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Original article

ANTIGEN FREQUENCY OF KELL, DUFFY, KIDD, MNS AND LUTHERAN BLOOD GROUP SYSTEM IN POPULATION OF NORTH MACEDONIA – TOWARDS RARE BLOOD GROUP REGISTRY

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Abstract

The frequency of red blood cell antigen is variable among different populations. Extended red blood cell (RBC) typing beyond the ABO and Rh system will broaden the possibility of finding compatible blood for alloimmunized patients.

To perform RBC antigen typing of: Kell, Duffy, Kidd, MNS and Lutheran systems and to calculate antigen and phenotype frequency.

In 920 blood donors, RBC typing of K, k, Kpa, Kpb, Fya, Fyb, Jka, Jkb, S, s, Lua and Lub antigens was performed using specific monoclonal antisera, antihuman globulin and column agglutination technique with gel cards (BioRad). Antigen and phenotype frequencies were calculated from the statistics module of the donor information system (database for blood donors).

The prevalence of Kell antigens is 7.5% for K and 99.94% for k. The phenotype (K+k-) is present in 21 (0.06%) blood donors. The frequency of other clinically significant antigens is as follows: 1.1% (Kp^a), 100.0% (Kp^b), 60.3% (Jk^a), 76.2% (Jk^b), 65.5% (Fy^a), 79.5% (Fy^b), 59.8% (S), 86.5 (s), 7.2% (Lu^a) and 92.8% (Lu^b). The most frequent phenotypes are Jk(a+b+) with 41.5%, Fy(a+b+) with 48.5%, (S+ s+) with 46.3% and Lu(a-b+) with 92.8%. Fy(a-b-) phenotype was detected in 0.21% of blood donors.

The estimated RBC antigen frequency in our blood donor population differs from the antigen frequency in different populations. Because of that extended RBC typing is necessary for identifying rare blood group donors within the local population. This strategy enables to meet the needs for RBC transfusion in patients with rare phenotypes and with antibodies against high frequency antigens or multiple antibodies, as well as to prevent RBC alloimmunization in polytransfused patients providing antigen matched RBC.

Keywords: blood group system, RBC antigen frequency, phenotype

Introduction

Blood groups represent molecules on the erythrocyte membrane with a certain biochemical structure (oligosaccharides bound with glycoproteins and glycolipids or amino acids from a particular protein), which are defined with specific antibodies, indicating the fact that some individuals do not possess the appropriate antigen.

Blood type is defined as an antigen on the erythrocyte membrane that can cause an immune response and subsequent production of alloantibodies. According to the International Society of Blood Transfusion (ISBT), 43 blood group systems with 378 antigens have been classified[1]. For production of these erythrocyte antigens 45 genes are responsible, all of which have been sequenced, so the polymorphisms associated with the blood group antigens are known.

Most polymorphisms occur as a result of single nucleotide polymorphism (Single nucleotide polymorphism-SNP), which conditions the replacement of one amino acid with another in a certain glycosyltransferase or in the extracellular domain of a certain protein in the composition of the erythrocyte membrane[2].

According to the biochemical composition, blood group antigens can be oligosaccharides, such as A, B and H (ABO system) and Lea, Leb (Lewis system); antigens D, C, c, E, e and Cw from the Rh system and antigens Jka and Jkb from the Kidd system are proteins; antigens M, N, S and s from the MNS system are sialoglycoproteins; antigens K, k, Jsa, Jsb, Kpa and Kpb from the Kell system, antigens Lua, Lub from the Lutheran system and antigens Fya, Fyb from the Duffy system are glycoproteins; the P1 antigen of the P system is a glycolipid.

Blood group antigens such as Diego, Scianna, Dombrock, Colton, Chido/Rodgers systems are glycoproteins of the erythrocyte membrane[3-5]. The biological and clinical significance of erythrocyte antigens depends on the biochemical composition, molecular structure and position within the erythrocyte membrane[6].

The biological significance of blood group antigens is connected with their function (structural proteins of the red blood cell membrane, receptors, ligands and adhesive molecules for different cytokines and microbial agents, and membrane transporters for different molecules), which are important for the viability of the erythrocytes, as well as for the human organism in general.

Antigen systems Rh (for ammonia ions), Kidd (for urea) and Colton (for water molecules) have a function of membrane transporter and ion channels[6-10]. Systems Lewis (Leb e receptor for Helicobacter pylori), P (Parvovirus B19), Duffy (Plasmodium vivax, IL-8), Knops (complement receptor) have a function of receptor and ligands [11,12]. As adhesive molecules are known antigen complexes Lutheran system/B-CAM antigen-CD29, Landsteiner Wiener/ ICAM-4 CD242, CD44, etc.)[13,14].

Basic proteins for the structural integrity of the erythrocyte membrane are proteins from the Rh system and protein 3[15,16]. The Kell protein is considered a part of the M13 zinc-endopeptidases and converts endothelin 3 to its biologically active form, which has a role in the regulation of vascular tone, as well as in the contractility and proliferation of vascular smooth muscle[17].

The clinical significance of erythrocyte antigens is related to blood transfusion, pregnancy, tissue and organ transplantation. The recipient's immune system is challenged by blood cells that differ in terms of different antigenic systems (erythrocyte, leukocyte, platelet antigens, etc.) and a number of recipients will develop alloantibodies.

The incidence of erythrocyte alloimmunization is estimated to be from 2% to 10% and it can be much higher in patients who are chronically transfused and have a 3-4 times higher risk of developing other antibodies[18]. The most frequently identified antibodies have specificity to E, K, Fya, Kidd, s and C antigens. Clinically, erythrocyte alloimmunization leads to delayed transfusion therapy, hemolytic transfusion reactions (HTR), hemolytic disease of the fetus and newborn, and increased morbidity in organ transplantation. Hemolytic transfusion reactions are among the most common causes of immediate life-threatening transfusion-related events. Their incidence worldwide is about 1:4000-12000 units of blood[19].

The clinical importance of erythrocyte antigens is due to their immunogenic potential for the creation of alloantibodies, which is especially evident in patients who are on a chronic program for erythrocyte transfusion due to congenital or acquired hematological diseases, chronic renal failure, malignant diseases and other polytransfused patients. Often, one or a complex mixture of specific erythrocyte alloantibodies is detected, especially if they possess a rare blood group phenotype.

The Kell blood group system is considered the third clinically significant blood group system, due to the high immunogenicity of the antigens. Anti-Kell antibodies can cause a hemolytic transfusion reaction and hemolytic disease of the fetus and newborn (HDFN), where the antibodies suppress erythropoiesis and cause severe fetal anemia. The Kell protein is anchored to the erythrocyte surface and linked to the erythrocyte integral membrane protein XK by a single disulfide bond. XK is a transmembrane protein that crosses the erythrocyte membrane 10 times. If XK is absent, McLeod multisystem syndrome occurs. In McLeod syndrome, Kell antigens are only weakly expressed on erythrocytes. Anti-Ku antibody production in patients with a Ko(Kell-null) phenotype would result in a fatal hemolytic transfusion reaction in case of incompatible transfusion[20].

Duffy protein plays a role in inflammation and in malaria infection. The protein is a member of the chemokine receptor superfamily. Duffy-negative individuals, or Fy(a-b-), lack the Duffy protein on erythrocytes, a phenotype found predominantly in African-American blacks. They have the FYB(Es) allele with a mutation in the promoter region, which abolishes expression of the protein only on erythrocytes. In a few cases in non-black Fy(a-b-) individuals, this phenotype has been determined to be the result of nonsense mutations such that Duffy glycoprotein synthesis is prevented.

The functional role of the Kidd protein is a urea transporter in erythrocytes and kidneys. Recent discoveries have expanded the system, which now includes 23 variant alleles recognized by the ISBT that reduce protein expression and 7 variant alleles responsible for the production of weak or partial JK antigens. Null phenotypes have been identified in individuals from several populations, including those of African, Indian, and Chinese descent, in addition to well-documented findings in Polynesian and Finnish populations.

MNS is a second system in manner of complexity after the Rh blood group system. MNS antigens show a dose effect, that is, M and N antigens give a stronger reaction when they are in homozygous expression, (M+N-) or (M-N+). Weaker reactions occur when they are in heterozygous expression (M+N+). Antigens are destroyed if they are treated with enzymes. Many of the alloantibodies within the MNS blood group system are generally not clinically significant.

The Lutheran null phenotype, Lu(a–b–), is characterized by the lack of all antigens from the Lutheran system. It can result from recessive, dominant or X-linked inheritance. The Lutheran recessive type is the result of homozygosity for an inactive LU gene.

Blood group antigens are represented with different frequency in different populations. Antigens that are represented with a frequency below 1% are called low-frequency antigens, and those that are represented over 90% are called high-frequency antigens[21]. About 160 out of 380 blood group antigens are of high frequency, such as the Cellano (k) antigen which frequency is 99.8%[22]. Individuals who do not possess the k-antigen and possess the Kell (K) antigen in homozygous form (KK), are considered to have a rare blood type. In the case of transfusion, such individuals should receive erythrocytes that do not possess k-antigen because there is a high probability that erythrocytes given at random will possess k-antigen and lead to the formation of anti-k antibodies. In the absence of database of typed donors (K-antigen homozygotes) finding compatible blood for a patient with an antibody to a high-frequency antigen is a long-term process that greatly complicates transfusion treatment and increases morbidity.

The term "rare blood group" is defined according to the following criteria: absence of a high-frequency antigen (< 1/1000) within the general population (Vel-, Lan-, k- or Lub-), absence of more common antigens within one blood group system (D-c- or D+C+E+c-e-), absence of more frequent antigens within different blood group systems (O, e-, k-, Fyb-, Jka-, s-) or presence of the so-called null-phenotype characterized by the absence of part or all erythrocyte antigens[23-25].

The Kell system has a null phenotype (Ko) in which none of the Kell antigens are present. As a result of transfusion, Ko-individuals can develop an anti-Ku antibody which reacts with all erythrocytes except those with the Ko-phenotype and can cause a fatal hemolytic transfusion reaction[26,27].

In the rare McLeod phenotype, as part of the McLeod syndrome, antigens from the Kell system are very weakly expressed, while Km and Kx-antigens are absent. As a result of transfusion, patients with McLeod syndrome usually develop anti-Km and anti-Kx antibodies, making almost impossible to find a compatible donor[28].

In general, antibodies to high-frequency antigens are problem for blood transfusion due to the unavailability of compatible rare blood. Anti-k, anti-Lan and anti-Vel are particularly dangerous antibodies that can cause an immediate and severe hemolytic transfusion reaction[6].

In order to provide blood for the needs of patients with rare blood groups, in 1965, on the recommendation of the ISBT, the World Health Organization (WHO) established the so-called International Rare Blood Group Donor Panel (IRDP) within the International Blood Group Reference Laboratory (IBGRL) in UK.

The goal of the IRDP is to identify donors with rare blood groups and to facilitate international exchange for patients in need of rare blood transfusions[29]. The first panel consisting of 300 donors from 10 countries was published in 1968[30]. Today, the IRDP consists of about 8000 blood donors from 27 countries in which blood banks are stored frozen erythrocytes with rare phenotypes[31].

Erythrocyte alloimmunization and hemolytic transfusion reactions represent a current problem, both in the world and in our transfusion practice. The detection and identification of erythrocyte alloantibodies provides information about the selection of compatible blood for transfusion.

Extended erythrocyte typing within the Kell, Duffy, Kidd, MNS and Lutheran system will be the basis for finding compatible blood for patients who have a rare blood group or who are alloimmunized to one or more high-frequency erythrocyte antigens, which is a challenge for any transfusion facility.

With a pro-active approach to erythrocyte typing and the formation of a donor base with a certain antigenic profile, it will be possible, the blood to wait for the patient and not the other way around.

The aim of this study is to estimate RBC antigen frequency of clinically significant blood group systems such as Kell (K, k, Kpa, Kpb), Duffy (Fya, Fyb), Kidd (Jka, Jkb) MNS (S, s) and Lutheran (Lua, Lub) in our blood donors in order to identify rare blood group phenotypes.

Material and methods

Extended erythrocyte typing was performed in 920 voluntary blood donors. The criteria for the selection of donors included in the study were in accordance with the Law on safety in the blood supply in R. Macedonia from 2007, as well as with the recommendations for the selection of voluntary blood donors of the European Directorate for the Quality of Medical Products (EDQM) at the Council of Europe (CE).

Donors younger than 18 years and older than 65 years, as well as donors in whom reactivity was determined to blood transmisible microorganisms, such as HBV, HCV, HIV and Treponema pallidum, were not included in the study.

Blood samples for erythrocyte typing were taken in a test tube with EDTA in the amount of 4 ml. The samples were appropriately marked with a barcode that linked them to the donor's identification number.

Extended erythrocyte typing included determination of antigens K, k, Kpa, Kpb, Fya, Fyb, Jka, Jkb, S, s, Lua and Lub by microgel technique in a microtube or by column agglutination technique (CAT). Appropriate specific sera of monoclonal origin and gel cards containing polyspecific monoclonal anti-human globulin (Anti-IgG + C3d) incorporated in the gel are used (ID-Microtyping system BioRad). The test is based on the principle of indirect agglutination of the examined erythrocytes with the help of anti-human globulin, i.e., indirect antiglobulin test (IAT). The test procedure is as follows:

a). Preparation of 1.0% erythrocyte suspension by adding 10 µl of whole blood to 1000 µl of low ionic strength solution (LISS).

b). Pipette 50 µl of the erythrocyte suspension into the microtube chamber of the card and add 25 µl of the appropriate serum.

c). The card is incubated for 15 minutes at 37^{o}C and centrifuged for 10 minutes at 1000 revolutions per minute (rpm).

The interpretation of serological reactions is performed on the basis of the presence of agglutination (i.e., presence of antigen) or absence of agglutination (i.e., absence of antigen) on the membrane of the examined erythrocytes with the appropriate serum. The gel card result is considered positive if agglutinated cells form a red line on the surface of the gel or agglutinates are dispensed in the gel. The result is considered negative if a compact button of cells is formed on the bottom of the microtube.

The results are considered valid only if the positive and negative serum controls show a positive and negative reaction respectively. Direct antiglobulin test (DAT) was performed on each sample before phenotyping on the principle of indirect antiglobulin test (IAT) was performed (the erythrocytes that are phenotyped must have a negative DAT for the accuracy of the obtained results).

After interpretation and validation, the results were entered into the database for donors.

The estimation of frequency of antigens and phenotypes was performed by using the statistical processing modules of the donor information system.

Results

The results of routine blood group typing of antigens from the Kell system (K-KEL1, k-KEL2) are shown as well as the results of extended blood group typing of antigens Kpa-KEL3, Kpb-KEL4, Kidd (Jka-JK1, Jkb-JK2); Duffy (Fya-FY1, Fyb-FY2); Lutheran (Lua-LU1, Lub-LU2) and MNS (S-MNS3, s-MNS4).

The frequency of Kell (K or K1) and Cellano (k or K2) antigens of the Kell blood group system and Kell phenotype in 35017 typed blood donors, as well as the extremely rare expression of K antigen in homozygous form (K+k-) is shown in Table 1.

Kpa and Kpb (Kpa-KEL3, Kpb-KEL4) antigens were typed in 920 voluntary blood donors; their frequency is expressed in percentage.

Table 1. Frequency of Kell-antigens and phenotypes

Kell-antigen	Frequency (%)	Kell-phenotype	Frequency (%)
K	7.5	K+k-	0.06
K	99.94	K+k+	7.44
		K-k+	92.5
Kpa	1,1	Kpa+Kpb-	0.0
Kpb	100	Kpa+Kpb+	1.1
		Kpa-Kpb+	98.9

Table 2. Frequency of other clinically significant blood group antigens in blood donors

Antigen	Frequency (%)
Jk^a	60.26
Jk^b	76.2
Fy^a	65.5
Fy^b	79.5
S	59.8
S	86.5
Lu^a	7.2
Lu^b	92.8

Fig. 1. Positive and negative agglutination reactions

The prevalence of Kell antigens is 7.5% for K and 99.94% for k. The rare Kell phenotype (K+k-) is present in 21 (0.06%) blood donors (Table 1). Erythrocytes with this rare phenotype are necessary for transfusion of alloimmunized patients who have developed anti-k antibodies.

The frequency of antigens from other clinically significant blood group systems, such as Kidd (Jka, Jkb), Duffy (Fya, Fyb), MNS (S, s) and Lutheran (Lua, Lub) in 920 blood donors is shown in Table 2. Of the examined donors, 736 (80%) were men, and 184 (20%) women. The average age of donors was 35.4 years.

The frequencies of certain phenotypes within the mentioned blood group systems are shown in Tables 3, 4, 5, 6 and 7.

Table 3. Frequency of other Kell-phenotypes

Phenotype	Kp(a+b−)	Kp(a−b+)	Kp(a+b+)	Kp(a−b−)
Frequency (%)	0	98.9	1.1	0

Table 4. Frequency of Kidd-phenotypes

Phenotype	Jk(a+b−)	Jk(a−b+)	Jk(a+b+)	Jk(a−b−)
Frequency (%)	23.58	34.9	41.48	0

Table 5. Frequency of Duffy-phenotypes

Phenotype	Fy(a+b−)	Fy(a−b+)	Fy(a+b+)	Fy(a−b−)
Frequency (%)	20.32	31.0	48.47	0.21

Table 6. Frequency of MNS-phenotypes

Phenotype	(S+s−)	(S−s+)	(S+s+)	(S−s−)
Frequency (%)	13.5	40.2	46.3	0

Table 7. Frequency of Lutheran-phenotypes

Phenotype	Lu(a+b−)	Lu(a−b+)	Lu(a+b+)	Lu(a−b−)
Frequency (%)	0	92.8	7.2	0

In all blood samples that were subjected to serological blood group typing based on the principle of IAT, the direct antiglobulin test (DAT) was negative, which is a prerequisite for the accuracy of the obtained results.

Each batch of tested blood samples included positive and negative control of the specific serum with test erythrocytes that are antigen-positive, in heterozygous form and antigen-negative for the tested antigen, respectively.

The results of the extended blood group typing were entered into the database for donors, as shown in Figure 2. It allows the search of the register when the required antigenic profile is entered in the appropriate module and a list of potential blood donors with a certain phenotype is generated (Figure 3).

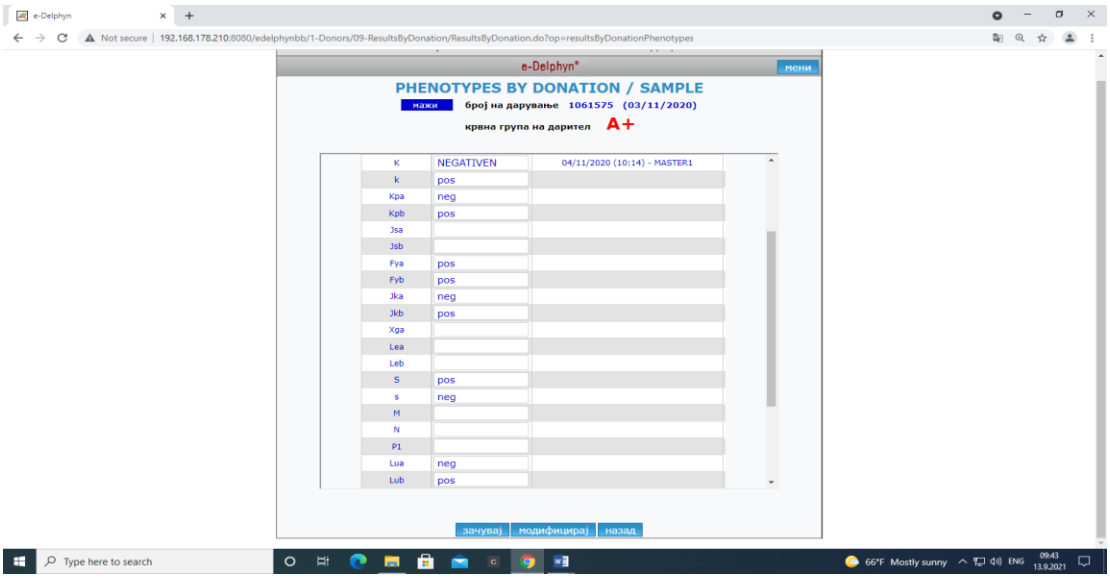

Fig 2. Records of RBC typing results in the information system

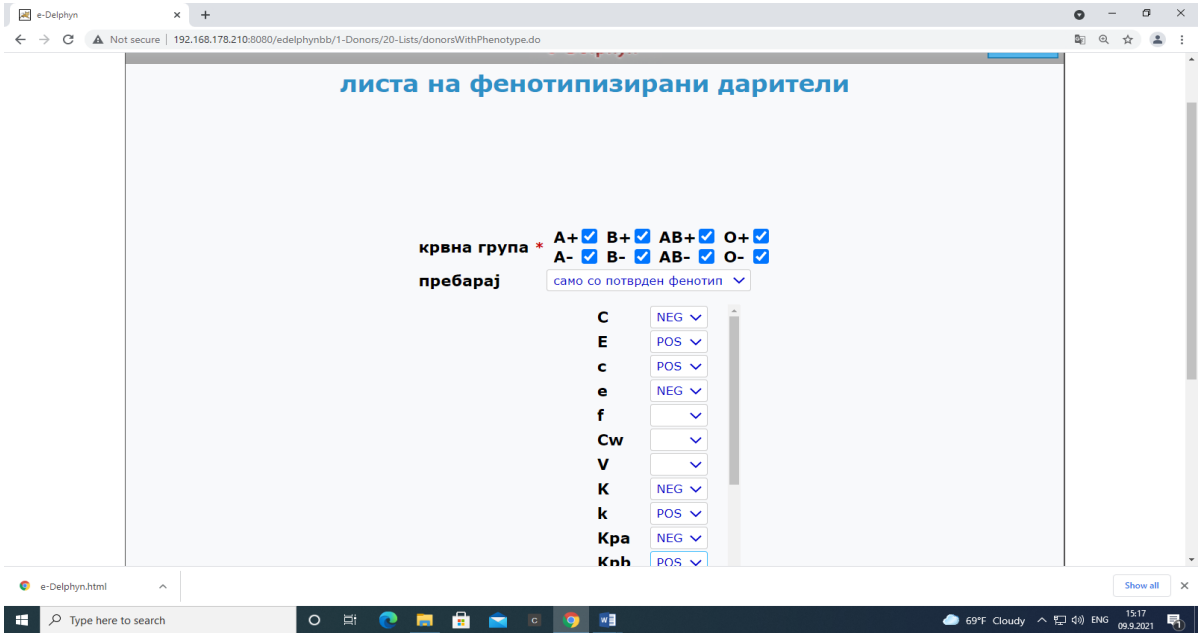

Fig 3. Blood donor search for a specific RBC phenotype

Discussion

The results of our study showed that there was a difference in the determined frequency of certain erythrocyte antigens in relation to African, Indian, Chinese and European populations.

In our study the prevalence of K antigen is 7.5%, which is lower than the prevalence of 9% in Caucasians. It differs significantly in relation to the Black race (2%) and the Arab population, in which the K antigen is represented by 25%[32,33]. The representation of the K-k+ (kk) phenotype in our study is 92.5%, which is similar to Caucasians with 91%. The frequency

of K-k+ (kk) is 98% in the Black race. The frequency of K+k- (KK) is 0.06% in our population and is much lower compared to the frequency of 0.2% in the Caucasians, while it is almost not present in the Black race.

Similar to our donor population, the high-frequency Kpb antigen is present in 97.7% of Caucasians and 100% in Blacks. The homozygous Kpa antigen expression is very rare, and in combination with the Kpb antigen it is present in 2.3% of the Caucasians[32]. The absence of the K-antigen is characteristic for the Japanese population, so that its allelic antigen k (K-k+ phenotype) is present in almost 100% which is similar to the Chinese population[33,34].

Jka and Jkb antigens have similar prevalence in Caucasian and Asian populations. Jka is much more common in the Black race than Jkb. Jk(a-b-) represents a null phenotype that is rare in most populations, but has an increased prevalence of 0.9% to 1.4% in Polynesia [32,34,35]. Anti-Jk3 is a very rare antibody found in alloimmunized patients with the Jk(a–b–) phenotype that can lead to an acute and delayed hemolytic transfusion reaction (HTR), necessitating the provision of rare phenotype blood for transfusion Jk(a–b–) [25]. According to the results of our study, the Jk (a-b+) phenotype is represented significantly more often (35%) compared to the frequency in the Caucasian race.

Table 8. Frequency of Kidd-phenotype in different populations

Phenotype	Caucasians (%)	Black race (%)	Asia (%)
$Jk^a + Jk^b–$	26	52	23
$Jk^a + Jk^b+$	50	40	50
$Jk^a–Jk^b+$	24	8	27

Differences in distribution of Duffy antigens became known in 1954 with the discovery that 68% of African Americans and 88-100% of Africans have the Fy(a-b-) phenotype[32]. Duffy-null phenotype Fy(a-b-) is also present in 61% of blood donors in Saudi Arabia[36-38].

This phenotype is extremely rare in the Caucasian race. In our donor population, the Fy(a-b-) phenotype is represented by 0.21%. Such individuals may develop a rare anti-Fy3 antibody that reacts with all erythrocytes except those with the Fy(a–b–) phenotype. This antibody causes acute or delayed HTR, so rare Duffy-antigen negative blood must be provided for transfusion[38].

The frequency of Fya and Fyb antigens in our population is similar with Caucasian where the frequency is about 66% and 83%, respectively, but differs from Asians and the Black race where the frequency is 99% and 18.5%, and 10% and 23%, respectively [36]. The frequency of the Fy(a+b+) phenotype is 49% in the Caucasians, 1% in the Black race and 9% in the Chinese. The frequency of the Fy(a-b+) phenotype is 34% in Caucasians, 22% in Blacks, and <1% in Chinese. The frequency of the Fy(a+b-) phenotype is 17% in Caucasians, 9% in Blacks and 91% in Chinese[34,38].

The frequency of antigens from the MNS system in Caucasians is: M-78%, N- 72%, S-55%, s-89%, while in the Black race it is: M-74%, N-75%, S- 31% and s-93% [32]. The phenotypes M+N-S-s-, M+N+S-s-, and M-N+S-s- are rare in Caucasians, but occur with a frequency of about 0.5% in the Black race[32,38].

In our study, the Lu(a+b+) phenotype is represented by 7.2%, which is very similar to the frequency in Caucasians where it is represented by 7.5%. The Lu(a-b+) phenotype, with a

frequency of 92.8%, is most frequently found in our population and can be compared to a frequency of 92.35% in Caucasians[32]. The Lu(a+b-) phenotype is very rare, accounting for 0% in our study and 0.15% in Caucasians. Thus, the total frequency of the Lub antigen in our study is 100%, which is very similar to that of Caucasians (99.85%)[33]. The Lu(a-b-) phenotype in Caucasians is very rare, while different studies of Indian population which is also part of Caucasians report a frequency of 2.61% and 3.15%[19, 37].

There are other blood group systems, such as the Dombrock and Colton systems, with less clinical significance because antibodies rarely cause a hemolytic transfusion reaction. The blood group systems Landsteiner-Wiener, Sciana, Yt, Gerbich, Cromer, Cnops, Indidian are not clinically significant for blood transfusion and pregnancy because alloantibodies that cause a hemolytic reaction have not been described. Therefore, antigens from systems that have no clinical significance are not included in routine erythrocyte test panels for antibody identification, nor are a subject to extended erythrocyte typing in blood donors.

The enzyme-converting strategy was proposed to overcome the barrier of ABO-incompatibility in organ transplantation[38]. To obtain universally compatible erythrocytes, a strategy was proposed for masking antigens using polyethylene glycol, as well as in vitro production of erythrocytes with a previously defined antigenic profile, from genetically modified stem cells[39].

Such approaches to overcome the differences in the erythrocyte antigenic profile between the donor and the recipient are still in the experimental phase, so attention of today's transfusion practice is focused on the most accurate erythrocyte typing[40]. Molecular testing is more accurate compared to serological testing and today has a wide application in genotyping of blood group antigens. With molecular technique, multiple clinically relevant antigens that are not included in routine ABO and Rh typing can be simultaneously tested, which makes it practical and more accessible, especially for polytransfused and alloimmunized patients[40-42]. Molecular tests are also increasingly used to identify rare blood group antigens[43].

Comparative studies have shown that the results of serological typing are consistent with those of molecular typing depending on the availability of quality specific sera. But, in cases where testing of a large number of antigens and a large number of samples is required at the same time, such as in the case of donor typing for a registry of rare blood groups, the molecular method is far more practical and cost-effective[44]. The existence of a register of donors with rare blood groups that are typed by a molecular method also offers the opportunity for the blood banks to create their own panel of test erythrocytes for screening and identification of anti-erythrocyte antibodies.

Blood groups are represented differently in different populations and different ethnic groups, which is why finding a donor with a suitable phenotype can be challenging. Blood units (erythrocytes) from such donors can be kept frozen for future use. For this purpose, the existence of an international database of donors with rare blood groups is necessary to promptly meet the need for transfusion.

Conclusion

The estimated RBC antigen frequency in our blood donor population differs from the antigen frequency in different populations. Therefore, RBC typing for clinically significant antigens is necessary for identifying rare blood group donors within the local population. Large scale extended blood group phenotyping or genotyping enables identification of blood donors

with rare blood groups for patients with rare phenotypes, with antibodies to high-frequency antigens or with multiple antibodies to antigens within one or more blood group systems.

For patients who need chronic transfusion, the database of typed blood donors will ensure regular and on time provision of antigen matched RBC compatible blood units, starting from the first transfusion, which will significantly reduce the rate of erythrocyte alloimmunization as well as morbidity related to hemolytic transfusion reactions.

Conflict of interest statement. None declared.

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