The frequencies of Kidd blood group antigens and phenotypes among Saudi blood donors in Southwestern 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, Jka and Jkb. Antibodies to these antigens may result in delayed hemolytic transfusion reactions. The present study investigated the frequencies of Jka and Jkb 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 Jka and Jkb using gel card technology and determine the phenotypes of the JK blood group system.

Results: The prevalence of Jka and Jkb 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 Jka and Jkb antigens and the distribution of the JK phenotypes in a group of Saudi blood donors in the Jazan Province. Furthermore, this study emphasizes the significance of identifying the frequency of JK antigens and phenotypes in the provinces of Saudi Arabia.

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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-Jka 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 Jk² after the name of the infant Jhon Kidd. Jk² antigen, an antithetical antigen of Jka, 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 (18q11–18q12). 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-
The surface of the RBC (Ekman and Hessner, 2000). Deletions, resulting in the absence of a functional JK antigen on the surface of Polynesian and Finnish ancestry (Irshaid et al., 2000). The 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 for the JK null phenotype, i.e., Jk(a– b–), is resistant to lysis for up to 30 min (Edwards-Moulds and Kasschau, 1988).

Although JK antigens are not very immunogenic, anti-Jk\textsuperscript{a} and anti-Jk\textsuperscript{b} are common causes of delayed hemolytic transfusion reactions (HTR). Anti-Jk\textsuperscript{a} and anti-Jk\textsuperscript{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. Frequency of Jk\textsuperscript{a} has been reported to be 83%, 77%, 92%, and 68% in Indian, Caucasian, African and Chinese population. While Jk\textsuperscript{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\textsuperscript{a} and Jk\textsuperscript{b} were 86% and 60%, respectively (Owaidah et al 2020).

The prevalence of ABO, RH, KEL1, Fya, and Fyb 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 frequency of Kidd blood antigens are in scarcity. 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\textsuperscript{a} and Jk\textsuperscript{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\textsuperscript{a} and DiaClon Anti-JK\textsuperscript{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\textsuperscript{a} and Jk\textsuperscript{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

| Antigen | Observation (n) | Frequency (%) |
|---------|----------------|---------------|
| Jk\textsuperscript{a} | 126 | 90.64% |
| Jk\textsuperscript{b} | 93 | 69.40% |

Table 2

| Phenotype | Observation | Frequency (%) |
|-----------|-------------|---------------|
| Jk(a + b –) | 51 | 34.96% |
| Jk(a + b +) | 75 | 52.45% |
| Jk(a – b +) | 18 | 12.50% |
| Jk(a – b –) | 0 | 0.00% |
|          | 143 | 100% |
3. Results

A total of 143 samples were investigated for their antigens and the phenotypes in the JK blood group system. The frequencies of Jka and Jkb antigens among the study population were examined; the prevalence of Jka and Jkb 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 (Thedssawal 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+ and Jk- 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 also 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 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 of 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, Fya, and Jkb 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 Jka and Jkb 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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