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## **Research Article**



# Metabolic health status and cardiovascular risk of different ABO blood group phenotypes

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#### Abstract

**Objectives:** ABO blood group antigens could play a role in the pathogenesis of cardiovascular disease (CVD). This study examined the metabolic health status (MHS) and CVD risk of apparently healthy individuals from across the ABO blood group system.

**Methods:** Demographic details as well as anthropometric and biochemical data were collected in a cross-sectional survey from 120 participants of different ABO groups (range: 18-70 years). Height, weight, and waist circumference were measured using standard procedures. Body mass index was calculated as weight divided by height squared (kg/m<sup>2</sup>). A blood sample of approximately 5 mL was collected after an overnight fast. Fasting blood glucose was estimated using a glucometer. The blood group was determined using a monoclonal ABO blood grouping reagent. Direct enzymatic methods and a commercial kit were used to measure the level of total cholesterol (TC), triglycerides, and high-density lipoprotein. Low-density lipoprotein (LDL) and very low-density lipoproteins were estimated using the Friede-wald equation. Metabolically healthy (MH) and metabolically unhealthy (MUH) individuals were identified based on the presence of metabolic syndrome using the Joint Interim Statement criteria. CVD risk was determined using the Systematic Coronary Risk Evaluation chart.

**Results:** Females showed significant differences in TC across the ABO system: The O group (mean±SD: 4.85±0.77 mmol/L) demonstrated a significantly higher TC level compared with the A group (mean±SD: 4.22±0.72 mmol/L; p=0.015). The LDL in females was also significantly higher in the O group samples (mean±SD: 3.06±0.75 mmol/L) compared with the A samples (mean±SD: 2.53±0.62 mmol/L; p=0.042). There was no significant difference between the MUH and MH groups based on ABO blood phenotype (p>0.05). The CVD risk among those with the O phenotype (51.7%) was significantly higher than in the non-O blood groups among male subjects ( $\chi^2$ =6.213; p=0.045).

**Conclusion:** MHS was not associated with the ABO system, but there is a possibility that male members of blood group O are more susceptible to CVD than men with non-O phenotypes.

**Keywords:** ABO blood group system, cardiovascular disease risk, metabolically (un)healthy, metabolic health status, metabolic syndrome

Clinically, certain cardio-metabolic risk determinants often occur in a cluster of components of obesity, dyslipidemia, hypertension, and hyperglycemia [1]. This formed the basis of the definition of metabolic syndrome (MetSyn). Various sets of criteria for the diagnosis of MetSyn have been proposed using a different number and combination of these compo-

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nents [2, 3]. As defined by the Joint Interim Statement (JIS), the MetSyn components are an excessive waist circumference, high triglyceride (TG) level, low high-density lipoprotein (HDL) cholesterol level, elevated blood pressure, and a high fasting plasma glucose (FPG) level. The presence of at least 3 of the 5 components meets the definition of MetSyn (termed metabolically unhealthy [MUH] in this study) [2]. Regardless of which definition is adopted, prior evidence underpins the understanding that MetSyn is significantly linked with a greater risk for cardiovascular disease (CVD) and type 2 diabetes, especially in men [4, 5]. Notably, a 2-fold increase in CVD has been reported [6].

The ABO blood group is considered an overarching genetic determinant of CVD risk [7]. Advances in technology, biochemistry, and genetics have clarified to a plausible extent the association of blood group types – especially the human blood group antigens, A, B, and H (O) – and their relationship to risk for disease [8]. Extensive, evidence-based, scientific validation has substantiated the association between ABO blood groups and diseases such as cancer, infection, coagulation disorders, diabetes, and CVD [8, 9]. Thus, the study of ABO blood group phenotypes remains a fascinating field, given its role in the pathogenesis of different diseases, particularly CVD [7, 9]. The influence of ABO blood groups on the cardio-metabolic health status of an individual is multifaceted, because MUH status and the risk of CVD is a multi-factorial condition that is not controlled by just a single blood group antigen [8]. This suggests the involvement of a complex etiological interaction of genetic and socio-environmental risk factors in the development of CVD [10].

Understanding the distribution of metabolic risk factors in different ABO blood phenotypes in a certain population is important because the distribution of blood group antigens differs across ethnicity and race [11]. There is increasing evidence reinforcing an association between the ABO blood group system and the risk of developing CVD, which may provide for tailored management of some disease conditions.

In an effort to understand the relationship between ABO blood group phenotypes and evidence underpinning an association between the ABO blood group system and the risk of developing CVD, several epidemiological studies have characterized lipid profile distributions in individuals with or without metabolic disease across the ABO blood group system [7, 10, 12-14]. However, research examining the metabolic health status of individuals according to ABO blood group, which may be an important genetic determinant for CVD processes, remains limited. Understanding metabolic health status (MHS) in the context of the ABO system may pave the way for improved CVD management, or better still, it could potentially serve as a predictive index of CVD in society at large. The goal of the present study was to analyze the MHS and CVD risk of apparently healthy participants from all of the ABO blood phenotypes with the following specifics objectives: (1) characterize and compare the level of different components of MetSyn

across ABO subtypes, (2) estimate the prevalence of MUH subjects across ABO subtypes by gender, and (3) determine the level of cardiovascular risk associated with each ABO subtype.

#### **Materials and Methods**

#### Study design and subject characteristics

A group of 120 apparently healthy individuals, comprised of males (n=60) and females (n=60) between the ages of 18 and 70 years, were recruited for a cross-sectional study in the city of Enugu, in southeastern Nigeria. The participants were sorted according to their ABO blood group type. MHS was determined using the Joint Interim Statement criteria on harmonizing a diagnosis of MetSyn, which requires the presence of 3 of 5 components for diagnosis:

- 1. Excessive waist circumference (WC) of ≥94 cm for men and ≥80 cm for females in sub-Saharan Africa
- 2. High TG level of ≥150 mg/dL (1.7 mmol/L) or use of lipidlowering drugs
- 3. Low HDL level of <40 mg/dL (1.04 mmol/L) for men and <50 mg/dL (1.3 mmol/L) for women
- Elevated blood pressure (BP) of systolic BP (SBP) ≥130 mmHg and/or diastolic BP (DBP) ≥85 mmHg, or use of or anti-hypertensive drugs.
- 5. High FPG level of ≥100 mg/dL (5.6 mmol/L) or medication for diabetes (insulin or oral anti-diabetic) [2].

Participants who did not meet at least 3 of the 5 criteria were considered metabolically healthy (MH), i.e., without MetSyn. This study was approved by the University of Nigeria Teaching Hospital Health Research Ethics Committee, Ituku-Ozalla Enugu (NHREC/05/01/2008B-FWA00002458-1RB00002323). Participants who willingly consented to participate after due explanation of the purpose and nature of the study were included in the study.

#### Social demographic details

All of the participants completed a well-structured, self-administered questionnaire that included social demographic variables, such as gender, age, alcohol use, smoking status, and physical (in)activity.

#### Anthropometric measurements

Body weight was measured in kilograms (kg). Patients were weighed after removing heavy clothing, such as shoes and belts, using a digital Soehnle electronic scale (Leifheit AS, Nassau/Lahn, Germany). Height was measured using a stadiometer, with the participant standing erect in bare feet with the head in the Frankfurt plane. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m<sup>2</sup>). WC was measured (cm) at the level of the iliac crest using a measuring tape while the participants exhaled. The blood pressure index was measured twice in a sitting position after 5 minutes of rest with a mercury sphygmomanometer according to standard protocol. The mean result was recorded in mmHg for each patient. The same measuring instruments were employed in the data collection of all patients to ensure reliability and validity of results.

#### Cardiovascular disease risk assessment

Assessment of CVD risk was performed using the Systematic Coronary Risk Evaluation (SCORE) chart [15], which has been recommended in European guidelines on CVD prevention in clinical practice based on large, representative, European cohort datasets. The SCORE chart estimates the 10-year risk of fatal CVD in high/low CVD risk populations based on certain risk components, such as age, gender, smoking, SBP, and total cholesterol (TC). It was designed to facilitate risk estimation in apparently healthy individuals with no documented CVD [16].

#### **Biochemical laboratory assessment**

A fasting blood sample of about 5 mL was collected from each participant using a sterile syringe. The FPG value was estimated using a point-of-care glucose testing device (glucometer). About 1.0 mL of the blood sample from each participant was added to an ethylenediaminetetraacetic acid sample container, then sealed and labeled for ABO grouping. The remaining 4 mL of blood was centrifuged after clotting and retraction to separate the serum for the estimation of the lipid profile. The serum samples were preserved in a refrigerator for a period of 24 to 48 hours while the lipid profile tests were conducted.

The blood group was determined using a monoclonal ABO blood grouping reagent (Clas Technology Ltd., Dungannon,

UK). The quantitative determination of the lipid profile parameters of TC, TG, and HDL was performed using direct enzymatic assay methods and a commercial kit (Randox Laboratories Ltd., Crumlin, UK). The low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) values were estimated using the Friedewald equation:

LDL-C (mmol/L)=TC-[HDL-C+TG/2.2]; where VLDL=TG/2.2.

#### **Data analysis**

The data were analyzed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, one-way analysis of variance with the Tukey post hoc multiple comparison test, and a chi-square test were used, as appropriate, to compare and estimate the metabolic health status (i.e., proportion of MH and MUH) and cardiovascular risk according to the ABO blood system group. Only the 3 predominant ABO blood group subtypes within the study population: O, A, and B, in that order, were used for analysis [13]. The AB blood subtype did not satisfy the statistical assumption of adequate cell size for analysis and it was excluded from the analysis. Significance was set at p<0.05.

#### Results

Table 1 demonstrates that there was no significant difference across the ABO system in the components of MetSyn in the studied population (p>0.05).

The proportion of study participants classified as MUH and those who were grouped as MH was not significantly different across ABO subtypes (p>0.05) (Table 2). This suggests that no ABO blood subtype is more or less likely to be metabolically healthy or unhealthy. The level of CVD risk for the A (19.4%) and B (27.8%) groups was significantly lower than that of the

Table 1. Components of metabolic syndrome according to ABO blood group in the study group (n=119)				
Parameters	Α	В	0	Р
	42 (35.3%)	20 (16.8%)	57 (47.9%)	
Age (years)	34.07±11.23	41.40±16.10	38.09±11.88	0.078
HDL (mmol/L)	1.27±0.19	1.23±0.17	1.29±0.18	0.439
LDL (mmol/L)	2.62±0.66	2.72±0.68	2.71±0.72	0.782
TG (mmol/L)	0.99±0.43	0.90±0.33	1.02±0.44	0.491
TC (mmol/L)	4.33±0.74	4.35±0.67	4.48±0.75	0.591
VLDL (mmol/L)	0.43±0.17	0.41±0.16	0.47±0.21	0.429
SBP (mmHg)	118.31±16.90	116.00±15.28	116.33±23.61	0.867
DBP (mmHg)	78.83±10.92	74.50±10.80	78.42±11.32	0.320
FPG (mg/dL)	88.95±15.11	88.70±17.32	92.00±0.00	0.505
BMI (kg/m <sup>2</sup> )	27.84±9.68	28.28±7.86	28.05±00.00	0.985
WC (cm)	92.29±10.44	87.81±7.99	92.33±0.00	0.163

Mean±SD; Statistical non-significance; P>0.05 with Turkey Post-Hoc tests used for multiple comparisons analysis between ABO groups for each parameter. BMI: Body mass index; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Total triglyceride; VLDL: Very low-density lipoprotein; WC: Waist circumference.

# Table 2. Metabolically healthy and metabolically unhealthy subjects and CVD risk across ABO subtypes among the general population studied (n=119)

Metabolically healthy, n (%)	Metabolically unhealthy, n (%)	χ² value P value
36 (35.0)	6 (37.5)	
17 (16.5)	3 (18.8)	χ²=0.133
50 (48.5)	7 (43.8)	P=0.935
103 (100)	16 (100)	
CVD-at risk	CVD-not	χ² value P value
	alfisk	P value
7 (19.4)	35 (42.2)	
10 (27.8)	10 (12.0)	χ²=7.627
20 (52.8)	37 (45.8)	P=0.022*
36 (100%)	83 (100%)	
	healthy, n (%) 36 (35.0) 17 (16.5) 50 (48.5) 103 (100) CVD-at risk 7 (19.4) 10 (27.8) 20 (52.8)	healthy, n (%)         unhealthy, n (%)           36 (35.0)         6 (37.5)           17 (16.5)         3 (18.8)           50 (48.5)         7 (43.8)           103 (100)         16 (100)           CVD-at risk         CVD-not at risk           7 (19.4)         35 (42.2)           10 (27.8)         10 (12.0)           20 (52.8)         37 (45.8)

\*Statistical significance: p<0.05; CVD: Cardiovascular disease.

O group (52.8%); the members of the O blood subtype group were more likely to be at risk of CVD ( $\chi^2$ =7.627; p=0.022).

Table 3 illustrates that significant differences in the TC and LDL (mmol/L) were observed across the ABO system among females. The O blood group had a significantly higher level of TC (mean±SD: 4.85±0.77 mmol/L) compared with the A group (mean±SD: 4.22±0.72 mmol/L; p=0.015). The LDL in blood group O (mean±SD: 3.06±0.75 mmol/L) was significantly higher compared with the A group (mean±SD: 2.53±0.62 mmol/L; p=0.042). However, none of the components of MetSyn revealed a significant difference between ABO blood groups.

In Table 4 it can be seen that there was no significant difference among female patients in the proportion of those with MUH status compared with the MH participants across each

#### Table 4. Proportion of females classified as metabolically healthy and unhealthy and the CVD risk across ABO blood groups

Blood group	Metabolically healthy, n (%)	Metabolically unhealthy, n (%)	χ² value P value
A	16 (35.6)	5 (35.7)	
В	7 (15.6)	2 (14.3)	χ²=0.014
0	22 (48.9)	7 (50.0)	P=0.993
Total	45 (100)	14 (100)	
Blood group	CVD-at risk	CVD-not	χ² value
Blood group	CVD-at risk	CVD-not at risk	χ² value P value
Blood group A	<b>CVD-at risk</b> 1 (14.3)		~
		at risk	~
A	1 (14.3)	at risk 20 (38.5)	P value
A B	1 (14.3) 2 (28.6)	at risk 20 (38.5) 7 (13.5)	<b>P value</b> χ <sup>2</sup> =2.040

CVD: Cardiovascular disease.

ABO subtype (p>0.05), suggesting that no ABO blood subtype was more or less likely than another to be metabolically healthy or unhealthy. Furthermore, the CVD risk did not differ significantly across the ABO blood group system among females ( $\chi^2$ =2.040; p=0.361). No ABO blood group was more or less likely at risk of CVD among the female subjects studied.

Table 5 demonstrates that there was no observed significant difference in any of the MetSyn components in the male subjects across the ABO subgroups (p>0.05).

In Table 6 it can be seen that the proportion of male subjects in each ABO group with MUH status was not significantly different from that of the MH participants ( $\chi^2$ =2.230; p=0.328). This indicates that no blood group was more or less metabolically

Table 5. Components of metabolic syndrome according to Abo blood group in the remain subjects (n=39, 49.0%)				
A (n=21)	B (n=9)	0 (n=29)	Р	
27.10±6.63	36.44±16.67	33.52±12.64	0.073	
1.27±0.23	1.24±0.21	1.31±0.23	0.698	
0.96±0.47	0.93±0.32	1.02±0.46	0.834	
4.22±0.72 <sup>a</sup>	4.34±0.82 <sup>b</sup>	4.85±0.77°	0.015*	
2.53±0.62ª	2.71±0.88 <sup>b</sup>	3.06±0.75 <sup>c</sup>	0.042*	
0.40±0.13	0.41±0.15	0.47±0.23	0.358	
119.43±16.78	116.22±13.53	117.79±28.47	0.935	
79.29±10.09	75.22±14.21	79.00±11.22	0.636	
90.19±19.41	81.67±15.93	93.86±16.91	0.203	
33.19±11.37	34.33±8.32	33.44±11.11	0.965	
98.96±8.59	90.59±9.33	98.10±9.37	0.063	
	A (n=21) 27.10±6.63 1.27±0.23 0.96±0.47 4.22±0.72 <sup>a</sup> 2.53±0.62 <sup>a</sup> 0.40±0.13 119.43±16.78 79.29±10.09 90.19±19.41 33.19±11.37	A (n=21)B (n=9) $27.10\pm 6.63$ $36.44\pm 16.67$ $1.27\pm 0.23$ $1.24\pm 0.21$ $0.96\pm 0.47$ $0.93\pm 0.32$ $4.22\pm 0.72^a$ $4.34\pm 0.82^b$ $2.53\pm 0.62^a$ $2.71\pm 0.88^b$ $0.40\pm 0.13$ $0.41\pm 0.15$ $119.43\pm 16.78$ $116.22\pm 13.53$ $79.29\pm 10.09$ $75.22\pm 14.21$ $90.19\pm 19.41$ $81.67\pm 15.93$ $33.19\pm 11.37$ $34.33\pm 8.32$	A (n=21)B (n=9)O (n=29)27.10±6.6336.44±16.6733.52±12.641.27±0.231.24±0.211.31±0.230.96±0.470.93±0.321.02±0.464.22±0.72°4.34±0.82°4.85±0.77°2.53±0.62°2.71±0.88°3.06±0.75°0.40±0.130.41±0.150.47±0.23119.43±16.78116.22±13.53117.79±28.4779.29±10.0975.22±14.2179.00±11.2290.19±19.4181.67±15.9393.86±16.9133.19±11.3734.33±8.3233.44±11.11	

Table 3. Components of metabolic syndrome according to ABO blood group in the female subjects (n=59, 49,6%)

Mean±SD; \* Statistical significance: p<0.05 with Tukey post hoc test used for multiple comparisons between ABO groups: \*=A vs O showed significant decrease; '=O vs A showed significant increase; b=B vs A and O, respectively, showed no significant difference; BMI: Body mass index; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Total triglyceride; VLDL: Very low-density lipoprotein; WC: Waist circumference.

Table 5. Components of metabolic syndrome according to ABO blood group in the male subjects (n=60, 50.4%)				
Parameters	Α	В	0	Р
	(n=21)	(n=11)	(n=28)	
Age (years)	41.05±10.59	45.45±15.16	42.82±9.02	0.554
LDL (mmol/L)	2.71±0.69	2.72±0.50	2.35±0.47	0.053
HDL (mmol/L)	1.26±0.14	1.22±0.13	1.27±0.11	0.516
TG (mmol/L)	1.01±0.39	0.86±0.34	1.02±0.43	0.495
TC (mmol/L)	4.44±0.76	4.35±0.55	4.08±0.51	0.124
VLDL (mmol/L)	0.47±0.19	0.40±0.17	0.46±0.19	0.588
SBP (mmHg)	117.19±17.48	115.82±17.24	114.82±17.65	0.896
DBP (mmHg)	78.38±11.94	73.91±7.70	77.82±11.59	0.531
FBS (mg/dl)	87.71±9.39	94.45±16.91	96.36±52.25	0.716
BMI (kg/m <sup>2</sup> )	22.49±1.67	23.31±1.36	22.46±1.91	0.357
WC (cm)	85.61±6.59	86.55±6.25	86.36±5.30	0.884

Mean±SD; Statistical non-significance; P>0.05 with Turkey Post-Hoc tests used for multiple comparisons analysis between ABO groups for each parameter; BMI: Body mass index; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Total triglyceride; VLDL: Very low-density lipoprotein; WC: Waist circumference.

healthy and unhealthy and the CVD risk across ABO blood groups				
Blood group	Metabolically healthy, n (%)	Metabolically unhealthy, n (%)	χ² value P value	
А	20 (34.5)	1 (50.0)		
В	10 (17.2)	1 (50.0)	χ²=2.230	
0	28 (48.3)	0 (0.0)	P=0.328	
Total	58 (100)	2 (100)		
Blood group	CVD-at risk	CVD-not at risk	χ² value P value	
A	6 (20.7%)	15 (48.4%)		
В	8 (27.6%)	3 (9.7%)	χ²=6.213	
0	15 (51.7%)	13 (41.9%)	P=0.045*	
Total	29 (100%)	31 (100%)		

Table 6. Dreportion of males classified as motabolically

\*Statistical significance: p<0.05.

unhealthy or healthy among the male subjects. However, the level of CVD risk among blood group O (51.7%) was significantly greater ( $\chi^2$ =6.213; p=0.045) compared with that of the non-O blood groups. Males in the O subtype group had the highest risk for CVD in the study population.

#### Discussion

This examination of the components of MetSyn, which are cardio-metabolic risk determinants (age, lipid profile parameters, FPG, BP, BMI, and WC), between blood subtypes revealed no significant difference across the ABO blood group system in the study group. The results were largely similar across the ABO groups among the male subjects. However, there were

significant differences observed in the TC and LDL values according to the ABO system group classification among the female subjects. The women in the blood group O category demonstrated a higher level of TC and LDL compared with those in blood group A. Our finding in the general populationparticularly among the males agreed with the documented evidence presented by Ghazaee et al. [17] and Farah et al., [18] which reported no significant difference in the lipid profile distribution among the different ABO blood groups. Some researchers [10, 13, 19-21] have reported a significant difference in lipid profile distribution between different ABO blood group antigens. For instance, a study of the Iranian population showed that hyperlipidemia was more frequent in other ABO groups than in blood group B [21], whereas other authors found that HDL and LDL had significantly different mean values across ABO blood groups [10]. Recently, Ureme et al. [13] revealed that blood group O might have a higher propensity for dyslipidemia, given that the highest level of LDL and the lowest level of HDL were reported in this blood group.

The results of this study indicated that there was no significant difference in the number of those with MUH or MH status according to ABO subtype. This was true for both female and male subjects. This implies that no blood group in the studied sample was more or less metabolically unhealthy than another. Many studies have revealed possible associations between various diseases, especially cardio-metabolic diseases, and the ABO blood groups, but the reasons for such an association remain controversial [8, 10, 22, 23].

The present study revealed that the level of CVD risk for blood groups A and B was significantly lower compared with that of the O group. The level of CVD risk among females did not differ significantly between groups; however, among male subjects, the level of CVD risk in members of blood group O was significantly increased compared to non-O blood groups. This finding is consistent with prior studies reporting evidence of an association between ABO blood subtypes and risk of CVD [10, 13, 17,18, 21, 23-27]. However, there is inconsistency in these prior findings as to which ABO blood subtype is at greater risk of CVD. Some studies [10, 13, 21] have reported that individuals with blood group O were at highest risk for CVD, but this was not replicated in other studies [17, 18, 23-27].

Our study results are similar to those of Anvari et al. [21], which indicated that the prevalence of coronary heart diseases was markedly higher in blood group O compared with the other ABO blood groups. Another study that was consistent with our findings was conducted among the Bengali population of eastern India. It found that a low HDL was the major CVD risk factor in healthy O blood group subjects [10]. Nafakhi et al. [27] suggested that there was no significant association between ABO blood group and CVD. Similarly, Jukic et al. [28] found there was no statistically significant difference between the blood groups in relation to their association with acute myocardial infarction. Anstee [29] reported that an association between blood group and CVD risk may only exist with non-O blood subtypes. Contrary to our findings, it was reported in a study performed in Senegal that the incidence of ischemic CVD in men was significantly higher in blood group A [23]. In the context of CVD in general, the level of risk of CVD associated with different ABO subtypes observed in our study, especially in blood group O, may not, in fact, differ from the study done in Senegal. The authors evaluated the prevalence of ischemic and non-ischemic CVD in patients of different ABO blood groups and reported that the diagnosis of ischemic disease (e.g., stroke, coronary artery disease, myocardial infarction) was 61.2% higher in blood group A compared with the other blood groups. The diagnosis of non-ischemic disease (e.g., heart failure, valvular disease, cerebral hemorrhage) was 73.6% higher in blood group O compared with the other blood groups [23]. Although our study did not stratify the type of CVD, both studies seem to indicate that individuals in sub-Saharan Africa with blood type O might be at increased risk of developing some form of CVD.

The inconsistent results in the literature may be attributable to ethnic variation in ABO antigens, varying sample size in different studies, and other unadjusted or unaccounted confounders for CVD. According to Liumbruno and Zranchini [22], the contrasting results on this issue suggest that the association between ABO blood group and risk of CVD is still unclear and deserves further investigation. A population-based prospective study is needed in Nigeria. This, in particular, could validate a possible etiological link between ABO blood group antigens and the risk of CVD, which could potentially serve as a predictive index for CVD in this population.

#### **Study limitations**

This study has some limitations. A causal link between ABO blood group and CVD risk cannot be ascertained as the study was a cross-sectional investigation and could only investigate an association. The AB blood group did not have an adequate representative sample in this study, likely because it is the

rarest of the ABO blood group subtypes in the studied population [13]. Only blood groups that satisfied the statistical assumption of adequate cell size for analysis were included: Our study examined the A, B, and O blood groups. Further study should be conducted with a well-represented sample for each ABO blood group. Additionally, a convenience sampling technique was used; therefore, generalization of results should be undertaken with caution. Covariates or confounders, such as smoking status, alcohol use, family history, physical inactivity, consumption of fruit and vegetables, and the use of some drugs, were not accounted for in the present study given that these data were generated from a self-administered questionnaire that produced a response favoring the positive/good replies, suggesting that the self-report process might have introduced social desirability bias.

The current study did not account for any underlying disorders, such as renal or liver disease, diabetes mellitus, a very high TG level of above 4.52 mmol/L (400 mg/dL), a very low level of triglyceride of below 1.13 mmol/L (100.10 mg/dL), or type III hyperlipidemia in the subjects recruited, which is capable of impacting the accuracy of Friedewald's formula used to estimate LDL [30]. LDL cholesterol overestimation is possible, as the formula does not differentiate between cholesterol derived from LDL and lipoprotein(a) in the face of elevated levels of lipoprotein(a) [30]. The Friedewald formula was applied in the current study because it had better agreement with a direct method for LDL measurement in healthy subjects [31] and appeared to have the best overall performance for LDL calculation when compared with other formulae in patients with dyslipidemias and co-morbidities [32].

#### Conclusion

The proportion of those classified as MUH in each ABO blood group was not significantly different from those who were considered MH. Male subjects of blood group O were associated with an increased risk for CVD, though the result may not have been independent of conventional cardio-metabolic risk factors. Consideration of blood group antigens alongside other convectional cardio-metabolic risk factors may offer helpful insights into understanding an individual's risk for developing CVD in the future.

Conflict of interest: None declared.

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– C.A.O.; Writing – I.C.A., P.N.K.; Critical review – I.C.A., C.A.O., I.N.O., P.N.K., B.C.O., F.A.

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