

Assessment of Cardiovascular Disease Risk in Type 2 Diabetic Patients: A Comparison of Risk Indices

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Abstract: Diabetes mellitus is a major public health problem; it is synchronized with the development of many complications of which cardiovascular disease is the most prevalent and detrimental. This study aimed at comparing the strength of various cardiovascular risk indices among diabetes type 2 patients. The risk indices evaluated were: Apoprotein A₁, Apoprotein B₁, lipoprotein (a), total cholesterol, (TCHOL), Triglyceride (TG), low density lipoprotein (HDL), TC/HDL, pentad and tetrad. Two hundred and four (204) subjects were studied comprising of 152 diabetes subjects and 52 non-diabetics as control. The result shows significantly higher values in the mean blood pressure of diabetic subjects when compared with the control at ($p < 0.05$). Mean HbA1C and total cholesterol values for diabetes subjects were significantly higher when compared with the control. However, the HDL-cholesterol of the diabetes subjects was significantly lower when compared to the control subjects. There was no significant difference in triglyceride level of both groups. The mean values of Apo A, Apo B and lipoprotein a, were higher in diabetic subjects compared to the control subjects at ($p < 0.05$). Comparison of the lipoprotein induces in terms of sensitivity, specificity and accuracy, Lpa had a sensitivity of 97.3%, specificity of 100% and accuracy of 95.7%, next was pentad with sensitivity of 91.45%, specificity of 100% and accuracy of 95.73%. Tetrad had a sensitivity of 81.05%, specificity of 100% and accuracy of 90.5%, the TC/HDL ratio and the least accuracy of 75.76%. Based on the overall accuracy Lpa tend to display highest accuracy followed by PENTAD and TETRAD.

Keywords: Diabetes, Cardiovascular Disease, Risk Indices, Lipoproteins

1. Introduction

Diabetes Type 2 goes on undiagnosed for many years; it is most predominant type of diabetes since it represents 90% of diabetes cases. The majority of new cases of Type 2 occur in the context of westernized lifestyles, high-fat diets and decreased exercise, leading to increasing levels of obesity, insulin resistance (IR), compensatory hyperinsulinaemia and ultimately, beta-cell failure and Type 2 [1].

The clustering of vascular risk seen in association with insulin resistance (IR), often referred to as the metabolic syndrome, has led to the view that cardiovascular risk appears early, prior to the development of Type 2, whilst the strong relationship between hyperglycaemia and microvascular disease (retinopathy, nephropathy, neuropathy) indicates that this risk is not apparent until 'frank' hyperglycaemia appears [2]. These concepts highlight the progressive nature of both Type 2 and associated

cardiovascular risk, which pose specific challenges at different stages of the life of an individual with diabetes mellitus (DM). The effects of advancing age, co-morbidities and problems associated with specific groups all indicate the need to manage risk in an individualized manner, empowering the patient to take a major role in the management of his or her condition [3].

As in the world generally and Europe particularly, changes in response to demographic and cultural shifts in societies also result in the pattern of disease and their implications vary. This largely depends on the genetic variation of the various races. The Middle East, Asia-Pacific rim and parts of both North and South America have experienced massive increases in the prevalence of DM over the past 20 years, changes mirrored in European populations over the same period [4]. Awareness of specific issues associated with gender and race and, particularly, the effects of DM in women including epigenetic and influences on non-

communicable diseases—are becoming of major importance.

Cardiovascular disease (CVD) is the leading cause of death and disability in the Western world and contributes substantially to healthcare budgets. Cardiovascular disease is defined collectively in these guidelines as coronary heart disease (CHD), stroke and other vascular disease including peripheral arterial disease (PAD) and renovascular disease, is a leading cause of death and disability in Australia and other parts of the world [5] and in 2003 accounted for approximately 18% of the total burden of disease in Australia [6].

Cardiovascular disease is the most prevalent and detrimental complication of diabetes mellitus. The incidence of cardiovascular mortality in diabetic subjects without a clinical history of previous cardiac events is as high as the incidence in non diabetic subjects with a history of myocardial infarction. This inordinate increase in the risk of coronary events in diabetic patients is attributed to multiple factors, including glycation and oxidation of proteins and increased prevalence of classic risk factors of coronary disease, such as hypertension, obesity, and dyslipidemia [7]. Despite advances in the management of cardiovascular disease, a large proportion of diabetic subjects continue to have uncontrolled hyperglycemia, hypertension, and dyslipidemia.

Lipid Tetrad Index (LTI) and Lipid Pentad Index (LPI) constitute a new and efficient evaluation of the lipid profile and cardiovascular disease risk. Lipid tetrad index is derived by the product of Total Cholesterol, Triglycerides and Lipoprotein-a divided by the High Density Lipoprotein (HDL) value. While a pentad index is determined as he product of Total Cholesterol, Triglycerides, Lipoprotein (A) and Apolipoprotein B divided by Apolipoprotein-AI. Substances such as cholesterol and triglyceride that are synthesized in the intestine or liver need to be transported to tissues and organs for their varied metabolic functions. Given the hydrophobic nature of the neutral fats, triglycerides, and cholesterol esters, lipid transport and delivery via plasma would not be possible without some form of hydrophilic adaptation. Lipoproteins are the particles that transport these lipids in the blood stream. Lipoproteins are composed of proteins (apolipoproteins or apoprotein) and lipids (phospholipids, triglycerides and cholesterol). The lipoproteins vary in the major lipoprotein present, and the relative contents of the different lipid components. Chylomicron, Low Density Lipoprotein (LDL), High density lipoprotein (HDL), Intermediate density lipoprotein, Very low density lipoprotein and free fatty acid are the classes of lipoproteins therein. Apoproteins (Apo) which attach to lipids to form lipoproteins includes; Apo A-I, Apo B-100, Apo B-48, Apo C-II and Apo E. A detailed and enhanced articulation of the relationship between lipoproteins, Apoprotein, Lipids and cardiovascular disease in Type 2 diabetes Mellitus and the use of tetrad and pentad indices will clearly reveal the risk profile involved. This study focused on comparing the strength of various cardiovascular risk indices on diabetes type 2 patients.

2. Material and Methods

2.1. Subjects

The subjects were patients diagnosed of diabetes types 2 that were attending routine fasting blood sugar checks at Braithwaite Memorial Specialist Hospital, Port Harcourt.

Fasting blood sugar and HbA1c tests were done to determine the diabetic status of the patients. The subjects were addressed and the purpose of the study made known to them. Upon receipt of consents, which were freely given by the patients, they were required to complete a set of questionnaire. Weight, height, blood pressure were measured as describe below and 4-5ml of venous blood sample were collected and dispensed into three different sample bottles.

2.2. Collection of Blood Specimen

The samples were collected between the hours of 7.00am to 9.00am. Daily samples for fasting sugars were centrifuged, the plasma was used for glucose estimations immediately while samples in the EDTA was kept in the refrigeration at 2-4°C for at3-4days in order to turn them in batches for glycosylated hemoglobin. The samples in plain container was allowed to clot, centrifuged, separated and stored for lipid profile, apolipoproteinA-1, Apolipoprotein B and Aplipoprotein A.

2.3. Weight, Height and Blood Pressure

The subjects were weighed with bathroom scale without shoes and object in their hands. They were made to stand erect when the readings were being taken with weighing balance and recorded on the questionnaire. The height was measured using a measurement tape and was recorded on the questionnaire.

The measurement of the blood pressure and was done twice at the intervals of 5minutes using automatic blood pressure monitor and the average taken.

2.4. Determination of Biochemical Indices

The biochemical indices determined were fasting blood glucose, fasting lipids, HbA1c, APO-A1, APO-B and lipoprotein a. All the biochemical parameters were determined using standard procedures and good laboratory practices.

3. Results

3.1. Biophysical Parameters of Diabetic Subject Compared with Control

The biophysical parameters of diabetic subjects for both control and test (diabetic) subjects are shown in table 1. The table shows that the mean \pm SD for systolic blood pressure for control and test subjects were 127.6 ± 12.8 mmHg and 139.5 ± 17.8 mmHg respectively. There was significant increase in mean systolic blood pressure of the diabetic group compared to the control at $p < 0.0001$. Also, mean values for

diastolic blood pressure of the diabetics was significantly higher than the control ($p=0.021$). Comparison of the mean

values of control and test subjects for both BMI and waist circumference was observed not to be statistically significant.

Table 1. Biophysical parameters of diabetic subject compared with control.

Biophysical Parameters	Diabetics N=152	Control N= 52	p values	Remark
Systolic Blood Pressure (mmHg)	139.52 \pm 17.83	127.55 \pm 12.81	0.0001	S
Diastolic Blood Pressure (mmHg)	82.89 \pm 13.46	78.13 \pm 7.63	0.0211	S
BMI(kg/m ²)	29.72 \pm 6.27	30.27 \pm 6.01	0.7678	NS
Waist Circumference(cm)	39.37 \pm 4.81	37.42 \pm 5.61	0.5774	NS

3.2. Levels of Glucose and Lipid Profile of Diabetic and Control Subjects

The levels of glucose and lipid profile of for both test and control subjects are displayed in table 2. The mean fasting blood sugar (FBS) values for control and test subjects were 4.77 \pm 0.65mmol/L and 7.34 \pm 1.78mmol/L respectively. The fasting blood sugar levels of the test group was significantly higher than the ($p=0.0001$). A comparison of the total cholesterol LDL levels showed that the mean levels of the test group was significantly higher than the control ($p=0.0001$). When compared, a significant decrease ($p=0.0001$) was observed for HDL in the test group compared with the control. However, there was no significant difference in TG levels.

Table 2. Levels of glucose and Lipid Profile of diabetic and control subjects.

Parameters	Diabetics N=152	Control	P values	Remark
FBS (mmol/L)	7.34 \pm 1.78	4.77 \pm 0.65	0.0001	S
HbA1c (%)	7.46 \pm 1.68	5.34 \pm 0.5	0.0001	S
Chol (mmol/L)	5.81 \pm 0.87	4.84 \pm 0.55	0.0001	S
HDL (mmol/L)	1.28 \pm 0.35	1.34 \pm 0.29	0.0001	S
TG (mmol/L)	1.42 \pm 0.31	1.03 \pm 0.25	0.2100	NS
LDL (mmol/L)	3.74 \pm 0.94	1.12 \pm 0.266	0.0001	S

3.3. Lipoprotein Indices for Diabetics and Control Subjects

The levels of lipoprotein indices comparing test and control groups are shown in table 3. Mean Apo A₁, Apo B, lipoprotein (a), Lipid tetrad indices (LTI) and lipid pentad indices (LPI) for diabetic group were significantly higher than the control ($p=0.0001$)

Table 3. Lipoprotein indices for Diabetics and Control Subjects.

Lipoprotein indices	Diabetics	Control	p-values	Remark
Apo A-1 (g/L)	1.59 \pm 0.46	1.12 \pm 0.26	0.0001	S
Apo B (g/L)	1.58 \pm 0.87	0.7 \pm 0.16	0.0001	S
Lipo (a) (mmol/L)	4.75 \pm 1.06	1.51 \pm 0.21	0.0001	S
LTI	33.00 \pm 18.83	2.7 \pm 2.2	0.0001	S
LPI	37.48 \pm 21.03	2.71 \pm 3.16	0.0001	S
TC/HDL	4.69 \pm 1.86	3.71 \pm 0.58	0.0001	S

4. Discussion

Cardiovascular disease (CVD) is a general health problem world wide, currently escalating in low income countries as an important component of non-communicable disease burden [8]. Type II diabetes and its complications constitute a major worldwide public health problem. Patients with type II diabetes have 2 - 4 times higher risk of experiencing cardiovascular disease (CVD) than adults without diabetes [9,10] and their relative risk for CVD is about twice as high [11] much of which may be preventable with appropriate treatment of dyslipidemia. The prevalence of CVD risk factors is dramatically increasing in low-and middle-income African countries, particularly in urban areas [12].

This study evaluated the cardiovascular risk profile in type 2 diabetes comparing various tools of assessment. In this study, systolic and diastolic blood pressure of diabetic subjects were significantly higher than the non-diabetic subjects ($p=0.001$ and $p=0.0211$) respectively. The results are consonance with the findings (Sowers et al., 2001). They stated that many factors, including hypertension, contribute to this high prevalence of CVDs among diabetic subjects. Stressing further that hypertension is approximately twice as frequent in patients with

diabetes compared with patients without the disease.

There was no significant difference between the mean BMI for control and that of diabetic subjects ($p=0.7678$), but both mean BMI values indicate that the subjects were overweight. Elevated BMI is known to increase the risk of CVDs and diabetes globally. [13] showed that BMI was an excellent predictor of elevated CVD risk. Although, the measurement of waist (WC) circumference is recommended in current clinical guidelines. This study recorded a non-significant difference in mean WC for diabetic and non-diabetic ($p=0.5774$) subjects.[14]reported in an observational study that progressively increasing risk of CHD, CVD and total mortality with higher HbA1c, and no risk increase at low HbA1c levels even with longer diabetes duration, previous CVD or treatment with either insulin or OHAs. Patients achieving HbA1c <7% showed benefits for risk reduction [14]. This study recorded a significant increase in the HbA1c levels for diabetic subjects ($p=0.0001$) compared with the control. In 2012, [15] examined the association between baseline HbA1c level and mortality attributable to all-cause, cardiovascular disease, coronary heart disease and stroke. They concluded that high HbA1c predicted excess risk of all-cause, cardiovascular disease, coronary heart disease and stroke mortality.

In this study, mean total cholesterol, and LDL values for test groups were significantly higher than the control ($p=0.0001$). While the HDL level was lower in the diabetic subjects than the control ($p=0.0001$). Diabetes from *abinitio* has been shown to increase the risk of coronary heart disease in all populations studied. The association of low plasma levels of high-density lipoprotein (HDL) with states of impaired glucose metabolism and type 2 diabetes mellitus is well established, but the mechanistic links remain to be fully elucidated. Recent data suggests that HDL directly influences glucose metabolism through multiple mechanisms, [16]. In another related study, diabetic individuals had elevated triglycerides, LDL cholesterol and low levels of high density lipoprotein [HDL] cholesterol, [17]. The mean Apo A₁, Apo B, lipoprotein (a), lipid tetrad and lipid pentad values for diabetic were significantly higher than the control subjects ($p=0.0001$). The need to search for these new methods of analysis has led to studies that more comprehensively describe patients' actual propensity to develop CVD, overcoming the analysis commonly based on individual lipid particles. The lipid tetrad (LTI) and pentad (LPI) indices have recently been described as a new form of assessment of lipid profiles, which have been analyzed in some populations [18, 19]. A characteristic of these new indices is distinguished by the broad approach of atherogenic and non-atherogenic lipid particles, resulting in a single value. Based on the conventional lipid profile and the emerging risk factors such as Lp (a), apolipoprotein AI (apoA-1) and apoB, the LTI and LPI appear as models in global risk assessment, considering the multifactorial nature of CVD. In this study, these emerging CVD risk assessment tools appear to have stronger accuracy over the traditional risk assessment tools.

5. Conclusion

The results from the study indicate that the traditional method of using lipid profile to assess cardiovascular risk is not sensitive and specific, and not predictive of CVD risk especially in diabetics.

Lipid tetrad and lipid pentad proved to be more sensitive and specific predictors of risk of CVD in the study subjects, although lipid pentad was more sensitive and specific than lipid tetrad. However both indices were better predictors than the conventional lipid profile.

These findings are significant, as early detection of CVD risk is important in the treatment and management of cardiovascular diseases. Thus, modern prognostic indices such as lipid tetrad and lipid pentad are invaluable in the management of cardiovascular diseases.

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