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## **A<sup>+</sup> and AB<sup>+</sup> blood groups are risk factors for coronary artery disease in Iranian men and women respectively**

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**Abstract**--The ABO blood group antigens, which represents genetic markers, are correlated with a number of diseases. However, the relationship between the ABO blood group system and coronary artery disease (CAD) is controversial. The aim of this study was to evaluate the association between ABO blood group system and CAD and its major risk factors. One thousand patients who underwent coronary angiography, were included. The study population comprised 590 males at a mean age of  $56 \pm 12$  years and 410 females at a mean age of  $59 \pm 13$  years. There was no difference in the distribution of the ABO blood groups between the study subjects and the general population (healthy blood donors). Excluding gender, there was no association between the ABO blood groups and CAD while, there was a significant correlation between CAD and the AB<sup>+</sup> blood group in the women ( $P=0.001$ ) and the A<sup>+</sup> blood group in the men ( $p=0.015$ ). There was also a significant association between the absence of the Rhesus antigen (Rh<sup>-</sup>) and normal coronary arteries ( $p=0.008$ ). Apropos the risk factors, the prevalence of the current risk factors of CAD was similar among the subjects with different ABO blood groups.

**Keywords**--ABO blood groups, coronary artery disease, risk factor, rhesus antigen.

## **Introduction**

The ABO blood group antigens, are present on the surfaces of red blood cells and in such a variety of human cells and tissues as the epithelium, vascular endothelium, and platelets; accordingly, it is highly probable that they are implicated in the pathophysiology of a wide range of human diseases (Chen et al., 2016; Dodiya et al., 2013; Franchini & Lippi, 2015; Zhang et al., 2015; Cesena & da Luz PL, 2006; Celebi et al., 2020; Zhou S, Welsby, 2014). A clear correlation has been established between the ABO blood group system and the blood levels of factor VIII and von Willebrand Factor (vWF), 2 proteins involved in blood clotting. Low levels of the proteins in individuals with the O blood group lead to excess bleeding and increased plasma levels of these proteins result in excess clotting and also increased risk of arterial and venous diseases in non – group of individuals (Ba et al., 2017; Natarajan et al., 2020; Hasan et al., 2014; Makoui, 2013; Clark & Wu, 2011; Anstee, 2010). Although the association between the ABO blood group system and different cardiovascular diseases has been previously underscored by a large number of studies, relationship between the ABO blood groups and CAD and its major risk factors is yet to be fully elucidated (Barzigar et al., 2015; Huang et al., 2017; Hassantash et al., 2007). Identification of the relationship between the ABO blood groups and CAD may play an important role in reducing morbidity and mortality of CAD by assisting in the selection of at risk patients for preventive treatment. The aim of the present study was to investigate the correlation between the ABO Blood group system and CAD and its major risk factors.

## **Materials and Methods**

This cross sectional study was conducted on 1000 patients who underwent coronary angiography in Rajaie Cardiovascular, Medical, and Research Center, Tehran, Iran, between March 2018 and September 2020. Patients were included if they had no history of cancer, coronary artery bypass graft surgery (CABG) percutaneous coronary intervention, or autoimmune or endocrine diseases. Patients were excluded if they were enrolled for a 2nd time or if they were aged >70 years. The patients' personal information and, medical history as well as the results of their physical examinations, laboratory tests and coronary angiography procedures were recorded and analyzed. The data were described as count (%). Comparison between the groups was performed using the Pearson's chi square or the fisher exact t. IBM SPSS statistics version 22 for Windows (IBM Inc. Armonk, NY USA) was used for the statistical analysis. The significance level was set at a P value = 0.05.

## **Results**

The distribution of the ABO blood groups between study subjects and general population were shown in table 1. Without considering gender, there was not any relationship between the blood group with CAD and also with the disease severity (Tables 2,3). In Table 4 development of CAD in patients with o Blood type compared with non – o blood type subjects. There was not any significant difference between these two groups. In the term of ABO with considering gender and Rh factor, our results determined that AB+ blood group in females and A+

group in males are associated with CAD ( $p=0.001$  and  $p=0.015$  and Table 5) and Rh - group (without considering ABO blood type) is associated with normal coronary artery ( $p=0.008$  Table 6)., related to risk factors no correlation was found between dyslipidemia, hypertension, Diabetes mellitus, smoking and family history of CAD with ABO blood type (Table 7).

Table 1  
Distribution of ABO blood group in our study subjects and general population (healthy blood donors)

Blood group	Distribution in study subjects	Distribution in general population*
A+	290 (29%)	27%
A-	32(3%)	3%
B+	177 (18%)	22%
B-	18 (2%)	2%
AB+	82 (8%)	7%
AB-	10 (1%)	1%
O+	349 (35%)	34%
O-	42 (4%)	4%
P=0.345		

\* Reported by Iranian blood transfusion organization Aug15 (2015) According to test of healthy blood donors

Table 2  
Relationship between ABO blood group and CAD

Blood group	CAD		Total
	Yes	No	
A+	244(29%)	46 (26%)	290
A-	24 (3%)	8 (5%)	32
B+	149 (18%)	28 (16%)	177
B-	14 (2%)	4 (2%)	18
AB+	69 (8%)	13 (8%)	82
AB-	7(1%)	3 (2%)	349
O+	291 (35%)	58 (34%)	349
O-	30 (4%)	12 (7%)	42
Total	828 (100%)	172 (100%)	1000
P=0.224			

Table 3  
Association between severities of coronary atherosclerosis (according to angiographic data) with ABO blood groups

Blood group	3VD	2VD	SVD	Min CAD	Normal	Total
A+	70	71	78	25	46	290
A-	7	5	9	3	8	32
B+	48	33	54	14	28	177

B-	4	2	5	3	4	18
AB+	21	18	19	11	13	82
AB-	3	-	3	1	3	10
O+	91	82	81	37	58	349
O-	10	5	7	8	12	42
Total	254	216	256	102	172	1000
P=0.195						

3VD = Three vessel disease

2VD = Two vessel disease

SVD = single vessel disease

Min CAD = minimal coronary artery disease

Table 4  
Relationship between CAD with o and non- o Blood groups

Blood group	CAD		Total
	Yes	No	
O	321 (39%)	70 (41%)	391
Non - O	507 (61%)	102 (59%)	609
Total	828 (100%)	172 (100%)	1000
P = 0.435			

Table 5  
Correlation between ABO blood group (with considering gender and Rh) with CAD in Male and Female

Blood group	Male CAD		Female CAD		Total
	Yes	No	Yes	No	
A	157(32%)	25(26%)	87(26%)	21(27%)	290
A-	15(3%)	5(5%)	9(3%)	3(4%)	32
B+	89(18%)	16(17%)	60(18%)	12(16%)	177
B-	9(2%)	2(2%)	5(1%)	2(3%)	18
AB+	28(6%)	7(7%)	41(12%)	6(8%)	82
AB-	3(1%)	1(1%)	4(1%)	2(3%)	10
O+	176(35%)	32(34%)	115(34%)	26(34%)	349
O-	18(4%)	7(8%)	12(4%)	5(6%)	42
Total	495(100%)	95(100%)	333(100%)	77(100%)	1000
	590		410		
P=0.001					

Table 6  
Correlation between Rhesus Antigen (without considering ABO blood group)

Blood group	CAD		Total
	NO	YES	
Rh+	145	753	898

Rh-	27	75	102
Total	172	828	10.0
P = 0.008			

Table 7  
Association between current risk factors of CAD and ABO Blood groups (with considering Rh)

Blood group	HLP		DM		HTN		Smoking		FH	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
A+	129(30%)	161(28%)	53(27%)	237(29%)	97(27%)	193(30%)	53(30%)	237(29%)	30(29%)	260(29%)
A-	13(2%)	19(3%)	7(4%)	25(3%)	13(4%)	19(3%)	8(5%)	24(3%)	4(4%)	28(3%)
B+	69(16%)	108(19%)	37(19%)	140(17%)	68(19%)	109(17%)	29(17%)	148(18%)	16(15%)	161(18%)
B-	7(2%)	11(2%)	5(3%)	13(2%)	8(2%)	10(2%)	3(2%)	15(2%)	3(3%)	15(2%)
AB+	38(9%)	44(8%)	15(8%)	67(8%)	35(10%)	47(7%)	16(9%)	66(8%)	9(9%)	73(8%)
AB-	4(1%)	6(1%)	2(1%)	8(1%)	5(1%)	5(1%)	2(1%)	8(1%)	2(2%)	8(1%)
O+	152(36%)	197(34%)	68(35%)	281(35%)	116(33%)	233(36%)	56(32%)	293(36%)	36(35%)	313(35%)
O-	11(3%)	31(5%)	8(4%)	34(4%)	13(4%)	29(4%)	7(4%)	35(4%)	4(4%)	38(4%)
Total	425	575	195	805	355	645	174	826	104	896
P value	P=0.083		P=0.967		P=0.092		P=0.394		P=0.940	

### Conclusion

The ABO blood group system was the first genetic polymorphism discovered in human thus research on this system has been of great interest because of its importance in different diseases (Zhang et al., 2015). Many studies were conducted to find association between this blood group system with coronary artery disease as to help in developing preventive strategies (Dodiya et al., 2013; Franchini & Lippi, 2015; Gorohi et al., 2018; Zhang et al., 2015; Cesena & da Luz PL, 2006) but the results of the studies were different and relationship between this blood groups and CAD is still unclear (Chen et al., 2016; Dodiya et al., 2013; Barzigar et al., 2015). The results of many studies determined that the risk of developing CAD in individuals with O blood group is significantly lower than those with non -o subjects. He, et al. (2012) in a meta – analysis study used the data obtained in two prospective cohort studies and showed with the O blood

group have moderately lower risk of developing CHD. Carpeggiani, et al. (2010) followed up 4901 patients for ten years and determined that non -O blood group is predictive factor for heart disease mortality in patients under 65 years old specially in females. Zhou Chen, et al [1] in updated systemic review and meta-analysis study combined results of 17 studies and showed that non - o and blood group A are risk factors of CAD. Takagi et al. (2015) enrolled data from 10 studies and demonstrated in subjects with non -o blood group 14% increase in CAD incidence compared to subject with O blood group. most of this group studies suggested that high plasma level of von Willebrand Factor (vWF) and factor VIII have important role in underlying mechanisms of association between CAD and non - o blood groups. The vWF has an important role in thrombosis by mediating platelet adhesion to the vascular wall. vWF also participates in platelet aggregation and play a role in development of atherosclerosis (Chen et al., 2016; Franchini & Lippi, 2015; Cesena & da Luz PL, 2006; He, et al., 2012)

Results obtained in another group of studies showed that the risk of CAD in subject with one of the ABO blood group is higher than other blood groups. Study of Biswas et al. (2013) in eastern of India showed that the risk of CHD in subjects with o blood is higher than individuals with other blood groups. Dhamendra et al. (2013) observed that in gujarati population, individual with O and A blood groups have high relative risk of CAD. Results of Sotodeh Anvari et al (2009) showed that among patients who admitted for CABG prevalence of ABO blood group was O. In the most this group studies ABO blood groups distribution in patients with CAD have been investigated but didn't compared with distribution of the blood groups in patients with normal coronary artery and also with general population (Suryasa et al., 2021).

The results obtained in another group of studies are similar to results of our study. Data obtained in Karabuva et al. (2013) same as our results showed that there was not significant difference in ABO blood group distribution between CAD patients (without considering gender and Rh factor) and general population (healthy blood donors) and also they didn't find any association between ABO blood group and extent of CAD. The data obtained in Amirzadegn et al. (2006) showed that the blood group could not serve as a risk factor for CAD. Our results determined that prevalence of CAD in patients with Rh<sup>+</sup> is higher and Rh<sup>-</sup> Blood groups significantly associated to normal coronary artery. In addition, we found a significant correlation between CAD with AB<sup>+</sup> blood group in women and with A<sup>+</sup> blood type in men.

The obtained data by Karabuva et al [22] showed that among CAD patients, men with AB blood group were significantly younger than their pairs with non- AB blood groups and The AB blood group might possibly identify Croatian males at risk of developing the premature CAD while Stakisaltis et al. (2002) didn't find any difference in distribution of AB blood group in women with CAD. In contrast to our data, results obtained by Biswas et al. (2013) determined that risk of developing CAD in subjects with AB blood group significantly lower than subjects with other ABO blood group, While obtained data in DR Meian He et al. (2012) (Harward school of Public health) showed that rates of CAD for women with AB blood type is higher than women with other ABO blood type. This results are similar to our data. We did not find any relationship between current risk factors

of CAD with ABO blood type while in Abdollahi et al. (2009) they found significant association between A Blood group with family history of CAD also obtained data by carpeggiani et al. (2010) determined that non - o blood group was significantly correlated with family history of CAD. Results of study done by Karabuva et al. (2013) showed, that, diabetes Mellitus and dyslipidemia were more predominant in AB blood group compared to non-AB blood groups and hypertension was predominant in B blood group but there were not statistically significant and data obtained in a study showed that the individual with A blood group have higher level of total and LDL cholesterol compared to other blood groups (Ashoori et al., 2018; He et al., 2012; Hajilou et al., 2021). In summery our data suggested that Rhesus antigen (Rh<sup>+</sup>), have a role in development of CAD in Iranian population. AB<sup>+</sup> and A<sup>+</sup> blood group have similar role in Iranian females and males. Determination of relationship between ABO blood group and CAD need to investigation with considering gender. Also probably dependent on ethnic and environmental characteristics, similar studies, may obtain different results.

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