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Distribution of Kell antigens K, k, Kp^a, and Kp^b among blood donors in Jeddah city of Western Saudi Arabia

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Abstract:

CONTEXT: Kell blood group system is considered as the third clinically significant blood group in blood transfusion due to the highly immunogenetic of their antigens. No data are available regarding the frequencies of the Kell blood group antigens in Jeddah city. Knowledge of the antigen and phenotype frequencies is crucial to assess the risk of alloimmunization and to guide the probability of finding antigen-negative donor blood, which can be useful when blood transfusion is required for a patient who has multiple red cell alloantibodies.

AIMS: The aim of this study was to determine the distribution of Kell blood group: K, k, Kp^a, and Kp^b antigens and phenotypes among blood donors in Jeddah city, western Saudi Arabia, to improve the transfusion services in the area.

SUBJECTS AND METHODS: Seven hundred and fifty-eight blood samples from blood donors were used in the study. The samples were collected from different national blood bank centers in Jeddah city hospitals. Kell antigens were typed through gel card method using commercial antisera.

STATISTICAL ANALYSIS USED: The gathered data were analyzed using the SPSS program. Frequency and crosstab tests were completed to achieve the objectives of the current study.

RESULTS: The most frequent Kell phenotype in this study was Kp^(a-b+), followed by K-k+, K+k+, and then Kp^(a+b+), and the less frequent was K+k-. K-k- and Kp^(a+b-) phenotypes were not observed in studied donors.

CONCLUSIONS: This study is the first report to determine the frequency of Kell antigens and phenotypes among blood donors in Jeddah city. These results appear to be useful in providing better care for patients by implementing tests that should become a routine in blood banks. The Kell system is very important in transfusion medicine practice.

Keywords:

Blood group, distribution, Kell antigen, phenotypes, transfusion

Introduction

A blood group is defined as an antigen on the membrane of red blood cells (RBCs) that may trigger an immune response and subsequent production of alloantibody.^[1] The blood group systems have expanded to 33 systems containing more than 400 antigens, which can be expressed on glycoproteins, proteins, and glycolipids

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on the RBC's surface membrane.^[2] The discovery of blood groups started with the detection of an alloantibody with possible clinical implications for transfusion services. The credit for this discovery goes to Karl Landsteiner, who in the 1900s discovered the first blood group system, the ABO blood group system. Blood groups are critical for transfusion medicine because of high immunogenicity and clinical significance in transfusion service.^[3] There are other significant blood group antibodies produced after exposure to foreign RBC antigens, such

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as Kell, MNS, Duffy, Kidd, Lutheran, P, MN, and Ii, and they too are important in the routine work of transfusion medicine.^[2]

One of the most clinically significant blood groups is the Kell blood group system, which includes several antigens. These Kell antigens are the third most immunogenic antigens, after the ABO and Rh systems.^[4] The first antibody was discovered in 1946 when Coombs described the antiglobulin testing and named it after Mrs. Kelleher, who had contracted anti-K (K1) from her newborn child, who had hemolytic disease of the newborn (HDN).^[5] In 1949, anti-K (K2) was described and named after another pregnant woman, Mrs. Cellano. Eight years later, the null phenotype (K0) was discovered with Kp^a in 1957, and in 1958, Kp^b was discovered. Kp^a (K3) is an antigen with low-frequency mutations, whereas the antithetical antigen Kp^b (K4) has high-frequency mutations.^[6]

The Kell blood group system has a highly polymorphic locus, with more than 30 antigens located on a glycoprotein. The K gene is defined as autosomal dominant encoded with 732 amino acids consisting of 2500 base pairs located on chromosome 7.^[7] The Kell antigen system is highly immunogenic and is clinically significant in transfusion medicine. The Kell antigen can be detected at 10 weeks of gestation in fetal RBCs. The anti-K appears as alloantibody immunoglobulin G class and crosses the placenta, causing extravascular hemolysis, such as severe hemolytic transfusion reaction, severe fetal anemia, and HDN.^[8] In HDN, the anti-K suppresses fetal synthesis of erythropoiesis in the mother's sensitized antigen from a previous pregnancy.^[9]

The main aim of blood transfusion is to transfuse compatible RBCs that will survive after transfusion. The selection of donor blood cells is determined by the absence of antigens against the corresponding antibody detected in patient serum. Multitransfused patients are at risk of developing alloantibodies but have no options other than receiving red cells with negative antigens to those alloantibodies.^[10] Here comes the importance of performing the phenotype test for donors, to create a database that facilitates finding compatible red cell units for patients with alloimmunization faster and improve the practice of blood transfusion.

Few studies have been published in Saudi Arabia on the frequency of antigens and phenotypes of blood group systems other than ABO system. No data have been reported on the Kell antigen prevalence in Jeddah city, western Saudi Arabia. Only a few blood bank centers in Jeddah city perform Kell phenotyping in the donor, thus exposing recipients to the risk of alloimmunization. Therefore, this study aims to study the phenotypic

prevalence of Kell blood group system among blood donors in Jeddah city. This will further improve blood transfusion services and facilitate in generating a donor database for preparation of red cell panels and supplying antigen-negative compatible blood unit to patients with multiple alloantibodies.

Subjects and Methods

Ethical approval

This study was approved by the Researches and Studies General Department of the Ministry of Health (MOH) and by the Research Ethics Committee, registered in the National Committee of Bio and Medical Ethics, Ref. No. (H-02-J-002).

Subjects studied

Blood samples were randomly collected from 758 donors from different blood donation centers of MOH hospitals in several areas in Jeddah, Saudi Arabia, from the North King Abdullah Medical Complex, the Middle Maternity and Children Al-Mosadiah Hospital, and the South King Abdulaziz Hospital. Inclusion criteria included healthy, unrelated, and male or female donors from the age 18 to 65 years who meet all the requirements for donating blood. The sample size was calculated based on the lowest nonzero prevalence of a phenotype in a geographically close region^[11] and at a 95% confidence level and margin of error of 1.25%.^[12,13] In total, 758 blood samples from blood donors were used in the study, which was adequate to draw conclusions on distribution of Kell antigens.

Samples were tested for red cell antigen typing of Kell blood group systems (K, k, Kp^a, and Kp^b). Each sample was tested using Immunodiffusion Gel System Card (ID-Gel System) and Seralclone anti-K, anti-k, anti-Kp^a, and anti-Kp^b (Bio-Rad Laboratories Inc., USA).

Red cells from each donor sample were prepared as 0.8% suspension in ID-Diluent 2, and Kell antigen (K, k, Kp^a, and Kp^b) typing was performed by gel card (Bio-Rad Laboratories Inc., USA). Fifty microliters of donor cell suspension was added to all microtubes, and 50 µl each of Seralclone reagents K, k, Kp^a, and Kp^b were pipetted into the appropriate microtubes. ID-Gel cards were incubated for 15 min followed by centrifuge for 10 min. Agglutinated cells forming a red line on the surface of gel or dispersed in gel are considered positive. A compact button of cells on the bottom of the microtube indicated the absence of the corresponding antigen.

Statistical analysis

The gathered data were analyzed and translated using the Statistical Package for the Social Science (SPSS) software (version 23.0; SPSS Inc., Chicago, IL, USA) program,

which encourages a definitive outcome. Frequency and crosstab tests were completed to achieve the objectives of the current study.

Results

The participants of this study comprised 758 donors; 745 of them were male (98.3%), and 13 of them were female (1.7%). In addition, 454 (59.9%) of the donors were Saudi nationals and 304 (40.1%) were non-Saudis.

Table 1 shows the frequency of Kell antigens, which there were Kp^{b+} 745 (100%) male donors, as majority of Kell antigens according to gender, followed by k+ 738 (99.1%), Kp^{a-} 725 (97.3%), K- 625 (87.5%), K+ 93 (12.5%), Kp^{a+} 20 (2.7%), and k- 7 (0.94%) donors. Only 13 (100%) female donors who participated in this study had K-, k+, Kp^{a-}, and Kp^{b+} antigens.

In addition, Table 1 shows that Saudi donors had Kp^{b+} 454 (100%) as the most common Kell antigens according to the nationality, followed by k+ 447 (98.5%), Kp^{a-} 436 (96%), K- 380 (83.7%), K+ 74 (16.3%), Kp^{a+} 18 (4%), and only 7 (1.5%) donors with the k-antigen. On the other hand, the non-Saudi donors had 304 (100%) results for both k+ and Kp^{b+} antigens, followed by 302 (99.3%) and 285 (93.8%) results for Kp^{a-} and K-antigens. The least common antigens for non-Saudi donors were K+ and Kp^{a+}, with only 19 (6.3%) and 2 (0.7%) results, respectively.

This study found that there were high-frequency antigens for the Kell blood group including K- 665 (87.7%), k+ 751 (99.1%), and Kp^{a-} 738 (97.4%). Moreover, all blood donors who participated in this study had

Kp^{b+} 758 (100%) antigens. It also showed that the antigens with the lowest frequency were k- 7 (0.9%), Kp^{a+} 20 (2.6%), and K+ 93 (12.3%). Kp^{b-} antigen was not observed among donors in Jeddah [Table 1].

As shown in Table 1, five Kell phenotypes were found to be present in participated donors. This study indicates that the most common Kell phenotype among donors being Kp^(a-b+) 738 (97.3%), followed by K-k+ 665 (87.8%), K+ k+ 86 (11.3%), Kp^(a+b+) 20 (2.6%), and K+k- 7 (0.92%), was the rarest phenotype observed. Three phenotypes, K-k-, Kp^(a-b-), and Kp^(a+b-), were not observed among blood donors. Furthermore, Table 1 shows Kp^(a-b+) 725 (97.3%) and K-k+ 652 (87.5%) for the males, and these are considered to be the most common Kell phenotypes according to the gender among blood donors participating in this study. The least common phenotypes were K+k+ 86 (11.5%) and Kp^(a+b+) 20 (2.7%), and only 7 (0.94%) male donors had K+k- phenotype. However, just 13 (100%) female donors had K-k+ and Kp^(a-b+) phenotypes.

According to nationality, Table 1 shows that 436 (96%) Saudi donors had Kp^(a-b+) and 380 (83.7%) had K-k+ phenotypes, which are considered as the most common Kell phenotypes according to nationality. The results for the same phenotypes were less for non-Saudi donors, with 302 (66.5%) and 285 (62.8%), respectively. For the other phenotypes, the Saudi donors had K+k+ 67 (14.8%) but only 19 (6.3%) for non-Saudi donors. This is followed by Kp^(a+b+) 18 (4%) for Saudi donors and finally only 2 (0.66%) for non-Saudi donors. Only Saudi donors had K+k- 7 (1.5%) phenotype.

Table 1: Frequency of Kell antigens and phenotypes among donors

	Frequency (n), n (%)	Gender (n)		Nationality (n)	
		Male, n (%)	Female, n (%)	Saudi, n (%)	Non-Saudi, n (%)
Antigens					
K+	93 (12.3)	93 (12.5)	0	74 (16.3)	19 (6.3)
K-	665 (87.7)	652 (87.5)	13 (100)	380 (83.7)	285 (93.8)
k+	751 (99.1)	738 (99.1)	13 (100)	447 (98.5)	304 (100)
k-	7 (0.9)	7 (0.94)	0	7 (1.5)	0
Kp ^{a+}	20 (2.6)	20 (2.7)	0	18 (4.0)	2 (0.7)
Kp ^{a-}	738 (97.4)	725 (97.3)	13 (100)	436 (96)	302 (99.3)
Kp ^{b+}	758 (100)	745 (100)	13 (100)	454 (100)	304 (100)
Kp ^{b-}	0	0	0	0	0
Phenotypes					
K-k+	665 (87.8)	652 (87.5)	13 (100)	380 (83.7)	285 (62.8)
K+k+	86 (11.3)	86 (11.5)	0	67 (14.8)	19 (6.3)
K+k-	7 (0.92)	7 (0.94)	0	7 (1.5)	0
K-k-	0	0	0	0	0
Kp ^(a+b+)	20 (2.6)	20 (2.7)	0	18 (4.0)	2 (0.66)
Kp ^(a-b+)	738 (97.3)	725 (97.3)	13 (100)	436 (96.0)	302 (66.5)
Kp ^(a+b-)	0	0	0	0	0
Kp ^(a-b-)	0	0	0	0	0

Discussion

Antigen and phenotype frequencies of Kell blood group system of this study were compared to other studies in the rest of the world [Table 2]. This study is the first report on the frequency of the Kell antigen system among blood donors from different blood donation centers in Jeddah city. However, there are few studies published in Saudi Arabia on the frequency of phenotypes or antigens of Kell blood group system.^[11,14,15] To find the ethical effect on the Kell phenotype distribution, many populations from different regions also have been tested to determine the prevalence of their Kell phenotype. The results of this study showed that 12.3% of the donors were K+ and the remaining 87.7% were K-. The prevalence of k antigen among the blood donors of our study group was 99.1%. This agrees with the results of Azarkeivan *et al.*^[16] who tested K antigen for 11,557 blood units, and they found that 96.2% were K- and 3.8% were K+. Furthermore, the present findings are consistent with the results of two studies: the first study was performed by Siransy Bogui *et al.*^[17] and showed that 5 blood donors (0.77%) were typed as K+ and 645 (98.08%) as k+ antigens. Accordingly, the K-k+ phenotype was the most common in these donors (98.92%). The second study was done by Vasquez *et al.*^[18] and screened for 200 blood donors, which revealed that the K+ frequency was 4%, while the k+ frequency was 99.5%, matching with our results of k+ frequency of 99.1%. Similar results have been seen in the study performed in Mauritania by Hamed *et al.*^[19] They identified the prevalence of ABO, Rh, and K antigen among 2094 Mauritanian donors from three blood groups. This study demonstrated that 2.96% of white moors were K+, 1.25% of black moors were K+, and no black Africans were K+, while the K- results were 97.04% for white moors, 98.75% for black moors, and 100% for black Africans. Furthermore, a study was conducted in North India (2010) among 1240 blood donors; it was demonstrated that 5.56% of donors were K positive with 100% k antigen. A rare antigen K+ was found in 5.5% of the donors. However, the k+ result was 100%.^[20] In 2013, of 3073 samples from randomly selected blood donors from Delhi and nearby areas, as another study, the k antigen came with high frequency 99.97% and 3.5% of K positive.^[21] Two years later, in 2015, Rani *et al.* showed that K positive was 3.17%, which is similar to the previous studies.^[22] In the same year, a study in Pakistan investigated 100 donors and showed 100% of K negative, and all donors were K- k+ phenotype.^[23] In 2016, 1412 samples were tested in Chinese population. In the Kell blood group system, k was present in 100% of the donors and a rare phenotype, Kp(a+b+), was found in 0.28% of the donors.^[24] A multiethnic cohort of 302 healthy Nigerian individuals was created to study Kell antigen prevalence. The prevalence of K was 0%.^[25] Our result of k antigen reveals that the k antigen is a

common antigen for blood donors, which indicates that the pretransfusion test of k antigen is a minor step for the blood bank.

Distributions of Kell blood group phenotypes among donors in this study are similar to other populations around the world. As previously shown, the most frequent Kell phenotype in this study is Kp(a-b+), followed by K-k+, K+ k+, Kp(a+b+), and finally, K+k-. There is no K-k-, Kp(a+b-), and Kp(a-b-) phenotypes among blood donors participating in this study. A study from Riyadh, Saudi Arabia, showed similar results and presented a frequency of Kell antigens; the results were K+ (18.2%), k+ (97%), Kp^a (11.7%), and Kp^b (96%). Among Saudi donors in Riyadh, the major Kell phenotypes were K-k+ (81.5%), followed by 16 K+k+ (15.5%), and K+k- (3%). No result observed for the K-k- phenotype. Furthermore, the major phenotypes that result from the antigens Kp^a and Kp^b were Kp^(a-b+) (88.0%), followed by Kp^(a+b+) (7.8%) and Kp^(a+b-) (4.2%), and there were no results for the Kp^(a-b-) phenotype.^[11] The similarity between our result in Jeddah and the result of Riyadh blood donors has indicated that all Saudi donors have the same genetic makeup for Kell expression. Kahar and Patel study, in blood donors of South Gujarat, India, showed that k was found to be positive in all donors, and no K+k- phenotype was found in Kell system.^[26] A rare phenotype Kp^(a+b+) was found in 0.95% of the donors.^[20] Another study tested frequencies of Kell phenotypes and demonstrated that Kp^(a-b+) was the most common phenotype among a population in the northeast of Iran.^[27] Kp^(a-b+) phenotype is considered as the most common phenotype in Saudi Arabia and other countries. However, our result reveals a slightly higher percentage than Riyadh blood donors, which might be due to the multicultural nature of Jeddah city.

In addition, the frequency of the K antigen was found to be 1.97%, and k was present in 100% of donors. Accordingly, the K-k+ phenotype was the most common in these donors 98.03% in a study that was done in North India.^[28] When assessing the prevalence with another study, there was no significant difference even with the most recent study done in 100 donors in the eastern region of Saudi Arabia in 2020. It showed 8% of K antigen with 100% of k antigen, with no detection of Kp^a and K+k- phenotypes. Furthermore, it showed a similar result of this study in Kp^b antigen that came positive in all donors.^[15] A total of 337 Omani blood donors were tested in another recent study. The k antigen was found at a frequency of 99.4%, while 4.5% of the blood donors studied were K+, which is similar to our study.^[29] Shah *et al.* studied phenotyping on a cohort of Indian voluntary blood donors. Of 200 blood donors, 2.5% were K positive and k antigen was found to be 100%. A rare phenotype Kp^(a+b+) was found in 1% of the

Table 2: Antigen and phenotype frequencies of Kell blood group system (compared to other studies in Saudi Arabia and the rest of the world)

Studies	Total Sample (n)	Antigens (%)										Phenotypes (%)									
		K+	K-	K+	K-	Kp ^{a+}	Kp ^{a-}	Kp ^{b+}	Kp ^{b-}	K-k+	K-k-	K+k+	K+k-	K-k-	Kp (a+b+)	Kp (a+b-)	Kp (a-b+)	Kp (a-b-)			
Present study, (2018) Jeddah	758	12.3	87.7	99.1	0.9	2.6	97.4	100	0	87.7	11.3	0.9	0	0	2.6	97.3	0	0			
Elsayid ^[11] (Riyadh)	400	18.2	81.2	97	3	11.7	88.3	96	4	81.5	15.5	3	0	7.8	88	4.2	0	0			
Owaidah <i>et al.</i> ^[15] (Eastern Region of KSA)	100	8	92	100	0	0	100	100	0	92	8	0	0	0	100	0	0	0			
Azarkeivani ^[16] (Iran)	11,557	3.8	96.2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
Siransy <i>et al.</i> ^[17] (Cote d'Ivoire)	651	0.77	-	98.1	-	0.61	-	82.8	-	98.9	-	-	-	-	-	-	-	-			
Vasquez ^[18] (Taica)	200	4	96	99.5	0.5	-	-	-	-	96	3.5	0.5	0	-	-	-	-	-			
Hamed <i>et al.</i> ^[19] (Mauritania)	2094	White 2.96 Black 1.3	White 97.0 Black 98.8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
Thakral <i>et al.</i> ^[20] (India)	1240	5.56	94.4	100	0	0.95	99.1	100	0	94.3	5.6	0	0	0.95	99.1	0	0	0			
Makroo <i>et al.</i> ^[21] (India)	3073	3.5	96.5	99.9	0.03	-	-	-	-	96.5	3.5	0.03	0	-	-	-	-	-			
Rani <i>et al.</i> ^[22] (India)	2000	3.5	96.9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
Karim <i>et al.</i> ^[23] (Karachi)	100	0	100	100	0	-	-	-	-	100	0	0	0	-	-	-	-	-			
Yu <i>et al.</i> ^[24] (China)	1412	0.14	99.8	100	0	0.28	99.7	100	0	99.8	0.14	0	0	0.28	99.7	0	0	0			
Adewoyin <i>et al.</i> ^[25] (Nigeria)	302	0	100	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
Kahar and Patel ^[26] (India)	115	6.09	93.9	100	0	1.74	98.3	100	0	93.9	6.09	0	-	1.74	98.3	-	-	-			
Keramati <i>et al.</i> ^[27] (Iran)	522	-	-	-	-	-	-	-	-	92	5.7	2.3	-	6	90.7	3.3	-	-			
Agarwal <i>et al.</i> ^[28] (North India)	9280	-	-	-	-	-	-	-	-	98.0	1.97	0	0	-	-	-	-	-			
Al-Riyami <i>et al.</i> ^[29] (Oman)	337	4.5	-	99.4	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
Shah <i>et al.</i> ^[30] (India)	200	2.5	-	100	-	-	-	-	-	-	-	-	-	1	-	-	-	-			

donors.^[30] This result indicates that the most common Kell phenotype is K–k+ phenotype for blood donors in Saudi Arabia and other countries.

There is a general lack of data about the frequency of blood groups among donors in the Middle East and Asia regions. Only the fundamental examinations, such as for ABO and D antigens, were performed, and additional examinations, such as for Rh and Kell phenotypes, were not performed. Moreover, there no studies were done to investigate the distribution of Kell antigens and phenotypes specifically in Jeddah, western Saudi Arabia. This is the first study to determine the distribution of Kell antigens and phenotypes among blood donors in Jeddah, western Saudi Arabia, and it aims to provide a better care for patients by enhancing the additional tests that should become a routine in blood bank centers.

Conclusions

This study found that there are three high-frequency antigens for the Kell blood group: K–, k+, and Kp^a–. Moreover, all blood donors participating in this study had Kp^b+ antigens for both gender and nationality. It also showed that the antigens with the lowest frequency were k–, Kp^a+, and K+, finding no Kp^b– antigens among donors in Jeddah. In addition, this study indicates that the most common Kell phenotype among donors is Kp(a–b+), followed by K–k+, K+k+, Kp(a+b+), and finally, K+k–. Furthermore, there was no K–k–, Kp(a–b), or Kp(a+b–) among blood donors participating in this study. Kp^b+ was the most common Kell antigen among Saudi donors, according to nationality. Finally, Kp(a–b+) and K–k+ were the most common Kell phenotypes according to nationality among blood donors participating in this study. This is the first study to determine the distribution of Kell antigens and phenotypes among blood donors in Jeddah city. This information can be useful to blood transfusion centers when deciding on the preventive measures to enhance safety in transfusion medicine.

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Conflicts of interest

There are no conflicts of interest.

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