

ABO BLOOD GROUPS: A POTENTIAL RISK FACTOR FOR CORONARY ARTERY DISEASE (CAD)

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Author's Contribution:

S.S. designed the model along with the computational framework and data analysis. S.T.A. and A.K. carried out the implementation. J.A. performed the calculations. R.P. and S.S. wrote the manuscript with input from all authors. S.T.A and A.K. conceived the study and were in charge of overall direction and planning.

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ABSTRACT:

Background:

Coronary artery disease (CAD) is a globally prevalent disease with high mortality rate. Pakistan suffers equally from a great burden of disease and it is anticipated that its toll may rise further by at least 50 % in the coming years. Therefore, a lot of work has been done on its associated risk

factors. Of them, one potential unmodifiable factor that has been under consideration in recent times which has an impact on CAD, is ABO blood groups. Researchers are extensively working on ABO blood groups with regard to its association with CAD and have achieved remarkable results. Pakistani literature in this regard is scarcely present, so this study aims to explore the association of ABO with CAD, using angiographs as a gold standard tool for diagnosing CAD.

Materials and Method:

This cross sectional study consists of 138 subjects of both the genders. After taking written consent, patients with angiographs having stenosis of more than 50% of one, two or three arteries were enrolled for the study and labeled as 1VD, 2VD and 3VD respectively. Involvement of left main artery was considered as presence or absence of left main stenosis. The blood groups of the subjects were determined using conventional tube agglutination method.

Results:

This study shows that A+ blood group was prevalent in all the coronary artery disease patients, showing its preponderance towards CAD, which is consistent with the findings of most of the Western researches. However, this study predicts that O+ blood group is the 2nd most frequent group in CAD subjects after A+, whereas according to a lot of Western studies, O blood group is considered as protective for CAD.

Conclusion:

Genetic studies are now required in this domain to help in evaluating the genetic polymorphisms that are occurring in the population related to ABO gene.

INTRODUCTION:

Coronary artery disease (CAD) is a complex multifactorial disease and accounts for the greatest number of deaths worldwide (1). Though its global prevalence is high but the mortality rate has declined in the western world due to routine screenings, early detection and timely clinical intervention. On the contrary, CAD is on an escalation in middle and low income countries (2). Pakistan unfortunately, categorized as the latter countries and therefore, suffers from a great burden of CAD. 30% of the middle aged Pakistani population is affected with the disease (3). The disease liability has approximately increased two-folds, particularly in Karachi since 1970 (4) and it is anticipated that its toll may rise further by at least 50 % in the coming years.

Because of all of these factors and future expectancies, researchers are trying to work upon the risk factors of CAD to help predict the vulnerability of the disease in the individuals who may otherwise, develop CAD in future. Some of the established and modifiable risk factors related to CAD are stress, sedentary life style, smoking, hypertension, dyslipidemia, diabetes and obesity. These have been found in about 80% of the CAD cases (5). But all these risk factors are acquired over a period of time and can be modified according to the situation. However, there is one

potential unmodifiable factor that has been under consideration in recent times which has an impact on CAD, is ABO blood groups.

An abundant amount of work has been done in the western world in regard to association of blood groups with CAD (6, 7) and majority of the studies are on the consensus that 'A' blood group is associated with CAD, whereas group 'O' is found protective against it. As, such associations may depend on ethnic and racial backgrounds, therefore studies were done in Asian countries also to explore this association in their respective populations (8, 9) The studies showed diverse results in a way that some showed significant association between the two variables and some showed contradictory results. An Indian researcher published an article showing B blood group to be associated with CAD (10) which was in contrast to what the various western studies have revealed.

In Pakistan, studies related to this association are scarcely available; and those that are done, are mainly survey based. Moreover, in those studies, CAD subjects were diagnosed by the cardiologists through the assessment of patients' ECG reports or through filled questionnaires (11, 12), although for confirming CAD, angiography is considered as the gold standard. But during literature review, merely single study could be accessed on the issue (13). It is, therefore, high time to explore whether the association between ABO and CAD exists among various ethnicities of local population or not. If any such co-relation exists, then which blood group is associated with it?

This study, hence aims to explore the association between ABO blood groups and CAD on the basis of angiographic assessment and to determine the blood group associated with CAD.

Materials and Method:

This is a cross-sectional study. The participants included in the study were 138. The sample size was estimated through Openepi software. The subjects selected were all those patients who visited the cardiology department of Ziauddin Hospital or visited Hussaini Blood Bank (May-Sept 2022), with coronary artery disease diagnosed on angiography. Normally, there are 3 main coronary arteries arising from the aorta, one right coronary artery (RCA) and two left arteries; left descending artery (LAD) and circumflex artery (Circ) along with a left main artery. Stenosis of more than 50% of one, two or three arteries was considered as one vessel (1 VD), two vessel (2 VD) and three vessel (3 VD) disease respectively. Involvement of left main artery was considered as presence or absence of left main stenosis. All the subjects of both the genders belonged to age group 25-75years. Written consent was acquired and details related to the demographics and medical history was obtained from the patients on a prescribed proforma. The angiography reports were kept for evaluating the degree of stenosis. Patients suffering from chronic liver disease, chronic kidney disease or any malignancy were excluded from the study. The study was approved by Ethical Review Committee of Ziauddin University (vide Reference No. 5230322SAPHY).

In the cases where patients had undergone multiple angiographies, their latest reports were used for the analysis. All the data collection was done under the supervision of a proficient cardiologist working at the teaching hospital attached to Ziauddin University. The blood groups of the subjects were determined using conventional tube agglutination method by forward and reverse typing from the freshly collected blood samples.

SPSS version 25 was used to analyze the data. The angiography findings were noted as 1VD, 2VD and 3VD. The missing data was reported as 0. Categorical data was represented by frequency and percentages and numeric data by mean and standard deviation. The categorical data included gender, ethnicity, family history of CAD, smoking, blood groups (A+, B+, O+, AB+, AB-, B- and O-), angiography findings (1 VD, 2 VD and 3VD), presence or absence of left main stenosis and hypertension and type II diabetes mellitus. Chi square test was used to show the association between coronary artery disease and ABO blood groups and also between the presence of left main stenosis and blood groups. A value of ≤ 0.05 was taken as statistically significant. The numeric data included age.

Results:

138 patients participated in the study. Table I shows the demographic characteristics of the participants. The mean age calculated was found 65 ± 9 years that shows that coronary artery disease is not solely restricted to old age, but affects young individuals as well. Comparing the genders, it was observed that 57.3% were males and 26.8% were females, showing the greater number of males were affected with CAD compared to females. Majority of the patients who participated in the study was Urdu speaking (46%), while the rest were Pathans(11%), Punjabis(6.1%), Sindhi(2.4%) and other minorities like Baloch and Hindku. This could be because of the greater number of Urdu speaking inhabitants in Karachi. When comorbids like hypertension and diabetes were evaluated on SPSS, 64.6% individuals had hypertension and 46.3% suffered from diabetes. This shows that most of the patients who had CAD, also had hypertension and diabetes simultaneously. The number of patients who presented with positive family history of CAD were 62(37.8%), which shows some genetic association of CAD like genetic polymorphism of blood groups. Majority of the patients (51.2%) were nonsmokers in this study.

TABLE I

Demographics Profile Of The Study Individuals			
		Frequency	Percent
Gender	Male	94	57.3
	Female	44	26.8
Ethnicity	Baloch	6	3.7

	Hindku	4	2.4
	Khaki	2	1.2
	Memon	2	1.2
	Pathan	18	11.0
	Punjabi	10	6.1
	Sindhi	4	2.4
	Urdu	76	46.3
Hypertension	No	32	19.5
	Yes	106	64.6
Diabetes	No	62	37.8
	Yes	76	46.3
Family History of CAD	No	72	43.9
	Yes	62	37.8
Smoking Status	Current	14	8.5
	Ex	22	13.4
	Never	84	51.2

Table II shows the cross tabulation between angiography findings and blood groups. It clearly reveals that number of patients with 3VD were greater than with 2VD or 1VD. Also, the patients with A+ blood group were seen higher amongst CAD. Fig#1 is a bar chart of the same variables showing that A+ blood group was prevalent in all the coronary artery disease patients, showing its preponderance towards CAD. The next prevalent blood group was O+ in 1 VD and 3VD, whereas in 2VD, B+ was the next prevalent blood group. We did not find any patient of CAD with A- blood group that's why it is eliminated from the analysis. '0' represents all those patients who had lost or missed their angiography reports and so the number of diseased vessels could not be recorded. When Chi square test was applied on these two variables, the p-value came out to be 0.000 which is highly significant (Table III). This indicated that CAD was vastly associated with blood groups, especially blood group A+ was seen to be significantly linked to CAD.

TABLE II

ANGIOGRAPHY FINDINGS & BLOOD GROUPS: Cross tabulation								
ANGIOGRAPHY FINDINGS	BLOOD GROUPS							Total
	A+	AB-	AB+	B-	B+	O-	O+	
0	2	0	0	0	4	0	2	8
1VD	10	4	0	0	4	0	8	26
2VD	14	0	0	2	12	8	4	40
3VD	20	0	6	4	14	2	18	64
Total	46	4	6	6	34	10	32	138

Fig:1

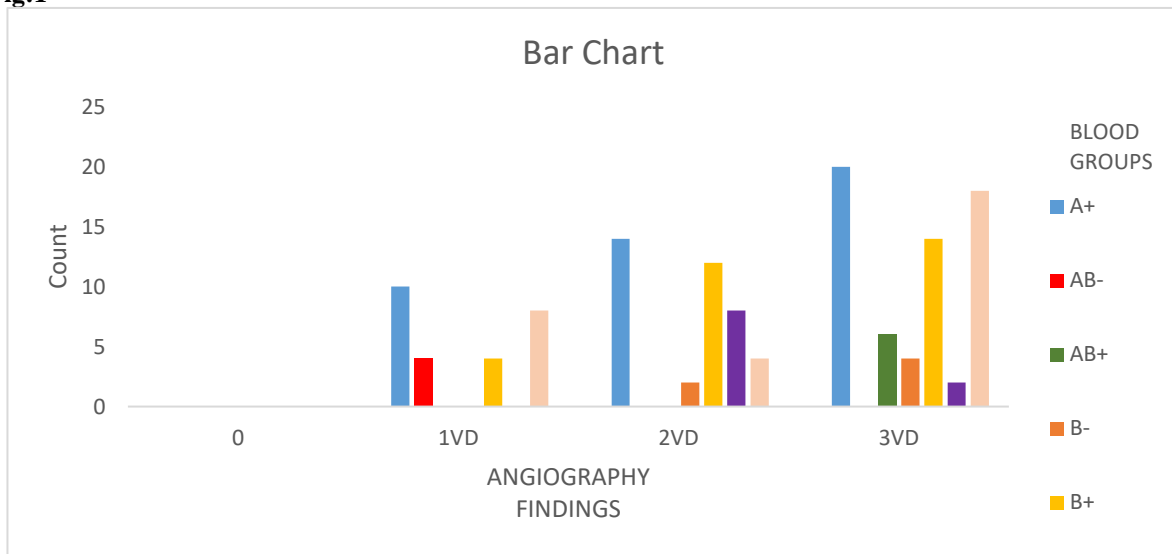


TABLE III

Chi-Square Test- CAD And Blood Groups			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	47.635 ^a	18	0.000
Likelihood Ratio	47.748	18	0.000
Linear-by-Linear Association	0.100	1	0.752
No of Valid Cases	138		

a. 19 cells (67.9%) have expected count less than 5. The minimum expected count is .23.

Table IV shows a cross tabulation between the left main stenosis and blood groups. The number of individuals presenting with left main stenosis was 12(9%). It is evident that despite A+ being prevalent in CAD, the left main stenosis is seen more in O+ patients. When Chi square test was applied between these variables, the p-value came out to be 0.023(Table V) which is significant, showing association between left main stenosis and blood groups, particularly O+ blood group.

TABLE IV

Left Main Stenosis And BLOOD GROUPS Crosstabulation								
Left Main Stenosis	GROUPS							Total
	A+	AB-	AB+	B-	B+	O-	O+	
No	44	4	6	6	32	10	24	126
Yes	2	0	0	0	2	0	8	12
Total	46	4	6	6	34	10	32	138

TABLE V

Chi-Square Test-Left Main Stenosis And Blood Groups			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	14.625 ^a	6	0.023
Likelihood Ratio	13.885	6	0.031
Linear-by-Linear Association	6.377	1	0.012
No. of Valid Cases	138		

a. 8 cells (57.1%) have expected count less than 5. The minimum expected count is .35.

DISCUSSION:

Blood groups acting as a risk factor for coronary artery disease are a longstanding subject of discussion for researchers. Most of the literature supports this idea (7, 14, 15). The most common blood group that is seen associated with CAD is 'A' which is consistent with our findings. A meta-analysis published in the year 2016 covering 17 studies concluded that 'A' and non O blood groups, both were risk factors of CAD. Even when the studies related to myocardial infarction were removed, the association between A blood group and CAD remained significant (16). Another study conducted in Africa to validate this association in their population also concluded that A blood group acts as a risk factor of ischemic heart disease involving CAD (17). The cause of this association is yet to be confirmed but most of the studies suggest that A blood group contains greater amount of vWF and factor VIII, due to which it confers the greater risk of venous and arterial thrombosis than group O. The previous researches usually have not

considered Rh factor in such association, but present study attempted to find this association as well. It was surprising to report that not a single participant with A- blood group was found amongst 138 patients under investigation. On the other hand, A+ was the most frequent in CAD.

In contrast to A blood group being the potential risk factor of CAD, O blood group is considered as the most protective group against CAD according to most of the western researches (16, 18). A study conducted in Italy recruited blood donors and allotted them a cardio risk score on the basis of some parameters. According to the study, subjects who although had a lower calculated risk score, but had a non O blood group were 3 times more prone of developing cardiovascular events than O blood group, suggesting O blood group to be protective for CAD (7). Another article intriguing the relationship of ABO blood groups with cardiovascular disease showed that O blood group because of its structure has less thrombotic risk and inflammation, making it protective for cardiovascular events (18). Quite contrary to the Western studies, this study shows that O blood group is the 2nd most frequent group in CAD subjects after A. This result matched with an Indian study that also showed O to be associated with CAD, suggesting that lower levels of HDL in this group poses the risk of CAD in such patients (19). This ambiguity still remains unanswered and hence needs to be explored that whether O is protective for CAD or not or maybe it is protective for some ethnicities and not for others, showing genetic predisposition.

In this study, majority of the subjects were nonsmokers which is quite surprising because smoking is one of the strongest known risk factors of CAD (20). It is difficult to explain the reason, however, lead toxicity may have a role in such cases because lead from the environment increases atherosclerotic cardiovascular risk (21). Major cause of lead exposure to the Karachi population is through water. A study reported that 86% of water samples, taken from various sources, have higher level of lead than recommended WHO level (22). A study done in the district east of the city, reported the similar findings (23). Moreover, Karachi is a highly populated industrial city having cosmopolitan status. Its environment remains polluted owing to industries and motorized vehicle traffic on the road. According to a study, main cause of atmospheric lead contamination is the exhausts from the vehicles which increases the lead concentration in the blood (24). Another factor that could play a role is blood group gene polymorphisms (25, 26). The western world has already started working on the genotypes of ABO and has explored most of the SNPs related to ABO gene. As a matter of fact, some of the researchers have emphasized on the importance of genotypes so much so that they feel the need to incorporate ABO genotypes in physician's history- taking forms.

Previously, CAD was considered a disease of old age, but since the last two decades, young individuals are also seen as a victim of the disease (27) which is in consensus with the findings of present study. Many reasons like sedentary lifestyle, environmental pollution, stress or genetic polymorphisms might be the cause of this undesirable burden.

In this study, patients suffering from chronic liver disease (CLD), chronic kidney disease (CKD) or any malignancy were excluded from the study. The reason for excluding patients with CLD

was that heart and liver dysfunction usually coexists because of some cardio-hepatic interactions (28). This meant that subjects with CLD in most of the instances would have some form of cardiac weakness as well. Coronary heart disease as a consequence of this cardiac weakness could have altered the results. Secondly, subjects with CKD were eliminated from the study as CKD itself is related to myocardial disease by causing hypertension, atherosclerotic vessels and ultimately CAD (29). Malignancy was excluded as cancerous treatments have many cardiovascular effects and in cases of metastasis, the deteriorating effects on heart and other vital organs are even vast (30). So, all these diseases could have caused biasedness in the results of this study.

Like other studies, this study has some shortcomings. The data was collected from merely two centers, which could affect the results in terms of ethnicity and socioeconomic status. The sample size was quite limited, which could increase the margin of error and reduce the power of study. A multi-centered study with larger sample size will confirm or contradict the findings of this study. To help in evaluating the genetic polymorphisms that are occurring in the population related to ABO gene, ABO genotype should have also been assessed. It is recommended to find out the influence of Rh factor on the severity of CAD, as in the present study, patients with A – ve blood group could not be accessed.

CONCLUSION:

The findings of the study divulge that ‘A+’ blood group has a statistically significant impact on the susceptibility of CAD. O+ blood group, however, does not seem to be protective in the population studied, unlike many western researches that declare it a safer blood group in terms of having CAD. The study also shows that despite A+ being the most relevant group to CAD, involvement of left main artery is seen to be linked with O+ blood group. Similar to other studies, this study also shows that males have a greater preponderance to CAD than females.

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CONFLICT OF INTEREST:

The authors do not have any conflict of interest regarding the manuscript.

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