PATTERN OF LIPID PROFILE IN CHRONIC RENAL FAILURE PATIENT WITH GFR < 60 ML/MIN/1.73 M^2 ON CONSERVATIVE TREATMENT VERSUS MAINTENANCE HAEMODIALYSIS

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Abstract:

The incidence and prevalence of chronic kidney disease (CKD) are increasing worldwide and are associated with poor outcomes. It becomes apparent that the severity of CKD along with CVD severity in any population makes a devastated combination for both patients and healthcare system. Identification of CKD as a major risk factor for cardiovascular morbidity and mortality is attributed to dyslipidemia, and therefore an expectation of effective intervention to diminish premature cardiovascular mortality and progression of renal disease to increase longevity is imperative, thus this study may explore the lipid profile in chronic renal failure patient; on conservative treatment and maintenance haemodailysis treatment.

A cross sectional comparative study was carried out to find out the Pattern of lipid profile in chronic renal failure patient with GFR < 60 ml/min on conservative treatment versus maintenance haemodialysis admitted in a selected hospital of Dhaka city. Total 128 study population were selected according to selection criteria among which 62 subjects were on maintenance dialysis (designated as group A) and 66 subjects were on conservative treatment of CKD (designated as group B).

On average cholesterol, LDL and triglyceride level were more in group B than group A. On the other hand, HDL level was more in group A than group B and it was statistically insignificant. At the same time average LDL/HDL ratio was higher in group B than group A. But all these differences were statistically insignificant. Among the group A patients average triglyceride, total cholesterol and LDL level were higher in stage 4 CKD patients than stage 5 CKD patients. Average HDL level was higher in stage 5 CKD patients than stage 4 CKD patients. Among the group B patients average triglyceride and LDL level were higher in stage 4 CKD patients. But none of these two differences were statistically significant. On the other hand, average total cholesterol level was higher in stage 3 CKD patients and it was statistically significant($p<0.05$). HDL level was higher in stage 5 patients. But this difference was not statistically significant. In group A LDL/HDL ratio was more in stage 4 CKD patients and it was statistically significant($p<0.05$). Average LDL/HDL ratio was highest in stage 4 CKD patients in group B and it was statistically significant ($p<0.05$).

Our study had showed that mean lipid profile is better in patients of CKD on dialysis than those on conservative treatment, but there is no statistical significance as sample size very small. A multicentric prospective study involving larger number of study population giving adequate statistical power is recommended for conclusive comment on the possible factors associated with dyslipidaemia in CKD patients.

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Introduction:

Chronic kidney disease or chronic renal failure is increasingly recognized as a global health problem. The incidence and prevalence of chronic kidney disease are increasing worldwide. According to the 1998-2004 National Health and Nutritional Survey (NHANBS), the prevalence of CKD in the US population is 15.2%[1]. Patient with CKD are in the

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highest risk category for coronary heart disease CHD[2]. The incidence of cardiovascular disease CVD is high in patient on haemodialysis[3].

CKD is defined as abnormalities of kidney structure or function, present for 3 months, with implications for health. It is diagnosed most frequently by the presence of micro albuminuria. Levels of urinary albumin excretion above 30 mg/day on at least 2 measurements are consistent with CKD, regardless of the level of the GFR.[4, 5, 6] We will focus primarily on the dyslipidaemia in patients with stage -3, stage-4, stage-5 CKD on conservative treatment and maintenance haemodialysis. Dyslipidaemia in common in patients with CKD and lipid profile varies widely depending on the level of kidney function and the degree of proteinurea.[7]

In CKD, the etiology of dyslipidemia may be reflected more accurately in the apolipoprotein profile. Levels of apoA-I and apoA-II are often reduced yielding decreased production of HDL-C. In addition, apoC-III, integral for the metabolism of both LDL-C and very low-density lipoprotein cholesterol (VLDL-C) is present in elevated levels. The accumulation of apoB-containing VLDL particles is also important in the development and maintenance of dyslipidemia in CKD.[8,9] Factors that may contribute to decreased catabolism and clearance of triglyceride –rich apoB-containing lipoproteins include 1) reduced activity of lipolytic enzymes; 2) compositional abnormalities in lipoproteins preventing binding to appropriate receptors, and 3) decreased uptake of lipoproteins from the circulation. [10]

Binding and uptake of lipoproteins may be affected by increased amounts of oxidant stress seen in CKD such that oxidative modification of lipoproteins leads to decreased uptake by the appropriate receptors and subsequent atherosclerosis.[11] In summary multiple factors interfere with uptake of triglyceride-rich apoB-containing lipoproteins by the liver and in the periphery, yielding increased circulation of these potentially atherogenic lipoproteins.[12] Prior to developing CKD, patient frequently have elevated total and LDL-C levels. However as CKD advances to kidney failure, the prevalence of elevated total and LDL-C levels decreases. In dialysis patient LDL-C levels generally are lower than in general population.[13, 14, 15.] The classic lipid profile of later stage CKD includes hyper triglyceridemia, low HDL-C, and low or normal LDL-C.[16]

Keeping in view the mortality in CKD patients, we investigate the serum lipid status in CKD patient undergoing on conservative treatment and maintenance haemodialysis. Identification of CKD as a major risk factor for cardiovascular morbidity and mortality is attributed to dyslipidemia, and therefore an expectation of effective intervention to diminish premature cardiovascular mortality and progression of renal disease to increase longevity is imperative, thus this study explore the lipid profile in chronic renal failure patient; on conservative treatment and maintenance haemodailysis treatment.

Materials and Methods

A cross sectional study was carried out in Dept. of Medicine and Dialysis Unit of BIRDEM hospital from February-2011 to September 2011. 128 sample was collected purposively among CKD patients admitted into BIRDEM hospital, due to CKD stge-3, stage-4, and stage-5. Respondents were divided into two groups. Patients on haemodyalysis were included in group A and patients on conservative treatment were included in group B. Patients less than 18 years, having hypothyroidism & Chronic Liver Disease, pregnant women, patients on lipid lowering drug were excluded from the study. Data was collected from all participants by direct interview and using structured questionnaires. Informed consent was obtained from all participants. Age, sex, occupation, marital status was noted as per statement of the participants at the time of interview. History regarding smoking habit, hypertension, diabetes mellitus. History of any cardiovascular events (Myocardial infarction, stroke, heart failure,) was taken. Drug history regarding anti-hypertensive, anti-diabetic, lipid-lowering, and anti-ischaemic drugs was noted. Then the participants were examined for height, weight, blood pressure, anemia, and edema. Laboratory data that was collected including FBG, serum creatinine, fasting lipid profiles, serum calcium, serum phosphate.

Data was processed and analyzed using computer software SPSS (Statistical Package for Social Science) version 16. The Test statistics used to analyze the data are descriptive statistics, chi square test, Student's t-test. The descriptive statistics are frequency, mean, and standard deviation. Continuous data was presented as mean and standard deviation from the mean and was compared using student's t-test. Categorical data was expressed as percentage and evaluated using chi-square test. P value < 0.05 was considered significant.

Results

The Socio-demographic characteristics of the respondents are shown in Table-I. Majority of the subjects were in 41 to 60 years age group both in group –A (58.1%) and group-B (47.0%).

Table I

Socio-demographic details of the respondents

Characteristics		No of the study subjects	
		Group A(n = 62)	Group B(n= 66)
Age (in years)	21-40	7 (11.3 %)	15 (22.7 %)
	41-60	36 (58.1 %)	31 (47.0%)
	Ø 60	19 (30.6 %)	20 (30.3 %)
Sex	Male	37 (59.7 %)	40 (60.6)
	Female	25 (40.3 %)	26 (39.4 %)
Educational status	Illiterate	8 (12.9 %)	9 (13.6 %)
	Primary	27 (43.5 %)	14 (21.2 %)
	Secondary	16 (25.8 %)	30 (45.5 %)
	Higher secondary and above	11 (17.7 %)	13 (19.7 %)
Occupation	Housewife	23 (37.1 %)	18 (27.3)
	Business	17 (27.4 %)	13 (19.7 %)
	Service holder	10 (16.1 %)	24 (36.4 %)
	Farmer	6 (9.7 %)	3 (4.5 %)
	Others	6 (9.7 %)	8 (12.1 %)

There are various risk factors among the respondents of our study. group A and group B 54 (87.1%) and 21 (31.8%) patients were hypertensive in group A and group B respectively. proportion of smoker greater in group A 46.8% than group B 30% and statistically was not significant. in group A and group B 31 50%) and 37 56.1%) were diabetic and 31 (50%) and 29 (43.9%) were nondiabetic, respectively. . More than half of the patients were anaemic in both Groups (67.7% in group A and 65.2% in group B). But statistically it was not significant.

Average age, BMI, systolic blood pressure and diastolic blood pressure were more in group A than group B. But statistically these differences were not significant. Average Hemoglobin level was more in group B (9.19±2.11 (SD). But this difference was also statistically insignificant. On the other hand, Calcium level on average in group A was 8.50±1.28 (SD) and in group B was 8.05±1.21 (SD) and statistically this difference was significant. Similarly average phosphate level was more in group A i.e. 5.21±1.97(SD) than group B i.e. 4.43±1.22(SD) and statistically this difference was also significant.

On average cholesterol, LDL and triglyceride level were more in group B than group A. But statistically these differences were not significant. On the other hand, HDL level was more in group A than group B and it was also statistically insignificant difference. At the same time average LDL/HDL ratio was higher in group B (3.86±1.93) than group A (3.43±1.85). But it was not statistically significant.

Table II

Comparison of lipid profiles between two groups

Characteristics	Group- A (on haemodialysis) n =62 Mean±SD	Group –B (on conservative) n=66 Mean±SD	P value
Cholesterol mg/dl	196.85±46.57	212.30±66.46	0.133
HDL mg/dl	36.79±9.88	33.39±10.11	0.057
LDL mg/dl	114.66±40.85	119.18±46.71	0.562
Triglyceride mg/dl	181.94±121.59	218.98±108.63	0.071
LDL/HDL	3.43±1.85	3.86±1.93	0.203

Table III showed that among the group A patients average triglyceride level(182.22±74.81), total cholesterol level(207.57±42.46) and LDL level(137.87207.57±42.46) were higher in stage 4 CKD patients than stage 5 CKD patients. Average HDL level was higher in stage 5 CKD patients (36.97±8.77) than stage 4 CKD patients (36.48±11.72). Serum LDL level is significantly lower among the patients of CKD stage 4 than stage 5 (p=0.000).

Among the group B patients average triglyceride level(231.63±124.67) and LDL level(127.37±38.35) were higher in stage 4 CKD patients. But none of these two differences were statistically significant. On the other hand, average total cholesterol level (244.48±57.62) was higher in stage 3 CKD patients and it was statistically significant(p<0.005). On average HDL level(35.56±10.49) was higher in stage 5 patients. But this difference was not statistically significant.

Table V showed that average triglyceride and total cholesterol was more in group B(TG=231.63±124,T. Choles=211.21±62.97) than group A(TG=182.22±74.81, T. Choles= 207.57±42.46) among the patients with CKD stage 4. On the other hand, average HDL and LDL was more in group A(HDL=36.48±11.72, LDL=137.87±33.71) than group B. But all the differences were statistically insignificant.

In stage 5 CKD patients Total cholesterol and HDL was more in group A(T. cholesterol=190.54±48.25, HDL=36.97±8.77) than in group B (T. cholesterol=174.74±63.34, HDL=35.56±10.49). On the other hand, average Triglyceride and LDL level was more in group B(TG=189.05±86.62, LDL=107.68±45.82) than group A(TG=181.77±143.15, LDL=100.97±38.76). But these differences were statistically insignificant.

Table III

Lipid profile in different stages of CKD in Group A

CKD stage	Triglyceridemg/dl	Total Cholesterolmg/dl	HDLmg/dl	LDLmg/dl
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Stage 4	182.22±74.81	207.57±42.46	36.48±11.72	137.87±33.71
Stage 5	181.77±143.15	190.54±48.25	36.97±8.77	100.97±38.76
P value	0.989	0.166	0.85	0.000

Table IV

Pattern of lipid profile in different stages CKD patients in group B

CKD stage	Triglyceride	Total Cholesterol	HDL	LDL
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Stage 3	230.52±106.72	244.48±57.62	35.05±8.66	120.13±54.80
Stage 4	231.63±124.67	211.21±62.97	30.08±10.64	127.37±38.35
Stage 5	189.05±86.62	174.74±63.34	35.56±10.49	107.68±45.82
P value	0.369	0.002	0.132	0.393

Table V

Lipid profiles status and stage 4 CKD patients between two group

Group	Triglyceride	Total Cholesterol	HDL	LDL
	Mean SD(±)	Mean SD(±)	Mean SD(±)	Mean SD(±)
Group A	182.22±74.81	207.57±42.46	36.48±11.72	137.87±3.71
Group B	231.63±124.67	211.21±62.97	30.08±10.64	127.38±8.35
P value	0.108	0.818	0.056	0.325

Table VI

Lipid profiles status and stage 5 CKD patients between two groups

Group	Triglyceride Mean SD(±)	Total Cholesterol Mean SD(±)	HDL Mean SD(±)	LDL MeanSD(±)
Group A	181.77 ±143.15	190.54±48.25	36.97±8.77	100.97±38.76
Group B	189.05±86.62	174.74±63.34	35.56±10.49	107.68±45.82
P value	0.839	0.296	0.591	0.562

Discussion

Chronic kidney disease (CKD) is a public health problem worldwide because of the increasing prevalence of type 2 diabetes mellitus and atherosclerosis-related renal disease. This creates an important health care problem because a high proportion of these patients will need renal replacement therapy. [17] Outcomes of chronic kidney disease include not only kidney failure but also complications of decreased kidney function and cardiovascular disease.

The worldwide rise in the number of patient with CKD and consequent end-stage renal failure necessitating renal replacement therapy is threatening to reach great proportions over the next decade, and only a small number of countries have robust economies able to meet the challenges posed. A change in global approach to CKD from treatment of ESRD to much more aggressive primary and secondary prevention is therefore imperative. A global and concerted approach to CKD must be adopted in both more and less developed countries to avoid a major catastrophe.

Dyslipidemia is often observed in patients with CKD, resulting in abnormal concentrations and composition of plasma lipoproteins. The prominent features of uremic dyslipidemia are an increase in plasma triglycerides and cholesterol in nearly all lipoproteins, and a reduction in HDL cholesterol.

The underlying mechanisms behind hyper-triglyceridemia may indeed be multifactorial. Hypertriglyceridemia are indeed contribute to the progression of atherosclerosis and cardiovascular disease. Cardiovascular disease (CVD) is a major cause of mortality in patients with CKD, caused by numerous factors defined as traditional and uremia-related risk factors. One of these risk factors, dyslipidemia is often observed in patients with CKD, resulting in abnormal concentrations and composition of plasma lipoproteins. The prominent features of uremic dyslipidemia are an increase in plasma triglycerides, slight increase in LDL and total cholesterol with increase in nearly all lipoproteins, and a reduction in HDL cholesterol. Therefore, it is essential to study the putative mechanisms for uremic dyslipidemia, since optimal treatment is essential for the prevention or delay of cardiovascular complications in patients with CKD.

Although lipid metabolism disorders have been consistently shown to predict atherosclerosis progression and subsequent CVD in the general population, their clinical implications in CKD patients are less clear.

the clinical implications of dyslipidemia in CKD patients are not limited solely to the development of atherosclerotic CVD but may also include an impact on the progression of renal insufficiency. Results, however, have been inconsistent as studies have shown detrimental effects of high concentrations of triglycerides, triglyceride-rich lipoproteins, apoB and total cholesterol, low levels of HDL-cholesterol or no associations at all.[18]

On average cholesterol, LDL and triglyceride level were more in group B than group A. On the other hand, HDL level was more in group A than group B and it was also statistically insignificant difference. At the same time average LDL/HDL ratio was higher in group B than group A. But all these differences were statistically insignificant.

Among the group A patients average triglyceride, total cholesterol and LDL level were higher in stage 4 CKD patients than stage 5 CKD patients. Average HDL level was higher in stage 5 CKD patients than stage 4 CKD patients. Among the group B patients average triglyceride and LDL level were higher in stage 4 CKD patients. But none of these two differences were statistically significant. On the other hand, average total cholesterol level was higher in stage 3 CKD patients and it was statistically significant ($p<0.05$).

On average HDL level was higher in stage 5 patients. But this difference was not statistically significant. In group A LDL/HDL ratio was more in stage 4 CKD patients and it was statistically significant($p<0.05$). Average LDL/HDL ratio was highest in stage 4 CKD patients in group B and it was statistically significant ($p<0.05$).

When comparing the results of the present study with that by Khalid [19] in Pakistan on the pattern of dyslipidemia in patients with CKD the following observations could be made CKD, a very common disease, is accompanied by many complications. One of such complications is abnormality of lipids. The lipids are disturbed in a characteristic manner. This disturbed lipid pattern predisposes the patients to atherosclerotic complications and increased mortality due to cardiovascular and cerebrovascular diseases. In the study conducted to determine the pattern of dyslipidemias in patients of CRF. Fifty (50) patients diagnosed to have CRF were subjected to fasting lipid profile, irrespective of cause and sex. Maximum patients had elevated triglyceride levels (46%25). A considerable percentage (16%25) had decreased HDL levels and a small percentage had elevated LDL (4%25) hence the LDL/HDL level were elevated. Total lipids were found to be elevated in 04 patients (8%25). Total cholesterol was elevated in 08 patients (16%25). This disturbed lipid pattern has role in atherosclerosis. The patients of CRF who are already having disturbed endothelial function are more prone to it.

Similarly, a study done in Argentina,[20] on lipid abnormalities in chronic renal failure patients undergoing haemodialysis. Lipid abnormalities were common in patients with renal disease, probably contributing to the high incidence of cardiovascular diseases in this population. In the study they determined the plasma and erythrocyte lipid profile in patients with chronic renal failure (CRF) along 30 months under haemodialysis. They conclude that CRF patients under regular haemodialysis evidence a gradual deterioration in the fatty acid and triglyceride abnormalities, a finding that might be relevant to the risk of cardiovascular disease in this setting.

Although optimum care had been tried in every step of this study, still some limitations existed. Single hospital based study, small sample size, sampling technique, exclusion of CKD stage 1 & 2, cofounders are the major limitations of the study. Though there is no statistical significance between two groups, but overall lipid profile is good in the patients who are on haemodyalysis. Small sample size may not reflect the whole scenario by statistical significance. A multicentric prospective study involving larger number of study population giving adequate statistical power is recommended for conclusive comment on the possible factors associated with dyslipidaemia in CKD patients.

Conclusion

Dyslipidemia represents an integral component of CKD, but it level depends on treatment moralities. Our study had showed that mean lipid profile is better in patients of CKD on dialysis than those on conservative treatment, but there is no statistical signifcance as sample size very small. When planning therapeutic approaches for CKD patients lipid profile should always be taken into consideration and identification and treatment of it should be an integral part of CKD patients management protocol.

References

1. Whaley-connel AT, Sowers JR, Stevens LA. CKD in the United states: Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) 1999-2004. Am J Kidney Dis 2008;5(Suppl 2): S13-20.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 2002;39: S1-266.
3. Gowdak LH, Arantes RL, de Paula FJ, Krieger EM, De Lima JJ. Under use of American College of cardiology: American heart Association Guidelines in hemodialysis patients. Ren Fail 2007; 29(5): 559-65.
4. Maheshwari N, Ansari MR, Laghari MS, Darshana, Lal K, Ahmed K. Pattern of lipid profile in patients on maintenance haemodialysis. Saudi J Kid dis transpl 2010; 21(3): 365-570.
5. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3:1-150.
6. Goddard J, Turner AN, Stewart LH. Davidson's principles and practice of medicine: Kidney and urinary tract disease. 21th ed. Churchill Livingston; 2010; 487-492.
7. Kasiske BL. Hyperlipidemia in patients with chronic renal disease. Am J Kidney Dis 1998;32 (5 suppl 3): S 142- S156.
8. Attman PO, Knight-Gibson C, Tavella M, Alaupovic P. The compositional abnormalities of lipoproteins in diabetic renal failure. Nephrol Dial. Transplant 1998;13: 2833-41.
9. Adeera L, Hemmelgarn B, Evil eton B, Tobe S, Farlane PM, Ruzicka et al. Medical Guideline for the management of chronic kidney disease. CMAJ 2008; 179(11).
10. Attman PO, Samuelsson O, Johansson AC, Moberly JB, Alaupovic P. Dialysis modalities and dyslipidemia. Kidney Int Suppl 2003;84:S110-S112.
11. Quaschning T, Krane V, Metzger T, Wanner C. Abnormalities in uremic lipoprotein metabolism and its impact on cardiovascular disease. Am J Kidney Dis 2001; 38 (4 suppl 1): S 14- S19.

12. Attman PO, Samuelsson O, Alaupovic P. lipoprotein metabolism and renal failure. Am J Kidney Dis 1993; 21: 573-92.

13. National Kidney Foundation. K/DOQI clinical practice guidelines for managing dyslipidemias in chronic kidney disease. Am J Kidney Dis 2003; 41 (suppl 3): S1–S92.

14. Deighan CJ, Caslake MJ, Mc Connel M, Boulton JM, Packard CJ. Atherogenic lipoprotein phenotype in end stage renal failure origin and extent of small dense low density lipoprotein formation. Am J Kidney Dis 2000; 35: 852-62.

15. Harper CR, Jacobson TA. Hyperlipidaemia patient in chronic kidney disease. J Am Coll Cardio 2008; 51:2375-2384.

16. de Gomez Dumm NT, Giammona AM. Touceda LA, Raimondi C. Lipid abnormalities in chronic renal failure patients undergoing hemodailysis Medicina (Buenos Aires) 2001; 61:142-6.

17. Otero A, Gayoso P, Garcia F, Angel LD. Epidemiology of chronic renal disease in the Galician population: Results of the pilot Spanish EPIRCE study. Kidney International 2005; 68: S16–S19.

18. Chmielewski M, Carrero J, Nordforse L. Lipid disorders in chronic kidney disease: reverse epidemiology and therapeutic approach. JNEPHROL 2008; 21: 635-644.

19. Khalid Amin, Masud Javed, Muhammad Abid et al. Pattern of dyslipidaemia in patients with CRF. Professional Med J 2006 Jan-Mar; 13(1): 79-86.

20. Nelva T, Gomez, Ana M, Giammona L, Touceda et al. Medicina Lipid Abnormalities in CRF patients undergoing hemodialysis. Buenos Aires 2001; 61:142-146.