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HAPLOTYPES AND GENOTYPES;

THE FREQUENCY OF RHESUS ALLELES, HAPLOTYPES AND GENOTYPES IN MAJOR SAKAK CITY POPULATION, ALJOUF REGION, SAUDI ARABIA

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ABSTRACT… Rh-D distribution varies worldwide. **Objectives:** The aim of this study was to document the frequency of Rhesus alleles, haplotypes and genotypes in Aljouf region, Sakaka. The EE genotype is not generally represented in the Aljouf province, and DcE/Ce genotypes are the shared (30.8%), while Dce/Dce and Dce/ce genotypes are less familiar (1.4%). **Results:** The frequency distribution of Rh haplotypes among Aljouf population in the present study CDE(0.701) has the highest observed frequency followed by Cde (0.250), cDe (0.116) and CDe (0.040), cDE (0.028), cde(0.021) and cdE(0.008). The data generated during this study would be important, a base line for advance to be catalogued by molecular rather than serological criteria, and of polymorphisms between RHD and RHCE, which will be a useful for DNA typing and to provide the development of suitable DNA techniques.

Key word: Blood groups, Rhesus, Haplotypes, Genotypes

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INTRODUCTION

The Rhesus blood group system (ISBT 004) is the common complex blood group system; comprising 46 antigens numbered RH1 to RH53 with seven numbers obsolete1. It is the most polymorphic human blood group, and next to ABO. The clinically significant in transfusion medicine. In Rh blood system, 18 phenotypes can be distinguished by using five kinds of anti-D,C,c,E,e[1]. Eight basic haplotypes are formed from primitive haplotype cDe by a series of duplication, point mutation and recombination events[2,3]. The frequencies of these haplotypes vary among different populations. From serological results, it is often impossible to determine the true genotype of an individual and phenotypes are sometimes symbolized as the most probable genotypes deduced from known haplotype frequencies[1]. Serologically similar phenotypes have different molecular backgrounds[4]. The D unwilling phenotype has either rh specific sequences positive or rh complete deletion. The cumulative frequency of various rh alleles in D pessimistic Europeans is 1:1,500[5]. However, in Africans and Asians, the frequencies are much different. In D gloomy Han Chinese, about 1 9.9%(all C+) have a grossly intact Rh, 168 % carry at least one rh exon[6], and in D negative African, around 82 % African have RHDW and RHD-CE-D hybrid gene. The antigen D is the most immunogenic of the Rh antigens and the clinically most important[1]. Anti-D usually is introduced after blood transfusion or pregnancy. About 85 % of D negative recipients produce anti-D following transfusion of 200 ml or more of D clear red cells[7] and as little as 0.1 ml of D favorable blood can immunize D cynical recipient. Even weak D type 2[8] or DEL phenotype[9] red cells can cause D unwilling recipient to produce anti-D. Clinically, anti-D has the potential to cause hemolytic disease of the newborn, transfusion reactions and autoimmune hemolyticus disease. Knowledge of Rh phenotypes in given population is relevant for better planning and management of a blood bank; to find compatible blood for patients needing multiple blood transfusions, which would resolve the blood transfusion needs of recipients. A random survey for Rh in Aljouf, Sakaka population was revealed rh allele distribution characters and defines its frequencies; it was also be benefit for accumulating human genetic data and useful guidelines for transfusion strategies.

METHODOLOGY

A total of 422 subjects (unrelated individuals) of both sex (male and female) and all ages were included

within this study over two years. Essential information was noted and recorded on a printed form. Subject blood samples were collected under aseptic condition from an anti-cubital vein for determination of Rhesus blood groups. Rhesus blood alleles, haplotypes and Genotype's grouping were determined by ID-Card "DiaClon contains monoclonal anti C, anti c, anti D, anti E, anti e [cell lines LM 297/628 (LA-2) and Preservative: <0.1% NaN3. EDTA-anticoagulated blood samples (3-5 ml) were drawn from 422 unrelated Saudi Arabian populations after obtaining their consent. All study groups were living in Aljouf Region, Sakaka, chosen at random according to such characters as name, residence, appearance and tribe. The collectors labeled the samples anonymously to guarantee unconnected testing. The samples were sent to hematology laboratory, College of applied medical science, Aljouf University, Aljouf, Sakaka for Rhesus alleles and phenotype determination. The Rhesus alleles and haplotypes were determined by using monoclonal reagents according to the manufacturer's instructions. ID-Card "DiaClon anti-D (IgM or IgG) was used. The other rhesus antigens were determined using monoclonal or oligoclonal reagents (anti-D, anti-C, anti-c, anti-E, and anti-c). The genotype was determined using either: the sample was considered homozygous for Rh, if two unusual rh, alleles detected, when there was a discrepancy between them, we choose rh sequencing result. Alternatively, if distinctive combinations of genotypes could explain a given sample, the most likely genotype was chosen as the common plausible explanation.

RESULTS

A total of four hundred twenty two healthy Arab ethnic male persons from five common tribes in Aljouf(Sharary: n = 134, Shamari: n = 48, Rwealy: n = 126, Enazy: n = 106 and Sarhany: n = 8) in different age groups were randomly selected from Primary Health Centers (PHC) of Sakaka city, Jouf Province of Saudi Arabia. The Al Jouf Province forms a vital position of the North Arabian and Syrian desert and is enclosed by sandstone hills; its oases have played an significant role in the contacts between the Arabs in the Peninsula and the people of the Fertile Crescent. Al Jouf was an extremely consequential center and a summer camping ground for the nomads in ancient history. It was a confluence of various cultures. Sakaka, the capital from the province. The most common ABO blood group among the study groups was grouped O; Enazy (43.4%), Rwealy(40.5%), Shamari(45.8%), Sharary (47.0%) and Sarahny(50.0%) as shown in table I.

Table II shows the frequency of the five Rh antigens in the population. The alleles were found as follows: e 384(91.0%), D 393(93.1%), C 263(62.3%), c 176(41.7%) and E 188(44.5%). These alleles were varied between the five ethnic groups of Aljouf province. The studying of some genotypes of the Rh-system, high frequency distribution 192(45.5%)) of the Ee version was identified. The number of the cc

Blood groups	Ethnic group, n(%)				
	Enazy (n=106)	Rwealy (n=126)	Shamari (n=48)	Sharary (n=134)	Sarhany (n=8)
A	33 (31.1)	43 (34.1)	15 (31.3)	46 (34.3)	2 (25.0)
B	20 (18.9)	23 (18.3)	7 (14.6)	15 (11.2)	1 (12.5)
O	46 (43.4)	51 (40.5)	22 (45.8)	63 (47.0)	4 (50)
AB	7 (6.6)	9 (7.1)	4 (8.3)	10 (7.5)	1 (12.5)

Table-I. Frequency distribution of ABO blood groups among major Sakaka city population

genotype carrier was a little lesser 6(1.42%). The Cc genotype carriers' frequency made up 170(40.3%). As for the ee genotype frequency; it equaled 155(36.7%) and CC frequency up to be 93(22.0%). It is to be mentioned that the EE genotype is not generally represented in the Aljouf province (Table III).

The Rh-antigens complex's frequencies were shown in table 4. Only people belonging to Rwealy tribe have the complex DCce (31.7%). In Shamary tribe DCcEe is very dominant (66.7%). Rh null was high among Rwealy and Enazy 8.7% and 9.4% respectively, while DcEe, DcE and ce antigen complexes were absent from all stud groups. Table IV. The frequency distribution of Rh haplotypes among Aljouf population was depicted in Table V. In the present study, CDE(0.701) has the highest observed frequency followed by Cde (0.250), cDe (0.116) and CDe (0.040), cDE(0.028), cde(0.021) and cdE(0.008) respectively as shown in table V. Table VI showed the Rh genotypes expected frequencies were shown in table 6. DCe/DcE, DCe/cE and DcE/Ce genotypes were the joint (30.8%), while Dce/Dce and Dce/ce genotypes were less communal (1.4%).

DISCUSSION

The Rhesus (Rh)D was, in fact, the fourth blood group system to be discovered and later ranked second to ABO system in terms of clinical importance[10]. Both are of equal importance in simple and forensic medicine. The study of Rh blood group is important in simple practice it was felt desirable to find out the prevalence of Rh phenotypes and genotypes in Al-Jouf Province of the Saudi Arabia from where no earlier serological data

Antigen present	Sarhany (n=8)	Enazy (n=106)	Rwealy (n=126)	Shamari (n=48)	Sharary (n=134)	Total (N=422)
D	8 (100%)	96 (90.6%)	115 (91.3%)	47 (98.0%)	127 (94.8%)	393 (93.1%)
C	8 (100%)	58 (54.7%)	66 (52.4%)	39 (81.25%)	92 (68.7%)	263 (62.3%)
E	8 (100%)	32 (30.2%)	26 (20.6%)	38 (79.17%)	84 (62.7%)	188 (44.5%)
c	4 (50%)	24 (22.4%)	72 (57.1%)	32 (66.7%)	44 (32.8%)	176 (41.7%)
e	8 (100%)	94 (88.9%)	100 (79.4%)	48 (100%)	134 (100%)	384 (91.0%)

Table-II. The frequencies of rh alleles in Aljouf region population of the Saudi Arabia

Antigen present	Sarhany (n=8)	Enazy (n=106)	Rwealy (n=126)	Shamari (n=48)	Sharary (n=134)	Total (N=422)
CC	4 (50%)	34 (32%)	-	7 (14.6%)	48 (35.9%)	93 (22.0%)
Cc	4 (50%)	24 (22.6%)	66 (52.4%)	32 (66.7%)	44 (32.8%)	170 (40.3%)
cc	-	-	6 (4.8%)	-	-	6 (1.42%)
EE	-	-	-	-	-	-
Ee	8 (100%)	32 (30.2%)	26 (20.6%)	38 (79.2%)	88 (62.7%)	192 (45.5%)
ee	-	62 (58.5%)	34 (27.0%)	9 (18.8%)	50 (37.3%)	155 (36.7%)

Table-III. Distribution peculiarities of the CC, Cc, cc, Ee, EE, ee genotypes in the Aljouf region population of the Saudi Arabia

Antigen present	Sarhany (n=8)	Enazy (n=106)	Rwealy (n=126)	Shamari (n=48)	Sharary (n=134)	Total (N=422)	Whites*	Blacks *
DCcEe	4 (50%)	24 (22.6%)	26 (20.6%)	32 (66.7%)	44 (32.8%)	130 (30.8%)	13.2%	4.2%
DCEe	4 (50%)	8 (7.5%)	-	6 (12.5%)	40 (29.9%)	58 (13.7%)	-	-
DCce	-	-	40 (31.7%)	-	-	40 (9.5%)	34.7%	24.6%
DCe	-	6 (5.66%)	-	1 (2.1%)	8 (6.0%)	35 (8.3%)	19.3%	3.6%
Dce	-	-	6 (4.8%)	-	-	6 (1.4%)	3.2%	42.3%
De	-	36 (34%)	28 (22.2%)	8 (16.7%)	35 (26.1%)	107 (25.4%)	-	-
D	-	2 (1.9%)	15 (11.9%)	-	-	17 (4.0%)	-	-
E	-	-	-	-	7 (5.2%)	7 (1.7%)	-	-
null	-	10 (9.4%)	11 (8.7%)	1 (2.1%)	-	22 (5.2%)	-	-
DcEe	-	-	-	-	-	-	11.5%	15.4%
DcE	-	-	-	-	-	-	2.3%	1.4%
ce	-	-	-	-	-	-	15%	7%

Table-IV. Frequencies of Rh-antigens complexes among Aljouf region population of the Saudi Arabia

Expected haplotypes*	Frequency	Phenotypes
CDE	0.701	Rz
Cde	0.250	r'
cDe	0.116	R_0
CDe	0.040	R_1
cDE	0.028	R_2
cde	0.021	r
cdE	0.008	r"

Table-V. The most probable haplotypes frequencies among Aljouf region population
** calculated according to Mourant et al 1976.*
*2 (cde) = 2(176/422*29/422*383/422)*

are available. In our study, blood group O was found predominant and AB was stood on the lowest side among the five ethnic population in aljouf. Similar distribution pattern of ABO blood groups was reported in Egypt, Jordon, Nigeria, Kenya and Eastern region of Saudi Arabia. However, other countries such as Syria, Lebanon, Israel and Jordan have an unusual ABO distribution pattern in which blood group A was predominant. This may be attributed to their distinct ethnic background, besides sampling error, and

	Total (n=422)	Expected genotypes (Fisher)	Expected genotypes (Weiner)
DCcEe	130 (30.8%)	DCe/DcE DCe/cE DcE/Ce	R_1R_2 R_1r'' R_2r'
DCEe	58 (13.7%)	DCE/DCe Dce/cE DcE/Ce	R_zR_1 R_1r'' R_2r''
DCce	40 (9.5%)	Dce/ce Dce/Dce Dce/Ce	R_1r R_1R_0 R_0r'
DCe	35 (8.3%)	Dce/DCe DCe/Ce	R_1R_1 R_1r'
Dce	6 (1.4%)	Dce/Dce Dce/ce	R_0R_0 R_0r
De	107 (25.4%)	De/De De/e	R_0R_0 R_0r
D	17 (4.0%)	D–/D– D–/–	R_0R_0 R_0r
e	7 (1.7%)	–e/–e	r'r'
null	22 (5.2%)	– / –	R_0

Table-VI. The most probable genotypes among Aljouf population of Saudi Arabia

natural selection. Similarly, in agreement with previous studies[11,12,13].

The frequencies of Rh antigens; D frequency was related to that obtained among blacks (92%) and Asians (99%) populations, the c antigen frequency was like to Asians(47%), C antigens frequency was like to Caucasians(68%), E frequency was like to that obtained among Asians(39%) while the e frequency was alike to Caucasians(98%), Blacks(98%) and Asians(96%) populations[14]. In other studies done in ethnic nationalities of Calabar, Nigeria[15], it was revealed that D was 95%, C 17.7%, c 99.8%, e 98.7% and E 20.5%. In a study by Thakral et al from India, e antigen was 98.3%, D, C 84.7%, c 52.8% and E 17.9% among blood donors[16]. In this study, it was found that the most common probable Rh-genotypes present in decreasing order of frequency were R1R2, R1r'', R2r', R0R0, R0r, RzR1, R1r'', R2r'', R1r, R1R0, R0r', R1R1, R1r', R0, R0r, r'r'. This finding was in agreed to the study done[17]. And close to results that were obtained from Jordan[18]. Some genotypes of the Rh-system high frequencies of the ee, Ee, and cc versions were lower than those found by Marina et al. while, The Cc genotype carriers' frequency akin to that obtained by Marina et al. As for the CC genotype frequency was found among the Aljouf province only and not found in some studies. It is to be mentioned that the EE genotype is not generally present in aljouf population, and this finding was in agreement with other studies[19]. The Rh-antigens complexes present in this study; at most people belonging to Rwealy tribe had the complex DCce in agreement with frequencies reported in Caucasian, while in Shamary tribe, DCcEe was very dominant in contrary to report on whites and black populations[14]. The frequency of Rh null was similar in both Enazy (9.4%) and Rwealy(8.7%), this rare Rh phenotype was just found in Enazy and Rwealy because of their relatively and had a close system of marriage between them compared to the other ethnic groups of Aljouf region. Almost exactly 50 years ago, R.A.Fisher and R. Race proposed a model for the evolution of the RH (rhesus) genes in which the less common haplotypes were derived from the commoner ones by recombination, and in which the gene order was D-C-E. No direct evidence bearing on this model was available then, and has not been, until now[20]. The most probable haplotype frequencies in general the white group showed a close resemblance to those of the canary islands [21] and Southern Spain[22] with a nasty frequency of cDe haplotype and a towering frequency of cde. Negroes had the CDE haplotype, with moderately base frequency of cDe and elevated CDe frequency, distinctive from the majority of African samples[23]. The CDE haplotype in the current study was unlike from that obtained in whites, mulattoes and Negroes. Whiles Cde was similar to all of them; cDe

haplotype was found same as that among whites[24].

The cdE haplotype in the instant study was absent in the population of South – western Germany[25] and also in agreement to Pedro et al. findings. It is to be noted that the observed and expected frequencies of the Rh phenotype (CcDee) in the present study were similar to those previously reported by other workers in Germany[25]. However, frequency of the CcDee phenotype among Amis, Japanese, Vietnamese, Sudanese, Lepchas and Khasis was lower than that of the Aljouf populations[26,27,28,29].

CONCLUSIONS

The most frequently of Rh antigens occurring were e (91.0%), D (93.1%), C (62.3%), c (41.7%) and E (42.7%). The collective probable Rh-genotypes present in decreasing order of frequency were R1R2, R1r", R2r', R0R0, R0r, RzR1, R1r", R2r", R1r, R1R0, R0r', R1R1, R1r', R0, R0r, r'r', r'r', RzR2, RzRz, r'r" and r"r. The Rh antigens, alleles and phenotype frequencies within the population of Aljouf province; Saudia Arabia was different from those that were previously reported among the populations of Asian, African or European countries[30]. These differences may be of importance to the anthropologists, who are concerned with exploring the familiar populations based on the blood groups, and also in forensic medicine. The present study would provide the local Blood Transfusion Center in Sakaka city, Aljouf with the Rh blood types and frequencies that may play a role in the blood transfusion problems. From our point of view, the present study was original in that, it was the first comprehensive study that documented the distribution of frequency of Rhesus blood group alleles, haplotypes and genotypes in the Aljouf region of Saudia Arabia.

RECOMMENDATION

The data generated during this study would be helpful to the researchers within the field of population genetics to explore the factors responsible for the observed distribution patterns of these markers in this part of West Asia. Equally important, will be a base line for advance to be catalogued by molecular rather than serological criteria, and of polymorphisms between RHD and RHCE, which will be a useful for DNA typing and to provide the development of suitable DNA techniques. Further studies using complex antibodies and direct DNA analysis are recommended.

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"Good judgment comes from experience, and experience comes from bad judgment."

Rita Mae Brown