r	4	0.11	N/A
−	+	+	+	+	dcE/dCe	r''r'	3	0.08	N/A
−	−	+	+	−	dcE/dcE	r''r''	1	0.03	0.5
−	+	+	−	+	dCe/dce	r'r	8	0.22	1.5
−	+	−	−	+	dCe/dCe	r'r'	1	0.03	N/A
−	−	+	−	+	dce/dce	rr	221	6.20	13.7

These results are relatively similar to that of a retrospective study conducted by Abdullah that reported from a single hospital in Jazan region with a large number of blood donors (30,481) [11]. Frequencies reported in the current study were as follows: A (27.6%), B (8.7%), AB (1.7%), and O (62%). The presence of D antigen in this study was 93.32% in comparison to that of Abdullah, i.e., 95%, which is somewhat similar.

Regarding the RH blood group system, frequencies of RH antigens in this study were as follows: D (93.32%), C (70.97%), c (75.38%), E (18.91%), and e (97.95%). Elsayid et al. were the first group to conduct a retrospective study in Riyadh, Saudi Arabia, regarding the RH blood group system including five main antigens (D, C, c, E, and e). The prevalence of RH antigens was reported as follows: D (84.8%), C (62.3%), c (74.3%), E (23.5%), and e (95%) [16]. The outcome of the current study on c and e antigens is somewhat similar. However, differences in D, C, and E frequencies were observed between the Riyadh and Jazan population. Interestingly, the frequency of D antigen reported in Riyadh population was similar to that in the English population, i.e., approximately 85% [16,17]. Conversely, the frequency of D antigen in Jazan Province was 93.32%, which is slightly higher than 92% found in the Nigerian and West Bengal Indian population [14,18].

Table 3. Frequencies of RH haplotypes.

Haplotype	Frequency %			
	Jazan	English [17]	Nigerian [14]	Chinese [19]
	n = 3,563	n = 2,000	n = 274	n = 4,648
Dce (R_0)	0.0078	0.0257	0.5908	0.0334
DCe (R_1)	0.4723	0.4205	0.0602	0.7298
DcE (R_2)	0.2736	0.1411	0.1151	0.1870
DCE (R_Z)	0.0051	0.0024	0	0.0041
dce (r)	0.2410	0.3886	0.2028	0.0232
dCe (r')	0	0.0098	0.0311	0.0189
dcE (r'')	0.0001	0.0119	0	0
dCE (r^y)	0	0	0	0.0036
p-values *		Jazan/English p = 0.000 *	Jazan/Nigerian p = 0.000 *	Jazan/Chinese p = 0.000 *

*** highly significant, n - sample size.**
Chi-square test was performed to test the significant difference between ethnicities.

Table 2 demonstrates that RH phenotypes were determined in Jazan Province in the current study and compared it with that in Riyadh. The frequencies were not statistically significant between the Jazan (current study) and Riyadh population [16]. The most common RH phenotypes in the Jazan population was R_1r, 37.95%. When compared with the Riyadh population, i.e., 28.7%. The R_1R_1 phenotype was then observed in 23.96%, which is somewhat similar than that detected in Riyadh, i.e., 24.5%. The rarest phenotypes were found in the current study, which were only observed in a single sample each, were R_zR_z, r''r'' and r'r'. Elsayid et al. [16] investigated only 600 blood donors from a single hospital in Riyadh. A higher number of participants from various hospitals are highly recommended to cover all areas in Riyadh.

However, this is the first study to determine the RH haplotypes in Saudi Arabia. When comparing the identified haplotypes in this study with other populations, results were statistically significant. p-values were calculated using chi-square test between the Jazan population and other ethnic backgrounds, including English [17], Nigerian [14], and Chinese [19], were highly statistically significant (< 0.01) as shown in Table 3.

The most common RH haplotypes was R_1, i.e., 0.4723 of the total RH haplotypes. Indeed, this outcome reflects the most common phenotypes in this study, i.e., R_1r as mentioned above. This is slightly higher than that R_1 in the English population (0.4205). However, the R_1 haplotype found in this study is remarkably lower than the findings in Chinese population, i.e., 0.7298 [19]. The R_2 haplotype found in this study (0.2736) was almost two-fold higher than the frequency reported in the English population [17], as demonstrated in Table 3. The R_z haplotype in this study (0.0051) is somewhat similar to that in the Chinese group (0.0041).

The r haplotype found in this study was 0.2410, which is somewhat similar to the Nigerian population [14], i.e., 0.2028, which is markedly higher than that of the Chinese population, i.e., 0.0232 [19]. Conversely, the r haplotype in this study is lower than that in the English population (0.3886) [17].

The frequency of KEL1 antigen was shown to be 4.54%. This is the first study to report the prevalence of KEL1 antigen in Jazan, Saudi Arabia. Indeed, the prevalence of KEL1 antigen varies between this study and that of other populations, i.e., English (9.02%) [20], Parisians (8.55%) [21], African Americans (1.50%) [22], Japanese (0.02%) [23], and Arabs (25%) [24]. This percentage of KEL1 antigen is extremely lower than that of the Arab population, as previously reported above. The frequency of KEL1 antigen is somewhat similar to Finns, i.e., 4.10% [25].

The frequencies of ABO, RH, and KEL1 antigens and phenotypes were determined in Jazan, Saudi Arabia. In addition, RH haplotypes were identified as the first study conducted in Saudi Arabia. This study might be conducted in different provinces across Saudi Arabia. Other blood group antigens on the red cell surface are present, which can hamper the transfusion procedure particularly for transfusion-dependent patients. These antigens, including Duffy, Kidd, and MNS, were implicated in HTR and HDFN due to antigen incompatibilities. Therefore, further investigations and frequency determination should be performed in these antigens. The provision of these patients with a safe procedure requires an extended compatibility assay to include other blood group antigens. These recommendations will help reduce the alloimmunization in patients who underwent multiple transfusions and provide safe blood units.

Acknowledgment:
The authors would like to acknowledge the assistance provided by Dr. Mohammad Zaino in the calculation of haplotype frequencies.

Declaration of Interest:
The authors have no conflicts of interest to declare.

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