Volume 2. No 3/2015. ISSN 2313-0008 (Print); ISSN 2313-0016 (Online)

**Research Article**

Malays. j. med. biol. res.

**The Use of Atherogenic Index of Plasma in Assessing the Potential Cardiovascular Risk among ABO Blood Groups in Sickle Cell Disease Patients**

**Mathias Abiodun Emokpae1\*, Lynda Bose Akpologun2**

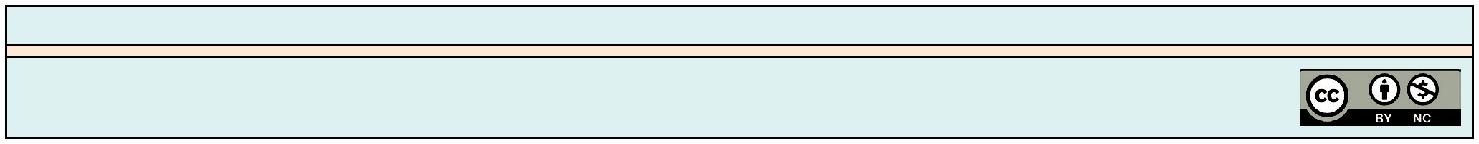
1Senior Lecturer, Department of Medical Laboratory Science, University of Benin, PMB 1154, **NIGERIA** 2Intern, Department of Medical Laboratory Science, University of Benin, PMB 1154, **NIGERIA**

\*Email: biodunemokpae@yahoo.com

**Abstract**

Studies have associated ABO blood groups with cardiovascular risk events in the general population and no significant association has yet been reported in sickle cell disease (SCD) patients. This study uses the atherogenic indices to evaluate the potential cardiovascular disease (CVD) risk of ABO blood groups in SCD patients. Lipoprotein concentrations were assayed in 200 SCD patients and 100 control subjects with normal haemoglobin using the enzymatic colorimetric method. The atherogenic indices were calculated and compared among the various blood groups to show which of the blood group has elevated atherogenic risk of CVD. The means total cholesterol, triglycerides and low-density lipoprotein cholesterol levels were highest in blood group A and lowest in blood group O while high-density lipoprotein cholesterol level was lowest in blood group A and highest in blood group O. All the atherogenic indices were highest in blood group A and lowest in blood group O. The mean levels of lipoprotein variables and atherogenic indices were not significantly different between the blood group B and AB. Atherogenic index of plasma (AIP), cardiac risk ratio (CRR) and atherogenic coefficient (AC) correlated positively (r=0.348,p=0.005; r=0.236, p=0.05; r=0.238,p=0.05) respectively with blood group A. Similarly AIP, CRR and AC correlated positively (r=0.316, p=0.05; r=0.311,p=0.05; r=0.310, p=0.05) with blood group B. On the other hand, AIP and AC failed to correlate with blood group AB but CRR correlated (r=0.321,p=0.05) with blood group AB. All the atherogenic indices did not correlate significantly with blood group O. Atherogenic indices were higher in non-O blood groups than blood group O. Patients with non-O blood groups may require detail evaluations and closer monitoring than those with blood group O with respect to CVD risk.

**Keywords:** ABO blood groups, atherogenic indices, cardiovascular disease, sickle cell disease.



**9/18/2015** **Source of Support:** None, **No Conflict of Interest:** Declared

This article is is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

**Attribution-NonCommercial (CC BY-NC)** license lets others remix, tweak, and build upon work non-commercially, and although the new works must alsoacknowledge & be non-commercial.

**Introduction**

The human blood group phenotype is determined by the presence of A or B antigen on the extra-cellular surface of the red blood cells. These antigens are made up of glycoproteins and glycolipids that are also present on a variety of tissues such as epithelium, sensory neurons, platelet and vascular endothelium (He etal, 2012). The biochemical compositions of ABO group system are terminal carbohydrate molecules that are synthesized by the sequential action of the enzymes ABO glycosyltransferase. The transferase A (α-1,3-N- acetylgalactosaminyltransferase) and transferase B (β-1,3-N-acetylgalactosaminytransferase) genes encode proteins associated with the ABO blood group system (Zhang etal, 2012). Any addition of specific monosaccharides to a common basic core precursor antigen H differentiates A from B antigens (Zhang etal, 2012), (Eastlund, 1998). On the other hand, blood O consists of only the basic H antigen without the addition of monosaccharide due to the deletion of guanine-258 in the region of the gene encoding the N-terminus of the protein (Jenkens and Donnell, 2006), (Storry and Olsson, 2009).

CC-BY-NC 2014. i-Proclaim | MJMBR Page 247

|  |  |
| --- | --- |
| Emokpae and Akpologun: The Use of Atherogenic Index of Plasma in Assessing the Potential Cardiovascular Risk among ABO Blood Groups in Sickle Cell Disease Patients | (247-251) |

ABO blood groups have been associated with the risk of cardiovascular diseases (CVDs), but no sufficient study has been done to prove it (Zera etal, 2015) and no significant association has yet been reported in Sickle cell disease patients. We previously reported the higher atherogenic index of plasma in SCD patients with chronic kidney disease than subjects with normal haemoglobin (Emokpae etal, 2010). Some studies have shown that blood group A and B are at higher risk of developing CVDs compared to blood group O (Emokpae etal, 2010), (Erikssen etal, 1980), (Nydegger etal, 2003). However, reports on the association of ABO blood group with CVD have not been consistent as some failed to show significant differences between the frequency of blood group and CVDs (Platt etal, 1985). No study to the best of our knowledge has used the atherogenic index of plasma to evaluate the relationship of ABO blood group with risk of CVDs. The association between total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c) with CVDs is recognized. Studies have indicated that about half of all CVD events occur in patients in whom plasma lipid levels are within normal limits (Amirzadegan etal, 2006), and it may be difficult to predict those at risk using conventional lipid profile parameters only (Blaton, 1997). Therefore, lipoprotein-related indices are used in clinical settings to indicate better those at risk of CVD events. The mathematical models used to assess how much atherogenic LDL-c is driving progression of CVD events (Emokpae etal, 2013) include: cardiac risk ratio (CRR) which measures the ratio of TC to HDL-c value (Tariq and Ali, 2012), atherogenic coefficient (AC) which is calculated by subtracting the value of HDL-c from TC, all divided by HDL-c value and atherogenic index of plasma (AIP), calculated as log(TG/HDL-c) is an indicator of plasma atherogenicity which is a significant independent predictor of CVD events (John and Brunzell, 2008). This study seeks to use atherogenic indices to evaluate the potential CVD risk among ABO blood group in SCD patients.

**Materials and Methods**

This study was conducted at the Department of Medical Laboratory Science, University of Benin, Benin City. The study subjects were Sickle cell disease patients in steady clinical state who were on a routine visit to the clinic. While the controls were apparently healthy subjects with normal haemoglobin who were recruited from among the staff and students of the University.

**Sample collection**: Five milliliters (5mL) of blood was collected ascetically in a fasting state with 4mL dispensed intoa plain container while 1mL was dispensed into EDTA container. The anticoagulated blood was used for blood group determination using tile method. The blood in the plain container was allowed to clot at room temperature and was centrifuged at 2000rpm for 10 minutes. The supernatant serum was separated into another container that was stored at -20oC for two weeks prior to analyses for lipid parameters. Total cholesterol, TG, and HDL-c were assayed by enzymatic colorimetric technique using reagents supplied by Randox Laboratories, UK. The low-density lipoprotein cholesterol (LDL-c) was calculated using Friedewald equation16. AIP was calculated as log[TG/HDL-c) with TG and HDL-c expressed in molar concentration15.Cardiac risk ratio (CRR) and AC were calculated as previously described7. **Statistical Analysis**: Statistical analysis was performed using the Statistical package for Social Sciences (SPSS 16,Chicago USA). Students’ t-test and ANOVA were used to compare mean values of the lipoprotein fractions and the atherogenic indices among the different blood groups. Results were expressed as mean±standard error of mean and p<0.05 was considered statistically significant.

**Results**

The results obtained are as shown in tables 1, 2 and 3. The study was conducted in 200 adult SCD patients (mean age 21±05years), and 100 apparently healthy HbAA controls (mean age 22±04).The lipoprotein variables were significantly lower in SCD patients compared to controls while atherogenic indices were significantly higher in SCD patients than controls. Table 2 shows that the means TC,TG and LDL-c levels were highest in blood group A and lowest in blood group O while HDL-c level was lowest in blood group A and highest in blood group O. All the atherogenic indices were highest in blood group A and lowest in blood group O. The mean levels of lipoprotein variables and atherogenic indices were not significantly different between the blood group B and AB. Total cholesterol, TG and LDL-c were significantly higher in blood group A than blood group B and blood group AB but higher than blood group O. The HDL-c levels in blood group B and AB were significantly higher than blood group A but lower than blood group O. The atherogenic indices of blood group B and AB were significantly lower than in blood group A but higher than blood group O. Table 3 shows that AIP, CRR and AC correlated positively (r=0.348,p=0.005; r=0.236, p=0.05; r=0.238,p=0.05) respectively with blood group A. Similarly AIP, CRR and AC correlated positively (r=0.316,p=0.05; r=0.311,p=0.05; r=0.310, p=0.05) with blood group B. On the other hand, AIP and AC failed to correlate with blood group AB but CRR correlated (r=0.321,p=0.05) with blood group AB. All the atherogenic indices did not correlate significantly with blood group O.

Page 248 Malaysian Journal of Medical and Biological Research **** Volume 2 **** Number 3/2015

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Volume 2. No 3/2015. |  | ISSN 2313-0008 (Print); ISSN 2313-0016 (Online) | |  |
| **Table 1:** Comparison of lipid profile and atherogenic indices in SCD patients with control (HbAA) subjects | | | | |
|  |  |  |  |  |
| **Variables** | **SCD patients** | **Control Subjects (HbAA)** |  | **p-value** |
|  |  |  |  |  |
| Number of Subjects | 200 | 100 |  |  |
|  |  |  |  |  |
| Total cholesterol (mmol/L) | 3.20±0.14 | 4.38±0.14 |  | 0.001 |
|  |  |  |  |  |
| Triglycerides (mmol/L) | 1.16±0.04 | 1.20±0.09 |  | 0.001 |
|  |  |  |  |  |
| HDL-c (mmol/L) | 0.70±0.15 | 1.08±0.05 |  | 0.001 |
|  |  |  |  |  |
| LDL-c (mmol/L) | 1.96±0.12 | 2.60±0.01 |  | 0.001 |
|  |  |  |  |  |
| AIP | 0.22±0.03 | 0.05±0.04 |  | 0.001 |
|  |  |  |  |  |
| CRR | 4.56±0.02 | 4.05±0.02 |  | 0.001 |
|  |  |  |  |  |
| AC | 3.56±0.02 | 3.05±0.02 |  | 0.001 |
|  |  |  |  |  |

**Table 2:** Distribution of measured variables among ABO blood group types in Sickle cell disease patients

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Measured variables** | | |  |  | **Blood Group A** | | **Blood Group B** | | |  | **Blood Group AB** | | |  | **Blood Group O** | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Number of Subjects | |  |  | 70 | |  | 42 |  |  |  |  | 12 | |  | 76 | |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Age (years) | |  |  |  | 20.5±0.01b | | 21.3±0.02c | |  |  |  | 18.0±0.03a | |  |  | 21.1±0.04c |
| Total Cholesterol(mmolo/L) | | |  |  | 3.81±0.14c | | 3.52±0.15b | |  |  |  | 3.47±0.14b | |  |  | 3.18±0.12a |
| Triglycerides (mmol/L) | | |  |  | 1.13±0.05c | | 1.10±0.04a | |  |  |  | 1.13±0.04a | |  |  | 1.06±0.04b |
| HDL-cholesterol(mmol/L) | | |  |  | 0.56±0.03b | | 0.62±0.04a | |  |  |  | 0.63±0.05a | |  |  | 0.71±0.03c |
| LDL-cholesterol(mmol/L) | | |  |  | 2.70±0.01c | | 2.39±0.03b | |  |  |  | 2.98±0.06c | |  |  | 1.99±0.09a |
| AIP | |  |  |  | 0.30±0.01c | | 0.25±0.03b | |  |  |  | 0.25±0.03b | |  |  | 0.17±0.03a |
| CRR | |  |  |  | 6.80±0.15c | | 5.66±0.04b | |  |  |  | 5.50±0.08b | |  |  | 4.47±0.02a |
| AC | |  |  |  | 5.80±0.05c | | 4.67±0.04b | |  |  |  | 4.50±0.08b | |  |  | 3.47±0.02a |
| a=p>0.05; b=p<0.05; c= p<0.001 | | |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Table 3:** Correlation of atherogenic indices among ABO blood groups in Sickle cell disease patients | | | | | | | | | | | | | | | | |
|  |  |  | | |  |  |  |  |  |  |  |  |  |  |  |  |
| **Blood Groups** |  | **Atherogenic** | | | |  | **Indices** | |  |  |  |  |  |  |  |  |
|  |  |  |  | |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  | **AIP** | | |  | **CRR** | |  |  |  |  |  |  | **AC** | |
|  |  |  |  |  |  |  |  |  |  | | |  |  | |  |  |
|  |  | **R-value** |  |  | **p-value** |  | **R-value** |  | **p-value** | | |  | **R-value** | |  | **p-value** |
|  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |
| A |  | 0.348 |  |  | 0.005 |  | 0.236 |  |  | 0.05 | |  | 0.238 |  |  | 0.05 |
|  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |
| B |  | 0.316 |  |  | 0.05 |  | 0.311 |  |  | 0.05 | |  | 0.31 |  |  | 0.05 |
|  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |
| AB |  | 0.350 |  |  | 0.10 |  | 0.321 |  |  | 0.05 | |  | 0.312 |  |  | 0.10 |
|  |  |  |  | |  |  |  |  |  |  | |  |  |  |  |  |
| O |  | 0.201 |  |  | 0.10 |  | 0.198 |  |  | 0.10 | |  | 0.196 |  |  | 0.10 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

**Discussion**

The data presented in this study shows that the atherogenic indices were higher in SCD patients than controls. The atherogenic indices were also higher in blood group A compared to blood group B, AB and O with blood group O having the lowest atherogenic indices. The atherogenic indices correlated significantly with blood group A and B but not with blood group O. The data suggest that the potential atherogenic risk was higher in blood group A, B and AB than O. Epidemiological studies have associated CVD events with ABO blood group (Zhang etal, 2012), (Tarjan etal, 1995), (Wazirali etal, 2005) but none has studied the atherogenic indices to show their potential contributions to CVD events observed which are different between the various blood group systems. Our observation is consistent with previous reports (He etal, 2012), (Friedewald etal, 1972), (Whincup etal, 1990). Significantly elevated risk incident of coronary heart disease (CHD) was observed in subjects with blood group A or B or AB compared to blood group O (He etal, 2012). The incidence of Ischaemic heart disease and CHD were reported to be higher in patients with blood group A (Whincup etal, 1990) in British men. In a Pakistani cohort study, it was observed that the prevalence of CHD was higher in patients with blood group A than the other blood groups (Tarjan etal, 1995). On the other hand, the report from the Northwich Park heart study stated that the incidence of IHD was significantly higher in patients with blood group AB compared to those with O,

CC-BY-NC 2014. i-Proclaim | MJMBR Page 249

|  |  |
| --- | --- |
| Emokpae and Akpologun: The Use of Atherogenic Index of Plasma in Assessing the Potential Cardiovascular Risk among ABO Blood Groups in Sickle Cell Disease Patients | (247-251) |

A or B(Wazirali etal, 2005).The reason for the differences in risk of CVD events in different blood groups is not completely clear. Apart from the effect of the ABO blood group system on lipoprotein levels other mechanisms have been proposed (Fox etal, 1986). It was suggested that ABO blood group system exerts profound influence on blood haemostasis via modulation of the von Willebrand factor and factor VIII, the concentrations which have been reported to be 25% higher in non-O blood groups than in group O subjects (Biswas etal, 2013), (Franchini and Lippi, 2015). Others have suggested that ABO blood group system may have a wider impact on CVD events than simply through modulation of thrombosis (Zhang etal, 2012). Genetic studies have associated ABO locus with circulating levels of soluble intercellular adhesion molecule 1, soluble P-selectin and soluble E-selectin (Franchini et al, 2007), (Gaudreault et al, 2012). The loss of glycosyltransferase function in blood blood group O may confer some protection against the development of CVD while genotypes relating to specific A and B blood groups and glycosyltransferase function may adversely impact on the endothelial function, lipoproteins and CVDs (Zhang etal, 2012). In conclusion, the atherogenic indices were higher in non-O blood groups than blood group O. Patients with non-O blood groups may require detail evaluations and closer monitoring than those with blood group O with respect to CVD risk.

**References**

Amirzadegan A, Salarifar M, Sadeghian S, Davoodi G, Darabian C, Goodarzynejad H. Correlation between ABO blood groups, major risk factors and coronary artery disease. Int J Cardiol 2006; 110:256-258.

Biswas S, Ghoshal PK, Halder B,Mandal N. Distribution of ABO blood group and major cardiovascular risk factors with coronary heart disease.BioMed Res Int 2013; 782941:1-5.

Blaton V. The role of lipids in the development of atherosclerosis and coronary heart disease:guidelines for diagnosis and treatment. J Int Federat Clin Chem Lab Med 1997; 51:16-22.

Dobiasova M, Frohlich J. The plasma parameter log(TG/HDL-c) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apo B-lipoprotein-depleted plasma (FERsubHDL). Clin Biochem 2001; 34:583-585.

Eastlund T. The histo-blood group ABO system and tissue transplantation. Transfusion 1998; 38:975-988.

Emokpae MA, Abdu A, Uadia PO, Borodo MM. Lipid profile in Sickle Cell Disease patients with Chronic Kidney Disease. Sahel Med J 2010; 13(1):20-23.

Emokpae MA, Arogundade A, Adumanya SC. Use of atherogenic index of plasma in evaluating the potential cardioprotective effects of red wine consumption: Studies in Nigerian young adult volunteers. Biokemistri 2013; 25(3):118-123.

Erikssen J, Thaulow E, Stormorken H, Brendemoen O, Hellem A.ABO bllod groups and coronary heart disease (CHD). A study in subjects with severe and latent CHD. Thromb Haemost 1980; 43:137-140.

Fox MH, Webber LS, Thurmon TF, Berbenson GS. ABO blood group associations with cardiovascular risk factor variables. Hum Biol 1986; 58(4):549-584.

Franchini M, Capra F, Targher G, Montagnana M, Lippi G. Relationship between ABO blood group and von Willebrand factor levels: from biology to clinical implications. Thromb J. 2007; 5:14.

Franchini M, Lippi G. The intriguing relationship between the ABO blood group, cardiovascular disease and cancer. BMC Med 2015; 13:7

Friedewald WT, Levy RL, Fredrickson DS. Estimation of concentration of low density lipoprotein cholesterol in plasma without use of preparative ultracentrifuge. Clin Chem 1972; 10:499-502.

Gaudreault N, Kumar N, Posada JM et al. ApoE suppresses atherosclerosis by reducing lipid accumulation in circulating monocytes and the expression of inflammatory molecules on monocytes and vascular endothelium.Arterioscler Thromb Vasc Biol 2012; 32(2):264-272.

He M, Wolpin B, Rexrode K, Manson JE, RimmE, Hu FB, Qi L. ABO blood group and Risk of coronary heart disease in two prospective cohort studies. Arterioscler Thromb Vasc Biol 2012; Doi 10.1161/ATVBAHA.112.248757.

Jenkens PV, O’Donnell JS. ABO blood group determines plasma von Willebrand factor levels: a biologic function after all? Transfusion 2006; 46(10):1836-1844.

John D, Brunzell MD. Lipoprotein management in patients with cardiometabolic risk. J Am Coll Cardiol 2008; 51:1512-1524.

Nydegger UE, Wuillemin WA, Julmy F, Meyer BJ, Carrel TP. Association of ABO histo-blood B allele with myocardial infarction. Eur J Immunogenet 2003; 30:201-206.

Platt D, Muhlberg W, Kiehl L, Schmitt-Ruth R. ABO blood group system,age,sex,risk factors and cardiac infarction. Arch Gerontol Geriatr 1985; 4:241-249.

Storry JR, Olsson ML. The ABO blood group system revisited: a review and update. Immunohematology 2009; 25(2):48-59.

Takeshi T, Keisuke N, Takaaki I, Makoto Y, Tatsuji N. Involvement of adhesion molecule in in-vitro plaque-like formation of macrophages stimulated with Aggregatibacter actinimycetemcomitans lipopolysaccharide. J Periodont Res 2010; 45(4):550-556.

Tariq M, Ali R. Comparative study for atherogenic index of plasma (AIP) in patients with type 1 Diabetes mellitus, type 2 Diabetes mellitus, thalassemia and Hypothyroidism. Int J Chem Res 2012;02:10-14.

Page 250 Malaysian Journal of Medical and Biological Research **** Volume 2 **** Number 3/2015

Volume 2. No 3/2015. ISSN 2313-0008 (Print); ISSN 2313-0016 (Online)

Tarjan Z, Tonelli M, Duba J, Zorandi A. Correlation between ABO and Rh blood groups, serum cholesterol and ischaemic heart disease in patients undergoing coronarography. Orv Hetil 1995; 136(15):767-769.

Wazirali H, Ashaque 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):1-3.

Whincup PH, Cook DG, Phillips AN, Shaper AG. ABO blood group and ischaemic heart disease in British men. Br Med J 1990; 300:1679-1682.

Zera E, Xinxo S, Hatellari A. The evaluation of Relationship between ABO blood groups and Cardiovascular risk factors in patients with acute Myocardial infarction in Durres population. Saudi J Med Med Scis 2015; 3(1):40-43.

Zhang H, Mooney CJ, Reilly MP. ABO blood groups and Cardiovascular Diseases. Int J Vascular Med 2012;1-11.

CC-BY-NC 2014. i-Proclaim | MJMBR Page 251