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Original article

The frequencies of Kidd blood group antigens and phenotypes among Saudi blood donors in Southwestern Saudi Arabia

Amr J. Halawani [a,b,*], Muhammad Saboor [c,d], Hisham I. Abu-Tawil [e,f], Ali Y. Alhazmy [e], Waleed Q. Mashlawi [e], Farkad Bantun [b,g], Abdullah S. Mansor [b,c]

[a] Department of Laboratory Medicine, Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Saudi Arabia
[b] SMIRES for Consultation in Specialized Medical Laboratories, Jazan University, Jazan, Saudi Arabia
[c] Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, Jazan University, Jazan, Saudi Arabia
[d] Medical Research Center (MRC), Jazan University, Jazan, Saudi Arabia
[e] Department of Laboratory and Blood Bank, Prince Mohammed bin Nasser Hospital, Ministry of Health, Jazan, Saudi Arabia
[f] Department of Laboratory and Blood Bank, King Faisal Medical City for Southern Regions, Ministry of Health, Abha, Saudi Arabia
[g] Department of Microbiology, Faculty of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia

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ABSTRACT

Background: The patients who require transfusion are prevalent in the Jazan Province, Saudi Arabia. Therefore, it is essential to know the frequency of blood group antigens in such a population. The Kidd blood group system (JK) has two antithetical antigens, Jk^a and Jk^b. Antibodies to these antigens may result in delayed hemolytic transfusion reactions. The present study investigated the frequencies of Jk^a and Jk^b and the phenotypes among Saudi blood donors living in the Jazan Province.

Methods: One hundred and forty-three samples from anonymous Saudi volunteer blood donors in the Jazan Province were serotype to detect Jk^a and Jk^b using gel card technology and determine the phenotypes of the JK blood group system.

Results: The prevalence of Jk^a and Jk^b antigens were 90.64% (n = 126) and 69.40% (n = 93), respectively. The JK phenotypes were 34.96% Jk(a + b −) (n = 51), 12.59% Jk(a − b +) (n = 18), 52.45% Jk(a + b +) (n = 75), and 0% Jk(a − b −). The frequencies of the JK phenotypes in the Jazan population were significantly different from those in the Asian population ($P < 0.05$).

Conclusions: We reported the frequencies of the Jk^a and Jk^b antigens and the distribution of the JK phenotypes in a group of Saudi blood donors in the Jazan Province, Saudi Arabia. The phenotype Jk(a + b +) was the most common among the study population. Furthermore, this study emphasizes the significance of identifying the frequency of JK antigens and phenotypes in the provinces of Saudi Arabia.

1. Introduction

Kidd blood group system (JK) is designated by the International Society for Blood transfusion as 009. This blood group system was first reported in 1951 after the detection of anti-Jk^a antibodies in the serum of Mrs. Kidd, whose infant had a hemolytic disease of the fetus and newborn (HDFN) (Allen et al., 1951). The antigen was designated Jk^a after the name of the infant Jhon Kidd. Jk^b antigen, an antithetical antigen of Jk^a, was identified two years later (Plaut et al., 1953).

JK antigens are coded by the *SLC14A1* (solute carrier family 14, member 1) gene, also known as the human urea transporter (*HUT11*) gene, on chromosome 18 ($18q^{11}$–$18q^{12}$). *SLC14A1* spans approximately 30 Kbp of DNA containing 11 exons. The mature JK proteins are encoded by exons 4–11. This gene encoded three major alleles –*JK*01 (JK*A), JK*02 (JK*B), and JK,* which is the silent allele (Lucien et al., 1998).

SLC14A1 encodes for the 43-kDa JK glycoprotein of 389 amino acids. The Kidd glycoprotein has two N-glycosylation sites. It traverses the red blood cell (RBC) membrane ten times and creates five extracellular loops numbered from the intracellular N-

Abbreviations: HDFN, Hemolytic disease of the fetus and newborn; HTR, Hemolytic transfusion reactions; RBC, Red blood cell; SNP, Single nucleotide polymorphism.

* Corresponding author.
E-mail address: ajjhalawani@uqu.edu.sa (A.J. Halawani).

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Terminal (Lucien et al., 2002). The Jk^a and Jk^b antigens are located on the fourth extracellular loop. *JK*01* and *JK*02* alleles differ in a single nucleotide polymorphism (SNP) in exon 9 of the *SLC14A1* gene. The *JK*01* allele, with C838G, encodes aspartate at position 280, while JK*02, with C838A, encodes asparagine at the same position (Olivès et al., 1997). In addition to the Jk^a and Jk^b antigens, Jk3 is another antigen of the Kidd blood group system found in all populations possessing either Jk^a or Jk^b antigens. The JK null phenotype, i.e., Jk(a − b −), is rare and most common in individuals of Polynesian and Finnish ancestry (Irshaid et al., 2000). The null phenotype may be caused by mutations in the form of SNPs or deletions, resulting in the absence of a functional JK antigen on the surface of the RBC (Ekman and Hessner, 2000).

The JK antigens act as urea transporter and play a pivotal role in maintaining the structure of RBC (Sands et al., 1992). When the RBC pass through the renal medulla, the JK antigens rapidly transport urea across the RBC membrane to prevent the RBC from shrinking in the renal medulla and swelling when it leaves the medulla. The JK antigens' ability to transport urea can be utilized to screen for the Jk(a − b −) phenotype. In a high-molar (2 M) urea solution, RBC with the Jk(a +) or Jk(b +) phenotype or both will be lysed within 30 s due to the entrance of urea and the rapid influx of water into the RBC. However, RBC with the Jk(a − b −) phenotype, due to their absence of urea transport, will be able to resist lysis for up to 30 min (Edwards-Moulds and Kasschau, 1988).

Although JK antigens are not very immunogenic, anti-Jk^a and anti-Jk^b are common causes of delayed hemolytic transfusion reactions (HTR). Anti-Jk^a and anti-Jk^b antibodies are dangerous because they can be difficult to detect during routine blood cross-matching. Anti-Jk3 is more difficult to detect and shall be investigated in RBC with the Jk(a +) or Jk(b +) or both phenotypes. The JK antibodies deteriorate rapidly both *in vivo* and *in vitro*; the decrease in antibody reactivity and increased difficulty of detection make them a common cause of HTR (Sanford et al., 2015; Makroo et al., 2017). Furthermore, the JK blood group antibodies have been implicated in the development of HDFN. In addition to its importance in transfusion, the JK blood group system is involved in acute kidney transplant rejection (Hamilton et al., 2006).

Literature review shows almost similar frequencies of Kidd blood group antigens in different populations. Frequncy of Jk^a has been reported to be 83%, 77%, 92%, and 68% in Indian, Caucasian, African and Chinese population. While Jk^b was found to be 67%, 74%, 49%, and 76% in these popultions. (Kahar and Patel, 2014, Yu et al 2016, Thakral et al., Reid et al 2012). A local study was conducted in the Eastern Region of Saudi Arabia has reported the frequencies of Jk^a and Jk^b were 86% and 60%, respectively (Owaidah et al 2020).

The prevalence of ABO, RH, KEL1, Fy^a, and Fy^b antigens, as well as the corresponding phenotypes, were reported in Southwestern Saudi Arabia (Halawani et al., 2021; Halawani and Arjan, 2021). It is to noteworthy that studies related with the frequrncy of Kidd blood antigens are in scaricity. Given the significance of the blood group antigens in HTR in patients with hemoglobinopathies, this study aimed to investigate the prevalence of the JK antigens, Jk^a and Jk^b, among anonymous volunteer Saudi blood donors in Jazan Province. In addition, the prevalence of JK phenotypes was determined.

2. Materials and methods

2.1. Blood samples

One hundred and forty-three anonymous voluntary blood donors, who lived in Jazan Province, were recruited for this study. Blood samples were collected in anticoagulated tubes with ethylenediaminetetraacetate (EDTA) at Prince Muhammad bin Nasser Hospital in Jazan Province of Saudi Arabia.

The ethics of this research was approved by Jazan Hospital Institutional Review Board (NO. 2017). Prior to blood donation, all blood donors signed consent forms and answered a questionnaire regarding their general health. All blood donors underwent the blood donation procedure per the national blood transfusion guidelines. Blood samples were screened for any transfusion-transmitted diseases, including Hepatitis B, Hepatitis C, and Human immunodeficiency viruses.

2.2. Immunohematology

A serological investigation was carried out using a commercially available kit based on the gel card technology, ID-Cards (DiaClon Anti-JK^a and DiaClon Anti-JK^b), according to the manufacturer's instructions (DiaMed GmBH, Cressier, Switzerland). A 5% RBC suspension was prepared by mixing 50 µl of whole blood with ID-Diluent 1 followed by incubation at room temperature for 10 min. A total of 12.5 µl of the suspension was then added to the corresponding microtubes of the ID-Cards, followed by centrifugation in the ID-Centrifuge at 85 × g for 10 min (DiaMed GmBH, Cressier, Switzerland). Following the manufacturer's instructions, known positive and negative samples for both antigens, Jk^a and Jk^b, were included as positive and negative controls for the quality assurance.

2.3. Interpretation of results

A formation of a red line on the surface of the gel or a dispersed clumping indicated the existence of a relevant antigen, hence a positive result. On the other hand, a pellet at the bottom of the microtubes indicates the absence of a corresponding antigen, hence negative results.

2.4. Statistics

The sample size was calculated, as described by Halawani et al. (Halawani et al., 2021). The prevalence of JK antigens and phenotypes were presented as percentages. The *P*-values were calculated using a chi-square test to compare JK phenotypes of the Saudi Arabia population to other ethnicities. The difference in comparison with the *P*-value < 0.05 was considered significant.

Table 1
The frequency of JK blood group antigens in a population of Saudi blood donors in Jazan Province, Saudi Arabia.

Antigen	Observation (n)	Frequency (%)
Jk^a	126	90.64%
Jk^b	93	69.40%

Table 2
The frequencies of the JK phenotypes in a population of Saudi blood donors in Jazan Province

Phenotype	Observation	Frequency (%) n = 143
Jk(a + b −)	51	34.96%
Jk(a + b +)	75	52.45%
Jk(a − b +)	18	12.59%
Jk(a − b −)	0	0.00%
	143	100

Table 3
Comparison of frequencies of JK phenotypes between various ethnic groups and the population in the current study

Phenotype	Jazan (Saudi Arabia) (%)	White (%)	Black (%)	Asians (%)
Jk(a + b −)	34.96%	26.3	51.1	23.2
Jk(a + b +)	52.45%	50.3	40.8	49.1
Jk(a − b +)	12.59%	23.4	8.1	26.8
Jk(a − b −)	0.00%	Rare	Rare	0.9 (Polynesians)
P-values		Jazan compared to White	Jazan to Black	Jazan to Asians
		> 0.05	$P > 0.05$	$P < 0.05^*$

*significant.

3. Results

A total of 143 samples were investigated for their antigens and the phenotypes in the JK blood group system. The frequencies of Jk^a and Jk^b antigens among the study population were examined; the prevalence of Jk^a and Jk^b among the Jazan population was 126 (90.64%) and 93 (69.40%), respectively (Table 1).

Then, the frequencies of the four phenotypes in the samples were identified (Table 2). The Jk(a + b−) phenotype was observed in 34.96% or 51 of the total samples. Interestingly. the Jk(a + b +) was the most prevalent at 52.45%, or 75 of all the samples. The Jk(a − b +) phenotype was observed in 12.59% or 18 individuals of the total population. The null phenotype Jk(a − b −) was not detected in any samples. Lastly, the frequencies of the different Jk phenotypes among the Jazan population were compared to those in other ethnic groups (Table 3).

4. Discussion

Blood transfusion is required regularly for transfusion-dependent patients with sickle cell disease and thalassemia in pandemic areas, such as Jazan Province, Saudi Arabia (Alhamdan et al., 2007; Alsaeed et al., 2018; Memish et al., 2011). Knowing the prevalence of the antigens of different blood groups will optimize the matching of patients to donors by antigen. Consequently, it may prevent RBC alloimmunization and any HTR due to the transfusion of multiple blood units (Thedsawad et al., 2019; Yazdanbakhsh et al., 2012).

In this study, the frequency of the JK blood group antigens was determined. The prevalence of the Jk^a and Jk^b antigens was observed to be 90.64% and 69.40%, respectively, much higher than reported in the general populations (Lawicki et al., 2017). This is could be due to the basis of the geographic locations and the ethnicity of the Saudi individuals living in Jazan Province.

Of the JK phenotypes, the most common phenotype in Jazan Province was Jk(a + b +) at 52.45%, relatively similar to that reported among the White and Asian populations at 50.3% and 49.1%, respectively (Reid et al., 2012). However, there was a statistically significant difference between the Saudis living in Jazan Province and that in the general Asian population. On the other hand, the Jk(a + b −) phenotype was higher in Jazan Province at 34.96% than that in the general Asian population at 23.2%. Interestingly, Jk (a + b −), at 51.1%, is highly prevalent in the Black population. Meanwhile, the Jk(a − b +) phenotype was found to have a frequency of 12.59% in the Jazan population compared to the Asians at 26.8%. Lastly, the Jk(a − b −) phenotype, the rarest phenotype among the JK blood groups system, was not observed in the Jazan population.

Therefore, it is highly recommended to include typing the JK antigens in the screening panel for transfusion-dependent patients. Moreover, the JK antigens should be added to the routine panels of screening blood donors. These implementations might help reduce the occurrence of alloimmunization due to the mismatching of the JK antigens. According to Castro et al. (2002), matching of the D, C, c, E, e, KEL1, S, Fy^a, and Jk^b antigens could reduce the likelihood of alloimmunization by 70.8% in patients with SCD (Castro et al., 2002). However, adding antigens to the screening panel may reduce the protocol's feasibility as well as increase the cost of the serological reagents.

5. Conclusions

In summary, we have determined the frequencies of the Jk^a and Jk^b antigens in the population in Southwestern Saudi Arabia. Moreover, we measured the prevalence of the four JK phenotypes and found the Jk(a + b +) phenotype to be most common in the entire population. The extended typing of blood groups is highly recommended for both donors and transfusion-dependent patients.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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