

Assessment of Cardiovascular Risk indices in Type 2 Diabetes Mellitus

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Abstract

Background: Dyslipidemia a common feature of diabetes mellitus leads to cardiovascular complications. These complications are not detected early enough due to absence of cheap and routine biomarker.

Aim: Therefore, the aim of this study is to assess the cardiovascular risk indices of diabetes mellitus individuals using Atherogenic coefficient (Ac), Cardiac Risk Ratio (CRR), Atherogenic index of plasma (AIP) and Non-HDL – cholesterol (surrogate marker for apolipoprotein B) in this locality.

Methods: Serum Total Cholesterol (TC), Triglycerides (TG), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein-Cholesterol (LDL-C), Very Low Density Lipoprotein-Cholesterol (VLDL-C) as well as cardiovascular risk indices (Cardiac Risk Ratio (CRR), atherogenic coefficient (Ac), atherogenic index of plasma (AIP) and Non-HDL cholesterol) were assessed.

Results: The TC, TG, LDL-C, VLDL-C as well as all the cardiometabolic risk indices of diabetes were observed to be significantly high ($P < 0.05$) when compared with control subjects. HDL-C in diabetes was observed to be significantly low ($P < 0.05$) when compared with control subjects.

Conclusion: The results indicates greater propensity of diabetes to cardiovascular complications. We therefore advocate routine use of these indices as part of lipid profile in order to nip any cardiovascular complication early enough.

Keywords: Diabetes mellitus; Cardiovascular risk indices; Dyslipidemia; Biomarker; Atherogenic

Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterized by hyperglycemia resulting from a variable interaction of hereditary and environmental factors due to defects in insulin secretion, insulin inaction, or both (WHO, 1985). There are two types of DM (Type 1 and Type 2) depending on the availability or non-responses of the insulin. Type 2 DM makes up about 90% of the diabetic population in Nigeria [1]. Relevant abnormalities found in diabetes mellitus are chronic hyperglycemia, dyslipidemia and insulin resistance [2]. Previous authors have reported increased levels of total cholesterol, triglycerides as well as LDL-cholesterol but decreased levels of HDL-cholesterol in diabetes [1,2]. Dyslipidaemia is common in diabetes, as both insulin deficiency and insulin resistance affects enzymes and pathways of lipid metabolism. It has been observed that about seventy-eight percent of type 2 diabetic patients die from cardiovascular disease, due to premature atherosclerosis which involves dyslipidemia [3]. Many factors account for increased cardiovascular disease risk in diabetes but lipid abnormalities are major contributors. It is well known that people with type 2 diabetes have elevated cardiovascular risk. Adults with diabetes have a two to four fold higher risk of experiencing cardiovascular events than adults without diabetes [4,5]. Due to higher risk of diabetes mellitus to cardiovascular disease, it is

crucial to identify and address these cardiovascular risks. The measurement of LDL cholesterol alone does not provide sufficient measure of atherogenic risk in hypertriglyceridemic patients, and a second or several markers is warranted [6]. Literature showed that the association of LDL-C with CVD was weak and LDL-C was not a significant predictor of CHD mortality [7]. Although there are recent markers such as apolipoproteins, C-reactive Proteins and markers of insulin resistance in cardiovascular risk assessment still present but are expensive. Also these recent markers are not routinely examined to assess the patient vulnerability to cardiovascular diseases. Therefore, the aim of this study is to assess the cardiovascular risk of diabetes mellitus individuals using atherogenic coefficient (Ac), Cardiac Risk Ratio (CRR), Atherogenic index of plasma (AIP) and Non-HDL – cholesterol a surrogate marker for apolipoprotein B in this locality [8].

Materials and Methods

Study population

A total of Two hundred (200) participants were recruited for this study based on the prevalence of diabetes in this locality. This comprise of One hundred (100) Non- Insulin Dependent Diabetes Mellitus (NIDDM) and One hundred (100) non diabetes individuals as controls. Inclusion criteria include being diabetic while an exclusion criterion is non-diabetic, cigarette smoking and lipid lowering drugs. Routine urinalysis was also performed for participants to confirm

diabetes and rule out renal or liver pathology. Informed consent was obtained from participants as well as ethical clearance from the various institutional ethics committee.

Collection of samples

Fasting blood samples were collected by standard vein puncture into plain containers. The blood was allowed to clot and then centrifuged at 3000rpm for 10minutes. The serum was separated into a cryovail tubes and kept frozen until required for analysis.

Biochemical analysis

Serum Total Cholesterol and Triglycerides were analyzed using the enzymatic CHOD-PAP method of as modified by and HDL-Cholesterol analyzed by the method of Trinder as modified by Richmond and HDL-Cholesterol analyzed by the method of Burstein [9-11]. LDL-Cholesterol, VLDL-Cholesterol was calculated using equation Friedewald except for those that have triglycerides values of ≥ 400 mg/dl which were estimated directly [12]. Cardiac Risk Ratio (CRR) was calculated as TC/HDL, atherogenic coefficient (Ac) was

calculated as TC-HDL/HDL, and atherogenic index of plasma (AIP) as $\log(TG/HDL)$ [13,14]. Non-HDL cholesterol was calculated as TC-HDL [8]. All test kits used were commercially available and products of Randox Laboratories UK. In all analysis, manufacturer's instructions were adhered to strictly.

Statistical analysis

The groups mean \pm SD was calculated for each analyte and significant difference between means evaluated using the student t-test. Statistical Package for Social Science SPSS version 16.0 software (SPSS Inc., Chicago, IL USA) for windows was used, with $P < 0.05$ considered as statistically significant.

Results

The results of our study shows an increase in total cholesterol, triglycerides, VLDL and LDL cholesterol but decreased level of HDL Cholesterol in Diabetes subjects when compared with controls (Table 1 and Figure 1).

	Age (years)	BMI	FBS (mmol/l)	TC (mmol/l)	TG (mmol/l)	HDL (mmol/l)	LDL (mmol/l)	VLDL (mmol/l)
NIDDM	47.3 \pm 0.7	26.4 \pm 0.2	11.3 \pm 0.4	5.7 \pm 0.3	3.2 \pm 0.1	1.4 \pm 0.1	2.8 \pm 0.1	1.5 \pm 0.1
Controls	30.6 \pm 0.7	22.1 \pm 0.3	4.7 \pm 0.1	3.8 \pm 0.3	1.3 \pm 0.1	2.0 \pm 0.1	1.2 \pm 0.1	0.6 \pm 0.1
P value	P=16.7 < 0.05	P=43 < 0.05	P=22 < 0.05	P=1.9 < 0.05	P=1.9 < 0.05	P=0.6 < 0.05	P=1.6 < 0.05	P=0.6 < 0.05

Table 1: Lipid profile (mmol/l) of Diabetic subjects and Controls.

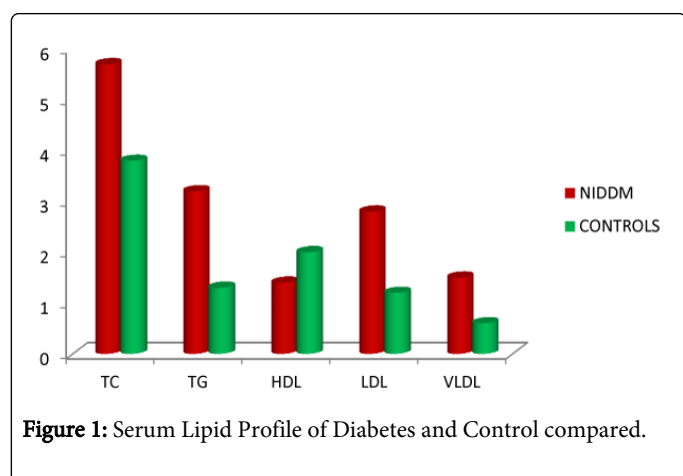


Figure 1: Serum Lipid Profile of Diabetes and Control compared.

	CRR	Ac	AIP	Non HDL
NIDDM	4.1 \pm 3.0	3.1 \pm 2.0	0.4 \pm 0.0	4.3 \pm 0.2
Controls	1.9 \pm 3.0	0.9 \pm 2.0	-0.2 \pm 0.0	1.8 \pm 0.2
P value	P=2.2<0.05	P=2.2<0.05	P=0.6<0.05	P=2.5<0.05

Table 2: Cardiovascular Disease Risk Indices of Diabetic and Control Subjects.

Table 2 shows increased cardiovascular risk indices in diabetes when compared with control subjects.

Discussion

Lipid tests, including triglycerides (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and low density lipoprotein cholesterol (LDL-C), are well accepted and widely used for the assessment of cardiovascular disease (CVD) and its equivalents, including peripheral vascular disease, abdominal aortic aneurysm, and ischemic cerebral vascular disease [6]. The results of this study show statistically significant increased total cholesterol, triglycerides, LDL-cholesterol and VLDL-cholesterol but decreased HDL-cholesterol in diabetes patients when compared with control subjects. This is in tandem with the work of Bello –Sani et al, Onyemelukwe and Stafford, and Rasha who did similar work on diabetes [1,15,16].

The Low Density Lipoprotein –Cholesterol (LDL-C) has been a prime index for assessing CVD but the measurement of LDL cholesterol alone does not provide sufficient measure of atherogenic risk in hypertriglyceridemic patients and second or other biomarkers is warranted. Literature showed that the association of LDL-C with CVD was weak and LDL-C was not a significant predictor of Coronary Heart Disease (CHD) mortality [6,7].

This study observed a statistically significant increased level of Cardiac risk ratio (CRR) in diabetes mellitus (4.1 \pm 3.0) when compared with controls (1.9 \pm 3.0). This is in accordance with the work of VinodMahato et al and Swaminathan et al who obtained a value of 4.3 \pm 0.13 and 4.5 \pm 2.5 for diabetes respectively [17,18]. When CRR of diabetes and controls were compared with the value of American Heart Association (≤ 3.5), the Diabetes shows greater propensity towards cardiovascular disease.

The Atherogenic Coefficient (Ac) of diabetes (3.1 ± 2.0) in our study was observed to be significantly increased when compared with the non-diabetes subjects (0.9 ± 2.0). This is in agreement with the work of Ikewuchi, who obtain Ac of 2.04 in diabetic rats. The observed value of 3.1 in diabetes shows a greater tendency towards cardiovascular disease [19].

The Atherogenic Index of Plasma (AIP) is a mathematical relationship between TG and HDL-C and an additional index for assessing cardiovascular (CV) risk factors [20]. The association of TGs and HDL-C in this simple ratio reflects the balance between risk and protective lipoprotein forces. The AIP of diabetes in this study was observed to be significantly increased (0.3 ± 0.0) when compared with the control (-0.2 ± 0.0). This is in accordance with Sushith et al., [21] who observed 0.24 in diabetic smokers and 0.49 diabetic nonsmokers. It has been suggested that AIP values of -0.3 to 0.1 are associated with low, 0.1 to 0.24 with medium and > 0.24 with high Cardiovascular risk [22]. Sushith and his coworkers [21] concluded that AIP has a better prediction of Coronary Artery Disease than triglycerides or High Density lipoprotein alone. This is because AIP is positively correlated with the fractional esterification rate of HDL (FERHDL), and also inversely correlated with LDL particle size. FERHDL predict particle size in HDL and LDL, which in turn predicts the risk of coronary heart disease. The simultaneous use of TG and HDL as AIP is useful in predicting plasma atherogenicity. This ratio has a strong predictor of myocardial infarction [23]. Atherogenic Index of Plasma provides information about the atherogenicity of plasma and quantifies the response to therapeutic intervention [14]. Also AIP correlate inversely with insulin sensitivity measurement [14].

Non HDL-C is calculated as total cholesterol minus HDL-C. It is a single index of all the Atherogenic, apolipoprotein (apo) B- containing lipoproteins, Low Density Lipoprotein, Very Low Density Lipoprotein, Intermediate Density Lipoprotein and lipoprotein (a). Although apo B can be measured directly, measurement of Non HDL cholesterol is more practical, reliable and inexpensive and is accepted as a surrogate marker for apoB in routine clinical practice [8]. The result of our study shows a significantly increased Non-HDL-C in Diabetes Mellitus patients (4.3 ± 0.2) when compared with non-diabetes (1.2 ± 0.2). The cut-off value for non HDL-c is 130 mg/dl (3.3 mmol/l) which shows that Diabetes Mellitus patients has a higher risk of cardiovascular disease [8]. Non-HDL-C has been observed to have the strongest relationship with small dense LDL-C (sdLDL-C) levels when compared with other lipid measurement [24]. The predictive value of non-HDL-C for cardiovascular risk and mortality is better than that of LDL-C [25]. The strong association between non-HDL-C and sdLDL-C adds additional support for using the non-HDL-C level as a predictor of CVD mortality [24].

Conclusion

In conclusion, it is worthy of note that these cardiovascular risk indices which are not routinely included in lipid profile are good and better biomarkers than the LDL-C alone in the assessment of cardiovascular risk in patients that are prone to cardiovascular diseases such as diabetes mellitus. We therefore advocate the inclusion of these cardiovascular risk indices in the routine lipid profile for a better assessment of the patient.

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