Relationship between lipid profile and severity of chronic kidney disease among patients attending the Nephrology Clinic of University of Ilorin Teaching Hospital, Ilorin

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Abstract

Back ground*: Chronic kidney disease (CKD) is a major public health problem worldwide with increasing incidence and prevalence with antecedent high medical cost and poor outcome. The increasing risk of cardiovascular disease (CVD) and the high prevalence of dyslipidaemia in patients with CKD coupled with paucity of data correlating lipid profile with stages of CKD necessitate this study.*

Methodology*: One hundred and twenty CKD patients were consecutively selected from among the predialysis CKD patients attending the nephrology unit of the University of Ilorin Teaching Hospital (U.I.T.H) Ilorin, Nigeria. Sixty (60) age and sex matched controls were also selected from among the staff and medical students. Creatinine, urea and lipid profile [total cholesterol (T-c), triglyceride (TG) high density lipoprotein (HDL-c) and low density lipoprotein (LDL-c)] were estimated in the serum of both patients and controls. Student t-test was used to compare means of results where appropriate. Pearson correlation formula was used to examine relationship between variables.*

Results*: There were statistically significant differences when the mean lipid profiles of the CKD patients were compared with that of the controls ($p<0.05$). Significant elevations were observed in the values of LDL-c, TG and T-c in CKD patients when compared with controls, while significant decrease was observed in the case of HDL-c. Significant negative correlations were observed when both HDL-c and coronary heart disease risk ratio were compared with stages of CKD ($r= 0.565$ and 0.542 respectively and p-value<0.05 for both). There was a significant positive correlation*

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between serum triglycerides level and stages of CKD (r = 0.601 and p<0.05). Correlation indices between BMI, T-c, LDL-c and stage of CKD were weakly positive with r values of 0.032, 0.032, 0.051 and 0.213 respectively with p-value>0.05 in all

***Conclusion**: We concluded that dyslipidaemia is common in chronic kidney disease and worsened with the severity of CKD. Therefore early lipid profile is advised in CKD patients as well as holistic interpretation of lipid profile as prompt treatment may prevent cardiovascular events and retard the progression of kidney disease.*

Keywords: Relationship, Lipid Profile and Severity of Chronic Kidney Disease

Introduction

Chronic kidney disease (CKD) is defined as kidney damage, as confirmed by kidney biopsy or markers of kidney damage, with or without a decrease in glomerular filtration rate (GFR) (or GFR < 60 mL/min/1.73m^2) for e" 3 months with or without Kidney damage.[1] Examples of these markers of kidney damage, such as urine abnormalities (proteinuria), blood abnormalities or abnormalities on imaging studies.

CKD is a public health problem worldwide with increasing incidence and prevalence with antecedent high medical cost and poor outcome.[2] According to 1999 – 2004 National Health and Nutritional Examination Survey (NHANES), the prevalence of CKD among the USA population is 15.3%.[3] In North America, up to 11% of the population (19 million) may have CKD[4] and survey in Australia, Europe and Japan described the prevalence of CKD to be 6– 16% of their respective populations [5, 6]. In Nigeria, the actual prevalence of this disease is not known but the hospital based studies showed that it accounts for 2-8% of all admissions [7, 8]. The current burden of CKD might be due to a change of its underlying pathogenicity. Glomerulonephritis was one of the leading causes of kidney disease several decades ago; infections have become a less important cause, at least in the western world.[9] Current evidence however suggests that hypertension and global epidemic of type II diabetes mellitus are primarily responsible for the increasing incidence of CKD worldwide.[10, 11]

Chronic Kidney Disease has a prolonged latent period during which the disease is present but asymptomatic with progressive renal damage. There is wide variability in the rate of progression among individuals even when similar risk factors are present.[12] Combinations of several risk factors that result in rapid progression to end stage renal disease define the course of the disease [13,14]. Chronic kidney disease itself, whether manifested by reduced GFR or microalbuminuria, is an independent risk factor for CVD outcomes[15]. There are several potential explanations for the finding but one possibility is that CKD may represent the kidney manifestation of a systemic burden of vascular and endothelial disease [16, 17]. Another possibility is that CKD reflects the severity and duration of traditional CVD risk factors such as hypertension, diabetes mellitus and dyslipidaemia[18].

National guidelines have identified dyslipidaemia, and elevated levels of love density lipoprotein cholesterol (LDL-c) in particular, as a key risk factor for CVD risk modification in the general population[14]. However spectrum of dyslipidaemia in patients with CKD is distinct from that of general population and it involves all classes of lipoprotein which varies with stages of CKD[14, 19]. There is elevation of total cholesterol and

LDL-c in patients prior to developing CKD, but as CKD advances to kidney failure there is decrease in total cholesterol and LDL-c[20], perhaps due in part to malnutrition[21]. The Plasma Triglyceride was elevated in patients with CKD, but as a consequence of high production rate which is related to impaired carbohydrate tolerance and enhances hepatic VLDL-c synthesis[22]. The low fractional catabolic rate is related to impaired lipase activity which in most cases is secondary to suppressed insulin level or hyperparathyroidism[23].

The lipid profile in late stage of CKD, include hypertriglyceridaemia: low HDL-c and low or normal LDL-c, a profile similar to that seen in patients with diabetes and metabolic syndrome[24]. Lipid abnormalities are associated with a reduction in kidney function in the general population. It is not certain if it is the lipid abnormalities that cause reductions in the kidney function, or if impaired renal function (or proteinuria) itself causes both the lipid abnormalities and reduction in renal function. Most studies have been small and a meta-analysis of these studies to assess the effect of lipid reduction on the progression of renal disease has shown that lipid reduction may preserve GFR and reduce proteinuria[25].

CKD patients have a higher burden of dyslipidaemia as compared to the general population and are at greater risk for cardiovascular morbidity and mortality. The unbalanced cardiovascular burden as well as high prevalence of dyslipidaemia in patients with CKD which has put CKD patients in the highest risk, according to the treatment guidelines of the Adult Treatment Panel III (ATP IIII) coupled with paucity of data correlating lipid profile with stages of CKD necessitate this study.

Materials and Methods

This was a cross sectional study of consenting chronic kidney disease patients attending nephrology unit of University of Ilorin Teaching Hospital (UITH) Ilorin, Kwara State, Nigeria. A total of 120 chronic kidney diseases (CKD) patients (male 63, and female 57) who met the inclusion criteria for the study were recruited after obtaining verbal consent. A total number of 60 (male 32 and female 28) age and sex matched controls consisting of consenting staff and students of U.I.T.H. were recruited. The exclusion criteria include patients on drugs that can affect lipid metabolism, patients on dialysis as well as patients with active infection.

Their height was determined with rigid measurement against a vertical wall. Weight was determined using a Hanson type bathroom weighing scale. Body Mass Index (BMI) was calculated using their height (m^2) and weight (kg).

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 lithium heparin 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. Estimation of urea was done by Diaminomonoxime Method while estimation of creatinine was done using Jaffe's method.

Total cholesterol was estimated by cholesterol oxidase method[26]. HDL-c and LDL-c were also estimated by enzymatic method while triglycerides were estimated using glycerol-3 phosphate oxidase method[27] using commercially prepared kit by AGGAPPE 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 Epi-info Version 6. The means

of the 3 groups were compared by ANOVA at significance level of a = 0.05. Correlation coefficient was determined for the dependent variables of lipid profiles and BMI (in kg/m^2) with stages of chronic kidney disease using stage 2 (mild) stage 3 (moderate) and stage 4 (severe) as the independent variables.

Results

Out of the one hundred and twenty CKD patients recruited, sixty three (52.5%) were males while fifty seven (47.5%) were females with mean age of both male and female as 41.6 ± 16.1 years ranging between 15 and 70 years. Mean age for males was 42.6 ± 17 years ranging between 17 and 70 years while mean age for female was 40.4 ± 15 years ranging between 15 and 67 years.

The mean BMI for subjects and controls were 22.73 ± 4.31kg/m^2 and 19.37± 2.43kg/m^2 respectively which were statistically significantly different ($p < 0.05$).

There were statistically significant difference when the mean lipid profiles of the CKD were compared with that of controls ($p < 0.05$).

Table 1: Means values of BMI and lipid profile in subjects and controls

Variables	Subjects	Controls	P-value
Mean BMI±SD (kg/m^2)	22.73±4.31	19.37±2.43	0.021*
Mean T-C(mmo1/L)±S.D	10.48±3.58	5.36±0.51	0.000*
Mean T.G (mmo1/L) ±S.D	3.40±1.46	1.70±0.17	0.000*
Mean HDL-C (mmo1/L) ±S.D	0.16±0.45	1.40±0.38	0.000*
Mean LDL-C (mmo1/L) ±S.D	8.10±2.92	2.90±0.33	0.000*
Mean CHD-RR ±S.D	0.07±0.07	0.21±0.05	0.000*

Table 2: Means values of BMI and lipid profile in male and female subjects

Variables	Male	Female	P-value
Mean BMI±SD (kg/m^2)	21.90±2.83	23.65±5.37	0.116
Mean T-C(mmo1/L)±S.D	10.39±3.73	10.59±3.43	0.873
Mean T.G (mmo1/L) ±S.D	3.54±1.48	3.24±1.45	0.437
Mean HDL-C (mmo1/L) ±S.D	0.53±0.46	0.69±0.42	0.426
Mean LDL-C (mmo1/L) ±S.D	7.80±2.54	7.92±2.49	0.751
Mean CHD-RR ±S.D	0.07±0.07	0.08±0.63	0.489

Significant elevations were observed in the values of total cholesterol, triglycerides, and LDL-C, TG, and T-c in CKD patients when compared with controls. Significant decrease was observed in the case of HDL-c in patients with CKD when compared with controls. Coronary heart disease risk ratio is statistically significantly different when mean value of patients is compared with that of controls.

ratio of male patients was compared with that of female CKD patients.

Significant negative correlation was observed when HDL-c was compared with stages of CKD (r = 0.565 and p-value <0.05). There was also a significant negative correlation when coronary heart disease risk ratio was compared with stages of CKD (r =0.542 and p-value <0.05). There was a significant positive

Table 3: Correlation of lipid profile and BMI with stages of CKD using pearson correlation

Stages of Kidney Disease	Mean BMI (Kg/m^2) ±S.D	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 ±S.D
Mild(eGFR-60-80ml/min) n = 27	23.03± 4.27	10.37± 3.62	2.93± 1.48	0.89± 0.05	8.10± 2.52	0.086± 0.06
Moderate (eGFR-30-59ml/min) n = 63	22.73± 4.29	10.68± 3.56	3.42± 1.46	0.65± 0.45	8.55± 2.52	0.061± 0.07
Severe (eGFR-15-29ml/min) n = 30	22.70± 4.60	11.60± 3.31	4.19± 1.37	0.45± 0.39	8.93± 2.46	0.040± 0.05
r =	**0.032**	**0.051**	**0.601**	**-0565**	**0.213**	**-0.542**
p-value	**0.364**	**0.435**	**0.019***	**0.047***	**0.444**	**0.039***

The mean BMI for male and female subjects were 21.90 ± 2.8kg/m^2 and 23.65 ± 5.37kg/m^2 respectively which was not statistically different when both were compared (p <0.05). There was no statistically significant difference when the mean lipid profiles of the male CKD patients were compared with that of female CKD patients (p <0.05). There was no significant difference observed in the values of total cholesterol, triglycerides, and LDL-c, in male CKD patients when compared with female CKD patients. There was also no significant decrease observed in the HDL-c in male patients with CKD when compared with female CKD patients. There was no significant difference when coronary heart disease risk

correlation between serum triglycerides level and stages of CKD (r=0.601 and p-value<0.05). Correlation indices between BMI, T-c, LDL-c and stages of CKD were weakly positive with r values of 0.032, 0.051, and 0.231 respectively with p-value>0.05 in all.

Discussion

This study shows that hyperlipidaemia was present in patients with CKD which was significantly higher than in the control subjects as was found in a previous study[14]. However, there was no correlation between total cholesterol and stages of chronic kidney

disease in our study. This is surprising as it has been found that abnormal serum lipid may contribute to renal disease progression because circulating lipids bind to and become trapped by extracellular matrix molecules[28]. There, they undergo oxidation thus increasing the formation of reactive oxygen species such as superoxide anion and hydrogen peroxide[29].

The resultant reduction in the action of endothelium-derived vasodilators/growth inhibitors, such as prostacyclin and nitric oxide, with maintenance of increased formation of endothelium-derived vasoconstrictors/growth promoters, such as Angiotensin II, endothelin-I and plasminogen activator inhibitor – 1, has significant vascular and renal pathophysiologic consequences. Macrophages derived foam cells release cytokines that recruit more macrophages to the lesion and influence lipid deposition, endothelial cell function, and vascular smooth muscle cell proliferation. Glomerular cells mimic some of these characteristics of cells in the atherosclerotic vessel wall; [30] therefore, similar pathogenetic mechanisms may contribute to the progression of atherosclerosis and chronic kidney disease.

The study also showed a high level of triglyceride in the patients than in the controls which was statistically significant and there was also correlation between triglyceride and stages of chronic kidney disease. Impaired clearance of chylomicrons and VDRL has emerged as the dominant factors for the increased serum triglyceride concentration. Lipoprotein lipase (LPL) is the rate limiting step in lipolysis of chylomicrons and VLDL. LPL binds to heparin sulphate proteoglycans on the cell surface of endothelium. In proteinuric renal diseases, a down regulation of LPL protein abundance and enzymatic activity were found[31]. These events were largely responsible for profound abnormalities in lipoprotein metabolism in nephritic syndrome and chronic renal failure rendering these lipoproteins more atherogenic.

There was decrease in the level of HDL-C in CKD patients when compared to that of r controls and was statistically significant. Also there was correlation in the levels of HDL-C and stages of chronic kidney disease. Low level of HDL with poor maturation of HDL-3 to cholesterol-rich HDL-2 is due to acquired lecithin-cholesterol acyltransferase deficiency secondary to abnormal urinary losses of this enzme[32]. The study showed lower level of CHD-RR in CKD patients when compared to those of our control and was statistically significant. There was also correlation in CHD-RR with stages of CKD.

Conclusion

We concluded that dyslipidaemia is common in chronic kidney disease with triglycerides, LDL-C and CHD-RR having correlation with stage of CKD. Therefore, early lipid profiling is advised in CKD-patients as well holistic interpretation of lipid profile as prompt treatment may prevent cardiovascular events and retard the progression of kidney disease.

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