Correlation between glycaemic control and lipid profile in Nigerian Type II diabetic patients

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Abstract

Background*: Hypercholesterolaemia is known to be frequently associated with diabetes mellitus. Lipid abnormalities in patients with diabetes are likely to play important role in the development of atherogenesis and so are called atherogenic dyslipidaemia. Improved glycaemic control may prevent the appearance and enhance the regression of macrovascular and microvascular complication. It has been noted that improved glycaemic control can alter the serum lipid level. This study demonstrates the effect of glycaemic control in Nigerians with type II diabetes on serum levels of lipid.*

Methodology*: A total of 160 consenting type II diabetic patients were recruited for the study consisting of 49(30.6%) male and 111(69.4%) female, while 70 non-diabetics subjects matched for age and sex with the patients were recruited as control consisting of 25 (35.7%) males and 45 (64.3%) females.*

A total of 5mls of blood sample was collected from each patient in sitting position after an overnight fast from the antecubital vein at the dorsum of the hand. Glucose, Total cholesterol, HDL-C and LDL-C were estimated. The absorbance of samples and standards were measured against reagent blank. Statistical analysis was done using Statistical Package for Social Science (SPSS version 15.0) results were expressed as means±SD. Paired sample t-test was used to compare means of results where appropriate, Pearson's correlation analysis was used to examine the relationships between the variables. A p-value less than 0.05 were considered statistically significant.

Results*: There were statistically significant difference when the mean lipid profiles of diabetic subjects were compared with that of controls ($p < 0.05$). Significant elevations were observed in the values of total cholesterol, triglycerides,*

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and LDL-C, in diabetic subjects when compared with that of controls. Coronary heart disease risk ratio was statistically significantly different when mean value of subjects is compared with that of controls. Significant positive correlation was observed when total cholesterol, triglyceride, LDL-c were compared with glycaemic control with r values of 0.613, 0.631 and 0.607 respectively with p-value <0.05 in all. There was also significant negative correlation when coronary heart disease risk ratio was compared with glycaemic control. (r = -0.595 and p-value <0.05).

***Conclusion**: This study has highlighted the fact that type II diabetic patients have a high frequency of atherogenic dyslipidaemia especially for TC, Tg and LDL-C. The study also shows that the poorer the glycaemic control the higher the incidence of dyslipidaemia. It is therefore suggested that along with glycaemic control, physicians should also focus on lipid profiles.*

Keywords: Correlation, Glycaemic control, Lipid profile and Type II diabetic patients

Introduction

Diabetes mellitus is heterogeneous metabolic disorder characterized by hyperglycaemia resulting from a variable interaction or hereditary and environmental factors of defects in insulin secretion, action or both. It is broadly classified into type I, type II, other specific types, and Gestational diabetes mellitus.[1,2]

Diabetes mellitus remains a significant health problem despite enormous research that has been undertaken on diabetes.[1 3,.4.] It is associated with considerable morbidity and mortality. In Nigeria where healthcare services and accessibility are poor, diabetes is associated with a high disease burden.[5]

The global estimate of the number of people with diabetes mellitus was about 175 million in 2000 and this is projected to reach about 353million by the year 2030.[6] Type II diabetes accounts for 85% to 95% of diabetes, depending on the population group in question.[7] There is gross under reporting of diabetes mellitus in African countries partly due to inadequate research funding and lack of technical expertise. A national survey in Nigeria showed a prevalence rate of about 2.8% amongst Nigerian.[8] Isolated reports from some regions of Nigeria have found prevalence rates in the range of 0.9-8.3%.[4, 8.] It is also estimated that not less than1.05million Nigerians are likely to be diabetic with only about 225,000 being aware of their condition and about 198,000 on treatment. [9]

The present global pandemic of type II diabetes is accounted for by westernization of lifestyle, population growth, ageing with consequent dietary change, sedentary lifestyle, and obesity.[10] As high as this prevalence figure is, it is thought to significantly underestimate the extent of the problem, since up to 50% of the population with diabetes are thought to remain undiagnosed and therefore untreated.[11] It is also a known fact that at the time of diagnosis, 50% of these patients already had micro and macrovascular complications which were known to adversely affect their quality of life and impose a heavy burden on healthcare system.[12-13] The burden of complications and premature mortality resulting from diabetes constitutes a major public health problem for most countries. The major risk factors in diabetes are hyperglycaemia, dyslipidaemia and hypertension.

Hypercholesterolaemia is known to be frequently associated with diabetes mellitus; it is widely acknowledged that in individuals with elevated levels of cholesterol, there is increased incidence of atherosclerosis and its complications. Diabetic dyslipidaemia is characterized by elevated levels of very low density lipoprotein cholesterol (VLDL-C) and

low density lipoprotein cholesterol (LDL-C) with lower levels of high density lipoprotein cholesterol (HDL-C) often referred to as lipid triad.[14] Lipid abnormalities in patients with diabetes are likely to play important role in the development of atherogenesis and so are called atherogenic dyslipidaemia.[15]

In type II diabetes, Insulin resistance leads to excess liberation of free fatty acids from adipose tissue, [16] which activates the signalling enzyme protein kinase C, inhibits phosphatidylinositol 1-3(P1-3)kinase (an enos agonist pathway), and increases the production of reactive oxygen species. This mechanism directly impairs nitric oxide (NO) production or decreases its bioavailability once produced. Localized accumulation of foam cells leads to formation of fatty streaks, the hallmark of early atherosclerotic lesions.[17] Improved glycaemic control may prevent the appearance and enhance the regression of macrovascular and microvascular complication. It has been noted that improved glycaemic control can alter the serum lipid level.[18] Also among type II diabetic patients with initial complications, good glycaemic control was associated with reduced risk of additional complications in other organs.[19]

This study demonstrates the effect of glycaemic control in Nigerians with type II diabetes on serum levels of lipid. Precise quantification of our finding was explored exclusively focusing on glycaemic control and its effect on serum lipid profile to assist and encourage patients and clinicians how good glycaemic control can lead to improved health, augment longevity, and enhance quality of life as obtained from previous studies in other countries.

Materials and Methods

This was a cross sectional study of consenting type II diabetic patients attending Medical Outpatient Department (MOPD) of the University of Ilorin Teaching Hospital (UITH) Ilorin, Kwara state Nigeria.

A total of 160 consenting type II diabetic patients were recruited for the study consisting of 49(30.6%) male and 111(69.4%) female, while 70 non-diabetic subjects matched for age and sex with the patients were recruited as control consisting of 25 (35.7%) males and 45 (64.3%) females. The exclusion criteria include patients on drugs that could affect glucose metabolism and lipids e.g. steroids, beta blockers, thiazide diuretics and lipid lowering drugs. Pregnant women were excluded by finding out about their last menstrual period. Patients with renal failure and liver diseases were also excluded.

Patients' preparation was done by advising patients to be on habitual diet for at least 2 weeks before taking samples. A total of 5mls of blood sample was collected from each patient in sitting position after an overnight fast from the antecubital vein at the dorsum of the hand. 2mls of collected blood sample was put into a fluoride oxalate bottle while the remaining 3mls was put into a plain bottle, allowed to clot with adequate retraction for about two hours before it was centrifuged at 3000 revolutions per minute for 15 minutes to harvest the serum into another clean covered plain sample bottle and stored at -20^{o}C before analysis.

Glucose analysis was carried out within 6 hours of sample collection. Plasma glucose was determined using glucose oxidase method with 4 aminoantipyrine as the oxygen acceptor as described by Trinder[20] using commercial kit produced by AGAPPE DIAGNOSTICS KERALA INDIA. Total cholesterol was estimated by Cholesterol Oxidase Method[21]. HDL-c and LDL-c were also estimated by enzymatic method while triglycerides were estimated using glycerol-3 phosphate oxidase method[22] using commercially prepared kit by AGAPPE DIGNOSTICS LTD. The absorbance of samples and standards were measured against reagent blank using Jenway 6300 spectrophotometer at 505nm. Conversion to SI units was done by dividing the values in mg/dl by 39 for the total cholesterol, HDL-C LDL-

C and by 88 for triglycerides. Statistical analysis was done using Statistical Package for Social Science (SPSS version 15.0); Results were expressed as means±SD. Paired sample t-test was used to compare means of results where appropriate, Pearson's correlation analysis was used to examine the relationships between variables. A p-value less than 0.05 was considered significant.

Results

There were statistically significant difference when the mean lipid profiles of diabetic subjects were compared with that of controls ($p < 0.05$). Significant elevations were observed in the values of total cholesterol, triglycerides, and LDL-C, in diabetic subjects when compared with controls. Coronary heart disease risk ratio is statistically significantly different when mean

Table 1: Comparing mean values of lipid profile in subjects and the control using paired sample t-test

Variables	Subjects	Control	P-value
Mean T-C(mmo1/L)±S.D	6.5±2.3	3.6±0.5	0.000*
Mean T.G (mmo1/L) ±S.D	1.5±0.6	0.6±1.1	0.000*
Mean HDL-C (mmo1/L) ±S.D	1.05±0.2	1.05±0.1	0.509
Mean LDL-C (mmo1/L) ±S.D	4.8±2.1	2.3±0.04	0.000*
Mean CHD-RR ±S.D	0.17±0.06	0.29±0.03	0.000*

Table 2: Correlation of level of glycaemic control using fasting plasma glucose with lipid profile using pearson correlation

Level of Glycaemic Using FPG	Mean T.C. (mmo1/L) ±S.D	Mean TG (mmo1/L) ±S.D	Mean HDL-C (mmo1/L) ±S.D	Mean LDL-C (mmo1/L) ±S.D	Mean CHD-RR (mmol/L) ±S.D
Good Glycaemic Control (<6.0)	4.7±0.9	1.1±0.3	1.1±0.2	3.1±0.8	0.237±0.046
Acceptable Glycaemic Control (6.1-6.9)	5.8±0.8	1.4±0.4	0.9±0.	4.2±0.7	0.163±0.030
Poor Glycaemic Control (>7.0)	8.4±2.0	2.0±0.3	1.1±0.2	6.5± 1.8	0.130±0.031
r =	**0.613**	**0.631**	**0.095**	**0.607**	**-0.595**
p-value	**0.000***	**0.000***	**0.234**	**0.000***	**0.000***

value of subjects is compared with that of controls.

Significant positive correlation was observed when total cholesterol, triglyceride, LDL-c were compared with glycaemic control with r values of 0.613, 0.631 and 0.607 respectively with p-value <0.05 in all. There was also Significant negative correlation when coronary heart disease risk ratio was compared with glycaemic control (r = -0.595 and p-value <0.05).

Discussion

This study shows that hyperlipidaemia was present in diabetic subjects which were significantly higher than in the control subjects as was found in a previous study[23]. The total cholesterol value is higher than in the previous study. The reason for the higher serum cholesterol in persons with diabetes in this study can be attributed to difference in dietary intake between the populations.[24] The presence of elevated cholesterol levels is known to play a key role in both the initiation and progression of atherosclerosis, as well as in the clinical consequences such as myocardial infarction, stroke, peripheral vascular disease, and heart failure.[25] Hypercholesterolaemia has also been implicated in the process of atherogenesis and a curvilinear relationship has been documented between increasing cholesterol and incidence of CVD.[26]

Hypertriglyceridaemia and low high-density lipoprotein are two components of the atherogenic profile also observed in our subjects to be high as was observed in previous works. Elevated low density lipoprotein has been found to be an independent risk factor for the development of cardiovascular disease and is often reported to be the commonest lipid abnormality found in patients with diabetes mellitus.[25, 27,28] The role of LDL-C in the development of CVD cannot be overemphasized as there is documented evidence that high levels of LDL-C not only cause atherosclerosis but pharmacological interventions that reduce LDL-C cholesterol are associated with stabilization and regression of atherosclerosis in proportion to the cholesterol lowering achieved.[29] Although the triglycerides have been found to be univariate predictors of CVD in many studies, no clinical trial data has established that lowering triglycerides in individuals with or without diabetes independently leads to lower CVD event rates after changes in HDL-cholesterol are adjusted for.

High density lipoprotein cholesterol (HDL-C) act by enhancing the removal of cholesterol from the peripheral tissues and so reduces the body cholesterol pool. No difference in mean values (1.05±0.2) of HDL-C was observed in the diabetic population in this study in comparison with controls as was in a previous study. [24.] This is in agreement with a belief in the past that the protective cholesterol HDL-C is significantly higher in tropical Africa.[24] Differences in dietary intake between the populations may explain the differences observed.[27] It is known that high total and saturated fat intake is associated with higher fasting plasma insulin concentrations which are associated with macrovascular complications and cardiovascular morbidity and mortality in some populations.[27] High dietary fiber diet is associated with hyperinsulinaemia.[25]

There is statistical significance increase in level of coronary heart disease risk ratio (CHD-RR) in controls than diabetic and also higher in patient with good glycaemic control than those with poor glycaemic control. CHD-RR explained a greater proportion of inter population variation in cardiovascular disease mortality than did either total cholesterol of HDL-C alone. CHD-RR was found to be the variable most predictive of the presence of cardiovascular disease and an increase in the CHD-RR accounted for reduction in the risk of cardiovascular disease.[28] It is therefore being suggested for routine use in screening to identify patients with dyslipidaemia as it is

identified as the most efficient predictor of cardiovascular disease at all ages.[30] In terms of benefit for cardiovascular protection, treatment of hyperlipidaemia was reported to be more beneficial than blood pressure or glycaemic control.[26]

Conclusion

The study showed that there is statistically significant association between glycaemic control and total cholesterol, low density lipoprotein cholesterol and triglycerides, with a strong positive correlation between TC, Tg, LDL-C and glycaemic control. When compared amongst our subjects, there was high statistical significant difference between levels of glycaemic control and coronary heart disease risk ratio with a strong and significant negative correlation with level of glycaemic control.

This study has highlighted the fact that type II diabetic patients have a high frequency of atherogenic dyslipidaemia especially for TC, Tg and LDL-C. The study also shows that the poorer the glycaemic control, the higher the incidence of dyslipidaemia. It is therefore suggested that along with glycaemic control, physicians should also focus on lipid profiles.

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