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Original Article

Serum lipid profile abnormalities among patients with nephrotic syndrome

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ABSTRACT

Background: Nephrotic syndrome is a multifactorial clinical condition characterized by increased glomerular permeability with consequent massive proteinuria. Hyperlipidaemia has been found to be one of the cardinal manifestations of nephrotic syndrome. **Aim**: The present study was conducted to determine the lipid profile and cardiovascular risk of nephrotics in this locality. **Methods:** Serum total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL) as well as atherogenic index (AI), coronary risk index (CRI) and non-HDL cholesterol were determined in ninety-six subjects. Forty-eight were nephrotic patients while others were apparently healthy individuals used as controls. **Result:** TC, TG, and LDL-C of nephrotics was observed to be significantly higher ($P<0.05$) when compared with control subjects. Similarly, AI, CRI and non-HDL-C of nephrotics were observed to be significantly higher ($P<0.05$) when compared with control subjects. VLDL-C of both groups was observed to show no significant difference statistically ($P>0.05$). HDL-C of nephrotics was observed to be significantly lower ($P<0.05$) when compared with control subjects. **Conclusion:** The result indicates apparent lipid derangement in nephrotic syndrome which may lead to cardiovascular disease. We therefore recommend that full lipid panel should be included in the investigation of suspected nephrotics to complement early diagnosis of the syndrome and to prevent further complications that could arise from the syndrome.

Keywords: Nephrotic syndrome, cardiovascular disease, lipid profile, hyperlipideamia, coronary risk index, atherogenic index

INTRODUCTION

Nephrotic syndrome (NS) is a multi-factorial clinical condition characterized by increased glomerular permeability with consequent massive proteinuria. There is a variable tendency towards developing edema, hypoalbuminemia and hyperlipidaemia.[1] The severity of lipid abnormalities also correlates with the degree of protienuria and a common

complication in patients with chronic kidney disease and Nephrotic syndrome is proteinuria>3g/day.[2] The specific causes of nephrotic syndrome include minimal-change nephropathy, focal glomerulosclerosis, and membranous nephropathy.[1] It can also result from systemic diseases that affect other organs in addition to the kidneys, such as diabetes, amyloidosis, and lupus erythromatous.[1]

Hyperlipidaemia is one of the cardinal manifestations of nephrotic syndrome.[3] Various studies have shown that the prevalence of hyperlipideamia or dyslipidaemia in patients with chronic kidney disease is higher than in the general population.[4] Nephrotics are at an increased risk for Cardiovascular disease due to the hyperlipidaemic state. The risk varies depending on the type of lipid abnormalities. Studies that reported the lipid profile in nephrotic patients are not consistent. Various authors have reported increased total cholesterol (TC), low density lipoprotein (LDL), very low density lipoprotein (VLDL), triglycerides (TG) and normal high density lipoprotein (HDL) in nephrotics[5-7] but Ohta and his co-worker[8]reported high level of HDL while Alexander and his colleagues[9] reported low level of HDL in nephrotic patients. This disagreement in data is probably because in most patients the nephrotic syndrome is accompanied by renal failure or other systemic disorders such as diabetes mellitus (or both), or because the patients are receiving treatment such as corticosteroids, that has a confounding effects on the lipoprotein patterns.[6] It has also been shown that the incidence of nephrotic syndrome varies from place to place due to factors such as changes in food, habits, climate, type of work, and ethnic origin.[1] Also, certain factors like diet, malnutrition, genetic traits are known to alter the frequency and severity of lipid pattern in an individual.[1] Hence, this study sought to determine the lipid pattern of nephrotics in this locality and by extension (if any), determine the atherogenic index (AI), coronary risk index (CRI) and non-HDL cholesterol a surrogate marker of Apo-lipoprotein B of these patients.

METHODOLOGY

Study population

Ninety six subjects comprising of forty eight certified nephrotics based on clinical manifestation and laboratory findings at the Nephrology and Paediatrics Clinic of the University of Benin Teaching Hospital (UBTH), and forty eight apparently healthy individuals without any clinical and laboratory findings of renal dysfunction, hypertension or systemic disease and non-smokers with age and sex-matched as controls were used for the study. Ethical clearance was obtained from the institution ethical committee and informed consent was obtained from patients.

Fasting venous blood samples were collected with minimum stasis into plain container. This was allowed to clot and spun in a centrifuge for 10 minutes. The serum was separated and kept frozen until required for analysis.

Biochemical assay

All parameters were assayed using standard methods. total cholesterol,[10] triglycerides,[11] HDL-cholesterol,[12] while others are by calculations LDL-cholesterol, VLDL-cholesterol,[13] atherogenic index, coronary risk index[14] and non-HDL-cholesterol (Apo lipoprotein B surrogate marker).[15] Commercially available standard kits (Randox Laboratories, U.K) were used. Manufacturer's instructions were strictly adhered to.

Statistical analysis

The mean ± SD was calculated for each analyte and significant differences between means were determined using the student t-test. $P<0.05$ was considered the level of significance.

RESULTS

The mean ± SD and the statistical comparison of serum total cholesterol, triglycerides, HDL-C, LDL-C and VLDL-C are as shown in Table1. Table 2 shows the mean±SD of the atherogenic index (AI), coronary risk index (CRI) and non-HDL-C (Apo lipoprotein B surrogate marker). Figure 1 and 2 shows the mean±SD of total cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C and AI,CRI, non-HDL-C in graphical form respectively.

Table 1: Serum total cholesterol, triglycerides, HDL-C, LDL-C and VLDL-C (mg/dl) in nephrotics and control subjects

PARAMETERS (mg/dl)	NEPHROTICS (N=48)	CONTROLS (N=48)	P<0.05
Total Cholesterol	242±28	190±18	**
Triglycerides	211±30	154±14	**
HDL-C	50±17	102±6.0	**
LDL-C	150±17	57±19	**
VLDL-C	42±6.0	31±3.0	*

** Significant, *not significant

Table 2: Atherogenic index (AI), coronary risk index (CRI) and non-HDL-C (Surrogate marker for Apo lipoprotein B) in nephrotics and controls

PARAMETERS (mg/dl)	NEPHROTICS (N=48)	CONTROLS (N=48)	P<0.05
AI	3.0±1.0	0.56±3.2	**
CRI	4.8±1.7	1.9±3.0	**
Non-HDL-C (Apo B) (mg/dl)	192±11	88±12	**

**Significant

Our results showed significant increase level of total cholesterol, triglycerides and LDL-C in nephrotic patients when compared with the control. Also, there was an increased level of VLDL-C in nephrotic patients but was not statistically significant when compared with control. Nephrotic patients showed a significantly reduced level of HDL-C when compared with control. The atherogenic and coronary risk indices as well as Apo lipoprotein B surrogate marker were significantly increased in nephrotic patients when compared with control.

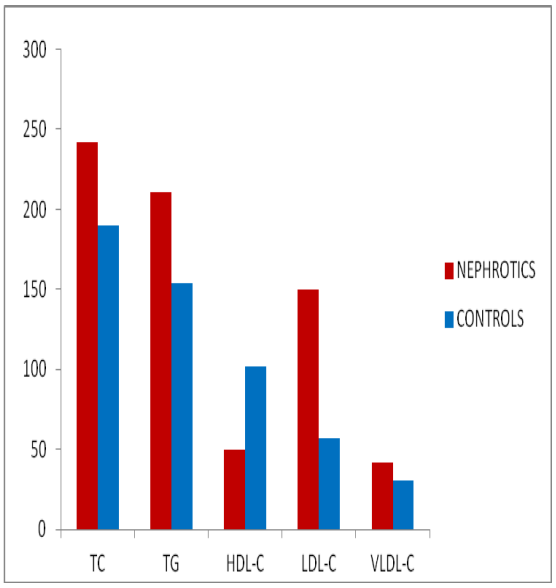

Figure 1: Serum total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL-C), low density lipoprotein (LDL-C), very low density lipoprotein (VLDL-C) of nephrotics and control

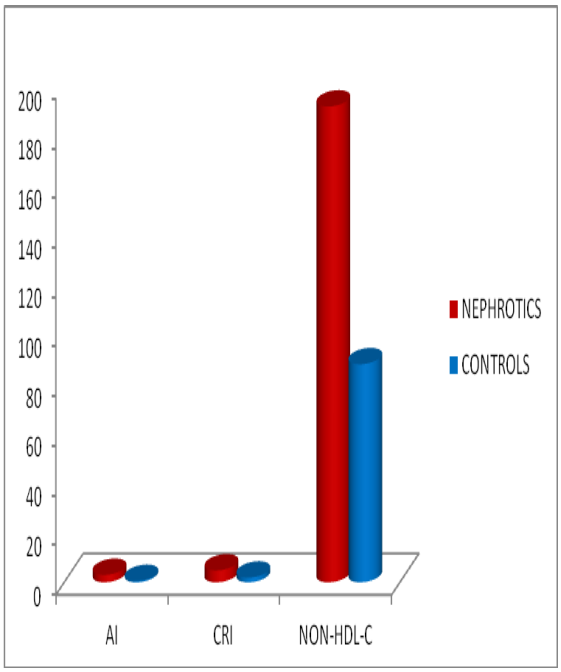

Figure 2: Atherogenic index (AI), coronary risk index (CRI) and non-HDL-C in nephrotics and control.

DISCUSSION

In our study, we observed hypercholesterolemia among nephrotics when compared with the control. This is in

accordance with the work of various authors[1,5-9] who did similar work on nephrotics. Vaziri[3] in his work attributed this hypercholesterolemia to a defective regulatory response of 3-hydroxy-3-methylglutararyl-coenzyme A (HMG-COA) reductase and hepatic cholesterol 7α-hydroxylase in nephrotics. These enzymes are rate–limiting enzymes in cholesterol biosynthesis and catabolism to bile acids in humans. There was also an increased level of triglycerides in nephrotics when compared with control. This is in agreement with the previous reports.[5-7] This hypertriglyceridaemia observed in nephrotics is attributed to down-regulation of lipoprotein lipase as found in nephrotics skeletal muscle, myocardium and adipose tissue, which is the principal sites of fatty acids consumption and storage.[3]

The HDL-C level of nephrotics was significantly decreased when compared to the control in this study. This is in accordance with the findings documented in some studies.[9,16] However, some conflicting findings exist which reported normal HDL-C in nephrotics,[5-7] while some reported high HDL-C in nephrotics.[8] A plausible explanation for the low level of HDL-C in nephrotics observed in the present study is the urinary losses of lecithin: cholesterol acyltransferase (LCAT) which leads to severe deficiency and limit the HDL-mediated uptake of surplus cholesterol from extra hepatic tissues. This is also compounded by marked reduction of the hepatic HDL-C receptor.[3] These limitations greatly affect the homeostasis of HDL-C in nephrotics. We also observed in this study increased level of LDL-C in nephrotics which is in agreement with previous studies.[1,5-7] The increased LDL can be explained by severe reduction of hepatic LDL receptor protein abundance in nephrotics despite normal LDL receptor mRNA abundance and gene translation rate.[17] These findings point to inefficient translation and/or increased LDL receptor protein turnover as a cause of LDL receptor deficiency in nephrotic syndrome.[17] Given the critical role of LDL receptor, acquired LDL receptor deficiency will contribute to hypercholesterolemia, elevation of plasma LDL-C, and impaired LDL clearance[17] as found in nephrotics. The VLDL-C of nephrotics is elevated but not statistically significant when compared with the control subjects .This is in variance with the work of previous authors.[1,5-7] The atherogenic index (AI), coronary risk index (CRI) and non-HDL-C in this study were observed to be elevated when compared with the control subjects. When the AI, CRI and Non-HDL of our study population were compared with the guidelines, the nephrotics seem to have unfavorable risk profile for cardiovascular disease. The recommended ratios for AI and CRI is ≤3.5,[14] while the AI observed in the study was 3.0±1.0 and 0.56±3.2 for nephrotics and control respectively, and CRI on the other hand was 4.8±1.7 and1.9±3.0 for nephrotics and controls respectively. The recommended value for non-HDL-C is <130mg/dl,[1,15] nephrotics had a value of 192±11 while control had 88±12. These findings suggest that nephrotics may be at risk of cardiovascular disease.

Conclusively, attempts have been made in this study to establish serum lipid pattern in the Nigerian nephrotics and we have also been able to affirm that nephrotics experience hyperlipideamia which predisposes to cardiovascular disease. We therefore advocate that lipid profile should be among the hallmarks of the biochemical investigation including these indices for any nephrotic syndrome patient for better management.

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