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Cardiovascular disease and ABO blood-groups in Africans. Are blood-group A individuals at higher risk of ischemic disease?: A pilot study



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Abstract *Background:* Since the discovery of the ABO blood group system by Karl Landsteiner in 1901, 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 pilot study was to identify a link between ABO blood group and ischemic disease (ID) in Africans, and to analyze whether A blood group individuals were at higher risk of ischemic disease or not.

Methods: A total of 299 medical records of patients over a three-year period admitted to the cardiology and internal medicine department of military hospital of Ouakam in Senegal were reviewed. We studied data on age, gender, past history of hypertension, diabetes, smoking, sedentarism, obesity, hyperlipidemia, use of estrogen-progestin contraceptives and blood group distribution.

In each blood group type, we evaluated the prevalence of ischemic and non-ischemic cardiovascular disease. The medical records were then stratified into two categories to evaluate incidence of ischemic disease: Group 1: Patients carrying blood-group A and Group 2: Patients carrying blood group non-A (O, AB and B).

Results: Of the 299 patients whose medical records were reviewed, 92 (30.8%) were carrying blood group A, 175 (58.5%) had blood group O, 13 (4.3%) had blood group B, and 19 (6.4%) had blood group AB.

The diagnosis of ischemic disease (ID) was higher in patients with blood group A (61.2%) than in other blood groups, and the diagnosis of non-ischemic disease (NID) was higher in patients with blood group O (73.6%) 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.

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Main risk factor for ID was smoking (56.5%), hypertension (18.4%) and diabetes (14.3%).

In our study, there was no statistical difference between blood group A and non-A in myocardial infarction (MI) incidence ($p = 0.09$, 95% CI = 0.99–2.83) but a statistically significant difference between blood group A and non-A in stroke and coronary artery disease (CAD) incidence ($p < 0.0001$, 95% CI = 1.80–3.37 and $p < 0.0001$ 95% CI = 1.82–3.41 respectively) was found. The incidence of ID in men was significantly higher in blood group A (95% CI = 2.26–4.57, $p < 0.0001$) compared with non-A group, while there was no statistically significant difference in women ($p = 0.35$). However, an overall effect was detected to be statistically significant regardless of gender ($p < 0.0001$).

Conclusion: Our study suggests an association between blood group A and ID in sub-Saharan Africans.

In African countries, where most of health facilities are understaffed, more rigorous studies with a larger population are needed to give a 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.

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1. Background

Since the discovery of the ABO blood group system by Karl Landsteiner in 1901, several reports have suggested an important involvement of the ABO blood group system in the susceptibility to infectious, neoplastic disease, bleeding, eclampsia, and even life expectancy.^{1–3}

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).⁴ 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.^{5–8}

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.

Although the importance of cardiovascular disease (CVD) epidemiology is well recognized, epidemiologic data are typically not available for all racial and ethnic groups.

Africans have significantly higher VWF levels compared to Caucasians and, Africans with blood group O show significantly lower VWF than the other ABO blood groups.⁹

The purpose of this pilot study was to identify a link between ABO blood group and ischemic disease (ID) such as CAD, MI and ischemic stroke in Africans, and to analyze whether A blood group individuals were at a higher risk of ID or not.

2. Methods

After approval by the Ethics Committee of the Ministry of Health and Social Welfare, Senegal (Comité d'éthique du

Ministère de la Santé et l'Action Sociale), medical records of patients over a three-year period admitted to the cardiology and internal medicine department of military hospital of Ouakam in Senegal were reviewed. Medical records of patients with venous thrombo-embolism (VTE) were excluded. A total of 57 patients were removed from the cohort secondary to incomplete medical records.

Medical records of 299 patients were evaluated. We studied data on age, gender, past history of hypertension, diabetes, smoking, sedentarism, obesity, hyperlipidemia, use of estrogen-progestin contraceptives and blood group distribution.

In each blood group type, we evaluated prevalence of ischemic disease (MI, CAD and ischemic stroke), and non-ischemic disease (NID) (Heart failure, valvular disease and cerebral hemorrhage).

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 including creatine kinase, creatine kinase-MB, and troponin I. CAD was determined by history of documented CAD, and abnormal ECG with changes questionable for ischemia and chest pain. Stroke was determined on the basis of cerebral scanner. The medical records were then stratified into two categories to evaluate incidence of ischemic disease:

Group 1: Patients carrying blood group A.

Group 2: Patients carrying blood group non-A (O, AB and B).

We also sought relation between blood group distribution in the cohort study and in the general population of Senegal.

The studied parameters were entered into an electronic questionnaire using GraphPad Prism 5. Data analyses were performed using chi-square (and Fisher's exact) test.

3. Results

Table 1 summarizes patient demographics. Of the 299 patients whose medical records were reviewed, 92 (30.8%) were carrying blood group A. Of the remaining 207 patients, 175 (58.5%)

had blood group O, 13 (4.3%) blood group B, and 19 (6.4%) blood group AB.

Among the patients 97% had rhesus positive and 3% had rhesus negative.

The risk factors for ID in our patients (Table 2) were dominated by active smoking found in 56 patients (56.5%), hypertension in 18 patients (18.4%) and diabetes in 14 patients (14.3%).

A total of 33 patients (33.7%) had no risk factor, 42 patients (42.8%) had one risk factor and the remaining patients (23.5%) had more than one.

Diabetes and hypertension were more common in non-A blood groups (95% CI = 0.015–0.60, $p = 0.015$ and 95% CI = 0.08–0.71, $p = 0.014$ respectively) compared with A blood group, while there was no statistically significant difference in smoking (95% CI = 0.59–3.06, $p = 0.523$).

The diagnosis of ischemic disease (ID) was higher in patients with blood group A (61.2%) than in other blood groups, and the diagnosis of non-ischemic disease (NID) was higher in patients with blood group O (73.6%) 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.

Distributions of blood groups in regard to diagnosis of ID or NID in our study and in comparison with general population are represented in Fig. 1.

Females were less representative in ID compared to males (18.4% vs 81.6%) but they were more representative in NID (60.2% vs 39.8%) (Table 3). This difference was statistically significant ($p < 0.0001$).

The incidence of ID in men was significantly higher in blood group A (95% CI = 2.26–4.57, $p < 0.0001$) compared with non-A group, while there was no statistically significant difference in women ($p = 0.35$). However, an overall effect was detected to be statistically significant when comparing blood group A with non-A for the incidence of ID regardless of gender ($p < 0.0001$). This difference remains statistically significant after adjustment for common cardiovascular risk factors. Distribution of blood group A and non-A in patients with ID and NID is represented in Fig. 2.

Table 2 Risk factors found in patients with ID.

Main risk factors	A Blood group (N = 60)	Non-A Blood group (N = 38)
Tobacco smoking	n = 36 (60%)	n = 20 (52.3%)
Hypertension	n = 6 (10%)	n = 12 (31.6%)
Diabetes	n = 4 (6.6%)	n = 10 (26.3%)

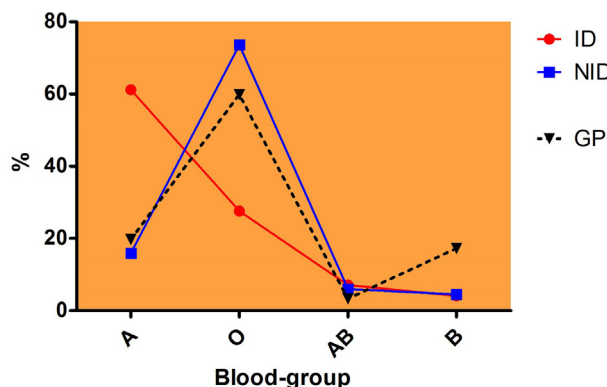


Figure 1 Comparison of ABO blood groups distribution between our study and general population.

In our study, there was no statistical difference between blood group A and non-A in MI incidence ($p = 0.09$, 95% CI = 0.99–2.83) but a significant statistical difference between blood group A and non-A in stroke and CAD incidence ($p < 0.0001$, 95%CI = 1.80–3.37 and $p < 0.0001$, 95% CI = 1.82–3.41 respectively) was found.

4. Discussion

In our study, blood group distribution frequency was found to be shown by formula $O > A > AB > B$, which is slightly in accordance with other studies carried out in Africa $O > A > B > AB$. The same formula is found in America and Europe but at different frequency percentage, in contrast to what is found in India and Pakistan, in which it is given by the formula $B > A = O > AB$ and $B > O > A > AB$ respectively (Table 4).

In our study, NID was more common in patients with O blood group (73.6%). This could be related to the high prevalence of this blood type in Africa.

There are a number of examples documenting that the blood type distribution among different populations in different times is driven by an evolutionary selective pressure, which acts by modifying susceptibility to various diseases. The best example is that of infectious diseases: the fact that O blood type provides a selective advantage against severe malaria probably explains the higher prevalence of this blood group in areas (i.e. Africa) in which malaria is endemic.¹⁷ Similarly, other authors have hypothesized that the relatively high prevalence of B blood group in India, which has been shown to protect against severe cholera, could be related to the selective pressure from this infectious disease endemic in that area.¹⁸

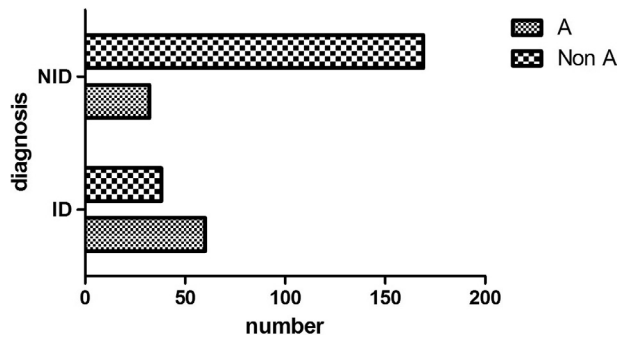
In our study, there was no statistical difference between blood group A and non-A in MI incidence ($p = 0.09$), and this

Table 1 Patient’s demographics.

	Mean age	54 Years old
	Gender	Males (n = 160; 53.5%) Females (n = 139; 46.5%)
Ischemic disease (ID)	Stroke	45 (A = 28 O = 12 AB = 3 B = 2)
	CAD	37 (A = 24 O = 8 AB = 3 B = 2)
	MI	16 (A = 8 O = 7 AB = 1 B = 0)
Non-ischemic disease (NID)	Heart failure	132 (A = 20 O = 102 AB = 6 B = 4)
	Valvular disease	59 (A = 10 O = 39 AB = 5 B = 5)
	Cerebral hemorrhage	10 (A = 2 O = 7 AB = 1 B = 0)

Table 3 Blood groups related to diagnosis in gender.

Blood Group	ID		NID		Total
	A	Non-A	A	Non-A	
Men	55	25	10	70	160
Women	5	13	22	99	139
Total	60	38	32	169	299

**Figure 2** Distribution of blood group A and non-A in patients with ID and NID.

could be due to the small number of patients admitted in our hospital for MI. A significant statistical difference between blood group A and non-A in stroke and CAD incidence ($p < 0.0001$) was found. However, an overall effect was detected to be statistically significant when comparing blood group A with non-A for the incidence of ID ($p < 0.0001$).

Previous systematic reviews and meta-analysis paid more attention to the relationship between MI and ABO blood group, but the link of ABO blood group system to CAD was rarely evaluated. Besides, almost all available studies principally focused on blood type non-O and O.

Whincup et al.¹⁹ found that the incidence of ischemic CAD was higher in those with blood group A than those with blood group non-A (OR = 1.21, 95% CI = 1.01–1.46).

Lee et al.,²⁰ in Taiwan, after adjustment for common cardiovascular risk factors, found that blood group A remains significantly associated with an increased risk of CAD and MI (OR = 2.61, CI = 1.11–6.14, $p = 0.028$, OR = 3.53, CI = 1.21–10.29, $p = 0.021$ respectively).

A study by Wazirali et al.²¹ suggested that blood group A was associated with a substantially increased risk of CAD,

which is independent of conventional cardiovascular risk factors.

Wu et al.²² performed a meta-analysis with regard to the relation of ABO blood group to MI and angina in 2008. In their study based upon 19 studies, group A was associated with a similar increase in MI risk (OR = 1.29, 95% CI = 1.16–1.45, $p < 0.00001$) to that observed with non-A.

Furthermore, a meta-analysis by Dentali et al.²³ found that patients with blood group non-O presented a higher prevalence of MI than that with blood group O (OR = 1.28, 95% CI = 1.17–1.40, $p < 0.001$).

Recently, Chen et al.,²⁴ in a meta-analysis involved 16 articles (17 studies) covering 225,810 individuals, found that risk of CAD in blood group A was mildly increased compared with that in blood group non-A (OR = 1.14), while there was no statistical difference between blood group B and AB compared with non-B and non-AB, respectively. Similar evidence was more robust in the analysis for MI incidence (OR = 1.24).

Moreover, their results indicated that the risk of CAD in blood group O was significantly lower than that in non-O blood groups (OR = 0.85), which is similar to previous studies.²³

Ischemic stroke accounts for considerable morbidity and mortality in either high or low income countries, and treatment is limited at present.

In our study, we found the incidence of ischemic stroke was higher in those with blood group A than those with blood group non-A ($p < 0.0001$, 95% CI = 1.80–3.37).

Ionescu et al.,²⁵ in a study of 329 cases of cerebral thrombosis, found that there was an excess of blood group A and AB and a deficiency of O and B with a statistically significant difference when the A + AB excess in thrombosis was contrasted with the O + B excess in hemorrhage, suggesting that this difference might be accounted for the major A subgroup.

Association between stroke and blood group A had been reported by many authors.^{26–28}

Wu et al., pooling 7 studies, showed that non-O significantly increased the risk of ischemic stroke (OR 1.14, 95%

Table 4 Comparison of frequency percentage of ABO in different countries.

Location of study		A (%)	B (%)	AB (%)	O (%)
Within Africa	Present study	30.8	14.3	6.4	58.5
	Senegal (Badiane et al.) ¹⁰	19.7	17.2	3.3	59.8
	Cameroon (Ndoula et al.) ¹¹	25.07	21.86	4.45	48.62
	Nigeria (Egesie et al.) ¹²	21.6	21.4	2.8	54.2
Outside Africa	USA (Mollison et al.) ¹³	41	9	4	46
	Britain (Frances et al.) ¹⁴	42	8	3	42
	India (Parul et al.) ¹⁵	28.7	32.07	10.53	28.7
	Pakistan (Khattak et al.) ¹⁶	27.92	32.4	10.58	29.10

CI 1.01–1.27). There was no evidence of heterogeneity ($P = 0.49$) and the findings of the individual studies were highly consistent (I² 0%). Meta-regression was not carried out to explore heterogeneity further due to the small number of studies. Only one of the seven did not provide data on group A. The pooled OR for group A relative to O was similar to that for non-O (OR 1.15, 95% CI 1.01–1.31).²²

The underlying mechanism of the relationship between ABO blood group and ischemic disease seems to be linked to plasma levels of VWF and coagulation FVIII.

In Euroclot study,²⁹ genetic variant of single nucleotide polymorphism (SNP) rs505922 in the ABO locus was found to be associated with ischemic stroke, and in particular subtypes large-vessels and cardioembolic stroke, but not small-vessel disease. This SNP was highly associated with VWF and FVIII.

Sanders et al.,³⁰ in a study including 635 adults with Von Willebrand Disease (VWD) compared the prevalence of arterial thrombosis with two reference population, found that the prevalence of ischemic cardiovascular disease was lower than in the general population.

Therefore, the link of blood group A to ID becomes plausible as ABO determinants occur on FVIII and on VWF, with the lowest levels seen in those of genotypes OO and the highest in those with the least O antigen expression (i.e.: A, AB, and B).^{31,32}

A better understanding of the increased incidence of ID among blood group A Africans could be due to the fact that Africans had significant higher VWF levels compared to Caucasians, and those with blood group O show significantly lower VWF than the other ABO blood group.⁹

5. Conclusion

Our study suggests an association between blood group A and ID in sub-Saharan Africans.

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.

Conflict of interest

There is no conflict of interest.

References

- Alpoim PN et al. Preeclampsia and ABO blood groups: a systematic review and meta-analysis. *Mol Biol Rep* 2013;**40**:2253–61.
- Liumbruno GM, Franchini M. Hemostasis, cancer, and ABO blood group: the most recent evidence of association. *J Thromb Thrombolysis* 2014;**38**:160–6.
- Franchini M, Bonfanti C. Evolutionary aspects of ABO blood group in humans. *Clin Chim Acta* 2015;**444**:66–71.
- Dentali F et al. Non-O blood type is the commonest genetic risk factor for VTE: results from a meta-analysis of the literature. *Semin Thromb Hemost* 2012;**38**:535–48.
- Medalie J, Levene C, Papier C, Goldbourt U, Dreyfuss F, Oron D. Blood groups, myocardial infarction and angina pectoris among 10,000 adult males. *N Engl J Med* 1971;**285**:1348–53.
- Garrison R, Havlik R, Harris R, Feinleib M, Kannel W, Padgett S. ABO blood group and cardiovascular disease. *Atheroscler* 1976;**25**:311–8.
- Jick H, Dinan B, Herman R, Rothman KJ. Myocardial infarction and other vascular diseases in young women. Role of estrogens and other factors. *Jama* 1978;**240**:2548–52.
- Erikssen J, Thaulow E, Stormorken H, Brendemoen O, Hellem A. ABO blood groups and coronary artery disease (CHD): a study in subjects with severe and latent CHD. *Thromb Haemost* 1980;**43**:137–40.
- Sukhu K, Poovalingam V, Mahomed R, Giangrand PL. Ethnic variation in Von Willebrand Factor levels can influence the diagnosis of Von Willebrand Disease. *Clin Lab Haematol* 2003;**25**(4):247–9.
- Badiane AS, Sarr O, Deme AB, Ahouidi AD, Gueye PE, Ndiaye M, et al. Distribution of erythrocyte binding antigen 175 (EBA-175) alleles and ABO blood groups in a hypoendemic area in senegal. *J Infect Dev Ctries* 2012;**6**(10):727–33.
- Ndoula ST, Noubiap JJN, Nansseu JRN, Wonkam A. Phenotypic and allelic distribution of the ABO and Rhesus (D) blood groups in the cameroonian population. *Int J Immunogenet* 2014;**41**(3):206–10.
- Egesie UG, Egesie OJ, Usar I, Johnbull TO. Distribution of ABO, Rhesus blood and haemoglobin electrophoresis among under-graduated students of Niger Delta state university, Nigeria. *Niger J Physiol Sci* 2008;**23**(1-2):5–8.
- Mollison PL, Engelfriet CP, Conteras M. The Rh blood Group system *Blood transfusion in clinical medicine*. 9th ed. Oxford: Black well Scientific Publication; 1993.
- Frances TF. Blood groups (ABO groups) *Common Laboratory and Diagnostic Tests*. third ed. Philadelphia: Lippincott; 2002, p. 19–15.
- Paul Garg, Saloni Upadhyay, Sanjay Singh Chufal, Yuman Tayal, Ishwer Tayal. Prevalence of ABO and Rhesus blood group in blood donors: a study from a tertiary care teaching hospital of Kumaou region in Uttarakhand. *J Clin Diagnosis Res* 2014;**8**(12):16–9, Dec.
- Khattak ID, Khan TM, Khan P Shah SM, Khattak ST, Ali A. Frequency of ABO and Rhesus blood group in district Swat, Pakistan. *J Ayub Med Coll* 2008;**20**(4):127–9.
- Cserti CM, Dzik WH. The ABO blood group system and Plasmodium falciparum malaria. *Blood* 2007;**110**:2250–8.
- Glass RI et al. Predisposition for cholera of individuals with O blood group. Possible evolutionary significance. *Am J Epidemiol* 1985;**121**:791–6.
- Whincup PH, Cook DG, Phillips AN, Shaper AG. ABO blood group and ischaemic heart disease in British men. *BMJ* 1990;**300**:1679–82.
- Lee HF, Lin YC, Lin CP, Wang CL, Chang CJ, Hsu LA. Association of blood group A with coronary artery disease in young adults in Taiwan. *Intern Med* 2012;**51**(14):1815–20.
- Wazirali H, Ashfaq RA, Herzig JW. Association of blood group A with increased risk of coronary heart disease in the pakistani population. *Pak J Physiol* 2005;**1**:1–2.
- Wu O, Bayoumi N, Vickers MA, Clark P. ABO(H) blood groups and vascular disease: a systematic review and meta-analysis. *J Thromb Haemost* 2008;**6**:62–9.
- Dentali F, Sironi AP, Ageno W, Crestani S, Franchini M. ABO blood group and vascular disease: an update. *Semin Thromb Hemost* 2014;**40**:49–59.
- Chen Z, Yang SH, Xu H, Li JJ. ABO blood group system and the coronary artery disease: an updated systematic review and meta-analysis. *Sci Rep* 2016;**6**:23250. <http://dx.doi.org/10.1038/srep23250>.
- Ionescu DA, Marcu I, Bicescu E. Cerebral thrombosis, cerebral haemorrhage, and ABO blood-groups. *Lancet* 1976;**1**:278–80.
- Sostaric V, Bozicevi D, Brinar V, Grbavac Z. Hereditary antigen characteristics of blood in ischemic cerebrovascular accident. *Neurol Croatica* 1991;**40**:3–11.

27. Herman B, Schmitz PI, Leyten AC, Van LJH, Frenken CW, Op DeCoul AA, et al. Multivariate logistic analysis of risk factors for stroke in Tilburg, The Netherlands. *Am J Epidemiol* 1983;**118**:514–25.
28. Larsen S, Anthonisen B, Marquardsen J. Cerebral infarction, cerebral haemorrhage, and ABO blood-groups. *Lancet* 1977;**1**:1064.
29. Williams et al. Ischemic stroke is associated with the ABO locus: the EuroCLOT Study. *Ann Neurol* 2012;**73**:16–31.
30. Sanders YV, Eikenboom J, de Wee EM, et al. Reduced prevalence of arterial thrombosis in Von Willebrand Disease. *J Thromb Haemost* 2013;**11**(5):845–54.
31. Stormorken H, Erikssen J. Plasma antithrombin III and factor VIII antigen in relation to angiographic findings, angina and blood groups in middle-aged men. *Thromb Haemost* 1977;**38**:874–80.
32. Jenkins P, O'Donnell J. ABO blood group determines plasma von Willebrand factor levels: a biological function after all. *Transfusion* 2006;**46**:1836–44.