

## **ABO Blood Group: A Risk Factor for a Cardiovascular Disease in Adults in Morocco**

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### **ABSTRACT**

#### **BACKGROUND**

The association between antigens A and B and cardiovascular disease is still unclear. Several reports have suggested an important involvement of the ABO blood group system in the susceptibility to thrombosis. Assessing that non-O blood groups in particular A blood group confer a higher risk of venous and arterial thrombosis than group O. Epidemiologic data are typically not available for all racial and ethnics groups. The purpose of this observational study was to identify a probable link between ABO blood group and ischemic and non-ischemic disease in subjects from the province of Casablanca, Morocco and to analyze whether A blood group individuals were at higher risk of ischemic disease or not.

#### **METHOD**

An observational study had been conducted from the beginning of 2017 until the end of 2019 in the Department of Cardiology, University Hospital Centre, Ibn Rochd, Casablanca, Morocco. We recruited consecutive subjects (549 men and 544 woman) at our center between 2017 and 2019. We studied data on age, gender, past history of hypertension, diabetes, smoking, sedentarism, obesity, hyperlipidemia, use of estrogen-progestin contraceptives and blood group distribution. Their ABO blood groups were determined using standard agglutination techniques. In each blood group type, we evaluated the prevalence of ischemic and non-ischemic cardiovascular disease.

#### **RESULT**

Of the 1093 patients whose medical records were reviewed, 482 (44.1%) were carrying blood group A. Of the remaining 611 patients, 353 (32.3%) had blood group O, 212 (19.4%) blood group B, and 46 (4.3%) blood group AB. The diagnosis of ischemic disease (ID) was higher in patients with blood group O (63.3%) than in other blood groups, and the diagnosis of valvular disease was higher in patients with blood group A (48.7%) compared to other groups. In patients with blood group B or AB compared to non-B or non-AB, respectively there was no statistically significant difference in ID incidence. The incidence of ID in men was significantly higher in blood group O (63.2%,  $p = 0.015$ ) compared with women, while there valvular disease was a statistically higher in women (54.5%,  $p = 0.035$ ). This difference remains statistically significant after adjustment for common cardiovascular risk factors.

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## CONCLUSION

Our study suggests an association between ABO blood group and Ischemic disease and non-ischemic disease in Moroccan population. In African countries, where most of health facilities are understaffed, more rigorous studies with a larger population are needed to give high level of evidence to confirm this association in order to establish the need to be more aggressive in risk factor control in these individuals.

## KEYWORDS

ABO blood, Risk factor; Cardiovascular disease; Ischemic disease; Prevention

## 1. INTRODUCTION

In 1901, Karl Landsteiner, a Viennese MD and pathologist, discovered ABO blood group system which was the first human blood group [1]. From then on, studies on relation of ABO blood group system to various diseases have never been interrupted for a century, even in the popular era of gene detection, as ABO blood group is inherent in human's body and easily to be tested. It has been reported that ABO blood group system is associated with cognitive impairment [2], preeclampsia [3], bleeding, neoplastic diseases [4], and even longevity [5].

The association with arterial thrombosis, coronary heart disease [6] (CHD) or cerebrovascular disease (CVD) [7,8] is less documented and is the subject of controversy. More recently, it has been reported that ABO blood group is associated with venous thrombosis (VT). The mechanism of relationship between ABO blood group and thrombosis is elucidated, and its major determinants are Von Willebrand Factor (VWF) and coagulation factor VIII (FVIII) [9]. This finding makes a theoretical hypothesis that ABO blood group may be also related to risk of coronary artery disease (CAD) and myocardial infarction (MI).

Furthermore, the association between thrombosis and ABO blood groups has a long history suggesting that non-O blood groups in particular A blood group confer a higher risk of myocardial infarction (MI), angina, peripheral vascular disease (PVD), cerebral ischemia of

arterial origin (CIAO), and venous thrombosis (VT) than group O [10-13]. Indeed, the link between ABO blood group and arterial thrombosis was assessed by a number of systematic reviews and meta-analyses, and the evidence from the literature on this association is less robust than that documenting the link with venous thrombosis.

Since the frequencies of the ABO system blood groups vary between populations [14], and since no studies had been performed in Morocco on severe arterial events resulting in hospitalization or death, we performed this study to determine the association of blood group and cardiovascular diseases in the province of Casablanca Morocco.

## 2. METHODS

### *Study population and protocol*

This study included 1093 consecutive patients (549 men and 544 women), admitted at cardiology for diverse diseases between 2017 and 2019 in the Department of Cardiology, University Hospital Centre, IBN Rochd, Casablanca, Morocco. We studied data on age, gender, past history of hypertension, diabetes, smoking, sedentarism, obesity, hyperlipidemia, and blood group distribution. In each blood group type, we evaluated prevalence of ischemic disease (CAD and ischemic stroke), and non-ischemic disease (NID) (Heart failure, valvular disease).

The study was conducted according to the principles of the Declaration of Helsinki after the approval from the local ethics committee had been obtained. The informed consent from the participants was not required due to the observational character of the study.

### **Collection of data**

Residents in cardiology filled out the questionnaire on the demographic and clinical characteristics (age, sex, height, weight, systolic and diastolic blood pressure), the patients self-reported presence of traditional cardiovascular risk factors (arterial hypertension, diabetes, hypercholesterolemia, hypertriglyceridemia, cigarette smoking), and values of laboratory parameters measured during the study (total cholesterol - TC, LDL cholesterol - LDL-C, HDL cholesterol - HDL-C, triglyceride - TG, glucose).

The presence of cardiovascular risk factors was defined as:

- Cigarette smoking was defined as smoking of at least 1 cigarette per day at the time of survey;
- Diabetes mellitus was defined as a fasting plasma glucose  $\geq 126$  mg/dL, glycohemoglobin value  $\geq 6.5\%$ , or the use of hypoglycemic agents;
- Hypertension was defined as systolic blood pressure (BP)  $>140$  mmHg and/or diastolic BP  $>90$  mmHg or use of antihypertensive drugs.
- Family history of CAD was self-reported by the patients and was defined as MI or known CAD in a parent or sibling before the age of 65-years.
- Blood samples for lipid profile were drawn after a 12-hours fast.
- Obesity was defined as a body mass index (BMI)  $\geq 27$  kg/m<sup>2</sup>.
- MI was determined by abnormal ECG showing evidence of ischemia (i.e. transient or permanent ST segment elevation or depression  $>0.1$  mv in two contiguous leads and q waves that are greater than

25% of the height of the subsequent R waves) and abnormal serum level of cardiac markers.

- Premature CAD was defined as a symptomatic CAD which emerged in men  $<50$  years and women  $<55$  years of age.

### **Laboratory methods**

All laboratory tests were performed immediately after the sample reception in the Department of Clinical Biochemistry, University Hospital Centre, Ibn Rochd, Casablanca, Morocco. ABO blood groups were determined in the Department of Blood Transfusion, Casablanca, by commercially available hemagglutination techniques (Erytype S ABO microplates, Biotest, Dreieich, Germany).

## **3. RESULTS**

Table 1 summarizes patient demographics. Of the 1093 patients whose medical records were reviewed, 482 (44.1%) were carrying blood group A. Of the remaining 611 patients, 353 (32.3%) had blood group O, 212 (19.4%) blood group B, and 46 (4.3%) blood group AB. Among the patients 99% had rhesus positive and 1% had rhesus negative.

The risk factors for ID in our patients were dominated by active smoking found in 470 patients (43%), diabetes in 411 patients (37.6%), hypertension in 470 patients (43%) and hypercholesterolemia in 106 patients (9.7%).

A total of 270 patients (24.7%) had no risk factor (table 2), 125 (46.34%) had blood group O, 100 (37%) blood group A, and 45 (16.66%) blood group B.

The diagnosis of ischemic disease (ID) was higher in patients with blood group O (63.3%) (95% CI = 2.26-4.57,  $p < 0.02$ ) than in other blood groups even in patients without risk factor (table 2) and the diagnosis of valvular disease was higher in patients with blood group A (48.7%,  $p < 0.03$ ) compared to other groups. Patients with

blood group B or AB compared to non-B or non-AB respectively, had no statistical differences in ID incidence or valvular disease.

The incidence of ID in men was significantly higher in blood group O 63.2% (95%, p = 0.015) compared with women, while there valvular disease was a statistically higher in women 54.5% (p = 0.035). This difference remains statistically significant after adjustment for common cardiovascular risk factors.

ABO type	A	B	AB	O
Total % (n°)	44.1(482)	19.4(212)	4.3(46)	32.3(353)
Age (years)	62.8 ± 12.2	59 ± 10.8	61 ± 7.4	52.8 ± 16.3
Men (%)	39	83.3	75	50
Diabetes (%)	34.1	38.8	75	36.6
Hypertension (%)	36.5	16.6	25	36.6
Smoking (%)	29.2	77.7	75	36.6
CAD (%)	46.3	44.4	50	63.3
Valvulopathy (%)	48.7	33.3	50	40
Embolic disease	0	22.2	0	0

Note: CAD: Coronary Artery Disease

Table 1: Clinical characteristics of the patients.

ABO type	A	B	O	AB
Non risk factors % (n° = 270)	37(100)	16.66(45)	46.34(125)	0
CAD % (n°)	37(37)	33.3(15)	75.2(94)	0

Table 2: Distribution of blood group in patients with CAD and no cardiovascular risk factors.

#### 4. DISCUSSION

In different regions of the world there is specific ABO blood group distribution. In our study, blood group distribution frequency was found to be shown by formula A>O>B>AB, which is in discordance with other studies carried out in Africa O>A>B>AB. The same formula is found in Europe but at different frequency percentage, in contrast to what is found in India, in which it is given by the formula B>A = O>AB (table 3) [15-18].

The association between ABO blood groups and CAD has been the subject of numerous studies and particularly non O blood groups have been reported to be related with atherosclerosis and ischemic heart disease. Investigators attribute this relation basically to increased levels of factor VIII, VWF, fragment 1 p 2 of prothrombin and

lower activated partial thromboplastin time (APTT) ratio in subjects with non O blood groups, which cause an increased prothrombotic tendency [19-22]. The results of majority of the studies are in concordance with the data, suggesting the association of CAD with non O blood group. The Framingham study and some other studies suggested that the incidence of ischemic heart disease was higher among subjects with blood group A phenotype [11].

Location of study	A%	O%	B%	AB%
Our study	44.1	32.3	19.4	4.3
Cameroon (Ndoula et al.) [15]	25.07	48.62	21.86	4.45
Senegal (Badiane et al.) [16]	19.7	59.8	17.2	3.3
Britain (Frances et al.) [17]	42	42	8	3
India (Parul et al.) [18]	28.7	28.7	32.07	10.53

Table 3: Comparison of frequency percentage of ABO in different countries.

Results of the Northwick Park Heart Study suggested an increased risk for blood group AB as compared with the groups O, A or B [20]. Stakisaitis et al. [23] suggested that blood group B was significantly more frequent in men aged less than 45 years suffering from coronary atherosclerosis. On the contrary, Mitchell [24] reported that towns with a higher prevalence of blood group O had higher rates of cardiovascular mortality. Finally, some investigators oppose the idea of association between ABO blood groups and CAD. Amirzadegan et al. [25] reported that there was no correlation between various ABO blood groups and development of CAD and premature CAD in individual subjects.

The results of our study showed a significant association (p-value <0.02) between CAD and blood group O even in patients without risk factors (75%) than others blood group, and we found that the patients with blood group O were younger than the patients with other blood groups. Association of major cardiovascular risk factors with ABO blood groups and CAD precocity with blood group A need to be elucidated with large-scale prospective studies. Also our observational study showed a significant

association between blood group A and valvular disease (p-value = 0.03). Blood group A had higher prevalence (44.1%). The sample size of our study was relatively small and we do not know whether we can extend our results to the general population; Association of ABO blood group distribution with cardiovascular risk factors, CAD and valvular disease needs to be clarified with multicenter, prospective and large scale studies.

## **5. CONCLUSION**

Our study suggests an association between ABO blood group and Ischemic disease and non-ischemic disease in Moroccan population. In African countries, where most of health facilities are understaffed, more rigorous studies with a larger population are needed to give high level of evidence to confirm the association in order to establish the need to be more aggressive in risk factor control in these individuals.

## **6. CONFLICT OF INTEREST**

The authors declare no competing interest.

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