

LIPID PROFILE IN PRE-DIALYSIS CHRONIC KIDNEY DISEASE PATIENTS ATTENDING UNIVERSITY OF MAIDUGURI TEACHING HOSPITAL, MAIDUGURI-NIGERIA.

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ABSTRACT

Background/objectives: Cardiovascular disease is a major cause of morbidity and mortality among patients with chronic kidney disease, and accounts for 50% of all deaths in them. Dyslipidaemia does not only accelerate atherosclerosis in these patients but also progresses the renal disease. This study therefore set to investigate the pattern of lipid profile in pre-dialysis chronic kidney disease patients.

Methods: This was case control study of 63 pre-dialysis chronic kidney disease patients attending University of Maiduguri teaching Hospital and 60 control subjects. All factors that may lead to dyslipidaemia were excluded in all subjects except hypertension. Lipid profiles were measured by standard methods. Data were analyzed using a statistical software SPSS version 11.0. Their observed differences in mean-SEM values were analyzed for statistical significance using Student's t-test and p-value <0.05 was considered significant.

Results: the mean+SEM of total cholesterol 4.50+0.14mmol/L and triglycerides 2.18+0.10mmol/L in patients were significantly higher than that of the controls 3.79+0.11mmol/L and 1.19+0.06mmol/L respectively, $p < 0.05$. Similarly the mean+SEM of LDL 2.62+0.16mmol/L and LDL/HDL ratio 3.53+0.12 in patients were significantly higher when compared to that of the controls 2.04+0.16mmol/L and 2.04+0.08 respectively, $p < 0.05$. However, although the mean+SEM HDL in patient 1.07+0.07mmol/L, was lower than that of the controls 1.21+0.06mmol/L, the difference was not statistically significant, $p > 0.05$. The pattern of lipid profile did not change with severity of disease and dyslipidaemia in patients were more in triglycerides, 68.3% and HDL, 63.5% than in TC, 22.2% and LDL, 17.5%.

Conclusion: Dyslipidaemia is common in pre-dialysis chronic kidney disease patients. It is pertinent to investigate and treat dyslipidaemia early in the course of the disease as it may prevent further progression of the renal damage.

Key Words: Chronic kidney disease, dyslipidaemia, atherosclerosis, Maiduguri, Nigeria. (Accepted 25 April 2008)

INTRODUCTION

Chronic Kidney Disease (CKD) is common in Nigeria, with prevalence rates derived from hospital based studies ranging between 2 - 8% of all hospital admission. Although the prevalence of CKD in Maiduguri is undetermined the Kidney Center in the Teaching Hospital started its dialysis program in 1999. From inception to July 2006, a total of 356 patients with chronic renal failure (CRF) were dialyzed with an increasing trend, 23 patients, 51 patients and 67 patients in the year 1999, 2002 and 2006 respectively. Out of this number, only 20 patients are alive indicating the high mortality rate associated with the disease. Cardiovascular disease is a major cause of morbidity and mortality among patients with CRF⁶⁻⁸, and accounts for 50% of all

Deaths⁶. Consequently, the importance of cardiovascular illness as the cause of death in these patients makes it imperative to consider the risk factors involved. Dyslipidaemia is common^{9,10} and it increases risk of cardiovascular disease (CVD) in CKD patients. This is independent factor and not merely reflecting the high prevalence of traditional cardiovascular risk factors such as hypertension and diabetes^{11,12}. In addition to the cause of CVD, dyslipidaemia has long been hypothesized that it plays a role in glomerular injury similar to their putative involvement in atherosclerosis^{10,13-15}. It was also hypothesized that the abnormality in lipid metabolism in CKD could be important in mediating not only glomerular but tubulo-interstitial injuries¹³. However, the first evidence that abnormalities of lipid metabolism might be linked to glomerular disease in man was provided by Gjone in his report of the rare familial condition of Lecithin Cholesterol

Acyltransferase (LCAT) deficiency¹⁶ and was later supported by the Multiple Risk Factor Intervention Trial (MRFIT) study¹⁷. Several patterns of lipid abnormalities have been described in patients with CKD but to date there is scanty or no data on serum lipid profile in CKD patients in the Northeastern Nigeria. This study therefore focused on pattern of serum lipid profile in pre-dialysis chronic kidney disease patients attending University of Maiduguri Teaching Hospital, Nigeria.

MATERIALS AND METHODS

This study was a prospective case control study which included 63 males and females with chronic kidney disease, who were among those attending the Nephrology Clinic of the University of Maiduguri, Nigeria. These subjects were diagnosed for chronic kidney disease and managed without dialysis. Sixty non-renal disease subjects who were matched for sex and age served as controls. The control subjects were recruited from patients' relatives, hospital workers and medical students. Subjects who were with diabetes, obesity, or those who smoke or take alcohol were excluded from the study. Also excluded among the CKD patients were those who had gone for dialysis. Similarly, those excluded among the controls were hypertensive, who were later discovered to have some degree of renal impairment by results of their renal function tests, and females on oral contraceptives. In all the subjects, weight (Kg), height (M) and blood pressure (mmHg) were measured. Body Mass Index (BMI) was calculated from the values of weight and height ($BMI = Kg/M^2$). All subjects were properly instructed to collect complete 24hr-urine and glomerular filtration rate (GFR) was determined using the formula $GFR = UV/P \times 1.73/S$ ml/min/S where S= body surface area of subjects determined from a nomogram using wt and ht of subjects¹⁹. In serum the following were determined by their respective methods use in department of Chemical Pathology of the hospital, urea²⁰, creatinine²¹, total cholesterol (TC)²², Triglycerides²³, and high density lipoprotein cholesterol (HDL-C)²⁴. The value of low density lipoprotein was calculated using the Friedwald formula²⁵. Data obtained from the study were analyzed using statistical software SPSS version 11.0. The mean±SEM was calculated for all the variables. Their observed differences in mean±SEM value were analyzed for statistical significance using Student's t-tests and p-value <0.05 was considered significant. Lipid profile was also related to the severity of disease. We determined the prevalence of dyslipidaemia in each component of lipid profile in patients and controls.

RESULTS

From the study, one hundred and twenty three (123) subjects were recruited out of which sixty-three (51.2%) had chronic kidney disease. Sixty (48.8%) subjects served as control. Table 1 shows a demographic and baseline data of subjects in the study. Patients and controls were matched for number and sex, however, the patients were older (42.18 ± 1.61 yrs vs. 37.75 ± 1.27 yrs), $p < 0.05$. While the controls were significantly heavier (25.59 ± 0.85 kg/m²) than the CKD patients (22.8 ± 0.45 kg/m²), $p < 0.05$. The mean±SEM urea value was significantly higher in CKD patients (26.28 ± 1.10 mmol/l) when compared to that of the controls (3.86 ± 0.12 mmol/l) $p < 0.05$. Similarly the mean±SEM creatinine of CKD patients was significantly higher (1127.39 ± 53.60 µmol/L) compared to the controls (82.93 ± 2.53 µmol/L) $p < 0.05$. Meanwhile the GFR was significantly lower in patients (8.01 ± 0.37 ml/min/s) than that of the controls (103.65 ± 2.87 ml/min/s) $p < 0.05$. Both systolic (169.68 ± 2.55 mmHg) and diastolic (111.43 ± 1.81 mmHg) blood pressure in patients were significantly higher than when compared to that of the controls (127.17 ± 2.15 mmHg and 86.00 ± 1.62 mmHg respectively), $p < 0.05$ in both. Table 2 shows comparisons of mean±SEM of lipid profile in CKD patients as compared to that of the controls. Total cholesterol (4.50 ± 0.14 mmol/L) and triglyceride (2.18 ± 0.10 mmol/L) were significantly higher in patients than in the controls (3.79 ± 0.11 mmol/L and 1.19 ± 0.06 mmol/L respectively), in both $p < 0.05$. Similarly the mean±SEM of both LDL (2.62 ± 0.16 mmol/L) and LDL/HDL ratio (3.53 ± 0.12 mmol/L) in patients were significantly higher as compared to that in the controls (2.04 ± 0.16 mmol/L and 2.04 ± 0.08 mmol/L respectively), $p < 0.05$ in both cases. Although the mean±SEM of HDL (1.07 ± 0.07 mmol/L) in CKD patients was lower than that of controls (1.21 ± 0.06 mmol/L), the difference was not statistically significant, $p < 0.05$. Table 3 shows comparison of mean±SEM of lipid profile in CKD patients whose GFR were less than or equal to 10ml/min/s and those whose GFR were greater than 10ml/min/s. All the mean±SEM of variable compared showed no significant differences ($p > 0.05$) between the two groups of patients except that of the GFR (6.58 ± 0.30 ml/min/s vs. 11.60 ± 0.35 ml/min/s), $p < 0.05$, indicating no change in the quality of dyslipidaemia with the severity of the disease. Table 4 shows prevalence of dyslipidaemia of lipid profile components in both patients and controls. The dyslipidaemia was more in triglycerides (63%) and HDL (63.5%) than in TC (22.2%) or LDL (17.5%) in the CKD patients, meanwhile the prevalence of HDL was also higher in controls, but the other components of lipid profile were homogeneously lower than in patients.

Table 1: Demographic Profile and Baseline Data of Subjects in the Study.

| Variables | CKD (N=63) | Controls (N=60) | P-Value |
|--|---------------|-----------------|---------|
| Male | 37(58.7%) | 36(60.0%) | |
| Female | 26(41.3%) | 24(40.0%) | |
| Age (yrs) | 42.98±1.61 | 37.75±1.27 | 0.012 |
| BMI (kg/m ²) | 22.78±0.45 | 25.59±0.85 | 0.007 |
| Systolic Bp (mmHg) | 169.68±2.55 | 127.17±2.15 | 0.000 |
| Diastolic BP (mmHg) | 111.43±1.81 | 86.00±1.62 | 0.000 |
| GFR (ml/min/s) | 8.01±0.37 | 103.65±2.85 | 0.000 |
| Creatinine (umol/L) | 1127.39±53.60 | 82.93±2.53 | 0.000 |
| Urea (mmol/L) | 26.27±1.11 | 3.86±0.12 | 0.000 |
| Na ⁺ (mmol/L) | 130.4±0.7 | 136.9±0.3 | 0.000 |
| K ⁺ (mmol/L) | 4.99±0.1 | 3.7±0.1 | 0.000 |
| HCO ₃ ⁻ (mmol/L) | 15.9±0.27 | 22.6±0.2 | 0.000 |

Table 2: Comparison of Mean±SEM of Lipid Profile in CKD Patients and Controls.

| Variables | CKD Patients (N=63) | Controls | P-Values |
|----------------------------|---------------------|-----------|----------|
| Total Cholesterol (mmol/L) | 4.50±0.15 | 3.79±0.12 | 0.000 |
| Triglycerides (mmol/L) | 2.18±0.10 | 1.19±0.06 | 0.000 |
| HDL-C (mmol/L) | 1.07±0.07 | 1.21±0.06 | 0.157 |
| LDL (mmol/L) | 2.62±0.16 | 2.04±0.16 | 0.005 |
| LDL/HDL ratio | 3.53±0.12 | 2.04±0.08 | 0.000 |

HDL-C=High-density Lipoprotein Cholesterol
LDL=Low-density lipoprotein

Table 3: Comparison of Mean±SEM of Lipid Profile in CKD Patients Whose GFR is <10ml/Min/s and Whose GFR is >10ml/Min/s.

| Variables | GFR<10ml/Min/s (N=45) | GFR>10ml/Min/s(N=18) | P-Values |
|----------------|-----------------------|----------------------|----------|
| GFR (ml/min/s) | 6.58±0.30 | 11.60±0.36 | 0.000 |
| TC (mmol/L) | 4.61±0.16 | 4.22±0.31 | 1.523 |
| TG (mmol/L) | 2.26±0.09 | 2.00±0.19 | 0.075 |
| HDL-C (mmol/L) | 1.10±0.09 | 0.99±0.14 | 0.264 |
| LDL (mmol/L) | 2.64±0.18 | 2.00±0.19 | 2.168 |

GFR=Glomerular Filtration rate
TC=Total Cholesterol
TG=Triglycerides
HDL-C=High-density Lipoprotein Cholesterol
LDL=Low-density Lipoprotein

Table 4: Prevalence of Dyslipidaemia in Subjects

| Variables | CKDPatients (N=63) | Controls (N=60) | P-Values |
|-----------|--------------------|-----------------|----------|
| TC | 14(22.2%) | 6(10.0%) | 0.000 |
| TG | 43(68.3%) | 6(10.0%) | 0.000 |
| HDL | 40(63.3%) | 12(20.0%) | 0.000 |
| LDL | 11(17.5%) | 2(3.3%) | 0.000 |

TC=Total Cholesterol
TG=Triglycerides
HDL=High-density Lipoprotein
LDL=Low-density Lipoprotein

DISCUSSION

The mean age of the patients in the study was 42.98±1.61 years (range 20 to 70 years), with a peak between 21 to 50 year(68.3%), while 28.6% were 51 years or older and only 1.6% were 20 years or below. Our observations are in keeping with earlier studies²⁶ in Nigeria which showed that the peak incidence of CKD is between the third and fourth decades. This indicates that CKD imposes a severe economic burden on the society. Most patients were also in their reproductive age. In developed countries however, the prevalence of CKD increases with age^{27,28}, where the incidence of ESRD is 6-to 10 times higher in patients between 70 and 90 of age compared with those ages between 21 and 50 years in the study. The CKD patients were older however; their BMI was significantly lower than that of the controls. It is therefore critical to note here that malnutrition in CKD patients. The mean values of GFR (8.01±0.37ml/min/s), urea (26.27±1.11mmol/L), and creatinine (1127.39±53.60umol/L) at recruitment implies most of the patients in the study presented or are referred late to the hospital and already had profoundly altered plasma biochemistry. Screening for kidney diseases as well as dyslipidaemia in the community is important. This will identify those at risk especially for dyslipidaemia and plan preventive measures instituted and/or appropriate referral of patients. In our study, about 98.4% of CKD patients had hypertension as compared to 85% in another study in Nigeria²⁶. Hypertension a cardiovascular risk factor accelerates progression of chronic renal disease in humans, whether it results from, or cause, the renal disease²⁶. The hypertension in these patients may accelerate the development of dyslipidaemia. In our study, although the mean±SEM of both total cholesterol as well as LDL were significantly higher than that of the controls, the values were within the reference value of the study laboratory, however, the results concur with findings in other studies^{10,29,30}. This signifies the importance of quality of requests for lipid investigations in CKD patients, where the total cholesterol alone will give little or no information, total lipid profile is preferred. Similarly, there is

strong clinical evidence that not only elevated plasma LDL but also the quality is associated with atherosclerosis especially in a milieu where free radical generations are accelerated as in the CKD^{12,31-33}. The presence of small-dense LDL, which is more susceptible to oxidation, accelerates atherosclerosis in the presence of normal total cholesterol and LDL values as observed in this study. Subsequently, the LDL/HDL ratio has been shown to be a better index of coronary artery disease risk than LDL or HDL alone^{34,35}. The ratio was increased in CKD patients in this study indicating the atherogenic burden imposes on its sufferers in Nigeria. Although hypertriglyceridaemia is now an acceptable independent risk factor of coronary artery disease, the mild form is usually not sufficient to increase the risk of coronary artery disease³⁶. However, as observed in our study, the moderate to severe type correlates with an increased risk of cardiovascular disease particularly in the context of low HDL-C levels, elevated LDL or both³⁶⁻³⁸. Consequently, the low HDL-C found in patients in the study increases the risk for atherosclerosis³⁷. The decreased HDL-C observed in some controls may be related to their weight, as 61% of those with decreased HDL-C were overweight. This study did not show any correlation between dyslipidaemia and severity of disease. Thus, many cases of CKD with relatively stable renal function may not have been included in the study; hence, our conclusion may apply more to CKD cases with acute deterioration. Consequently as it is imperative to screen for CKD in the community, it is significant as well investigating lipids abnormalities early in the course of the disease since treating the dyslipidaemia may prevent the progression of disease^{14,15}.

The study also showed that dyslipidaemia occurred in almost all the components of lipid profile, however, the most prevalent in pre-dialysis CKD patients observed in the study was hypertriglyceridaemia (68.3%) and decreased HDL-C (63.5%). This is in keeping with findings of Sniderman *et al*³⁰ who reported that hypertriglyceridaemia is the most common lipid abnormality in adults and children with chronic renal failure. The finding in the study of moderate to severe hypertriglyceridaemia in the presence of decreased HDL-C and increased LDL/HDL ration predisposes patients of CKD in environment to atherosclerosis. This may not only accelerate atherosclerosis in them but may lead to progression of disease. The magnitude of the existing burden of illness caused by renal disease, the projections for increasing incidence of CKD, and the limitation of the existing treatments for renal insufficiency in Nigeria all point to the need for clinical and population based intervention aimed at prevention of

ESRD. The cost of treating this condition is enormous. Appropriate management should preferably involve a multidisciplinary approach targeting the control of dyslipidaemia, hypertension, obesity, diabetes mellitus, smoking, alcohol consumption, and tropical diseases that progress to CKD¹. Free annual screening and health eradication will go a long way in elucidation, increasing awareness and preventing the deleterious condition that may lead to dyslipidaemia and CKD. There is a need to embark on an increase health education campaign and screening of the study populace for early detection of dyslipidaemia as well as kidney disease. In conclusion, dyslipidaemia is common in pre-dialysis CKD patients in this environment. It is pertinent therefore to investigate for lipid abnormalities early in this category of patients, the treatment of which may prevent the progression of the disease who may later require dialysis.

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