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Onovughakpo-Sakpa
O. Ejuoghanran
Department of Chemical Pathology,
University of Benin,
PMB 1154 Benin-City, Nigeria

The Effect of Diabetic Nephropathy on the Lipid Profile of Diabetics in Southern Nigeria

[1]Onovughakpo-Sakpa O. Ejuoghanran,
[2]Onyeneke E. Chukwu and [3]Sakpa L. Christopher

Diabetic Nephropathy (DN) is a common cause of abnormal lipoprotein metabolism and can be influenced by impairment of renal function and metabolic control in diabetes. The aim of this study was to explore the lipid abnormalities in diabetic patients with nephropathy in comparison with diabetic patients without nephropathy. This was achieved by assaying plasma lipid fractions in diabetic patients and control. A total of 95 diabetic patients and 19 non-diabetic control subjects were used for the study. The patients were divided into 2 groups-those with diabetic nephropathy and those without diabetic nephropathy, using ACR = 30 mg g^{-1}. Urinary albumin and creatinine were assayed by the Lowry method and the modified Jaffe method, respectively. Triglyceride was assayed by the glycerol-3-phosphate dehydrogenase method while total cholesterol and High Density Lipoprotein (HDL) cholesterol were assayed using the enzymatic end point method. Low Density Lipoprotein (LDL) cholesterol was determined by the Friedewald equation. Body Mass Index (BMI, kg m^{-2}) was calculated from height and weight which were obtained from a questionnaire used to record the demographic features of all the volunteers/subject. Results obtained showed that plasma total cholesterol was significantly increased in diabetic volunteers without nephropathy (197.29 ± 8.20, $p<0.05$) and in those with nephropathy (211.58 ± 7.49, $p<0.05$) when compared with the control subjects (161.84 ± 8.98, $p<0.05$). There were also significant increases ($p<0.05$) in mean plasma Low Density Lipoprotein (LDL) cholesterol (137.51 ± 7.27) in diabetics without nephropathy and 149.49 ± 6.97 in those with nephropathy and triglyceride (113.58 ± 9.56) in diabetics without nephropathy and (123.52 ± 6.62) in those with nephropathy when compared to the control subjects (93.95 ± 7.53, 107.11 ± 8.73, respectively). However, there was a significant decrease ($p<0.05$) in plasma High Density Lipoprotein (HDL) cholesterol in diabetics without nephropathy (42.75 ± 2.30) and those with nephropathy (37.5 ± 3.31) when compared to the control subjects (46.47 ± 2.42). A positive correlation was obtained between microalbuminuria (ACR = 30 mg g^{-1}) and total cholesterol ($R^2=0.028$, $P<0.05$), triglyceride ($R^2 = 0.123$, $p<0.05$), low density lipoprotein cholesterol ($R^2 = 0.012$, $p<0.05$) and body mass index ($R^2 = 0.005$, $p<0.05$). This study showed that total cholesterol, low density lipoprotein cholesterol, triglyceride and body mass index increased with persistent albumuinuria or nephropathy amongst diabetics in Southern Nigeria.

Key words: Diabetic nephropathy, lipid profile, albumin creatinine ratio, body mass index

[1]Department of Chemical Pathology,
[2]Department of Biochemistry,
[3]Department of Anatomy, University of Benin, PMB 1154 Benin-City, Nigeria

INTRODUCTION

According to Crook (2006) Diabetes Mellitus (DM) is caused by an absolute or relative insulin deficiency. Insulin affects many sites of mammalian lipid metabolism and it stimulates synthesis of fatty acid in liver, adipose tissue and in the intestine. Insulin has also been reported to increase cholesterol synthesis in the liver and enhances the activity of lipoprotein lipase in white adipocytes (Suryawanshi *et al.*, 2006). Abnormalities of plasma lipids other than elevated cholesterol play a major role in the enhanced atherosclerosis that occurs with diabetes (Best *et al.*, 1994). Glycation of apolipoproteins may alter Lipoprotein (LP) metabolism and may increase susceptibility to oxidation (Best *et al.*, 1994).

Furthermore albuminuria and even microalbuminuria have been associated with increased Low Density Lipoprotein Cholesterol (LDL-C) and decreased high density lipoprotein cholesterol. Because of the high prevalence of vascular disease in patients with diabetes, screening for lipid abnormalities is an essential component of routine clinical management. Also because triglycerides are frequently abnormal in diabetes and because it is greatly influenced by diet, screening is done in the fasting state (Best *et al.*, 1994). Bonnet and Cooper (2000) have reported studies in both types of diabetes indicating an independent deleterious influence of serum total cholesterol on the decline in renal function and progression of albuminuria. According to Rosenson (2005) and Martinez-Castelao *et al.* (2002) low level of HDL-C is a key feature of type 2 diabetes. Arora *et al.* (2007) in their study revealed that diabetes often coexists with obesity, hypertension and dyslipidaemia and that Africans, Americans and Asians have a greater risk of developing diabetes. This study was done to assess plasma lipids in patients with complicated (those with nephropathy) and uncomplicated (those without nephropathy) DM in Southern Nigeria.

MATERIALS AND METHODS

Data collection: A total of 95 diabetic volunteers and 19 apparently healthy control subjects gave their consent for the study. Specific questionnaire was used to document height (m), weight (kg), Blood Pressure (BP, mmHg), demographic and socio-economic features of all the volunteers/subjects.

Specimen collection

Blood: Subjects/volunteers were fasted overnight and blood samples were collected at about 8.00AM and dispensed into 3 different specimen bottles: 1.5 mL into fluoride oxalate (for fasting plasma glucose estimation), 1.5 mL into ethylenediaminetetraacetic acid (EDTA, for glycosylated heamoglobin estimation) and 4.0 mL into lithium heparin (for total cholesterol, triglyceride, High Density Lipoprotein-Cholesterol (HDL-C), estimation while Low Density Lipoprotein-Cholesterol (LDL-C) was obtained by calculation).

Urine: A spot urine sample (mid-stream) was collected into a sterile universal bottle for urine albumin (protein) and creatinine estimation. This is more convenient for the subjects/volunteers than a timed (24 h, 4 h or overnight) urine collection.

Analysis: Glucose levels were estimated by the glucose oxidase method as outlined by Barham and Trinder (1972); glycosylated haemoglobin (HbA$_1$c) by the fast ion exchange separation method as outlined by Nuttall (1998); creatinine by the modified Jaffe's method as outlined by Spierto *et al.* (1979), urinary albumin (protein) by the Lowry method (Lowry *et al.*, 1951) and lipid profile by the Rosechlau method (Rosechlau *et al.*, 1974). Body Mass Index (BMI) was calculated as weight divided by height in squared meter (kg m^{-2}) (WHO, 1995).

RESULTS

This study was based on 69 (72.63%) volunteers diagnosed with Diabetic Nephropathy (DN) of the 95 diabetic volunteers who consented to the study. Of the 69 volunteers 25 (36.23%) were males and 44 (63.77%) were females. Results obtained (Table 1) showed mean significant increases (p<0.05) in mean diastolic BP (82.86±1.77 mmHg) in diabetics without nephropathy and (86.2±4.66 mmHg) in those with nephropathy and systolic BP (137.32±3.15) in diabetics without nephropathy and 140.48±4.66 in those with nephropathy when compared to the control subjects (76.84±2.54; 120.53±3.01), respectively. BMI was also significantly increased in diabetic volunteers without nephropathy (25.49±0.58, p<0.05) and in those with nephropathy (27.38±0.58, p<0.05) when compared with the control subjects (23.24±0.98, p<0.05). Table 2, showed that plasma total cholesterol was significantly increased in diabetic

Table 1: Physical parameters in diabetic subjects with and without nephropathy as compared to control

Parameters	Control	Diabetic subjects without nephropathy	Diabetic subject with nephropathy
Diastolic BP	76.84±2.54	82.86±1.77*	86.21±4.66*
Systolic BP	120.53±3.01	137.32±3.15*	140.48±4.66*
BMI(kg m^{-2})	23.24±0.98	25.49±0.58	27.38±0.58

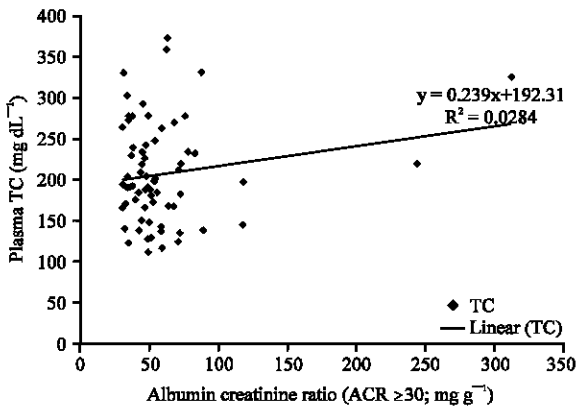Values are Mean±SEM, *p<0.05 as compared to control, BP: Blood pressure, BMI: Body mass index

Fig. 1: Correlation between ACR≥30 and plasma TC

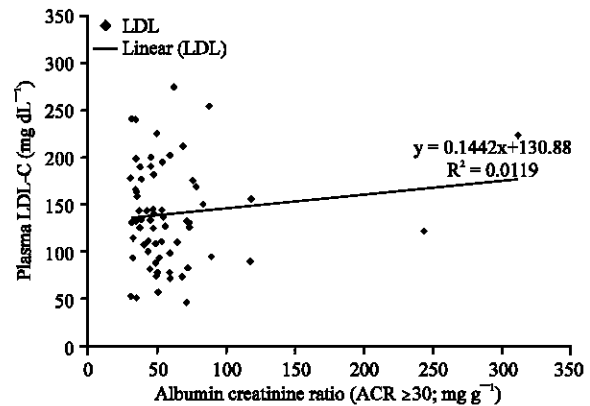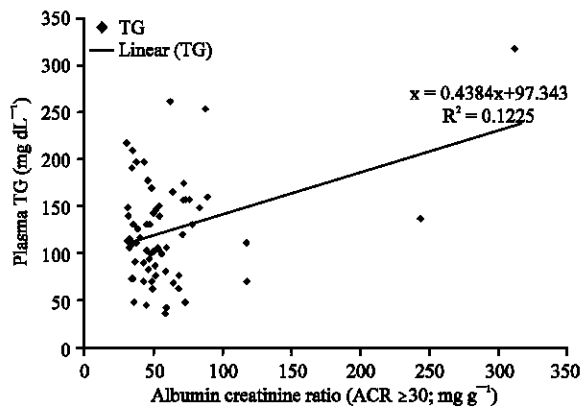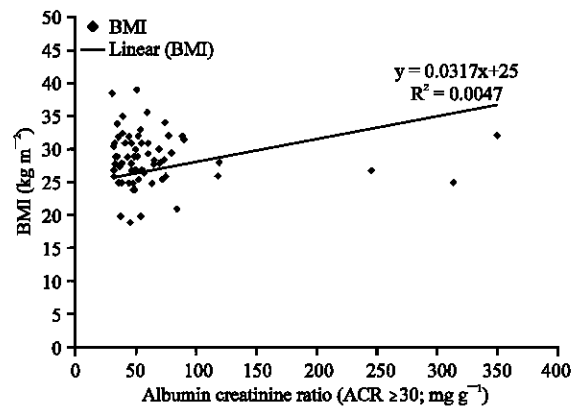Fig. 2: Relationship between ACR≥30 and TG

Table 2: Biochemical parameters in diabetic subjects with and without nephropathy as compared to control

Parameters	Control	Diabetic subjects without nephropathy	Diabetic subjects with nephropathy
Total cholesterol (mg dL^{-1})	161.84±8.98	197.29±8.20*	211.58±7.49*
HDL-C (mg dL^{-1})	46.47±2.42	42.75±2.30*	37.50±3.13*
LDL-C (mg dL^{-1})	93.95±7.53	137.51±7.27*	149.49±6.97*
Triglyceride (mg dL^{-1})	107.11±8.73	113.58±9.56*	123.57±6.62*
FPG (mg dL^{-1})	86.05±2.47	141.59±7.80*	150.48±8.76*
HbA$_1$c (%)	3.72±0.13	5.71±0.40*	5.98±0.34*
ACR (mg g^{-1})	22.76±5.14	29.91±1.23*	59.71±5.28*

Values are Mean±SEM, $p<0.05$ as compared to control

volunteers without nephropathy (197.29±8.20, $p<0.05$) and in those with nephropathy (211.58±7.49, $p<0.05$) when compared with the control subjects (161.84±8.98, $p<0.05$). There were also significant increases ($p<0.05$) in mean plasma Low Density Lipoprotein (LDL) cholesterol (137.51±7.27 in diabetics without nephropathy and 149.49±6.97 in those with nephropathy) and triglyceride (113.58±9.56 in diabetics without nephropathy and 123.52±6.62 in those with nephropathy) when compared to the control subjects (93.95±7.53; 107.11±8.73,

Fig. 3: Correlation between ACR≥30 and LDL-C

Fig. 4: Correlation between ACR≥30 and BMI

respectively). However, there was a significant decrease ($p<0.05$) in plasma High Density Lipoprotein (HDL) cholesterol in diabetics without nephropathy (42.75±2.30) and those with nephropathy (37.5±3.31) when compared to the control subjects (46.47±2.42). A positive correlation was obtained between microalbuminuria (ACR = 30 mg g^{-1}) and total cholesterol (R^2 = 0.028, $p<0.05$; Fig. 1), triglyceride (R^2 = 0.123, $p<0.05$; Fig. 2), low density lipoprotein cholesterol (R^2 = 0.012, $p<0.05$; Fig. 3) and body mass index (R^2 = 0.005, $p<0.05$; Fig. 4).

DISCUSSION

Diabetic Nephropathy (DN) is a clinical syndrome characterized by persistent albuminuria, a relentless decline in glomerular filtration rate, raised arterial blood pressure and increased relative mortality from cardiovascular disease (Rehman and Hamayun, 2004). Albuminuria and even microalbuminuria have been associated with increased LDL-C and decreased HDL-C

(Best *et al.*, 1994). According to Attman *et al.* (1998) lipoprotein abnormalities are more pronounced in patients with HbA_{1c} levels.

In a study by Rehman and Hamayun (2004), 35.58% of the total patients examined were diagnosed with Insulin Dependent Diabetes Mellitus (IDDM) nephropathy. The mean Body Mass Index (BMI) in DN patient was 26.49 ± 0.23 kg m^{-2}. The present study showed the incidence of diabetic nephropathy in diabetic patients aged 20-70 years as 72.63% and BMI in these patients as 27.38 ± 0.58 kg m^{-2}. This is higher than the earlier result of Rehman and Hamayun (2004), although they considered only patients with IDDM in their study.

Bonnet and Cooper (2000) stated that DN is associated with an altered lipid profile characterized by elevated triglyceride rich lipoproteins even in the early stages of the renal disease. In this study the plasma Total Cholesterol (TC), LDL-C and triglyceride were significantly higher in diabetic nephropathy than in diabetics without nephropathy while HDL-C was significantly lower in DN than in diabetics without nephropathy. Significant positive correlation were also found between microalbuminuria (ACR = 30 mg g^{-1}) and TC, triglyceride, LDL-C and BMI. These results were in favour of the study that showed an association between albuminuria and even microalbuminuria with increased LDL-C and decreased HDL-C (Best *et al.*, 1994).

Our study was also in agreement with the findings by Arora *et al.* (2007) on the relationship between BMI and serum lipids. This study showed a relationship between microalbuminuria and plasma cholesterol, BMI, HbA_1c and BP. This is in favour of the study by Ravid *et al.* (1998) which showed the risk of developing microalbuminuria to be independently predicted by total cholesterol, mean BP, HbA_1c, HDL cholesterol and BMI.

CONCLUSION

Diabetic Nephropathy (DN) is a common cause of abnormal lipoprotein metabolism and can be influenced by impairment of renal function and metabolic control of diabetes. This study showed that total cholesterol, low density lipoprotein cholesterol, triglyceride and body mass index increased with persistent albuminuria or nephropathy amongst diabetics in Southern Nigeria.

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