

## Prevalence of Red Cell Blood Group Antigens Among Egyptian Population in Comparison with Other Ethnic Groups

RANDA M. ABOU EL-FETOUH, M.D.\*; TAREK M.A. EL-GEMMEZI, E.F.B.T.M.\*\*;  
MERHAN A. FOUDA, M.D.\* and FATEN M. MOFTAH, C.T.M-R.C.P.S. of Edinburgh\*\*\*

*The Departments of Clinical Pathology (Blood Bank Unit), National Cancer Institute, Cairo University\*, Red Cell Reference Laboratory, National Blood Transfusion Services, Ministry of Health and Population\*\* and International Blood Transfusion Services\*\*\*, Cairo, Egypt*

### Abstract

**Background:** Blood group antigens differ in their distribution among different ethnic populations, knowledge of the different blood antigen frequency in a population is important for safe blood transfusion, as cases of multi-transfused patients with multiple allo-antibodies, where antigen-negative blood should be provided.

**Aim of the Work:** Is to detect the prevalence of red cell blood group antigens among Egyptian population and compare it with other ethnic groups. This information can be used to establish the correlation between blood group genotype and phenotype, and to help managing cases of alloimmunization in multiply transfused patients.

**Methodology:** A total number of 3219 regular blood donors in NBTC and the blood bank of the National Cancer Institute, Cairo University, were subjected to extended Rh system phenotyping (D, C, E, c and e), and to phenotyping for other blood group systems. Colum Agglutination Technique was used to test the red cells of the blood donors.

**Results:** Our study showed that in the Rh system, the D+(84%), e+(97.4%), C+(67.5%) prevalence was close to Caucasians. The K antigen (8.23%) was also almost close to Caucasian, while the k antigen (99%) was equal to other ethnic population. The S and s antigens (56.77%, 86.1% respectively) were almost the same as that of Caucasian and Indian population. Duffy blood group was different as Fya (26.66%) and Fyb (48.87%) antigens results were unique to our studied population. The Lea (26.26%) antigen was almost the same as both Caucasians and African population. While the Jka (83.88%) antigen was close to the Indians population, the Jkb (58.75%), the Leb (46.49%) and the N (40.1%) antigens were unique to our studied group. The M antigen (78.99%) result was almost the same as Caucasian and Asian population.

**Conclusion:** The distribution of the blood group antigens among different races shows different findings. Knowledge of the prevalence of different blood group antigens in any given population is helpful in managing cases of alloimmunization in multiply transfused patients.

**Key Words:** Red cell – Blood group antigens – Egyptians – Ethnic groups – Prevalence.

### Introduction

**BLOOD** group antigens are inherited macromolecules on the outer surface of the red blood cell, and some of these antigens are present on the cell surface of various tissues, as they are not red cell specific. They may be proteins, glycolipids and mostly glycoproteins e.g. the ABO system specificity is determined by the oligosaccharide sequence, while the MN, Kell, Duffy, Kidd, and Diego system specificities are determined by the amino acid sequence [1].

The International Society of Blood Transfusion (ISBT) identifies almost 344 red cell surface antigenic determinants classified according to the following: 36 blood group Systems consisting of one or more antigens controlled at a single gene locus, or by two or more very closely linked homologous genes with little or no observable recombination between them; Collections (200 series) consist of serologically, biochemically, or genetically related antigens, which do not fit the criteria required for system status; 700 Series or low incidence antigens with an incidence of less than 1% and cannot be included in a system or collection and 901 Series or high incidence antigens with an incidence of greater than 90% and can't be included in a system or collection [2].

Knowledge of the prevalence of different blood group antigens in any given population is always helpful in managing cases of allo-immunization especially multi-transfused patients. Several studies compared the phenotype frequencies among different ethnic groups and populations, especially those

**Correspondence to:** Dr. Randa M. Abou El-Fetouh,  
[E-Mail: randafetouh@yahoo.com](mailto:randafetouh@yahoo.com)

important in blood transfusion and in transplantation. As blood transfusion can carry immediate or delayed immunological risks; the most common and most serious is the hemolytic transfusion reaction by antibody incompatibility. Multi-transfused patients (who often require chronic blood transfusion) such as patients suffering from thalassemia, sickle cell anemia, patients on dialysis, cancer patients, etc., are more likely to develop antibodies against minor blood group antigens, thus, antigen negative blood is required for those patients who are already allo-immunized and sometimes with more than one antibody. Finding compatible units for such patients without having any knowledge of the prevalence of the implicated antigens in the local population is a laborious and time consuming process [3-5].

Absence of surface antigenic expression in any blood group systems is known as null phenotype; they are rare and found accidentally when this person is immunized either by transfusion or pregnancy [1]. Though the D antigen is the most potent immunogen in the Rh system, other antigens in this system are capable of sensitizing the immune system giving rise to clinically significant antibodies, as when transfusing compatible Rh D blood units but are incompatible for C, c, E or e antigens. Antibodies specific to the Rh system are the most frequent antibodies encountered in pre-transfusion testing, and are the main cause of hemolytic disease of fetus and newborn (HDFN), and hemolytic transfusion reactions (HTRs) and antigen-negative blood should be available whenever possible. The c antigen is clinically the most important Rh antigen after the D antigen, causing severe HDFN, whereas antibodies to the C, E, and rarely e antigen can cause mild (but not always) HDFN [3,6].

Delayed hemolytic transfusion reactions can be caused by some blood group systems as the Rh system where Anti-D, Anti-c, Anti-C, and anti-e, which can cause severe hemolytic transfusion reaction with extra vascular hemolysis. The K antigen is the most immunogenic antigen after the antigens of the ABO and Rh blood group systems causing severe hemolytic transfusion reaction [5,7]. Other antigens are also capable of producing antibodies causing HTRs, HDFN or even decrease red cell life span [8]. Knowledge of the phenotypic frequency of these antigens is required both in managing and preventing the development of allo-antibodies in multi-transfused patients.

One-third of all non-Rh allo-antibodies are mainly anti-K, so providing K-persons with K-blood units is essential [7,9-12]. The Kell system is

the third potent system capable of initiating an immune response after ABO and Rh systems due to the strong immunogenic K antigen, which is a low frequency allele in all studied populations. Anti-K antibodies should be considered potentially clinically significant, in causing severe HDFN and HTRs requiring transfusion with antigen-negative blood whenever possible. Mainly anti-K antibodies are known to cause severe reactions in numerous occasions causing HDFN, due to immune destruction of RBCs with significant suppression of erythropoiesis resulting in severe anemia, which may be prolonged and without overt signs of hemolysis. [3,13,14].

The Kidd blood group system has two major antigens Jka and Jkb, besides being antigenic; they are the major urea transporters on erythrocytes. Jk (a-b-) individuals have no clinical symptoms, but have their urine concentrating ability reduced by about one-third [15]. Anti-Jka and anti-Jkb can cause severe immediate HTRs and sometimes delayed HTRs. As their plasma level drop to low or undetectable levels, they are often not detected and rarely can cause severe HDFN [3]. Duffy blood group antigens are glycoprotein in nature functioning as receptors for cytokines and malaria parasite, *Plasmodium vivax*. Antigens of the Duffy system, (Fya and Fyb antigens) are capable of producing antibodies causing immediate or delayed HTRs, although mild, but sometime could be fatal, and being responsible for varying degree of HDFN, ranging from mild to severe. The phenotype Fy (a-b-), found mainly in Africans, lacking the Duffy glycoprotein from their red cells, affecting the susceptibility to malarial infections, resulting in natural selection. This phenotype is less common in other ethnic groups [16,3,2,5]. Duffy and Kidd blood group antigens may act as a minor histocompatibility antigen in renal allograft rejection [17].

The MNS system have four major glycoprotein antigens M, N, S and s, functioning as receptors for cytokines and *Plasmodium falciparum*. Anti-S and anti-s were found to be implicated in HTRs and causing severe and fatal HDFN [3,18].

The Lewis system antigens, Lea and Leb, are adsorbed from the plasma, as they are not intrinsic to erythrocytes. The Leb antigen in the gastric mucosal epithelium is the receptor for *Helicobacter pylori*, which is the major causative agent of gastric ulcers [19,20]. It is extremely rare for Le(a+) or Le(b+) red cells to cause HTR as specific naturally occurring antibodies are almost exclusively in the sera of Le(a-b-) individuals [3,9].

Different antigen phenotyping is essential in initiating a donor blood bank registering all known antigen phenotypes as it would be helpful for patients with rare phenotype, or multi-transfused patients with multiple antibodies [21,22]. Donor bank registration could be helpful in prophylactic prevention of alloimmunization in young or pregnant females, and patients expecting to have multi-transfusion in life, as in cases of thalassemia, sickle cell disease and patients with refractory aplastic anemia [23,24].

Racial and ethnic variation in different blood group antigens frequency in Africa, Asia, Europe, North and South America was reported by several authors [25-29].

### Material and Methods

A total number of 3219 regular blood donors from April 2015 to December 2016 in NBTC and the blood bank of the National Cancer Institute were subjected to extended Rh system phenotyping (D, C, E, c and e), and to other blood group systems phenotyping. The donation included both sexes, with 4/1 male to female ratio, age ranging from 18 to 45 years. All donors were asked to fill in a questionnaire to determine their eligibility for blood donation. Those considered as eligible donors were physically examined by a physician prior to acceptance of donation. Specimens were collected, stored and handled according to the assay manufacturers' instructions. The study was approved by the Institutional Review Board of the National Cancer Institute (NCI), Cairo University.

The classical method used for testing the blood group antigens was hemagglutination; Colum Ag-

glutination Technique using Mono-specific anti sera (Biorad Laboratories, Inc., Hercules, California, USA) as this serological technique used to test the red cells of the blood donors being simple, inexpensive with appropriate specificity and sensitivity. For collection of specimen, a 3ml fresh, non-hemolysed EDTA blood sample was used for preparation of 5% RBCs suspension to detect RBCs antigens. Quality Control was done using positive & negative control specific for each Anti-serum, refereeing to standard operating procedures (SOPs) of preparation of controls for different immune-hematological reagents to ensure specificity of reagent and to avoid false positive and negative results. Red cell suspension was tested with the mono specific anti sera using Biorad (Biorad Laboratories, Inc., Hercules, California, USA) column agglutination cards. Positive test results in case of red cell agglutination and negative test results in case of no agglutination of RBCs.

This study was approved by the Institutional Review board of the National Cancer Institute on 3rd of March 2015 and the IRB approval number is 201001415020.2.

### Results

A total number of 3219 regular blood donors in NBTC and the blood bank of the National Cancer Institute were subjected to extended Rh system phenotyping (D, C, E, c and e), and to phenotyping for other blood group systems. Our results are shown in Table (1,2). The prevalence of phenotypes associated with the blood group antigens among our study group in comparison with other ethnic groups are shown in Tables (3,4,5).

Table (1): Results of the study group showing the prevalence of Rh Phenotype.

	Cases tested	Prevalanceof RBC antigens (%)	D	C	E	c	e
R2r	283	8.79%	+		+	+	+
R1R1	683	21.22%	+	+	-	-	+
R1r	1125	34.95%	+	+	-	+	+
R1R2 (R <sub>Zr</sub> )	271	8.42%	+	+	+	+	+
R0r	297	9.23%	+	-	-	+	+
R2R2	67	2.1%	+	-	+	+	--
rr	446	13.86%	-	-	-	+	+
r'r	34	1.1%	--	+	-	+	+
r''r	13	0.40%	-	-	+	+	+
Total	3219	Number %	2726 84.68	2113 65.64	634 19.7	2536 78.78	3152 97.92

Table (2): The prevalence of the different minor blood groups in the study group.

	Kell		Duffy		Kidd		Lewis		MNSs			
	K	k	Fya	Fyb	JKa	JKb	Lea	Leb	M	N	S	s
Total tested samples	3222	2200	2251	2204	2270	2240	2239	2205	2208	2200	2276	2203
Positive cases	265	2172	600	1077	1904	1316	588	1025	1744	880	1292	1896
Positive cases (%)	8.23	99	26.66	48.87	83.88	58.75	26.26	46.49	78.99	40.1	56.77	86.1

Table (3): Comparison of the different minor blood groups in our study with other ethnic groups.

	K	k	Fya	Fyb	JKa	JKb	M	N	S	s	Lea	Leb
Egyptians (%)	8.23	99	26.66	48.87	83.88	58.75	78.99	40.1	56.77	86.1	26.26	46.49
Caucasians (%)	9	98	66	83	77	74	78	72	55	89	22	72
Black (%)	2	100	10	23	92	49	74	75	31	93.0	23	55
Asians (%)	Rare	100	99	18.5	72	76	79.7	67.4	8.7	100	–	–
Indians (%)	3.5	99.7	87.4	57.7	81.4	67.6	88.8	65.4	54.8	88.7	–	–

Table (4): Comparison of the Rh phenotype between our study group and other ethnic groups.

	Egyptians (%)	Cote d'Ivoire (%)§	Indians (%)	Caucasians/ Whites (%)	Blacks (%)	Iran (%)*	Asians (%)¶
D	84.68	92.93	93.4	85	92	90.2	99.0
C	65.64	21.97	84.8	68	27	75.9	93.0
E	19.7	13.82	17.9	29	22	29.5	39.0
c	78.78	99.85	52.8	80	98	73.9	47.0
e	97.92	99.85	98.3	98	98	97.9	96.0

Please see references for the detailed data ¶: [30]. §: [31]. \*: [32].

Table (5): Comparison between Rh phenotype (Weiner notation) prevalence between our study group and other ethnic groups.

Rh-Phenotype	Egyptians (%)	Whites [Caucasian] (%)	Blacks (%)	Asians (%)	South Indians (%)*
R <sub>1</sub> R <sub>1</sub>	21.22	18.5	2.0	51.8	40.87
R <sub>2</sub> R <sub>2</sub>	2.1	2.3	0.2	4.4	
R <sub>1</sub> R <sub>2</sub> (R <sub>z</sub> r)	8.42	0.2	rare	1.4	13.91
R <sub>1</sub> r	34.95	34.9	21.0	8.5	23.48
R <sub>2</sub> r	8.79	11.8	18.6	2.5	4.35
R <sub>0</sub> r	9.23	2.1	45.8	0.3	0.87
rr	13.86	15.1	6.8	0.1	11.3
r'r	1.1	0.8	rare	0.1	–
r''r	0.40	0.9	rare	rare	–

Please see references for the detailed data \*: [33]

## Discussion

Knowledge about the frequency of red cells antigens phenotypes in our population can be useful in initiating a donor data bank for minimizing the risks of alloimmunization for multi-transfused patients as most transfusions are done based only on the ABO and D antigens with little or no data available for the frequency of other blood group antigens. Blood transfusion is used mainly to save life, but this is not without risk, as an immediate or delayed hemolytic transfusion reaction due to antigen incompatibility could occur. Knowing the frequency of the blood group antigens phenotype

in our population is important in managing alloimmunization in multi-transfused patients, as finding compatible units without knowing the prevalence of the desired antigen in our population or in any ethnic population is a time and reagent consuming work [3,4,28].

Studying the Rh phenotype it was found that R<sub>1</sub>r was highest in value (34.95%) which is equal to that of Caucasian, followed by R<sub>1</sub>R<sub>1</sub> with a result of 21.22% and rr with 13.86% both values are almost close to Caucasian population. R<sub>0</sub>r (9.23%), R<sub>1</sub>R<sub>2</sub> (R<sub>z</sub>r) (8.42%), R<sub>2</sub>r (8.79%), and r''r (0.4%) showed a percentage unique to our

studied population. The D, C, c, e antigens in our study showed a percentage of (84.68%, 65.64%, 78.78% and 97.92% respectively) which is almost the same as that in Caucasians except for the E antigen (19.7%) giving a value which was close to Indians and black population than to Caucasians. The Kell phenotype showed a different result for both antigens were the K antigen (8.23%) showed a value almost close to Caucasian than to other ethnic population, while the k antigen (99%) was equal to other ethnic population. The Duffy blood group was different as Fya (26.66%) and Fyb (48.87%) antigens results were unique to our studied population. As for the Kidd blood group antigen the Jka (83.88%) result was close to the Indians population, while the Jkb (58.75%) was unique to our studied group. The M antigen (78.99%) result was almost the same Caucasian and Asian population, while the N antigen (40.1%) showed a unique percentage to our studied group.

The S and s antigens (56.77%, 86.1% respectively) in our studied group were almost the same as that of Caucasian and Indian population. The Lewis blood group showed difference in the expression of both the antigens as Lea (26.26%) was almost the same as both Caucasians and African population, while the Leb (46.49%) was unique to our studied group [25,29].

#### Conclusion :

The distribution of the blood group antigens among different races shows different findings. This has clinical significance in transfusion medicine and in hemolytic disease of fetus and newborn (HDFN), as it is essential to provide antigen-negative blood to patients with medical conditions, who often require regular blood transfusion and who may have developed multiple antibodies. This study has provided us with donor database of regular repeat voluntary blood donors with known antigenic profile. Although our studied blood donor group are considered a small group compared to our country population, but still, it gives an estimate of the frequencies of minor blood group antigens. It is recommended that extended phenotypic status for Rh and Kell systems be determined routinely along with ABO and Rh (D) typing before the first transfusion as a preventive measure reducing potential allo-immunization, especially in multi-transfused patients.

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## مقارنة بين فصائل الدم المختلفة بكرات الدم الحمراء ونسب تواجدها بين المجتمع المصري والجناس الأخرى

الهدف من البحث: هو معرفة نسبة تواجد فصائل الدم الحمراء المختلفة في المجتمع المصري ومقارنتها بالجناس الأخرى وهذا يساعد على تجنب المشاكل الناجمة عن تكوين الاجسام المضادة في حالات نقل الدم المتكررة. بالاضافة إلى تكوين الارتباط بين النمط الجيني والنمط الظاهري لفصائل الدم تم اختيار عدد ٣٢١٩ متبرع بالدم بالمركز القومي لخدمات نقل الدم ومعهد الاورام القومي بجامعة القاهرة. تم عمل الاختيار بطريقة الالتصاق باستخدام العمود وكانت النتيجة كالتالي: وجد أنه في حالة عامل ريسوس ان نسبة تواجد المستضدات في المجتمع المصري هي  $D+/\%٨٤$  و  $e+/\%٩٧$  و  $C+/\%٦٧$  وهذه النسب قريبة من نسب تواجد هذه المستضدات في العرق القوقازي. كما لوحظ أن نسبة تواجد المستضاد مشابهة أيضاً للعرق القوقازي وبالنسبة لنسبة تواجد المستضاد فهي مشابهة للجناس الأخرى.

بالنسبة للمستضادات  $s,S$  فهي نسب تواجدها في المجتمع المصري هي  $[S+/\%٥٦.٧]$  و  $[s+/\%٨٦.١]$  هي مشابهة لنسب تواجدها في الشعوب القوقازية والهندية. بالنسبة الفصيلة دم دافي فقد اختلف حيث أن نسب تواجد المستضدات كانت  $[Fya+/\%٢٦.٦٦]$  و  $[Fyb+/\%٤٨.٨٧]$  وهذه النسب هي فريدة بالشعب المصري فقط ولا تتشابه مع أي من شعوب العالم أما بالنسبة للمستضاد كانت نسبة تواجده هي  $[Lea+/\%٢٦.٢٦]$  وهي مشابهة للشعوب القوقازية وشعوب القارة الأفريقية. بالنسبة للمستضاد والتي كانت نسبة تواجده  $[JKa+/\%٨٣.٨٨]$  فكانت قريبة من الشعب الهندي بينما المستضادين والتي كانت نسب تواجدهما  $[JKb+/\%٥٨.٧٥]$  و  $[Leb+/\%٤٦.٤٩]$  و  $[N+/\%٤٠.١٠]$  فكانت هذه النسب فريدة للشعب المصري فقط أما المستضاد والتي كانت نسبة تواجده  $[M+/\%٧٨.٩٩]$  فكانت هذه النسب شبيهة بالشعوب القوقازية والاسيوية.