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DYSLIPIDAEMIA IN NON INSULIN DEPENDENT DIABETES MELLITUS

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ABSTRACT

Lipid is one of the identifiable deranged disorder in type - 2 diabetics, therefore the study was conducted to measure the serum lipids in type-2 diabetics subjects attending clinic in ABUTH, Shika, Zaria, Nigeria. Thirty - three type – 2 diabetic subjects and 13 healthy subjects participated in the study. Serum concentrations of total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), Triacylglycerol (TG), very low-density lipoprotein (VLDL-C) cholesterol and TC/HDL-C ratio (atherogenic index) were measured. The total cholesterol means in both type 2 diabetics (2.83±0.81) and control (3.21±0.75) were within normal limits. In the type 2 diabetic subjects, the mean value of Triacylglycerol TG was 3.91±3.54 while the control subjects value was 1.83±1.05 ($p<0.05$) and also was higher than the normal range. The mean HDL-Cholesterol was 0.81±0.92mmol/L in diabetic subjects while it was 0.56±0.27 ($p>0.5$) in control subjects and both were within normal range. The LDL was significantly higher in the diabetic group than the control subjects although both were within normal range. The atherogenic index was significantly higher in the apparently healthy subjects than the diabetics' subjects. This study therefore emphasizes that in this condition, lipid profile analysis is still essential and the effective management of lipid abnormalities is required when diabetes is diagnosed to improve and reduce the morbidity and mortality associated with lipid derangements.

Key words: *Type- 2 diabetes, serum lipid, total cholesterol, low density lipoprotein cholesterol, Triacylglycerol, very low-density lipoprotein cholesterol and atherogenic index*

INTRODUCTION

Diabetic mellitus has been recognized as an important public health problem in developing countries, where its prevalence is increasing steadily and adequate treatment is often expensive and unaffordable (Djrolo *et al*., 1998). As type - 2 diabetics become more prevalent, there will be an associated rise in the number of individuals with its related disorders. Again, the incidence of cardiovascular diseases has been found to increase two-to-fourfold in people with type 2 diabetes mellitus (Raza and Movahed, 2003). Study by Kelley and Simoneau (1994) attributed to diabetes-related condition as enhancer of free fatty acid (FFA) liberation, a crucial role in producing the well described changes in lipid profile. Excess circulating levels of FFA results from both enhanced release from adipose tissue and reduced uptake by skeletal muscle. The liver responds to FFA excess by increasing VLDL (very low density lipoprotein) production and cholesteryl ester synthesis (Sniderman *et al.,* 2001). The accumulation of triacylglycerol-rich lipoproteins, depends also on their reduced clearance by lipoprotein lipase, triggers hypertriglycaeridaemia and lowers HDL (High Density Lipoprotein) levels by promoting exchanges from HDL to VLDL via cholesteryl ester transfer protein (Sniderman *et al.,* 2001). HDLs are not only reduced in quantity, but also impaired in

function. Classically, diabetes mellitus induces elevation in triacylglycerol and LDL, and decline in HDL serum levels. These changes clearly affect the natural history of the atherosclerotic disease, and render patients with diabetes more prone to develop cardio - vascular disease, stroke, and peripheral vascular disease. HDL from poorly controlled type 2 diabetic patients are less effective in preventing LDL oxidation compared to those from non-diabetic subjects (Gowri *et al.,* 1999). Inreased VLDL production and abnormal cholesterol and triacylglycerol transfer between VLDL andLDL enhances serum levels of small and dense pro-atherogenic LDLs (Sniderman *et al.,* 1978), which are in addition more prone to oxidation due to impaired antioxidant defense mechanisms in the serum of diabetics (Tsai *et al.,* 1994). The pro-atherosclerotic effects of these particles on coronary, carotid, and peripheral arteries have important clinical consequences, thus representing an important treatment target. Type 2 diabetes mellitus is associated with several lipid-related conditions, namely hypertriglyceridaemia, elevated VLDL cholesterol, and reduced HDL cholesterol. Both hyperglyceamia and dislipidaemia are implicated in the development of diabetic complications (Defronzo *et al.,* 1992; Laakso, 1996). The aim of this study was therefore to measure the serum lipids in type-2 diabetics' subjects.

SUBJECTS, MATERIALS AND METHODS

The sample size that participated in the study was 33 type – 2 diabetic subjects and 13 healthy subjects. The Type-2 diabetic subjects were classified purely based on non-dependence on insulin for survival, and the currently valid clinical classification criteria issued by WHO (1995), WHO (1999) and ADA (2003). The subjects of study were volunteers from the population of patients attending diabetic clinics of Ahmadu Bello University Teaching Hospital (ABUTH) Shika, Zaria, Nigeria. The control subjects were volunteers who had no personal or family history of diabetes and were selected from Ahmadu Bello University (ABU) and Ahmadu Bello University Teaching Hospital and were apparently healthy. Informed consent for inclusion into the study was obtained from the subjects who fulfilled the inclusion criteria. The proposal was approved by the scientific and ethical committee of ABUTH, Zaria.

Blood sample was collected into plain tubes using a sterile technique and was left to clot for about 15 minutes which was promptly centrifuged. The serum was carefully drawn into sample bottles and then stored frozen at -20^{o}C until the time for analysis. Concentration of serum total cholesterol and high density lipoprotein cholesterol were determined using enzymatic procedure test kits by RANDOX Laboratory Ltd Ardmore United Kingdom using the principle of (Roeschlau *et al.,* 1974). Measurement of serum triacylglycerol concentration was performed using the method of Levy (1972) of enzymatic colorimetric Test Kits for triacylglycerol with Lipid Clearing Factor by RANDOX Laboratory Ltd Ardmore United Kingdom were used. Serum very low-density lipoprotein triacylglycerol concentration and serumLDL cholesterol concentration were estimated using Friedewald formular (Friedewald *et al.,* 1972).

Statistical Analysis

All values were expressed as mean ± SD. The statistical analysis were carried out using students't-test to detect differences in the concentrations of serum lipid between different groups. Tests with a probability value <0.05 were considered statistically significant.

RESULT

The total cholesterol mean in both type 2 diabetics (2.83±0.81) and control (3.21±0.75) were within normal limits (Table 1). Although the mean was higher in magnitude in the control than the diabetic subjects, it was not significant at $p>0.05$. In the type 2 diabetic subjects, the mean value of TG was 3.91±3.54 which was significantly higher than that for the control subjects with the value of 1.83±1.05 and also was higher than the normal range ($p<0.05$) (Table 1). The mean HDL-Cholesterol was 0.81±0.92mmol/L in diabetic subjects while it was 0.56±0.27 in control subjects and both were within normal range (Table 1). This was similar ($p>0.5$) The LDL was significantly lower in diabetic group than the control subjects although both were within normal range (Table 1) ($p<0.05$). The atherogenic index was significantly higher in the apparently healthy subjects than the diabetics subjects (Table 1).

DISCUSSION

This study on lipid profile showed significant lipid abnormality in diabetic subjects especially TG. Supportive evidence to this study was reported by Ononogbu (1988) that there were changes in lipid concentration and consequent disorders of lipid metabolism have been observed in diabetes mellitus. With Ketosis of diabetes mellitus, hyperlipidaemia and hypercholesterolaemia may lead to increased level of lipid peroxidation. This enhances the oxidation of lipids and lipoproteins exposing a diabetic to dangers of atherosclerosis (Halliwell, 1990). Hence there may be an elevated lipid peroxidation in the plasma of diabetic patients. Supportive evidence to this approach was the finding of increased concentration of plasma lipid peroxides in diabetic patients with angiopathy (Sato and Hotta, 1979), hyperlipidaemic patients (Leoper *et al.*, 1993) and patients with acute myocardial infarction (Loeper *et al.*, 1987). WHO multinational study and the Paris Prospective study predicted that high serum TG may lead to vascular disease (Frontbonne *et al.,* 1989; Stephen *et al.,* 1991). It has been shown that an abnormally high triacylglycerol level is a feature of type 2 diabetics (Albrink, 1974). It has also been previously documented that there was elevated serum triacylglycerol and lipid peroxide levels in diabetic subjects (Oberley, 1988). This may be due to reduced clearance and increased production of TGs as a result of insulin deficiency or insulin resistance which may be the reason why the insulinogenic index and insulin level were low in this study. It has been reported that one function of insulin in non-diabetics is to maintain the balance between intestinally derived and liver derived triacylglycerol-rich lipoproteins. Insulin also normally suppresses fatty acids released from adipose tissue in the postprandial state (Frayn, 1993; Taskinen, *et al.,* 1996). However, in insulin resistance or lack, these regulatory functions fail with consequent flux of FFAs and inappropriate production of VLDL (VLDL) by the liver from these substrates. These in turn slightly lower the activity of lipoprotein lipase which may be generally lower in type 2 diabetes than control (Frayn, 1993; Taskinen, *et al.,* 1996; Mikko and Marja-Ritta., 1997). Hypertriglyceriadaemia

was found in 52% of the diabetic group as against 18.1% in the control group which is similar to the study of Anaja *et al.* (1995) that showed frequency of 64% in type 2 diabetic subjects. Stampfer *et al.* (1996) from the Physicians Health study confirmed that a rise in fasting triacylglycerol was a powerful independent pointer to likely risk of cardiovascular problems. The total cholesterol in both type 2 diabetics and control were within normal limits. None of them was even in border line to raise some suspicion. The mean HDL cholesterol in both groups was within normal. Though LDL was significantly lower in the diabetic than the control group. It has been reported that dyslipidemia is also characterized by elevations of apolipoprotein B (apoB) and a shift of the low-density lipoprotein (LDL) pool toward small, dense LDL (sdLDL) particles that are cholesteryl ester depleted (Brunzell and Ayyobi, 2003). Central abnormalities of dyslipidemia are increases in apo B-carrying lipoproteins and decreases in apolipoprotein A-I–carrying lipoproteins. It is believed that this complex dyslipidemia, which is termed atherogenic dyslipidemia, diabetic dyslipidemia, or dyslipidemia of insulin resistance, reflects underlying insulin resistance and plays a key role in the increased cardiovascular risk in patients with type - 2 diabetics.

It is critical to remember that because of the clustering of several major risk factors for type - 2 diabetics, multiple preventive strategies may be required, often simultaneously. Of importance is lifestyle modifications, including reductions in dietary cholesterol, reductions in saturated and trans fatty acids, and increased physical activity, remain central to any therapeutic programme. It is clear from the Finnish Diabetes Prevention Study and the Diabetes Prevention Programme that modest weight loss and moderate increases in exercise can significantly reduce the incidence of diabetes in individuals with glucose intolerance (Hamman *et al.,* 2006; Laaksonen *et al.,* 2005). In addition, the Steno-2 study demonstrated dramatic reductions in cardio - vascular disease events in patients with type - 2 diabetics who were treated with intensive lifestyle modification and pharmacologic agents (Gaede *et al.,* 2003).

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Table 1: Lipid profile of diabetic and control subjects

	Diabetics	Control
TC (mmol/L)	2.83±0.81	3.21±0.75
TG (mmol/L)	3.91±3.54[a]	1.83±1.05[b]
HDL-C (mmol/L)	0.81±0.92	0.55±0.27
LDL (mmol/L)	1.78±1.61[c]	0.83±0.93[d]
TC: HDL-C (atherogenic index)	3.49±4.60[e]	5.73±3.75[f]

Values in the same row with different superscripts are significantly different ($p<0.5$).