

# Association of Blood Groups with the Extent and Severity of Coronary Lesions in Patients with Acute Myocardial Infarction

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## ABSTRACT

**Background:** Coronary Artery Disease (CAD) is a complex interaction of genetic and multifactorial environmental factors. This study was conducted to evaluate the association of blood groups with the severity of coronary artery lesions in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention (PCI).

**Methods:** This descriptive cross-sectional study was conducted at a tertiary cardiac care center in Karachi, Pakistan. Consecutive adult patients of either gender diagnosed with ST-segment elevation myocardial infarction (STEMI) undergone primary PCI during the study period of November 2020 to February 2021 were included. Based on blood grouping patients were stratified into two groups, non-O and O. comparative analysis of clinical and angiographic findings was performed and Chi-square test was used with  $p$ -value  $\leq 0.05$  was considered statistically significant.

**Results:** A total of 398 patients were included in this study out of which 296(74.4%) were males (mean age:  $57.15 \pm 10.95$  years) and 102(25.6%) females. Type O blood group distribution was 107(26.9%) and non-O blood groups were 291(73.1%). The non-O blood group included A=110(27.6%), AB=43(10.8%), and B=138(34.7%). Significant results in type O and non-O group were seen among single vessel diseases (41.1%, 29.6%) ( $p=0.029$ ) and circumflex artery as culprit (16.8%,9.6%) ( $p=0.046$ ), whereas in post-procedure complication no significant results were found ( $p=0.554$ ) with in-hospital mortality rate ( $p=0.642$ ).

**Conclusion:** Blood group type O was found to be associated with single-vessel coronary artery diseases. However, no association of blood groups was observed with lesion complexity, post-procedure complications and mortality.

**Keywords:** Ischemic Heart Diseases; Coronary Artery Diseases; Myocardial Infarction; Blood Group.

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## INTRODUCTION

The Asian population, especially South Asians, remains at an increased risk of ischemic heart diseases (IHD), contrary to the western world, an increase in the prevalence of coronary artery diseases (CAD) is expected for this region in the next few decades<sup>1</sup>. Increased efforts in the last decades towards primary prevention, evidence-based medicines, treatments, and diagnosis have resulted in a dramatic decline in mortalities and morbidities due to IHD in Western countries<sup>2</sup>. However, increasing trends in low and middle-income countries (LMCs) pose new challenges for global public health, collectively. LMCs contribute to 80% of global deaths due to cardiovascular diseases (CVD)<sup>2,3</sup>. Drastic preventive and curative measures with a deeper understanding of underlying indigenous causative factors are crucial to tackling the impending epidemic of CAD in these regions<sup>4,5</sup>.

Worsening of metabolic risk factors is among the leading factors associated with CAD, these include high body fat (cholesterol), obesity (high body mass index), hypertension, and diabetes. Tobacco consumption, mainly in the form of smoking, has also been the leading risk factor for years of life lost due to CAD<sup>6</sup>. Previously, mass media campaigns to promote a healthy lifestyle along with preventive measures such as increased taxation on tobacco products, restrictions on smoking in public places, health warnings on the packaging of cigarettes, and free blood pressure screening events in major cities have proved effective in decreasing disease burden in high-income countries<sup>7</sup>. However, the increasing trend of CAD in low- and middle-income countries can be partly associated with the increasing urbanization and adoption of westernized lifestyles without proper access to such programs<sup>8</sup>.

Pathogenesis of CAD is a complex interaction of genetic and multifactorial environmental factors<sup>9</sup>. In addition to the traditional risk factors, blood group antigens are thought to have an association with CAD but the mechanism behind this association is not very clear<sup>10,11</sup>. Ethnic differences in ABO blood type locus have been reported which can be a major determinant of differences in CAD risk among various ethnicities, however, evidence is inconsistent for linking of ABO groups to coronary atherosclerosis<sup>12</sup>. Some studies have reported an association between increased risk of CAD and ABO group,<sup>13,14</sup> while other studies have shown no evidence of reported association<sup>15,16</sup>. Local evidence is lacking regarding the association of ABO distribution with the extent and severity of CAD, especially in the context of acute myocardial infarction (AMI), in the Pakistani population. Therefore, this study was conducted to evaluate the non-O and O blood group distribution and its

association with the extent and severity of coronary artery lesions in AMI patients with acute myocardial infarction undergoing primary percutaneous coronary intervention (PCI) at a tertiary care cardiac hospital in Karachi, Pakistan.

## METHODS

This descriptive cross-sectional study was conducted at a tertiary care public sector cardiac center of Karachi, Pakistan. This study was approved by the ethical review committee of the National Institute of Cardiovascular Diseases (NICVD), Karachi (ER-45/2020). The consent for participation and publication was obtained from all the patients included in the study. Inclusion criteria for the study were consecutive adult patients of either gender diagnosed with ST-segment elevation myocardial infarction (STEMI) undergone primary PCI during the study period of four months from November 2020 to February 2021. Exclusion criteria for the study were patients with a history of cardiac intervention or surgery for any valvular, congenital, or ischemic heart diseases, patients with dilated cardiomyopathy, thyroid diseases, or chronic kidney disease as such patients were expected to have more severe coronary lesions.

Data for this study were collected on a structured proforma consisting of demographic characteristics (gender, age, weight, and height), co-morbid conditions (diabetes, hypertension, positive family history for coronary artery diseases (CAD), obesity, and smoking), presentation details (Killip class, time of presentation, and vital signs at presentation), angiographic findings (coronary dominance, number of diseased vessels, localization of diseases (culprit artery), stenosis (%), lesion length, lesion complexity (Syntax score II), pre and post-procedure thrombolysis in myocardial infarction (TIMI) flow grade, and procedural details), and post-procedure complications and in-hospital outcomes (requirement of mechanical ventilation, arrhythmias/heart block, cardiogenic shock, acute kidney injury (AKI), slow/no-reflow, bleeding (gastrointestinal/ access site), sepsis, acute stent thrombosis, cardiac arrest, pulmonary edema, or in-hospital mortality).

ABO and Rh(D) blood grouping of the patients were determined by the conventional blood grouping test using the tile and tube method as well as anti-AB Immonet Kit in the hospital pathology laboratory. All primary PCI procedures were performed by experienced interventional cardiologists using a femoral or radial approach. Pre-treatment with anti-platelet drugs according to standard guidelines were initiated includes a 600 mg loading dose of clopidogrel plus 325 mg aspirin before the procedure and 70–100 IU/kg intravenous unfractionated heparin during the procedure.

Analysis of collected data was performed by using IBM SPSS version 21. Based on blood grouping patients were stratified into two groups, non-O and O, and comparative analyses were performed. Continuous variables such as age, weight, height, body mass index (BMI), symptom to hospital arrival time, door to balloon time, total ischemic time, systolic blood pressure, diastolic blood pressure, heart rate, stenosis (%), LVEF (%), and length of the lesion were summarized with mean  $\pm$  standard deviation (SD) or median [interquartile range (IQR)]. The blood group was compared for the continuous variables by applying an independent sample t-test. Frequency and percentages were computed for categorical variables and their association with non-O and O groups were assessed by applying the Chi-square test. The p-value of  $\leq 0.05$  was taken statistically significant.

**RESULTS**

A total of 398 patients were included in this study out of which 74.4% (296) were male patients and the mean age of the study sample was  $57.15 \pm 10.95$  years with 28.1% (112) of the patients aged above 64 years of age. Blood group distribution was 26.9% (107) blood group type O. While remaining 73.1% (291) with non-O blood groups consisted of 27.6% (110) type A, 10.8% (43) type AB, and 34.7% (138) type B (Figure 1). Demographic and clinical characteristics of the patients stratified by the blood group type are presented in Table 1. Comparative analysis of the patients in blood group type O and non-O showed no statistically significant differences in demographic distribution, the prevalence of co-morbid conditions, type of myocardial infarction, and clinical presentation.

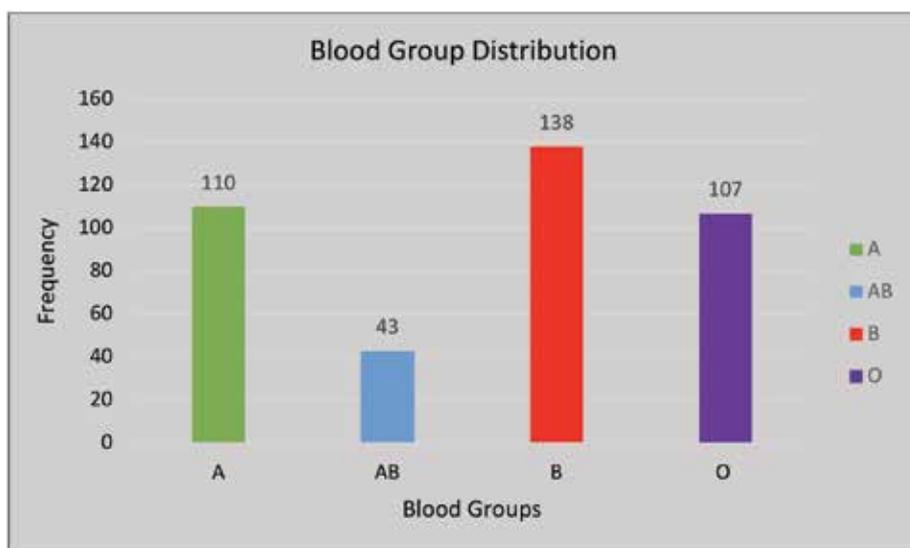


Figure 1: Blood groups distribution of the participants.

Table 1: Demographic and clinical characteristics of the patients stratified by the blood group type.

Parameters	Frequency (n) (%) /Mean $\pm$ SD/ Interquartile Range	Blood Group		p-Value
		Non-O	O	
N=398		291 (73.1%)	107 (26.9%)	-
<b>Baseline demographic</b>				
Males	296(74.4%)	212(72.9%)	84(78.5%)	0.252
Female	102(25.6%)	79(27.1)	23(21.5%)	
Mean age (years)	57.15 $\pm$ 10.95	56.82 $\pm$ 10.59	58.07 $\pm$ 11.88	0.314
Elderly ( $\geq 65$ years)	112(28.1%)	78(26.8%)	34(31.8%)	0.328
Weight (kg)	71.16 $\pm$ 7.62	70.73 $\pm$ 7.66	72.31 $\pm$ 7.4	0.067
Height (cm)	169.97 $\pm$ 4.31	169.81 $\pm$ 4.42	170.4 $\pm$ 3.98	0.226
BMI (kg/m <sup>2</sup> )	24.63 $\pm$ 2.57	24.53 $\pm$ 2.56	24.91 $\pm$ 2.58	0.186

Type of myocardial infarction				
Anterior	227(57%)	163(56%)	64(59.8%)	0.497
Inferior	119(29.9%)	89(30.6%)	30(28%)	0.623
Inferior with RV	31(7.8%)	26(8.9%)	5(4.7%)	0.160
Lateral	11(2.8%)	8(2.7%)	3(2.8%)	0.976
Posterior	10(2.5%)	5(1.7%)	5(4.7%)	0.095
Co-morbid conditions				
Diabetes	167(42%)	124(42.6%)	43(40.2%)	0.664
Hypertension	214(53.8%)	161(55.3%)	53(49.5%)	0.304
Obesity	50(12.6%)	37(12.7%)	13(12.1%)	0.880
Family history of CAD	7(1.8%)	5(1.7%)	2(1.9%)	0.919
Smoking	118(29.6%)	78(26.8%)	40(37.4%)	0.04*
Presentation				
Symptom to hospital arrival time (minutes)	240[120-400]	240[120-420]	240[120-360]	0.242
Door to balloon time (minutes)	100[100-150]	100[100-150]	100[100-150]	0.966
Total ischemic time (minutes)	367.5[250-545]	380[250-580]	340[240-510]	0.330
Systolic blood pressure (mmHg)	129.6 ± 27.1	130.5 ± 28.1	127.3 ± 24.1	0.292
Diastolic blood pressure (mmHg)	80.5 ± 16.5	81 ± 17.2	79.3 ± 14.4	0.382
Heart rate (bpm)	86.2 ± 19.9	86.7 ± 20.5	84.6 ± 18.2	0.335
Killip class III or IV	49(12.3%)	37(12.7%)	12(11.2%)	0.686
Rh(D) grouping				
Negative	22(5.5%)	17(5.8%)	5(4.7%)	0.651
Positive	376(94.5%)	274(94.2%)	102(95.3%)	

BMI = body mass index, RV = right ventricular, CAD = coronary artery diseases, \* statistically significant.

Angiographic findings and procedural characteristics are summarized in Table 2. Single vessel diseases were found to be significantly more prevalent among patients with blood group type O with a distribution of 41.1% (44/107) vs. 29.6% (86/291);  $p=0.029$  in type O and non-O group respectively. Similarly, circumflex artery as the culprit was more common among type

O group with the distribution of 16.8% (18/107) vs. 9.6% (28/291);  $p=0.046$  in type O and non-O group respectively. Distribution of coronary dominance, pre-and post-procedure TIMI flow lesion length and complexity, stenosis (%), and left ventricular ejection fraction showed no significant association with blood group type O and non-O.

**Table 2: Angiographic findings and procedural characteristics of the patients stratified by the blood group type.**

Parameters	Frequency (n) (%) /Mean±SD	Blood Group		p-Value
		Non-O	O	
N=398		291 (73.1%)	107 (26.9%)	-
Coronary dominance				
Right	348(87.4%)	251(86.3%)	97(90.7%)	0.240
Left	9.8% (39)	11.3% (33)	5.6% (6)	0.088
Co-dominance	2.8% (11)	2.4% (7)	3.7% (4)	0.472
Number of vessels involved				
Normal	3(0.8%)	2(0.7%)	1(0.9%)	0.800
Single vessel disease	130(32.7%)	86(29.6%)	44(41.1%)	0.029*
Two vessel disease	119(29.9%)	93(32%)	26(24.3%)	0.139
Three vessel disease	146(36.7%)	110(37.8%)	36(33.6%)	0.446

<b>Culprit artery</b>				
Normal/non-obstructive coronaries	3(0.8%)	2(0.7%)	1(0.9%)	0.800
Left anterior descending artery	229(57.5%)	167(57.4%)	62(57.9%)	0.921
Right coronary artery	112(28.1%)	88(30.2%)	24(22.4%)	0.124
Circumflex	46(11.6%)	28(9.6%)	18(16.8%)	0.046*
Left main	1(0.3%)	1(0.3%)		0.544
Diagonal	2(0.5%)	1(0.3%)	1(0.9%)	0.460
Obtuse marginal	3(0.8%)	2(0.7%)	1(0.9%)	0.800
Ramus	2(0.5%)	2(0.7%)	0(0%)	0.390
<b>Pre-procedure TIMI flow</b>				
0	217(54.5%)	161(55.3%)	56(52.3%)	0.595
I	28(7%)	20(6.9%)	8(7.5%)	0.835
II	93(23.4%)	66(22.7%)	27(25.2%)	0.594
III	60(15.1%)	44(15.1%)	16(15%)	0.967
<b>Stenosis (%)</b>	94.25 ± 12.98	92.58 ± 17.67	95.1 ± 11.06	0.169
<b>LVEF (%)</b>	38.15 ± 9.24	37.72 ± 9.04	38.36 ± 9.56	0.534
<b>Length of lesion (mm)</b>	21.83 ± 9.04	21.46 ± 10.31	21.42 ± 8.52	0.969
<b>Lesion complexity</b>				
Low (Syntax: 0-22)	295(74.1%)	215(73.9%)	80(74.8%)	0.858
Intermediate (Syntax: 23-32)	68(17.1%)	55(18.9%)	13(12.1%)	0.113
High (Syntax:> 32)	35(8.8%)	21(7.2%)	14(13.1%)	0.067
<b>Stenting</b>				
Stent placed	346(86.9%)	257(88.3%)	89(83.2%)	0.177
POBA	39(9.8%)	24(8.2%)	15(14%)	0.086
Unsuccessful	13(3.3%)	10(3.4%)	3(2.8%)	0.753
<b>Collaterals</b>	19(4.8%)	14(4.8%)	5(4.7%)	0.954
<b>Severe calcification</b>	87(21.9%)	66(22.7%)	21(19.6%)	0.513
<b>Thrombus present</b>	333(83.7%)	242(83.2%)	91(85%)	0.652
<b>Bifurcation</b>	59(14.8%)	46(15.8%)	13(12.1%)	0.363
<b>Export use</b>	59(14.8%)	42(14.4%)	17(15.9%)	0.717
<b>Post-procedure TIMI flow</b>				
0	12(3%)	8(2.7%)	4(3.7%)	0.609
I	6(1.5%)	4(1.4%)	2(1.9%)	0.720
II	29(7.3%)	22(7.6%)	7(6.5%)	0.729
III	351(88.2%)	257(88.3%)	94(87.9%)	0.898
<b>Post-procedure myocardial blush grade</b>				
0	14(3.5%)	9(3.1%)	5(4.7%)	0.448
1	17(4.3%)	14(4.8%)	3(2.8%)	0.380
2	57(14.3%)	47(16.2%)	10(9.3%)	0.086
3	310(77.9%)	221(75.9%)	89(83.2%)	0.123

TIMI = thrombolysis in myocardial infarction, LVEF = left ventricular ejection fraction, POBA = plain old balloon angioplasty, \*significant at 5%

Post procedure complications and in-hospital outcomes are summarized in Table 3. Cumulative post procedure complications were noted in 27.1% (108) with requirement of mechanical ventilation (12.1%), slow/no-reflow (11.8%), and cardiogenic shock (9.8%) as commonly observed complications.

In-hospital mortality rate was found to be 0.5% (2/398). Complication (23.4% (25/107) vs. 28.5% (83/291);  $p=0.554$ ) and in-hospital mortality rate (0.9% (1/107) vs. 0.3% (1/291);  $p=0.642$ ) was not statistically significant between blood group type O and non-O respectively.

**Table 3: Post-procedure complications and in-hospital outcomes of the patients stratified by the blood group type.**

Characteristics	Frequency (n) (%)	Blood Group		p-Value
		Non - O	O	
N=398		291 (73.1%)	107 (26.9%)	-
Clinical Complications/Outcomes				
Overall complication	108 (27.1%)	83 (28.5%)	25 (23.4%)	0.554
Mechanical ventilation	48 (12.1%)	36 (12.4%)	12 (11.2%)	0.220
Heart block	19 (4.8%)	17 (5.8%)	2 (1.9%)	0.079
Cardiogenic shock	39 (9.8%)	29 (10%)	10 (9.3%)	0.429
Acute kidney injury	3 (0.8%)	3 (1%)	0 (0%)	0.559
Sepsis	1 (0.3%)	1 (0.3%)	0 (0%)	0.596
Acute stent thrombosis	5 (1.3%)	4 (1.4%)	1 (0.9%)	0.889
Cardiac arrest	3 (0.8%)	2 (0.7%)	1 (0.9%)	0.512
Arrhythmias	8 (2%)	3 (1%)	5 (4.7%)	0.096
Pulmonary edema	17 (4.3%)	15 (5.2%)	2 (1.9%)	0.252
Slow/no-reflow	47 (11.8%)	35 (12%)	12 (11.2%)	0.813
Bleeding	2 (0.5%)	2 (0.7%)	0 (0%)	0.154
Mortality	2 (0.5%)	1 (0.3%)	1 (0.9%)	0.642

## DISCUSSION

This descriptive cross-sectional study was conducted to evaluate the association of the non-O and O blood group distribution with the extent and severity of coronary artery lesions in AMI patients. No association was observed between the lesion complexity, as assessed by Syntax score, and blood group type O and non-O. Patients with blood group type O had a lower burden of disease with single vessel diseases more common in this group as compared to the non-O group. Post-procedure complications and in-hospital mortality rates were not significantly different between the two groups. Among the significant differences, the smoking tendency was found to be significantly higher among the patients in blood group type O with the frequency of 37.4% vs. 26.8% ( $p=0.04$ ) as compared to the patients in a non-O blood group type. Such a relationship can partly be explained by the relatively higher age (78.5% vs. 72.9%) and relatively higher male gender dominance ( $58.07 \pm 11.88$  years vs.  $56.82 \pm 10.59$  years) among the O blood group patients.

A study conducted by Celebi et al. evaluated the association between blood group types and the development of coronary collateral circulation in 212 patients with CAD and reported that poor collateral development is associated with non-O blood group type<sup>17</sup>. However, like our findings, a study by Rasmi et al. in an Iranian population also observed no association between the number of diseased vessels and ABO distribution of blood group<sup>18</sup>. When ABO distribution was studied for association with thrombus burden in 369 patients with ST-segment elevation myocardial infarction (STEMI) by Askin et al., no relationship with thrombus burden and ABO blood type was noted<sup>19</sup>. But a study reported a positive relationship between spontaneous recanalization with blood group type O in patients with AMI<sup>20</sup>.

In contrary to our finding of no association between blood group type O and non-O and post-procedure complications and in-hospital mortality, a study by Cetin et al. on 1835 consecutive patients reported blood group type non-O as an indicator of the increased rate of in-hospital, short-term, long-term mortality, and adverse events in patients with STEMI after primary PCI<sup>21</sup>. However, this study also found no difference in lesion complexity (Gensini score) between the two groups. Similarly, Karabuva et al. also reported no association between the extent of coronary artery atherosclerosis and ABO blood groups<sup>22</sup>.

Among various other studies, a study of 3823 Chinese Han patients by Zhang et al. observed a strong association between non-O blood group and severe coronary atherosclerosis and higher inflammatory level with increased risk of cardiovascular event occurrence<sup>23</sup>. Similarly, blood group type A was reported as an independent risk factor of severe coronary artery disease (based on Gensini score)<sup>24</sup>. In this study involvement of circumflex was observed to be more common among the patients with type O blood group as compared to the non-O type with the frequency of 16.8% vs. 9.6%;  $p=0.046$  respectively. These findings along with a higher proportion of the patients with single-vessel coronary artery disease among the type O blood group indicate lesser complexity and severity of atherosclerosis among these patients as compared to their non-O type counterparts. A similar observation of lesser complex associated disease was reported by the studies in past<sup>23,24</sup>. However, literature negates such association in a study conducted by Kaya et al. They reported 620 subjects having no significant results among any blood group type and coronary artery ectasia. Upon comparison of outcomes, no statistically

significant difference was observed among the patients with type O and non-O blood group, however, a relatively higher rate of complications was observed among patients in the non-O group with a frequency of 28.5% vs. 23.4% as compared to type O groups. Relatively higher rates of complications among the non-O group were seen, including a higher rate of heart blocks (5.8% vs. 1.9%) and pulmonary edema (5.2% vs. 1.9%) as compared to the type O groups respectively. However, arrhythmias were relatively more common among patients in type O groups as compared to the non-O type with the frequency of 4.7% vs. 1.0% respectively<sup>25</sup>.

This study has certain limitations such as it was conducted in a single center with a relatively small sample size and due to the difference in the number of patients in blood group type O and non-O, some of the differences may not be evident in statistical analysis. Cohort studies with a large sample size may be needed to validate the study findings.

#### CONCLUSION

Blood group type O was found to be associated with single-vessel coronary artery diseases in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention (PCI). However, no association of blood group type O and non-O has been observed with the severity of coronary artery lesion and post-procedure complication and mortality.

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#### CONFLICT OF INTEREST

All authors have no conflict of interest to disclose.

#### ETHICS APPROVAL

This study was approved by the ethical review committee of the National Institute of Cardiovascular Diseases (NICVD), Karachi (ER-45/2020).

#### PATIENT CONSENT

Verbal informed consent was obtained from all the patients regarding their participation in the study and publication of data while maintaining confidentiality and anonymity.

#### AUTHORS' CONTRIBUTION

The idea conceived by JAS and GA study designed by JAS, GA, RK, KAK, and MK, study execution and data collection was done by JAS, GA, RK, KAK, AH, DQ, MZ, and FN manuscript drafted by JAS, GA, RK, KAK, AH, FN, and MK, the manuscript was critically

reviewed by MZ, JS, TS and MK, and the study was supervised by JAS. All authors have read and approved the manuscript.

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