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# Identification of major effects of cardiovascular disease on different blood group samples: A case study Aminu Kano Teaching Hospital, Kano State, Nigeria

**R Ibrahim[1*], Tahir H[2], Magnus Ezihe I[3], Samaila Y Dogon Jeji[4]**
[1-4] Department of Sciences Laboratory Technology, Abubakar Tatari Ali Polytechnic, Bauchi, Nigeria

**Abstract**
This study was designed to investigate whether there was an association between ABO blood groups and cardiovascular diseases in Nigerian population. The present retrospective study analyzed ABO blood groups among 721 patients with documented CVD, who were treated at Malam Aminu Kano Teaching Hospital in Kano State from January 2013 to December, 2016 comparing with a control group of 120 subjects. Data were analyzed with computer software MS-Excel SPSS and Minitab by using cross tabulation, ANOVA and Latin square design. A p-value less than 0.05 were considered as statistically significant. Also significant difference in distribution of ABO blood groups was seen in patients with CVD (A, 32%; B, 26%; AB, 11%; O, 31%) and also after adjustment for common cardiovascular risk factors such as age, gender, (A, 24%; B, 27%; AB, 12%; O, 36%) as compared to the controls (A, 22%; B, 23%; AB, 20%; O, 34%), p value = 0.000 respectively. The findings of the study suggest that there seems to be no correlation between various ABO blood groups and development of cardiovascular diseases. Moreover, the prevalence of major risk factors was not equal in patients with different blood groups and blood groups had impact on development of cardiovascular pathogenesis in individual subjects.

**Keywords:** cardiovascular diseases, blood groups, Nigerian population

## Introduction

ABO blood groups have been associated with various disease phenotypes, particularly cardiovascular diseases. Cardiovascular diseases are the most common causes of death in developed countries and their prevalence rate is rapidly growing in developing countries including Nigeria. There have been substantial historical associations between non-O blood group status and an increase in some cardiovascular disorders. Recent Genome-Wide Association Study (GWASs) have identified ABO as a locus for thrombosis, myocardial infarction, and multiple cardiovascular risk biomarkers, refocusing attention on mechanisms and potential for clinical advances. As I highlight in this project, more recent work is beginning to probe the molecular basis of the disease associations observed in these observational studies. Advances in our understanding of the physiologic importance of various endothelial and platelet-derived circulating glycoproteins are elucidating the mechanisms through which the ABO blood group may determine overall cardiovascular disease risk. The role of blood group antigens in the pathogens is of various cardiovascular disorders remains a fascinating subject with potential to lead to novel therapeutics and prognostics and to reduce the global burden of cardiovascular diseases.

After the discovery of ABO blood groups numerous studies have been reported correlating the frequency of various diseases with the blood groups e.g. Carcinoma of stomach (Aird *et al.* 1953), duodenal and gastric ulcers (Clarke *et al*.1955), cholera (Glass *et al*.1985), and cardio metabolic diseases (Bates, 1971; Cronenwett *et al.* 1983; Erikssen *et al*.1980). As a matter of serious concern, cardiovascular diseases (CVD) have emerged as the leading causes of death, the world over, including Nigeria (http://www.who.int/mediacentre/factsheets/fs317/en/index.html). Gender, age, obesity, smoking, diabetes mellitus, hypertension and family history are considered major cardiovascular risk factors. Several studies have revealed that the ABO blood group phenotype of individuals, particularly non O groups are associated with major cardiovascular risk factors and/or increased rate of cardiovascular events (Erikssen *et al.* 1980; Platt *et al.* 1985; Whincup *et al.* 1990) [15, 24]. However there is limited consensus regarding the magnitude and significance of the ABO effects at the population level and whether it relates to all disorders equally or mainly modulates thrombotic pathways and disorders, as outlined in a meta-analysis (Wu *et al.*2008).In Nigeria, Kano state has one of the highest incidences of cardiovascular diseases and contributes to the highest number of deaths by these diseases (http://www.harneedi.com/index.php/healthcare/4362-ahmedabad-tops-heartdisease-emergencies-in-state). Lack of investigations examining the association between ABO blood groups and CVD in Nigeria and absence of such study in Kano was recognized as an important lacuna to be filled. I conducted a retrospective case-control study to evaluate the effect of the ABO blood groups on the risk of CVD, in a cohort who had undergone coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA). In the majority of previous studies subjects who were understudy were known cases of CAD, however, presence of major cardiovascular risk factors (i.e. hypertension, smoking, diabetes and obesity) was not taken into account, and therefore I investigated data with cardiovascular risk factors in my study to investigate the relation between ABO blood groups and cardiovascular pathogenesis in documented CVD patients.

It is reported that there is lower incidence of coronary heart disease with blood group O as compared with group A in Western countries1, 2, 3, 4, 5, 6. It is also reported that men

belonging to groups O or B had a lower mean cholesterol level than group A, a finding that emphasizes the genetic pathogenesis of is chaemic heart disease. On the other hand, Amirzadegan *et al* and Sari *et al*8 showed that there was no correlation between various blood groups and development of coronary artery disease. These authors observed that the prevalence of major risk factors was equal in patients with different blood groups and had no impact on development of premature coronary artery disease in individual subjects.
Hence this was undertaken to study the effect of cardiovascular on blood

**Aim and objectives**
The aim of this study is to examine the traditional heart hypothesis through recovery and analysis of previously unpublished data from the Minnesota CVD Experiment and to put findings in the context of existing cardiovascular cases, randomized controlled trials through a systematic review and Latin square design.

1. To observe the association between ABO blood group and Rheumatic heart disease.
2. To observe which blood group is more vulnerable to cardiovascular diseases.
3. To observe which of the heart diseases is more prevalent to each blood group.

**Methodology**
The study was conducted at Aminu Kano Teaching Hospital, Kano State, Nigeria from 2013 to 2016. A total of 721 patients with confirmed CVD were taken as cases. On the other hand, 120 subjects without CVD were taken as controls. All the cases were obtained from case file records of Aminu Kano Teaching Hospital and the controls were volunteers. Data on each case and control subject was recorded. Statistical analyses was performed according to Statistical Package for the Social Sciences (SPSS) version 23. Based on the Latin Square design, all probability values were two-tailed and probability values below 0.05 were considered statistically significant. Confidence intervals (CI) was 95%, R-square was 0.746 and ratio of control to case was 0.17. R-square and the CI were used to describe the association between CVD and group.

**Result**
Out of 721 cases, 232 patients were of group 'A' (32%), 187 patients were of group 'B' (26%), 81 were of group 'AB' (11%) and 221 cases were of group 'O' (31%). In control cases, 22% belongs to group 'A', 23% to blood group 'B'. 20% to blood group 'AB' and 34% to O. Its comparison with control series revealed that there was an apparently increased frequency of disease in the 'A', while 'B' and 'O' blood group have the same increase frequency and there is a decrease in blood group 'AB'. Finally there is increased incidence in blood group 'A' and low incidence in Blood group 'AB'.
This Latin-square value revealed and it is significant [P value 0.000 i.e. < 0.05 and Degree of freedom (D.F.) = 3].
Figure

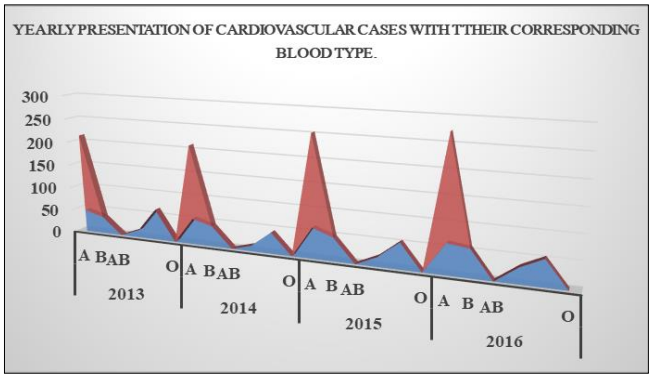


**Fig 1:** Above present the annual cases of cardiovascular together with their corresponding ABO blood group.

**Table 1:** Yearly Distribution of Cardiovascular In Akth (2013-2016)

| CVD Disease | 2013 | | | | 2014 | | | | 2015 | | | | 2016 | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | A | B | AB | O | A | B | AB | O | A | B | AB | O | A | B | AB | O | |
| Rheumatic Heart Disease | 19 | 10 | 6 | 14 | 16 | 18 | 5 | 7 | 12 | 14 | 3 | 13 | 9 | 12 | 11 | 7 | 176 |
| Coronary heart disease | 21 | 16 | 9 | 35 | 32 | 23 | 6 | 18 | 40 | 26 | 11 | 31 | 43 | 31 | 14 | 30 | 386 |
| Heart attack | 8 | 10 | 1 | 17 | 7 | 3 | 1 | 20 | 13 | 9 | 6 | 11 | 12 | 15 | 8 | 18 | 159 |
| TOTAL | 48 | 36 | 16 | 66 | 55 | 44 | 12 | 45 | 65 | 49 | 20 | 55 | 64 | 58 | 33 | 55 | 721 |
| | 166 | | | | 156 | | | | 189 | | | | 210 | | | | 721 |

**Table 2:** Above show the observed and corresponding expected frequency of each cell.

| Group | Gender | | | | | Total |
|---|---|---|---|---|---|---|
| | Male with risk factor | | Female with risk factor | Male without risk factor | Female without risk factor | |
| A | Count | 92 | 17 | 50 | 31 | 190 |
| | Expected Count | 63.8 | 21.1 | 84.9 | 20.3 | 190.0 |
| | % within GENDER | 38.0% | 21.3% | 15.5% | 40.3% | 26.4% |
| B | Count | 42 | 20 | 85 | 4 | 151 |
| | Expected Count | 50.7 | 16.8 | 67.4 | 16.1 | 151.0 |
| | % within GENDER | 17.4% | 25.0% | 26.4% | 5.2% | 20.9% |
| AB | Count | 15 | 31 | 104 | 26 | 176 |
| | Expected Count | 59.1 | 19.5 | 78.6 | 18.8 | 176.0 |
| | % within GENDER | 6.2% | 38.8% | 32.3% | 33.8% | 24.4% |
| O | Count | 93 | 12 | 83 | 16 | 204 |
| | Expected Count | 68.5 | 22.6 | 91.1 | 21.8 | 204.0 |
| | % within GENDER | 38.4% | 15.0% | 25.8% | 20.8% | 28.3% |
| Total | Count | 242 | 80 | 322 | 77 | 721 |
| | Expected Count | 242.0 | 80.0 | 322.0 | 77.0 | 721.0 |
| | % within GENDER | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

**Post Hoc Tests Blood Group (Multiple Comparisons)**

**Table 3**

| Dependent Variable: DATA1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| | (I) Blood group | (j) Blood group | Mean difference (i-j) | Std. Error | Sig. | 95% confidence interval | |
| | | | | | | Lower bound | Upper bound |
| LSD | A | B | 1.4289* | .40590 | .000 | .6320 | 2.2258 |
| | | AB | -.4960 | .53304 | .352 | -1.5425 | .5506 |
| | | O | -16.6945* | .38823 | .000 | -17.4567 | -15.9323 |
| | B | A | -1.4289* | .40590 | .000 | -2.2258 | -.6320 |
| | | AB | -1.9249* | .54939 | .000 | -3.0035 | -.8463 |
| | | O | -18.1234* | .41038 | .000 | -18.9291 | -17.3177 |
| | AB | A | .4960 | .53304 | .352 | -.5506 | 1.5425 |
| | | B | 1.9249* | .54939 | .000 | .8463 | 3.0035 |
| | | O | -16.1985* | .53647 | .000 | -17.2518 | -15.1453 |
| | O | A | 16.6945* | .38823 | .000 | 15.9323 | 17.4567 |
| | | B | 18.1234* | .41038 | .000 | 17.3177 | 18.9291 |
| | | AB | 16.1985* | .53647 | .000 | 15.1453 | 17.2518 |

Based on observed means.
The error term is Mean Square (Error) = 17.059

**Latin square design**

**Table 4:** Tests of Between-Subjects Effects

| Dependent Variable: Data | | | | | |
|---|---|---|---|---|---|
| Source | Type III Sum of Squares | Df | Mean Square | F | Sig. |
| Corrected Model | 49710.910[a] | 9 | 5523.434 | 231.599 | .000 |
| Intercept | 128438.975 | 1 | 128438.975 | 5385.471 | .000 |
| CVD | 21469.971 | 3 | 7156.657 | 300.080 | .000 |
| PERIOD | 960.073 | 3 | 320.024 | 13.419 | .000 |
| TREATMENT | 28865.029 | 3 | 9621.676 | 403.439 | .000 |
| Error | 16956.755 | 711 | 23.849 | | |
| Total | 222595.000 | 721 | | | |
| Corrected Total | 66667.664 | 720 | | | |

a. R Squared =.746 (74.6%) [Adjusted R Squared =.742 (74.2%)]

R-square→ describes the amount of variation in the observed response values that is explained by the predictors. Adjusted $R^2$-is a modified $R^2$ that has been adjusted for the number of terms in the model.

Table 4 gives the sum of square, degrees of freedom, mean square and F-statistic for the model, blood group, period and type of heart diseases (block error and total) our concern is on the p-value of the treatment (blood group) and the block which are both 0.000 respectively. Both of the three values are less than 0.05 we therefore reject both of the null hypothesis and conclude that there is significance difference in the mean of treatment(blood group), blocks (CVD type) and the periods.

**Table 5:** Homogeneous Subsets of the ABO blood group

| DATA2 | | | | |
|---|---|---|---|---|
| Turkey B[a,b,c] | | | | |
| Blood Group | N | Subset | | |
| | | 1 | 2 | 3 |
| AB | 176 | 4.8580 | | |
| O | 204 | | 16.1324 | |
| B | 151 | | 16.4967 | |
| A | 190 | | | 20.8737 |

Means for groups in homogeneous subsets are displayed Based on observed means. The error term is Mean Square (Error) = 23.849

a) Uses Harmonic Mean Sample Size = 178.019.
b) The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.
c) Alpha = 0.05.

From table above, Turkey's multiple comparison procedure, shows that there are three homogeneous subsets. There is no significant difference between blood group O and B. A and AB are different from each other and also significantly different from A and AB.

Hence blood group A is having highest increased of cardiovascular diseases.

**Discussion**

The present study aimed to find out the effect of cardiovascular diseases on blood groups i.e. IHD, RHD, CAD and Heart Attack. Results of this study showed significant association between ABO blood groups and cardiovascular pathologies. The control group in this study showed a proportionate frequency of the ABO blood groups as: A (22%), B (23%), AB (20%), and O (34%). This is different to the findings of POOJA, INDERMEET and MANISHA (2013) in their study conducted at Ahmedabad, India (A, 25.47%; B, 37.53%; AB, 9.04%; O, 27.94%). It is also comparable to findings in the studies at nearby areas of Eastern Ahmedabad, Punjab and Pakistan (Patel *et al.*, 2012). All these studies described B as the most frequent blood group, O being the second most common blood group and AB as the least common blood group. Southern India have described contrast findings with O being the most common blood group, followed by B, A and AB. In Nepal, which is connected to northeast of India, as well as Australia, Britain and USA, O and A are the common blood

groups that are followed by B and AB (Patel *et al*., 2012). The distribution of blood groups varies regionally, ethnically and from one population to another. While looking at

Rh grouping, 89-95% donors all over the world are detected as Rh +ve, except at Britain and USA where the frequency of Rh positivity is 83-85% (Patel *et al*., 2012).

A multitude of risk factors are responsible for development of cardiovascular diseases (CVDs) including environmental factors. Control of these risk factors has been shown to reduce the severity and complications of the disease. In this study, correlation between blood groups and IHD was examined in three different Heart diseases: rheumatic, coronary and heart attack. Similar distribution of ABO blood groups was found in patients with CVD in both groups ($p<0.05$), however, after excluding patients with risk factor/s, there was significant association in CVD patients between Heart disease and different blood groups ($p<0.05$). Similar results were found in the studies of Amirzadegan *et al*. (2006) [2], Abdollahi *et al*. (2009) and Lutfullah *et al*. (2010) in which they found that distribution of age was similar between ABO blood groups. This was in contradiction to the findings of Platt *et al*. (1985) [15] who studied correlation between blood groups and cardiac infarction in two different age groups: those who were 65 years old and older, and younger patients and observed that the predominance of blood type A in patients with cardiac infarction was even higher in more elderly population (i.e. $p<0.001$). Gender distribution was also found to have no significant association with blood groups in CVD patients in this study, as also observed by Abdollahi *et al*. (2009) and Lutfullah *et al*. (2010).

This study was distinct in that the other risk factors such as addiction history, obesity, diabetes, high blood pressure were excluded from each category of patients to know the existence of genetic impact of ABO blood groups and independent of the other factors specifically, as was done in the studies of Platt *et al*. (1985) [15]. Almost 60% of population in our control group had blood groups A and O. Similar pattern was also seen in CVD patients. Gender had no significant association with blood group distribution in CVD, however blood group A showed more association in both RHD, CAD and heart attack patients without risk factor/s. In summary, the results in this study showed that, in this Nigerian cohort, the prevalence of various blood groups was almost similar to that in controls and significant association was found between ABO blood groups and CVD. Some of the recent studies have also shown similar results. Omnath, Hiteshkumar, Krishna, Gopinath, and Sushil,(2014) [14]. Reported that group 'A' individuals are more susceptible to rheumatic heart disease while group 'O' individuals are relatively resistant to the disease. Amirzadegan *et al*. (2006) [2] investigated a possible relationship of ABO blood groups with coronary artery disease in 2026 CAD patients. Their results did not show any significant difference between the prevalence of ABO blood groups in coronary artery disease patients compared to the Iranian general population. Their analysis suggests that there is no relationship between various ABO blood groups and development of coronary artery disease. Moreover, the incidence of major risk factors was found equal in patients with different blood groups, and hence, blood groups had no impact on development of premature coronary artery disease in individual subjects.

In contrast, results in various investigations are conflicting. Several clinical studies have shown that individuals of the A phenotype blood group are more susceptible to cardiovascular diseases. In British men and in the Hungarian population, the incidence of ischemic heart disease is higher in patients with blood group A (Whincup *et al*., 1990; Tarjan *et al*., 1995) [24]. Also, Skaik (2009) found that group A was the most common (57%) and the group O was the second (30.5%) among the MI patients in Gaza Stripe of Palestine. Abdollahi and his colleagues (2009) observed that group A subjectsreported more family history of CAD than the subjects with other blood groups. Tarjan *et al*. (1995) concluded that blood group A was more frequent and the blood group O was less frequent among the patients with positive coronary angiography. Stakishaitis *et al*.(2002) found that the blood group B can be related with coronary atherosclerosis in women. The blood group O can possibly serve as a protective antiatherogenic factor in women. The blood group A is not a risk factor for atherosclerosis in women in Lithuanian population. Again, Nydegger *et al*. (2003) [13] indicated that the ABO blood group B allele was an independent risk factor for myocardial infarction.In a study in Bangladesh, Biswas *et al*. (2008) found that the prevalence of Coronary Artery Disease (CAD) was invariably higher in blood group O than all other blood groups while the major blood group in Bangladeshi people is phenotype B. It is consistent with the observation of Anvari and his colleagues (2009), and Mitchell (1977) who concluded that towns with a higher prevalence of blood group O had higher rates of cardiovascular mortality, whereas Meade *et al*. (1994) reported significantly higher incidence of IHD in blood group AB as compared to those of B & O, which were in contrast with other studies done in Europe and United States. Thus looking to the contradictory results from cross-sectional studies of various racial groups, relationship between ABO blood groups and CVDs is still not clear signifying need for more research to draw a decisive conclusion. In recent Indian studies, Garg *et al*. (2012) concluded that there is a significant association between MI and blood group B; and Banerjee and Datta (2011) indicated that incidence of ischemic heart disease is highest in blood type A, wherein comparatively a smaller number of subjects (n=400 and 300 respectively) were investigated. Hence these variations could be a result of biological variations or could be because of sample size. Further investigations in other regional settings with much larger study population may more fully elucidate these findings.

## Conclusion

From the results we can conclude that there is significant relation or impact of ABO blood groups on major cardiovascular diseases (RHD, CAD AND HEART ATTACK), however we get no significant difference in distribution of blood groups in male and female patients with CVD after excluding patients with risk factor/s. Further investigations in other regional settings with much larger population may more fully elucidate these findings.

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