

Genetically Determined ABO and (Rh) Rhesus Blood Groups and Their Associations with Diabetes Mellitus

Louay Al-Ani¹, Huda M. Mahmood², Noor Abdulhaleem³

¹College of Applied Sciences-Biotechnology, Department-Fallujah, University of Fallujah.

^{2,3}College of Science, Biotechnology Department, Ramadi, University of Anbar

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ABSTRACT

The current study was designed to explore the distribution of blood groups ABO and Rh and to find out the association of diabetes mellitus type II with blood groups. The study was performed on a sample of data consisting of records of blood groups were collected from different cities in Al Anbar Province in Iraq. A total of (23022) individuals were included in this study. All the information about ABO and Rhesus (Rh) blood group systems serological and diabetic patients' results were obtained from the survey of (1092) pedigrees.

In the population under investigation the overall proportions of different alleles of ABO were 0.20, 0.14 and 0.64 for A, B, and O, correspondingly. This happened in the direction of $O > A > B$. Phenotypic proportions were $O = 40.17\%$, $A = 29\%$, $B = 20\%$ and $AB = 11.54\%$. The proportion of O allele was the maximum in the population, whereas allele frequency for allele B was the lowest at 0.20. The observed distribution of ABO does not differ from the expected and the population under investigation was in Hardy-Weinberg equilibrium (Goodness – of – fit, $\chi^2 = 7.12$, d.f = 3, $p \geq 0.05$).

Concerning Rhesus D antigens, the current study found allele frequency for D+ and D- alleles was 0.65 and 0.35, correspondingly. While, the genotypic proportions to the Rh blood group were $D+D+ = 0.42$, $D+D- = 0.46$ and $D-D- = 0.12$, and the phenotypic frequencies

were $D+D+ = 87.5\%$ and $D-D- = 12.5\%$. There was a greater percentage of Rh (D) +ve persons than the Rh (D)-ve in over-all the people under investigation.

Our results backing a robust association among blood group and diabetes incidence, with the contribution of AB blood type which have a minor chance of increasing diabetes type II. It has been detected minor rise of risk of increasing DM II amongst A and B blood group while AB was a lesser amount of probable to develop diabetes compared to blood group O. Consequently, the impact of blood groups would be examined in upcoming medical and epidemiological pieces of training on diabetes. Additional pathological and physiological investigation is furthermore required to answer the reason why people with type AB has a minor chance of diabetes.

Key words: Blood group, ABO, Rhesus (Rh), Diabetes Mellitus, Gene frequency

Correspondence:

Louay Al – Ani

College of Applied Sciences, Biotechnology Department, University of Fallujah, Fallujah

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INTRODUCTION

The ABO and Rhesus (Rh) both continue to be the maximum significant and well-known blood group systems in the medical field. Karl Landsteiner in 1900 was discovered the first blood system of ABO. Blood group can be detected by the existence or lack of two genes, A and B. The gene is found on chromosome 9q34 which contains 7 exons extent over 18 kb named ABO groups (Glycoconj, et al., 1997; Farhud., et al., 2013). No illnesses are identified as a consequence of deficiency of manifestation of ABO antigens, but the vulnerability to some illnesses related to the ABO phenotype. For instance, gastric cancer occurs more in people with A group, while duodenal and gastric ulcers happen more amongst people with (O) group (Groot et al., 2020).

Relationship of data on the spreading of the ABO blood types and diabetes mellitus type II (DMII) is contradictory, some researches recording no relationship and others showed an affirmative link. So, the prevalence of DM II has been connected to several aspects such as genetic, environment, diet, obesity, lack of exercise. But, still very inadequate studies in the contemporary scientific works concerning the relationship between ABO and Rhesus blood group systems and DMII (Kamil, et al., 2010; Mandal, et al., 2018; Groot et al., 2020).

Even the link between ABO blood groups and DM was detected earlier in numerous epidemiological and hereditary investigations and lead to varying results. Group A was found to be related to DM II in certain researches, however still, there was insufficient researches in the works about the relationship between ABO blood groups with DM. (Kamil, et al., 2010; Karagoz, et al., 2015; Mandal, et al., 2018).

There is inadequate evidence available on ABO and Rh systems gene occurrence, and their clinical importance among the resident of the province of Al Anbar. Therefore, the objectives of this study were 1) to establish as accurately as possible the normal phenotype and genotype proportions of several alleles in ABO and” Rh” group systems of a sample of the population from different cities in Al Anbar province, Iraq. 2) to document the relationship between blood group with diabetes mellitus type II. Finding of this study may be used by researchers and health professionals as a reference in production and power to face any future challenges in health issues in this region.

MATERIAL AND METHODS

A total of (23022) individuals were included in this study. Those individuals residing in Al Anbar province of Iraq. All ABO and Rhesus (Rh) serological results and diabetic patients' information obtained from the survey of (1092) pedigrees. Pedigree tree was constructed according to the rule of construction of human pedigree (Young, 2007).

Allele frequency of the antigens was calculated by using of Hardy-Weinberg law based on the number of individuals with diverse blood groups (Hamilton, 2009). The departure from Hardy- Weinberg equilibrium was calculated for each blood system using standard Chi- squared goodness – of – fit – test (IBM Corp. Released, 2015).

RESULTS AND DISCUSSION

This study had a population containing of 51.54% males and 48.45 % females. Mostly diabetic patients were in <5years of duration. The overall percentages of diabetic individuals from the population under investigation were 2.93%of males and 2.12% females. Diabetic patient percentages were

5.17%, 5.42% , 4.96% and 3.91% distributed in groups of O,A,B and AB, correspondingly. Table (1) indicated the whole allele proportions for the ABO in the investigated population. Allele proportions of ABO were 0.20, 0.14 and 0.64 for A, B and O, correspondingly.

This happened in the direction of O > A > B. The phenotypic proportions were O = 40.17%, A = 29%, B =20% and AB = 11.54%. Allele O proportion was the maximum in the tested population, whereas allele frequency for allele B was the lowest 0.20 (Table 1).

Table 1: Over all blood group and their phenotypic and genotypic frequencies

BG	PF	G	GF	Allele	AF
A	0.290	I ^A I ^A	0.040	I ^A	0.20
		I ^A I ^O	0.252	I ^B	0.14
B	0.200	I ^B I ^B	0.019	I ^O	0.64
		I ^B I ^O	0.176		
AB	0.115	I ^A I ^B	0.056		
O	0.401	I ^O I ^O	0.396		

BG= Blood Group, PF=Phenotypic Frequency, G=Genotype, GF=Genotypic Frequency, AF=Allele Frequency

Table (2) shows a alike distribution of ABO blood groups to this study was set up in Iraq, Gaza – strip, Egypt, Saudi Arabia, and Kuwait (Awny, et al., 1965; Bashwari, et al., 2001; Al-Bustan, et al., 2002; Skaik, et al., 2007). They autonomously stated ABO groups frequencies in the order of O>A > B >AB, the expected percentages of these blood groups were as follow 40.1%, 28.66%, 19.60% and 11.54%

for O, A, B, and AB, respectively. This results is in agreement with (Bakere, et al., 2006), who explain the reason behind the high frequency of O blood group may be due to the fact that several subjects have A or B with heterozygous genotype, having O allele at the same time with an A or B gene.

Table 2: ABO Blood group of present study in comparison with different countries

Regions	Countries	Frequency of blood groups				References
		O	A	B	AB	
North America	American Indian	0.950	0.039	0.011	0.000	Mourant, et.al ,(1976)
Africa	Nairobi	0.690	0.158	0.126	0.023	Lyko, et.al ,(1992)
	Sudan	0.668	0.181	0.123	0.026	Khalil, et.al ,(1989)
	Libya	0.324	0.410	0.195	0.080	Al-Ani, et.al ,(1996)
	Egypt	0.364	0.339	0.209	0.086	Awny et.al ,(1965)
	Nigeria	0.489	0.244	0.238	0.027	Raji, et.al ,(2000)
	Nairobi	0.474	0.262	0.220	0.044	Lyko, et.al ,(1992)
Europe	UK	0.467	0.417	0.086	0.030	Talib, et.al ,(1991)
	Germany	0.640	0.256	0.081	0.022	Wagner, et.al ,(1995)
	Ukraine	0.576	0.236	0.225	0.070	Mukhin, et.al ,(2003)
	Hungary	0.559	0.276	0.121	0.042	Tuaszik et.al ,(1995)
Asia	Turkey	0.739	0.122	0.121	0.008	Akbas et.al ,(2003)
	India	0.325	0.247	0.375	0.053	Talib, et.al ,(1991)
	Gujarat	0.559	0.174	0.222	0.043	Anees, et.al ,(2005)
Middle East	Gaza –Strip.	0.381	0.331	0.213	0.075	Skaik, et.al ,(2007)
	Kuwait	0.667	0.160	0.140	0.026	Al-Bustan, et.al ,(2002)
	Saudi Arabia	0.520	0.240	0.170	0.040	Bashwari et.al ,(2001)
	Syria	0.375	0.462	0.131	0.031	Sakharov et.al ,(1996)
	Lebanon	0.361	0.472	0.115	0.051	Nasif et.al ,(1953)
	Jordan	0.366	0.383	0.180	0.069	Hanania et.al ,(2007)
	Iraq-Anbar	0.401	0.290	0.200	0.115	Present study

Though, further countries such as Syria, Lebanon, Jordan and Libya have a diverse range in blood group A which is the main group (Nasif., 1953; Talib, 1991; Al-Ani et al., 1996; Sakharov and Nofal., 1996; Hanania et al., 2007) (Table 2). The fluctuation in the distribution of ABO blood groups may be due to genetic factors, migration and natural

selection which are affected by tradition and habits and may be due to the differences in sample size and sample error (Hamilton, 2009).

The observed distribution of ABO blood groups is insignificant with expected under Hardy-Weinberg equilibrium ($X^2 = 7.12$, d.f =3, $p>0.05$). By convention, we

would reject chance as the explanation for the differences. The observed and expected patterns are the same. The critical value above which we except the null hypothesis for a X² test is 7.12 with 3 df. In this case, we can clearly see the population under investigation is under Hardy–Weinberg equilibrium between the observed and expected ABO blood group loci.

Gene frequency could be altered over time since the difference in genetic variance can change, the difference due to environmental elements alteration, or the association between a genetic factor and environment can be altered.

Genetic variation can be modified if allele occurrences altered which might be due to consanguinity, novel variations obtained by the population by mutation or immigration which will add to the genetic difference resulting from the change in genetic bases or the environment. These results confirm that the above factors have no effect on the population under investigation in regard to the gene frequency therefore the results showed the population was in Hardy-Weinberg equilibrium (Hamilton, 2009).

Table 3: The ABO frequencies in males and females

BG	Male					Female					
	G	GF	PF	Allele	AF	G	GF	PF	Allele	AF	
A	I ^A I ^A	0.040	0.298	I ^A	0.202	A	I ^A I ^A	0.035	0.274	I ^A	0.188
	I ^A I ^O	0.256		I ^B	0.132		I ^A I ^O	0.238		I ^B	0.146
B	I ^B I ^B	0.017	0.185	I ^O	0.634	B	I ^B I ^B	0.021	0.207	I ^O	0.633
	I ^B I ^O	0.167					I ^B I ^O	0.184			
AB	I ^A I ^B	0.053	0.113			AB	I ^A I ^B	0.054	0.117		
O	I ^O I ^O	0.401	0.402			O	I ^O I ^O	0.400	0.401		

BG= Blood Group, PF=Phenotypic Frequency, G=Genotype, GF=Genotypic, Frequency, AF=Allele Frequency

Table (3) displays whole alleles proportions for the ABO on the examined population in males and females. The allele frequencies of males ABO blood group were 0.202, 0.132 and 0.634 for A, B and O, correspondingly. While females were 0.188, 0.146 and 0.633 for blood groups A, B and O, respectively. This happened in the direction of O > A > B. The phenotypic proportions were O = 40.2%, A = 29.8%, B

=18.5% and AB = 11.3% for males. The phenotypic proportions for females were O = 40.1%, A = 27.4%, B = 20.7% and AB = 11.3%. The proportion of O allele was the maximum of entire population, whereas allele frequency of B was the lowest 0.20 (Table 3). In general the phenotypic, genotypic and allele frequency for males and females are in the same trends of overall population parameters.

Table 4: Blood group Rhesus (Rh) and their phenotypic and genotypic frequencies.

Allele	Allele Frequency		Genotype	Frequency
D ⁺	0.65	Rh(D) ^{+ve}	D ⁺ D ⁺	0.42
D ⁻	0.35	Rh(D) ^{+ve}	D ⁺ D ⁻	0.46
		Rh(D) ^{-ve}	D ⁻ D ⁻	0.12

In respect to Rhesus D antigens, the study indicated allele rate of recurrence for D⁺ and D⁻ alleles were 0.65 and 0.35, correspondingly. While, the genotypic proportions to the Rh blood group were D⁺D⁺ = 0.42, D⁺D⁻ = 0.46 and D⁻D⁻ = 0.12, and the phenotypic frequencies were D⁺D⁺ = 87.5% and D⁻D⁻ = 12.5%. There was a greater percentage of Rh(D)+ve persons more than Rh(D)-ve in the overall investigated residents (Table4). The results of this study are in steady with existing information from earlier researches amongst Nigerian people, researchers found greater Rh (D) +ve percentage than the Rh(D)-ve (Meo, et al., 2016).

To give details about the great proportion of the D⁻ allele in Europe (Anstee, 2010) suggested a socializing of two people groups with a high frequency of D⁻. They were mixing between the Paleolithic with Neolithic immigrants. This hypothesis recently used mt DNA and Y-chromosome which confirmed the acceptance of the people mixing theory (Wells et al., 2001). Tracing of haplotypes evolving from the Basque and Ukrainian refugees has revealed that these populations traveled all over Europe and Asia. (Wells et al.,

2001) Hemolytic disease of the fetus and newborn (HDFN) is created in all these areas. Mourant (1976) also proposed an association between the Basques and the Berbers due to the great proportion of D⁻ in phenotypes amongst Berbers. The assumption is now reinforced through confirmation from motherly DNA indicators presenting that ancestral Berbers reside in the Basque safe haven region than coming back to North Africa (Achilli. et al., 2005).

DIABETES

The information on the link of diabetes with ABO and Rhesus (Rh) blood group systems is flimsy and typically demonstrate no relationship. It is essential to strain that we come across several earlier researches on this topic where there was a greater conflicting argument on the association between blood groups ABO/Rh and diabetes.

Chi- square analysis between the whole blood groups for normal (21857) and diabetic people (1165) showed highly substantial association of blood group with DM II which was observed (X²=9.48, d.f= 3, P<0.024). But relative risk

(RR) were estimated on the basis of O group, it has been detected that minor rise of chance of emerging DMII amongst A(RR 1.102 [95% CI 0.964-1.129]), B(1.006 [95% 0.900- 1.124]), while blood group AB(RR=0.824 [95% 0.690-0.984]) was less possible to develop diabetes in connection with blood group O. The current research showed that certain ABO system is linked with a rise of DM II risk. Subjects with the AB blood group were showed the lower most risk of developing DM II.

The relationship between ABO system types and diabetes is inconsistent, several researches recorded no correlation and others presented a positive relationships.

Results of this research consistent with the observation of the study carried out by (Fagherazzi et al., 2015) a total of 82,104 females from big potential E3N cohort study from 1990- 2008. They detected people with any of the A (HR 1.10 [95% CI 1.02- 1.18]) or B (HR 1.35[95% CI 1.13- 1.60]) group were at the upsurge of DM II risk in comparison with people with the O group. The greatest rise in the chance of DM II was acquired in people with the A group.

Several types of researches showed no relationship between ABO system with DM II which suggested that there was an insignificant relationship between the ABO system and diabetes. Rahman (1976) showed in Bangladesh a sample size of 2312 patients and 8936 normal there was no relationship between the ABO system and DM. Rahman clarified no affirmative relationship, but our results show a considerably greater proportion of A and B blood groups amongst patients, which showed an adverse relationship with these blood groups.

Chi-square analysis showed a significant relationship between Rh and diabetes($X^2=4.52$, d.f=1, $P\leq 0.03$). The relative risk was calculated in reference to Rh(D)+ve, which was 1.009 (CI 1 -1.0109) , therefore, the people with Rh(D)-ve have 1.009 time of chance in developing diabetes than people with Rh(D)+ve. This result was in disagreement with (Meo, et al., 2016; Gusto et al., 2015) they showed no difference in DM II risk between Rhesus+ve and negative groups. This is maybe due to different races reside in study regions and may be due to differences in sample size. Whereas (Sadhu et al., 1988) found are lationship of DM with blood group “Rh+ve”.

As evident from the argument above, definitely the finding showed an affirmative relationship with ABO groups however the confirmation is blended. Current results indicated an adverse relationship among the AB group and DM II, with AB being less common in the diabetic group. The finding that AB has an adverse relationship with DM II, which appears to have a defensive impact. Still, it is early on time to spot any actual assumptions from the research without a using ghuge sample study is being directed. Qureshi and Bhatti (2003) revealed that DM II and ABO groups are interconnected; they showed that amongst 70 patients with DMII, B group stayed most communal and was 35.71% in comparison to normal, which was 22.14%

CONCLUSION

This results in backing a robust association among blood group and DM II incidence. AB has a very low contribution to the incidence of DM II. Subsequently, the impacts of

blood groups would be examined in future medical and epidemiological researches on diabetes. Extra pathological and physiological investigations are additionally required to characterize why the people with group AB have a lesser chance to have DMII.

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