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RARE BLOOD GROUPS IN ABO, RH, KELL SYSTEMS – BIOLOGICAL AND CLINICAL SIGNIFICANCE

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ABSTRACT

Background: The frequency of ABO, Rh and Kell blood group antigens differs among populations of different ethnic ancestry. There are low-frequency antigens (<1%) and high-frequency antigens (>90%). A rare blood group is defined as the absence of a high-frequency antigen in the general population, as well as absence of multiple frequent antigens within a single or multiple blood group systems.

Aim: To perform red blood cell typing and to calculate the antigen and phenotype frequencies, in order to identify rare blood group donors within the clinically most important ABO, Rh and Kell systems.

Material and Methods: ABO, Rh (D, C, E, c, e) and Kell (K) antigen typing was performed using specific monoclonal sera and microplate technique, while Cellano (k) typing was performed with a monoclonal anti-k, antihuman globulin and column agglutination technique. Weak ABO subgroups were determined using the absorption elution method or molecular genotyping (PCR-SSP).

Results: ABO antigen frequency is: A (40.89%), O (34.22%), B (16.97%), AB (7.92%) and weak ABO subgroups (0, 009 %). The established genotypes were AxO1 (0, 0026%) and AxB (0, 001%). Rh antigen frequency is: D (85.79%), C (71.7%), c (76.0%), E (26.0%) and e (97.95%). The most common Rh phenotype is the DCcee (32.7%) while the rarest phenotype is the DCCEE phenotype (0. 003%). The prevalence of K and k antigen is 7.5% and 99.94%, respectively. The frequency of the rare phenotype K+k- is 0.06%.

Conclusion: Large scale phenotyping of blood group antigens enables the identification of blood donors with rare blood groups for patients with rare phenotypes or with antibodies to high-frequency antigens and to frequent antigens within one or more blood group systems.

Keywords: rare blood group, red blood cell antigen frequency, blood donor registry

INTRODUCTION

The term "blood group" refers to a certain blood group system which contains red blood cell antigens under the control of serial allelic genes or genes which are very closely linked via the chromosome. The term "blood group phenotype" refers to a specific pattern of antigen reactions within the specific sera. According to the International Society of Blood Transfusion, red blood cell antigens are classified in 38 blood group systems, with more than 340 RBC anti-

gens, from which ABO, Rh, Kell, Duffy, Kidd, Lutheran and MNS are clinically the most important for transfusion, pregnancy and transplantation.

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 RBC, as for the human organism in general.

The structures and functions of the RBC antigens and, the correlation of blood group antigens with some conditions and diseases is well established, especially the antigens of the ABO, Rh and Kell systems [1].

The ABO blood group system has a great impact on blood coagulation [2]. The ABO genotype determines the plasma level of the von Willebrand factor (vWF), a glycoprotein which takes part in blood coagulation, and is 25-30% lower in blood group O individuals in comparison to other blood groups who have no greater risk of bleeding [3]. In individuals who are in the non-O blood groups, a greater risk for arterial and venous thromboembolism has been established, especially according to their ABO genotype [4, 5]. The AB blood group is associated with a two-fold greater risk of preeclampsia [6]. Some studies have shown the association of the ABO blood group with malignant diseases [7]. The A blood group is associated with a greater risk of gastric and colon cancer [8]. The risk of pancreatic cancer is less in blood O individuals [9]. The B antigen is associated with a greater risk of ovarian cancer [10]. In rare cases of colorectal malignancy, individuals which are in the A blood group may have so called acquired the B antigen and their phenotype may be similar to AB blood group [11]. In some malignant blood diseases, the expression of ABO antigens may be changed. Weak expression of the A, B, and H antigen has been reported in 17% to 37% of the patients with different types of leukaemia [12,13].

The association of RBC antigens and susceptibility to infection has been well established. Individuals in the O blood group are protected from heavy forms of malaria, caused by plasmodium falciparum, but they have a greater risk of infection, caused by Vibrio cholera type 01, while AB individuals are less susceptible [14, 15]. ABO antigens and antibodies have a modulatory effect on the SARS-Cov-2 infection as well as on the outcome of the COVID-19 [16].

ABO subgroups are characterised by different expressions of the antigens, such as A1 A2, A 3, A x, A end, A m, Ael. B3, Bx, Bm, Bel, AxB, A1Bx, AmB, A1Bm, AelB, A1Bel, cisA2B3, cisA2B, cisA1B3. Except for A1, A2, A1B and A2B, other ABO subgroups have very weak A or B antigen expression and are very rare. They may have clinical significance if irregular natural anti-A1 antibodies, reactive at 37oC, are present. Should this be the case, an RBC with the A2 phenotype must be provided for transfusion. A subgroups are more frequent in whites, while B subgroups are more frequent among the Japanese population [17].

There are rare phenotypes (Rh-null, McLeod) as a result of deletions or inactivating mutations in the genes of the Rh, Kell and Kx blood group systems. The Kx gene encodes the RBC membrane structural proteins and an absent expression of the Kx antigen is associated with stomatocytosis, acanthocytosis, and haemolytic anemia [18, 19].

ABO, Rh and Kell blood group antigens have the greatest clinical significance. The ABO system is characterised by natural anti-A and anti-B antibodies which are responsible for acute haemolytic transfusion reactions in the case of ABO incompatible blood transfusion. Rh (D, E, C, c, e) and Kell (K, k) antigens, however, are immunogenic and represent the most frequent reason for RBC alloimmunization associated with RBC transfusion and pregnancy. The incidence of RBC alloimmunizataion in general is 2-10% and it can be up to 60% in some groups of multi-transfused patients [20]. RBC compatibility in ABO, Rh, and Kell system provides prevention of most of the alloimmunizations and consequently haemolytic transfusion reactions; these have an incidence of about 1:4000-12000 blood transfusions [21].

The frequency of the blood group antigens from ABO, Rh and Kell blood group systems differs among populations from different ethnic ancestries. The antigens which have an incidence below <1% are low-frequency antigens, and those which have a frequency >90% are high-frequency antigens [22]. The term "rare blood group" is defined by the following criteria: the absence of a high-frequency antigen among the general population (Vel-, k- or Lub-), the absence of multiple frequent antigens within a sin-

gle blood group system (D-c- or D+C+E+c-e-) or the absence of multiple frequent antigens within different blood systems (O, e-, k-, Fyb-, Jka-, s-) [24,25]. About 160 of 340 blood group antigens are high frequency antigens, such as the Cellano (k) antigen with a frequency of 99, 8% [23]. That is why it is very difficult to provide homozygous (K+k) red blood cells for patients with anti-k antibodies, especially in the absence of rare blood groups in the donor registry.

The individuals with null RBC phenotypes which are characterised with the absence of part or all of the antigens of a certain blood group system can form cross-reactive antibodies which react with all human RBC except with those with the same rare null phenotype, which makes the provision of compatible blood in case of transfusion very difficult [26].

Rh-null phenotype, discovered for the first time in 1961 among the Aborigines in Australia, is the rarest blood group and has been identified in about 50 individuals worldwide. Blood donations with this phenotype are from a small network of 9 regular blood donors and are intended for patients with the same phenotype [27, 28]. Individuals with the Rh-null phenotype form the anti-Rh29 antibody. This antibody reacts with epitopes common for the two Rh proteins (RhD and RhCE) on human RBC except with those with the same null phenotype [26,29]. This antibody can cause a severe haemolytic transfusion reaction, as well as haemolytic disease of the new-born [30].

The RBC of individuals with the Kell null phenotype (Ko) possess no Kell antigens, and after transfusion they can produce the anti-Ku antibody which reacts with all human RBC except with those with the Ko phenotype. This antibody can also cause fatal haemolytic transfusion reaction [31,32].

In individuals with the rare McLeod phenotype, antigens of the Kell system have a very weak expression, and Km and Kx antigens are absent. These individuals produce anti-Kx and anti-Km antibodies due to transfusion which makes the availability of compatible blood donors practically impossible [33].

Another rare blood group is the so-called Bombay phenotype or Oh. In the general population the Oh frequency is 0.0004%, while in some parts of India the frequency is 0.01% or 1 in 10,000 [34]. Individuals with Oh phenotype possess natural anti-H, anti-A, and anti-B antibodies which cause severe haemolytic transfusion reactions with all RBC groups except with those of the Oh-phenotype. This further complicates blood transfusion. [35].

In order to provide compatible blood for transfusion for the patients with rare blood groups and to enable international blood exchange, the World Health Organization established the International Rare Donor Panel (IRDP) in 1965. This was completed under the responsibility of the International Reference Blood Group Laboratory (IBGRL) in Great Britain. [36]. The first panel, which consisted of 300 blood donors from 10 countries, was established in 1968 [37]. Today, the IRDP consists of about 8000 blood donors from 27 countries in which there are blood banks, where frozen RBCs with rare blood groups are stored [38].

In the Information system of the Institute for transfusion medicine in Skopje, there are more than 70. 000 registered blood donors with their determined ABO, Rh (D, C, c, E, e) and Kell (K,k) antigens. This blood typing strategy is sufficient for most of the alloimmunized patients because about 60% of the identified antibodies are directed to the above-mentioned antigens [39].

The aim of this study is to determine the antigen frequency of the common and rare blood groups within the ABO, Rh and Kell blood system in our donor population with the intention to promote the establishment of a rare blood donor registry. This is the only option for the patients with a rare blood group or with antibodies to one or more high frequency antigens, and this is also a challenge for every blood transfusion facility.

MATERIALS AND METHODS

In 75,528, 28,946 and 35,017 of the registered blood donors, ABO/D, Rh (C, E, c, e) and Kell (K, k) antigens were found in the period of 2016 to 2021. We analysed the antigen frequency using data from the donor information system.

For the purpose of antigen typing, a blood sample of 5 mL was collected at the time of donation into a tube containing ethylenediaminetetraacetic acid (EDTA) and was identified with bar-coded number which connects the donor ID and the donation.

Blood typing was performed using serologic methods such as the microplate (MP) technique (DiaMed-MP Test) with different antigen/antibody profiles (MP-A, B, AB, DVI-, DVI+, ctl/A1, B and MP-C, c, E, e, K, ctl). The test is based on the direct agglutination of the RBC with the corresponding antigen by the specific sera. K (K1) antigen positive samples were further subjected to k (K2) antigen typing, using monoclonal anti-k sera, antihuman globulin (AHG) and the column agglutination technique (CAT). The test is based on the indirect agglutination of the RBC with the corresponding antigen by the specific sera and AHG.

If agglutination is present, there is a positive reaction (antigen/antibody is present) and the absence of agglutination provides a negative reaction (antigen/antibody is absent). Internal control using QS samples was also included.

ABO subgroups were determined by, using the absorption elution method or via the molecular genotyping technique. The ABO genotype was determined by 8 parallel PCR-SSP reactions in order to amplify exons 6 and 7 of the ABO blood group gene.

Upon validation, the results were transferred into the donor information system. Antigen frequency was calculated using a statistics-operating module from the donor information system.

RESULTS

Antigen frequency of ABO, Rh (D-RH1, C-RH2, c-RH4, E-RH3, e-RH5) and Kell (K-KEL1, k-KEL2) is shown in tables 1-5. The ABO antigen frequency among 75,528 blood donors is shown on table 1. There are 57,197 (75.73%) male and 18,331 (24.27%) female donors. The RhD antigen is present in 64,793 (85.79%) donors, referred as RhD positive, whereas the antigen is absent in 10,734 (14.21%) donors who are RhD negative.

Table 1. *ABO frequency*

Blood group	Frequency (%)
A	40.89
O	34.22
B	16.97
AB	7.92

The total number of those who were identified as belonging to the low ABO subgroups, with very weak A antigen expression, was 7 out of 75,528 blood donors (0, 009%). Three donors were classified in the A3 subgroup and one in the A3B subgroup, according to their very weak reactions with anti-A sera. The samples of the rest of the donors (three of them) were subjected to molecular genotyping, as there was no reaction with anti-A serum. The established genotypes were two belonging to the AxO1 (0, 0026 %) genotype and one belonging to AxB (0, 001 %) genotype. Irregular anti-A1 antibodies (non reactive at 37oC) were identified in 2 (0, 0026 %) donors, both with the AxO1 genotype.

Table 2. *Rare ABO phenotypes frequency*

Blood subgroup (phenotype)	Blood subgroup (genotype)	Frequency No (%)
A_3	not performed	3 (0.0039)
A_x	A_xO_1	2 (0.0026)
A_3B	not performed	1 (0.001)
AxB	A_xB	1 (0.001)
Total		7 (0.009)

The frequency of clinically significant Rh antigens among 28,946 blood donors is shown in table 3.

Table 3. *Rh antigen frequency*

Antigen	Frequency (%)
D (RH1)	85.79
C (RH2)	71.7
c (RH4)	76.0
E (RH3)	26.0
e (RH5)	97.95

Among the Rh positive phenotypes with D, C, or E antigens, most frequent phenotype is DCcee, at 32.7%, and the least frequent is the DCCEE phenotype at 0.003%. The frequency of the most common Rh negative phenotype ddccee at 15.1%, as it is shown in table 4.

Rh phenotypes with homozygous expression of the E antigen are considered to be rare because of their frequency in the presence of the D and C antigens is < 1%. RBC with such phenotypes are compatible for patients with the anti-e

antibody and are difficult to provide, especially if the patient is RhD negative (Table 4).

The Kell antigen and phenotype frequency among 35,017 blood donors is shown in table 5.

Table 4. *Rh phenotype frequency*

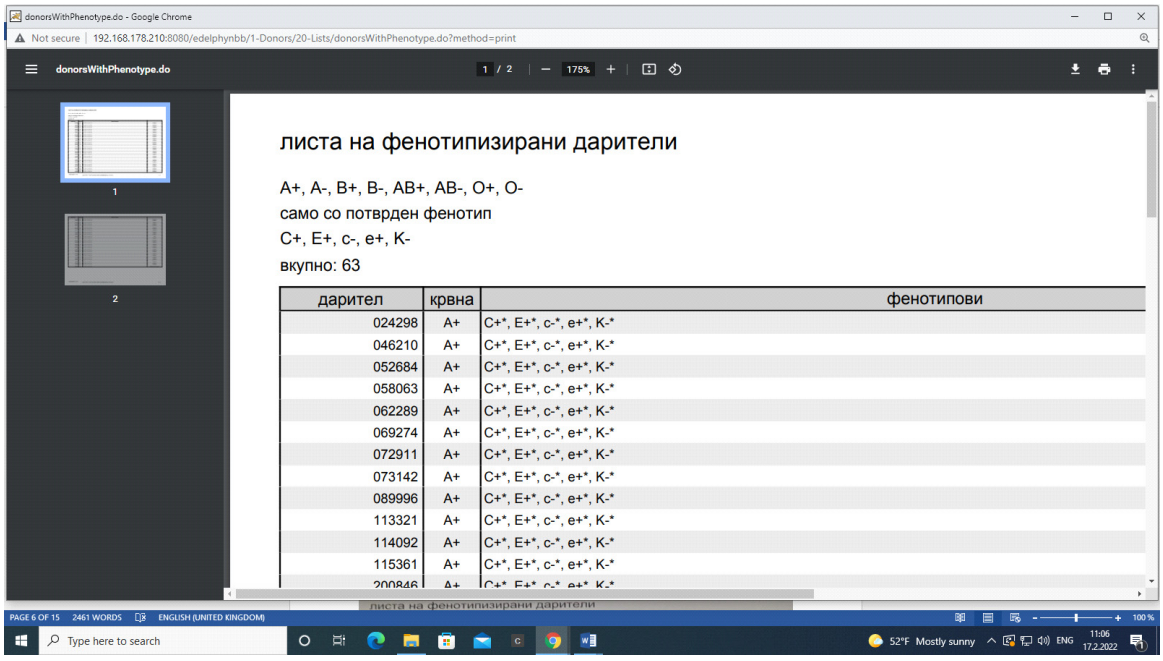
Rh-phenotype	Frequency (%)	Rh-phenotype	Frequency(%)
DCcee	32.7	ddccee	15.1
DCCee	23.7	ddCcee	1.28
DCcEe	13.7	ddccEe	0.2
DccEe	9.7	ddCCee	0.03
DccEE	1.9	ddCcEe	0.007
Dccee	1.2	ddccEE	0
DCCEe	0.2	ddCcEE	0
DCcEE	0.04	ddCCEE	0
DCCEE	0.003	ddCCEe	0

Table 5. *Kell-antigen and phenotype frequency*

Kell-antigen	Frequency (%)	Kell-phenotype	Frequency (%)
K (KEL1)	7.5	K+k-	0.06
k (KEL2)	99.94	K+k+	7.44
		K-k+	92.5

Kell phenotypes with the homozygous expression of the K antigen (K+k-) are considered to be rare, since their frequency is < 1%. In our donor population, the frequency of this phenotype is 0.06%. There are 21 regular blood donors typed as having the K+k- phenotype of all ABO blood groups in our donor registry. Their RBCs are the only compatible choice for patients with anti-k antibodies, and thus are directed to k antigen, which is present in 99.94% of the donors.

The donor information system enables centres to find a suitable donor from the register of phenotyped donors, and it generates a list of potential blood donors, according to the antigen profile of the patient (Figure 1).



DISCUSSION

Population studies have shown that there are significant differences in the erythrocyte antigens distribution in various ethnic groups. By comparing the Macedonian population with the general Caucasian population, the ABO antigen frequency differs except for the A antigen, which is not the case when comparing the ABO frequency in Britain with the general Caucasian population, as they are similar. The estimated ABO frequency in our study differs even more in comparison to the frequency reported for the African and Asian population as well as other groups within the Caucasian population (Table 6) [40, 41].

In the general Caucasian population, the frequency of Rh antigens D, C, c, E and e is 85%, 70%, 80%, 30% and 98% respectively, which is similar to our population [42]. In the Indian population, although also Caucasian, the Rh antigen frequency (93.6% - D, 87% - C, 20.0% - E, 58% - c) significantly differs in comparison to our population, with the exception of the Rh e antigen, with a similar frequency of 98.0% [43]. The most frequent Rh phenotype in our population is DCcee (32.7%), which is present only in 23.5% in the Indian population. The most frequent Rh phenotype in the Indian population is DCCee (40.87%) [44].

The prevalence of the K antigen in our study is 7.5%, whereas it is 9% in the general Caucasian population, 2% in Blacks, and 25% in the Arabic population [45]. The most common Kell phenotype is K-k+, not just in our donor population (92.5%) but also among Caucasians (91%), Blacks (98%) and Chinese (100%). In our study, the frequency of the rare K+k- phenotype is 0.06% in comparison with 0.2% in Caucasian population in general while it is almost absent in the Chinese population[46].

Demographic changes to our population may have had an impact on the RBC antigen frequency, which is shown in two antigen frequency studies performed in 1992 and 2009 on 1000 and 1600 blood donors from our donor population [39, 47, 48]. The comparative frequency of ABO, Rh, and Kell antigens is shown on tables 7–10.

There is no significant variation in the ABO distribution over the last 30 years in our donor population, except for the B blood group, where a slight increment is observed.

Table 6. *ABO distribution in different populations*

Blood group	Macedonia (%)	Caucasian* (%)	Britain (%)	Black (%)	Latino (%)	Asian (%)
O	33	45	47	50	57	43
A	41	43	42	26	31	27
B	18	9	8	20	10	25
AB	8	4	3	4	3	5

* General Caucasian population

Table 7. *Comparative ABO frequency*

Blood group	Current study(%)	Study 2009 (%)	Study 1992 (%)	Caucasian*(%)
O	33	38	35	45
A	41	39	40	43
B	18	14	16	9
AB	8	7	8	4

* General Caucasian population

Table 8. *Comparative Rh antigen frequency*

Antigen	Current study (%)	Study 2009 (%)	Study 1992 (%)	Caucasian* (%)
D (RH1)	86	79	86	85
C (RH2)	72	58	73	70
c (RH4)	76	82	80	80
E (RH3)	26	21	31	30
e (RH5)	98	97	95	98

* General Caucasian population

Table 9. *Comparative Kell system antigen frequency*

Antigen	Current study (%)	Study 2009 (%)	Study 1992 (%)	Caucasian*(%)
K (KEL1)	7.5	6.31	8.1	9.0
k (KEL2)	99.94	99.49	99.0	99.8

* General Caucasian population

Table 10. *Comparative Kell phenotype frequency*

Phenotype	Current study (%)	Study 2009 (%)	Study 1992 (%)	Caucasian* (%)
(K+ k-)	0.06	0.5	1.0	0.2
(K+ k+)	7.44	5.81	7.1	8.8
(K- k+)	92.5	93.68	91.9	91.0

* General Caucasian population

There is no significant variation observed in the distribution of the antigens of Rh blood group system in the last 30 years in our donor population, except for the C antigen where a frequency of 58% was observed in 2009 (Table 8).

Concerning the Kell system antigens, the homozygous expression of the K antigen (K+k-) is significantly lower in comparison to the previous studies of our population (table 10). This can be explained with the introduction of the micro-agglutination technique for RBC antigen typing which is more sensitive and specific in comparison to the previous tube method, as well as the fact that a very large number of more than 35,000 donors were typed for Kell system antigens in the current study (table 9).

Several strategies have been proposed in order to prevent immunological recognition of incompatible RBC antigens and to avoid haemolytic transfusion reactions. One of these strategies is based on technology which involves the enzymatic conversion of glucopolysaccharide A and B antigen in order to obtain "universal" O red blood cells using enzymes such as galactosidase and N-acetylgalactosaminidase [49, 50, 51]. This strategy has also been proposed to overcome ABO incompatibility in organ transplantation [52]. Another strategy for universally compatible RBCs is to mask RBC antigens with polyethylene glycol, as well as the in vitro production of RBCs with a predefined antigen profile from genetically modified stem cells. [53, 54, 55].

The concepts of universal RBC are still in the experimental phase, thus turning the attention of the current transfusion practice towards molecular red blood cell typing. This is more precise then serologic typing, especially in the context of large scale donor typing. Single nucleotide polymorphisms of blood group alleles can be determined with PCR-primer specific sequence techniques and can be used for simultaneous typing of multiple red blood cell antigens which are not included in the routine typing. Currently, blood group genotyping is widely performed on blood donors for the purposes of rare phenotype detection, in polytransfused patients, and in patients with multiple red cell alloantibodies, as well as for obtaining typed panel-test RBCs for antibody identification [56, 57].

According to the previous antigen frequency studies performed on our blood donors and transfused patients, there is no significant difference between the two groups in the estimated frequency of the clinically significant red blood cell antigens (ABO, Rh, Kell), except for the frequency of RhE which was found to be lower (13.5%) in polytransfused patients in comparison to blood donors (21.3%). The corresponding alloantibody (anti-E) was most frequent (35.7%) in comparison to all identified alloantibodies in polytransfused patients, followed by anti-K with the frequency of 26.5% [47].

What is, then, the potential impact of the estimated RBC antigen frequencies in this study on our transfusion practices? We must also, keep in mind that blood donors can represent the general population. ABO subgroups have no impact on transfusion practice, except in cases where warm reactive irregular anti-A1 is present and RBC with the A2 phenotype are compatible for transfusion. This is not a transfusion problem, as the frequency of A2 is 3.8% in our blood donors with A blood group, and the frequency of A2B is 1.25% in our AB blood group donors. Concerning low ABO subgroups, a transfusion recipient

could safely receive O red cells, which is not a case if the recipient is of the Oh (Bombay) phenotype. This phenotype has not been identified neither in our blood donors and nor in our blood recipients. According to the estimated Rh phenotype frequencies in this study, transfusion needs can be achieved for most of patients with rare anti-e antibodies, even in combination with anti-c, except for those who are RhD negative, as shown on table 4.

This study revealed the presence of the rare K+k- phenotype in 21 (0.06%) of the typed blood donors from all ABO groups, including O RhD positive and negative donors, who are active and can be invited to donate blood for patients with the same rare phenotype and with anti-k antibodies. As we have no identified donors with rare Oh, Rh-null and Ko phenotype, we should establish collaboration with the IRDP and IBGRL for blood provision if a rare blood group is in need.

The introduction of the donor information system in 2016 enabled more extensive blood typing and better management of data on RBC frequencies, as well as donor follow up when a specific blood type is needed. Our goal is to improve future blood transfusion practices by further large scale blood typing, not only within ABO, Rh, and Kell, but also in the other clinically significant blood group systems (Kidd, Duffy, Lutheran, MNS, etc.), all relevant to our population, possibly in combination with RBC cryopreservation.

CONCLUSION

Our blood donor registry is comprised of donors with rare blood group phenotypes within the ABO, Rh, and Kell system. This, is not enough to meet the need for compatible blood when another rare blood group is concerned or when antibodies to the other high frequency erythrocyte antigens are present.

In order to achieve large scale typing of multiple red blood cell antigens, which are not included in routine typing, it is necessary to implement a molecular technique as a prerequisite of a rare donor registry establishment. The existence of a rare blood donor registry improves the quality of blood transfusion practice for patients with high-frequency-antigen-negative and multiple-common-antigen-negative blood groups.

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Резиме

РЕТКИ КРВНИ ГРУПИ ОД СИСТЕМИТЕ ABO, RH, KELL – БИОЛОШКО И КЛИНИЧКО ЗНАЧЕЊЕ

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Вовед: Еритроцитните антигени од ABO, Rh и Kell-системот се застапени со различна фреквенција во различни популации. Антигените со фреквенција < 1 % се со ниска фреквенција, а оние со > 90 % се високофреквентни антигени. Поимот „ретка крвна група“ подразбира отсуство на високофреквентен антиген во општата популација или отсуство на повеќе чести антигени во рамките на еден или на повеќе крвногрупни системи.

Цел: Еритроцитна типизација и утврдувањето антигенска и фенотипска фреквенција за идентификација на дарители со ретки крвни групи од клинички најзначајните системи ABO, Rh и Kell.

Материјал и методи: Типизација на ABO, Rh (D, C, c, E, e) и Kell (K) антигени кај дарители на крв со моноклонални серуми и техника на микроплоча. Типизација на к (K) антиген со моноклонален анти-к-серум, антихуман глобулин и микроаглутинирачка техника. Слабите ABO-подгрупи беа одредени со метода на апсорпција и елуција или со молекуларна метода (PCR-SSP).

Резултати: ABO-антигенската фреквенција изнесува: A (40,89 %), O (34,22 %), B (16,97 %), AB (7,92 %) и ABO-подгрупи (0,009 %). Утврдените генотипови беа AxO1 (0,0026 %) и AxB (0,001 %). Rh-антигенската фреквенција изнесува: D (85,79 %), C (71,7 %), c (76 %), E (26 %), e (97,95 %). Најчест Rh-фенотип е DCcee (32,7 %), а најредок фенотип е DCCEE (0,003 %). Фреквенцијата на K- и k-антигенот изнесува 7,5 % и 99,94 %, соодветно. Реткиот фенотип K+k- е застапен со 0,06 %.

Заклучок: Вклучувањето на што поголем број фенотипизирани дарители во постојниот регистар, овозможува идентификација на дарители со ретки крвни групи. Тоа претставува основа за обезбедување компатибилниа крв за пациенти со ретки крвни групи, како и за пациенти со антитела кон високофреквентни антигени во рамките на еден или на повеќе крвногрупни системи.

Клучни зборови: ретки крвни групи, фреквенција на еритроцитни антигени, регистар на типизирани дарители на крв