ORIGINAL ARTICLE

Confederacy of ABO Alleles with Ischemic Heart Disease: An Angiographic Study

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ABSTRACT

Objective: To establish whether the ABO alleles are in confederacy with Ischemic Heart Disease (IHD) in Pakistani Population

Study Design: Analytic comparative study

Place and Duration: Punjab Institute of Cardiology Lahore, from September 2015 to September 2016

Methodology: About 734 IHD suspects and 500 controls were selected via non-probability purposive sampling techniques. Out of 734 suspects of IHD, 599 (81%) were diagnosed as confirmed IHD patients by interventional coronary. Control group were selected from adult healthy blood donors with no symptoms of IHD and normal ECG. All subjects were processed for ABO blood grouping, Baseline characteristics and cardio-vascular risk factors were assessed by a cardiologist. Chi-square test was used as a test of significance; p-value of <0.05 was considered statistically significant. Win Pepi software was used for statistical analysis of data

Results: Mean age of cases and control was 48±12.34 years and 47.3±2.38 years respectively. Both in cases and controls, number of males were more as compared to females. Blood group A and AB was significantly more in cases as compared to control. In control group blood group B and O was significantly more frequent as compared to cases. Among cases most common risk factrs were smoking (77.1%), ghee abuser (75%), hyperlipidemia (73.1%) and hypertension (71.1%). Majority of controls (59.2%) gave history of performing exercise (Table I). All the risk factors had a significant association with types of blood group.

Conclusion: Blood groups are significantly different between cases and controls. Risk factors have significant association with blood groups.

Keywords: ABO, Ischemic heart disease, Risk factors.

Introduction

ABO blood group system was revealed more than one century ago. [1] These are carbohydrate particles stated on the superficial area of red blood cells (RBC) .[2] Blood group A contain different glycosyl transferases as compare to blood Group B while O alleles do not have any transferase functional enzyme [3.] Furthermore ABO antigens are also present in different cells and tissue of human body i.e epithelium, sensory neurons, platelets, and vascular endothelium.[4]. ABO blood group alleles are seemingly associated with pathophysiology of multiple disease especially cardiac diseases [5,6] Therefore, clinical significance of ABO blood group alleles with heart disease is not astonishing.

Cardiovascular diseases (CVD) are considered as one of the foremost critical dilemmas among this civilized world. Disturbed the delivery of oxygenated blood, To the heart, which leads to development cardiac disabilities. CVD, are a group of multifactorial diseases, involves heart and blood vessels. The deposition of cholesterol plagues, blocked the blood vessels and as a result deprived the supply of the oxygen and nutrients to

the heart, which ultimately leads to the death of that different area of cardiac tissue, resulting in myocardial infarction. [7]

CVD is the major cause of mortality in the world with almost 17.3 million deaths annually.[8] In the year of 2000, almost 30.3% of all the deaths around the globe were due to CVD. Most of them were from developing countries.[9] National health survey of Pakistan (NHSP) in 2001, reported that IHD is the most common type of CVD, It is responsible for 12% adult mortality.[10] IHD is an inflammatory process with complicated pathology that plays a significant role in the commencement and progression.[11] The family history of hypertension, hyperlipidemias, diabetes mellitus and genetic properties are major risk factors associated with IHD.[12]

Various studies have been conducted to suggest the relationship of ABO blood groups and IHD, such that individuals of a non-O type (A, B, or AB) are more likely to have IHD than blood group "O" individuals.[13-15] But that doesn't mean an individual with blood group other than O should be excessively alarmed. Furthermore, studies have shown that non–O-type individuals with elevated cholesterol absorption rates.[16] Therefore, IHD susceptibility is influenced by ABO group due to its direct effect on cholesterol levels. Blood is a complete and unalterable moiety of any individual. ABO and Rh are major clinically significant blood Group Antigens. The antigens of the ABO blood group are composed of glycoproteins and glycolipids.

This ABO group contains A and B alleles on their locus which are responsible for glycosyl-transferase activities associated with A and B. The A and B alleles of the ABO locus encode A and B glycosyl-transferase activities, which alter the precursor H antigen. These antigens contain extra saccharide unit known as the O unit (N-acetyl galactosamine and galactose). This transferase enzyme activity is absent from O group individuals and unchanged H-antigen has expressed.[17] This study was planned to determine the association between ABO blood groups and IHD.

Methodology

A total of 734 suspects of IHD were selected randomly and processed for Interventional coronary angiography. Out of 734 total 599 (81%) confirmed IHD cases were included in the study. Total 500 individuals with no symptoms of IHD and normal ECG were selected as controls from adult healthy blood donors. About 2 ml EDTA blood samples were collected from every individual and processed for ABO blood grouping by standard hem-agglutination technique. Cardiovascular risk factors were assessed by a cardiologist. Clinical features along with demographical characteristic of patients, previous history of hypertension, diabetes and smoking were collected from medical records. All cases of valvular heart disease, congestive heart failure, autoimmune disease and rheumatic heart disease were excluded from the study. Frequencies and percentages were calculated by SPSS 21.0,

Results

Mean age of cases and control was 48±12.34 years and 47.3±2.38 years respectively. Both in cases and controls, number of males were more as compared to females (Table I). Blood group A and AB was significantly more in cases as compared to control. In control group blood group B and O was significantly more frequent as compared to cases (Table I). Among cases most common risk factrs were smoking (77.1%), ghee abuser (75%), hyperlipidemia (73.1%) and hypertension (71.1%). Majority of controls (59.2%) gave history of performing exercise (Table I). All the risk factors had a significant association with types of blood group (Table II).

Table I: Demographic variables and Risk factors among cases and control

Variables	Cases IHD (n=599)		Controls (n=500)		X^2 and p-Value
	Frequency	Percentage	Frequency	Percentage	
Male	419	69.9	382	76.4	
Female	180	30.1	118	23.6	$X^2 = 5.73$ $p = 0.017$
Blood group A	216	36.1	120	24	$X^2 = 18.67$ $p = 0.000$
Blood group B	162	27.0	170	34	$X^2 = 6.25$ $p = 0.012$
Blood group AB	115	19.2	45	9	$X^2 = 22.79$ $p = 0.000$
Blood group O	106	17.7	165	33	$X^2 = 34.35$ $p = 0.000$
Smoker	462	77.1	139	27.8	$X^2 = 323.48$ $p = 0.000$
Hypertension	426	71.1	211	42.2	$X^2 = 93.53$ $p = 0.000$
Hyperlipidemia	438	73.1	185	37.0	$X^2 = 144.82$ $p = 0.000$
Diabetic	246	41.1	75	15.0	$X^2 = 89.56$ $p = 0.000$
Family History	234	39.1	213	42.6	$X^2 = 1.41$ $p = 0.235$
Exercise habitual	216	36.1	296	59.2	$X^2 = 58.642$ $p = 0.000$
Banaspati abuser	449	75.0	173	34.6	$X^2 = 180.70$ $p = 0.000$

Table: II Association of risk factors and blood groups between cases and control

Risk factors	Blood Groups								X^2 and p-value
	A (n=336)		B (n=332)		AB (n=260)		O (n=271)		
	I n=216 n(%)	II n=120 n(%)	I n=162 n(%)	II n=170 n(%)	I n=115 n(%)	II n=145 n(%)	I n=106 n(%)	II n=165 n(%)	
Smoker	115 (53.2)	45 (37.5)	142 (87.6)	65 (38.2)	91 (79.1)	20 (13.7)	84 (79.2)	30 (18.1)	$X^2 = 10.21$ $p = 0.017$
Hypertension	112 (51.8)	86 (71.6)	144 (88.8)	75 (44.1)	75 (65.2)	35 (24.1)	95 (65.5)	15 (9.0)	$X^2 = 28.57$ $p = 0.000$
Hyperlipidemia	192 (88.8)	65 (54.1)	85 (52.4)	45 (26.4)	96 (83.4)	20 (13.7)	65 (61.3)	55 (33.3)	$X^2 = 12.91$ $p = 0.005$
Diabetic	58 (26.8)	25 (20.8)	82 (50.6)	15 (8.8)	86 (74.7)	17 (11.7)	20 (13.7)	18 (10.9)	$X^2 = 20.43$ $p = 0.000$
Family History	69 (31.9)	95 (79.1)	72 (44.4)	28 (16.4)	39 (33.9)	38 (26.2)	54 (50.9)	52 (31.5)	$X^2 = 42.55$ $p = 0.000$
Exercise habitual	63 (29.1)	69 (57.5)	54 (33.3)	112 (65.8)	49 (42.6)	47 (32.4)	50 (47.1)	69 (41.8)	$X^2 = 11.10$ $p = 0.011$
Banaspati abuser	141 (65.2)	81 (67.5)	132 (81.4)	24 (14.1)	86 (74.7)	30 (20.6)	77 (72.6)	38 (23.0)	$X^2 = 21.72$ $p = 0.000$
I=Cases, II = Control									

Discussion

In last few years multiple reports have reported significant association between blood group and coronary heart disease or Ischemic Heart Disease. Previous studies has reported high rate of stable angina and acute myocardial infarction among blood group AB. [18] A study from England also reported high rate of IHD among blood group AB population [19] Similarly a study conducted by Ali et showed blood group A was 3.14 fold more predominant than B, 6.35 fold than O, and 3.32 fold than AB. [20] Likewise, A was leading among the patients in Rawalpindi.[21]

It is very interesting for us to study about certain blood groups and their association with IHD and its development. The results of present study showed a significant association between IHD and ABO blood groups principally blood group "A". Among control group, the most common blood groups were "B"(34%). Among IHD confirm patients 420(78%) were male and

180(22%) were female. The blood group "A" was found to be a most prevalent group among IHD patients and "O" group was the least common with the frequency of 36 % and 17 % respectively. While in the category of the control group "B" was observed more common as compared to "A" and "AB" blood group. Among the risk factors associated with IHD, it was observed that lack of doing exercise is also a significant risk factor for IHD patient. The ratio of IHD is highest among people with a habit of not doing exercise on regular basis.

Clinically IHD in South Asians (Pakistani) is similar to the population of Europe. Whincup et al report very similar results to present study, from England[22] And from other parts of Europe, [23] and USA.[24] Modern science proves certain parameters as risk factors linked with IHD. According to researchers the age, gender, family history of IHD is considered as non-modifiable factors. Although other factors i.e; history of any comorbidities (hypertension, obesity, smoking, diabetes are more threatening factors**.** People with large BMI are more prone to develops IHD**.** In Pakistan gee is used as common cooking oil on daily basis and it is one of the major sources for Pakistani population to getting IHD. Researchers have been trying to find out any path-physiological co-relation among blood groups and IHD. Different theories about their mechanisms have been reported. Genetic Studies showed that genes for ABO group's inheritance were located on chromosome 9 (locus 9p34). At the same places, the genes responsible for the cholesterol balance is also found, so it was claimed by different genetic investigators that there would be the possibility of genetic exchange between IHD and ABO groups.[25]

In consistency to this proposal, non "O" group individuals have a significant tendency of developing a relationship with hypercholesterolemia and previous family history of IHD. Several biomarkers are also possible factors for IHD, predominantly von Willebrand factor (vWF) and factor VIII [26]. Factor VIII is more common in non-O blood group. While on the other side von Willebrand factor is found 25% more among non O people as compared to "O" blood group [27]**.** Therefore, elevated factor VIII–vWF levels have more chances to form blood clots and coagulation, which results in the development of more heart issues. vWF playing an important role in platelets and vascular

wall interaction, and acting as a significant factor in Factor VIII function. Deficiency of vWF is associated with bleeding, its redundancy was established to be coupled with thrombosis [28]. For that reason, coronary heart problems are connected with vWFlevelsin blood.[29]

Furthermore, the reason of fluctuation in vWF levels in blood groups is not clear yet. The interaction of different antigenic properties of ABO groups in endothelial cells may have an impact on the synthesis of vWF.[30] According to a study conducted by Gill et al., the lowest amount of vWF in "O" blood group people is 75IU/dL and highest levels reported in an "O" was 123 IU/dL) respectively.[27] But the high ratio of factor VIII levels were also reported in a study among ABO blood group.[31] The process of atherosclerosis is mediated by adhesion molecules. Different studies reported that inflammatory markers including soluble P-selection, soluble E selection, and insoluble intercellular adhesion molecules are closely linked with IHD.[32 ,33] Single nucleotide polymorphisms at ABO locus are associated with these inflammatory markers according to genetic studies. [34,35] Several previous studies have shown that patients of non-O blood group have significantly higher rates of myocardial infarction as compared to blood group O. [30,36] As per the report of Northwick Park Heart Study, "AB" group are at more risk for developing IHD as compared to other groups. Patient with phenotype showed the highest incidence of IHD by Framingham. [37] Lee et al declared group "A" as an independent risk factor for IHD [38]. While according to He et al.," B" is a sovereign aspect of myocardial infarction. [37] In a meta-analysis conducted on a time frame of 20 years on follow up patients, it was observed that blood group "O" had relatively at lower risk of acquiring IHD with respect to other groups [37]. In another study by Sharif et al showed The prevalence of blood groups in IHD group was 34% in blood group A, 29% in blood group B, 14% in blood group AB and 23% in blood group O. In control group the distribution of B, A, AB and O blood groups were 34.4%, 20.9%, 12.6%, 32.2% respectively. A Rh+ve factor was prevalent in 90.5% among IHD group and 92.6% in control subjects.

A previous study stated that frequency of IHD was 63.5% and 36.5% among males and females respectively, Hypertension was 58.5%, diabetes 53%, family history 45%, exercise habitual were only 35.5%, 58.5% were ghee abuser, and 58% were smokers.[39] No difference between blood groups and IHD were reported by Amirzadegan et al and biancari et al in their work. There are significantly higher chances of myocardial infarction was observed in individual with blood group B.[38] While people belonging to a non-O blood type people around the world still have not reported any case of developing IHD.

Conclusion

We conclude that there may be a significant association between various blood groups and IHD. Though the exact cause is unknown, a multitude of serious factors is linked with the development of IHD. "Thus, in our opinion, health status of any person is directly manipulated by the lifestyle of any individual.

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