VOLUME-7, ISSUE-3, MARCH-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Nephrology

STUDY OF SEVERITY AND PATTERN OF DYSLIPEDEMIA IN CHRONIC KIDNEY DISEASE

Dr. Amit Shah — Associate Professor, Department of General Medicine, S.B.K.S & Medical institute and Research Centre, Sumandeep Vidyapeeth, Vadodara, Gujarat

Dr. Mrugal Doshi* — Junior Resident, Department of General Medicine, S.B.K.S & Medical institute and Research Centre, Sumandeep Vidyapeeth, Vadodara, Gujarat *Corresponding Author

Dr. Jaydutt Patel — Assistant Professor, Department of General Medicine, S.B.K.S & Medical institute and Research Centre, Sumandeep Vidyapeeth, Vadodara, Gujarat

Dr. Hetal Pandya — Professor and head, Department of General Medicine, S.B.K.S & Medical institute and Research Centre, Sumandeep Vidyapeeth, Vadodara, Gujarat

ABSTRACT

Introduction: Coronary artery disease is a major cause of morbidity and mortality in patients with Chronic Kidney Disease (CKD). Dyslipidemia is an established coronary artery disease in the general population. Patients with CKD exhibit significant alterations in lipoprotein metabolism, which in their most advanced form may result in the development of severe dyslipidemia which can lead to increased risk of cardiovascular complications. However, this relationship is less clear, and many studies show that low, rather than high, cholesterol levels predict mortality in this patient population. The aim of this study was to determine the prevalence and pattern of dyslipidemia in patients of CKD.

Method: This study was carried out in Dhiraj Hospital affiliated with SBKS MIRC after IEC approval, 50 patients of CKD according to KDOQI guidelines were enrolled after obtained written informed consent. Patients who were already diagnosed as having CAD, receiving haemodialysis, were on statin therapy were excluded from study. Detailed history and clinical examination done in all patients. Fasting lipid profile was done in all participants. Abnormality in any one of lipid components (Cholesterol, Triglyceride, HDL-C, LDL-C, VLDL) considered as dyslipidemia.

Result: Out of 50 patients of CKD , 27(54%) patients were having dyslipidemia according to NCEP-ATP III guidelines. No correlation were found between in age, gender, BMI, HTN, DM and addiction with occurance of dyslipidemia in CKD patients (P-value=<0.05). Mean values of all lipid components were in normal range except for VLDL. Most common lipid abnormality found was increased VLDL (30%) followed by hypertriglyceridemia (24%), decreased HDL-C in (18%), increased LDL-C in (10%). Hypercholesterolemia was detected in only 8% of patients. Mixed dyslipidemia was also noted. Hypertriglyceridemia + Increase VLDL was most common (25.9%) among them. Mean CR/CL was 10.18±5.95 for study population. Stage 5 CKD patients are having slightly more prevalence of dyslipidemia (57.5%) than stage 4 CKD (40%).

Conclusion: Higher prevalence of cardiovascular complications are found in CKD patients due to accelerated atherosclerosis leading to high risk of mortality. Dyslipidemia is one of the common risk factor for atherosclerotic changes in patients of CKD. This study confirms the high prevalence for of atherogenic lipid profile in patients of CKD which can lead to increased morbidity and mortality due to additional cardiovascular risks.

KEYWORDS : Chronic Kidney Disease, Dyslipidemia.

INTRODUCTION

Chronic Kidney Disease(CKD) is defined as per The kidney disease outcomes quality initiative ,2003, of the National Kidney Foundation [NKF] as either kidney damage or a decreased kidney glomerular filtration rate of less than 60ml/min/1.73m^2 for 3 or more months (chronic renal failure corresponds to CKD stages 3-5)[1]. The frequency of CKD continues to increase worldwide as does the prevalence of end-stage renal disease (ESRD). The reported prevalence of CKD stages 1-4 in the most recent NHANES (National Health And Nutrition Examination Survey) between 1999 and 2006 was 26 million (13%) out of approximately 200 million United States residents aged 20 and older. Of these, 65.3% had CKD stage 3 or 4. It has been presumed that nearly 100,000 new patients with ESRD in India require renal replacement therapy every year based on data from tertiary referral centers.[2]

Most of the CKD Patients have morbidity and mortality due to various complications of CKD. Coronary artery disease is one of the major cause of mortality and morbidity among patients with CKD. More than 50% of patient die due to cardio vascular complication[1]. An increased prevalence of both CVD morbidity and mortality is evident at all ages among patients with CKD.[2]Both traditional risk factors, including diabetes, dyslipidemia, and hypertension, and non-traditional risk factors associated with CKD, including inflammation, oxidant stress, malnutrition, and proteinuria, may further increase CVD risk. In recent times dyslipidemia has been identified as a major risk factor for coronary artery disease in chronic kidney disease patients. This has renewed interest in the identification and management of abnormalities in the plasma lipids and lipoproteins. There is limited data on pattern and severity of Dyslipidemia of CKD patients so this study has taken to compare and analyze dyslipidemia prevalence and pattern in CKD patients especially from our region.

Material & Method

This study was done on 50 patients of Chronic Kidney Disease who were diagnosed according to KDOQI guidelines after approval of Sumandeep Vidhyapeeth Institutional Ethics Committee (SVIEC). Patients having CAD before having CKD, who were on maintenance haemodialysis, on statin therapy, refused to give consent were excluded from the study. Detailed history related to the risk factors, presentation and complications was taken of all patients. Detailed general and physical examination including anthropometric measurement was carried out of all patients. All the patients were subjected to renal function test. Creatinine clearance was calculated as per Cockcroft-Gault equation and patients were classified in stages according to it.

Table No.1: Stages of CKD according to KDOQI guidelines.[1]

Stages of chronic kidney disease	Description	GFR in ml/min/1.73m2
1	Kidney damage with Normal or increased Glomerular Filtration Rate	>90

2	Kidney damage with mild decreased Glomerular filtration rate	60-89
3	Moderate decreased Glomerular filtration rate	30-59
4	Severe Decreased Glomerular filtration rate	15-29
5	Kidney failure	<15

Fasting lipid profile was done in all patients. Reference values for various lipid components were as per *NCEP- ATP* III Classification. Abnormality in any one of the lipid components is considered as dyslipidemia.

Table No. 2 *NCEP- ATP*-III Classification of LDL, Total, and HDL Cholesterol (mg/dL)

LDL - low-density lipoproteins		**Total Cholesterol**		**HDL** - high-density lipoproteins	
<100	Optimal	<200	Desirable	<40	Low
100-129	Near Optimal /Above Optimal	200-239	Borderline High	≥60	High
130-159	Borderline High	≥240	High		
160-189	High				
190	Very high				

Other routine investigation like haemoglobin, liver function test, serum electrolytes, urine examination, electrocardiography was done to all patients.

RESULT

Out of 50 patients of CKD, 27 patients were detected to have having dyslipidemia suggestive of 54% prevalence of dyslipidemia in my study. The mean age of study population is 48.90±13.80 years. There is minimal difference in mean age of dyslipidemia(Group-D) and normal lipid(Group-M) group (Dyslipidemia: 51.04±13.77 , Normal : 46.39±13.71, P-value : 0.2). but prevalence of dyslipidemia increases with advancing of age. There was 66.6% of prevalence of dyslipidemia in patients of above 60 years of age while 51% of prevalence of dyslipidemia was seen in below 60 years of age patients. The Male : Female ratio of study group is almost 3 : 2 and prevalence of dyslipidemia is marginally higher in males and in urban population which is statistically not significant. Risk factors like hypertension, diabetes mellitus and addiction to smoking or alcohol were not found to affect prevalence of dyslipidemia in CKD as p value for each of them was >0.05. All patients enrolled in the study were having severe renal impairment , all were in stage 4(10%) or stage 5 CKD(80%) as per NFK KDOQI guidelines.

TABLE NO.3: Basic characteristics of study participants.

Charestristic	Groups	Total (N=50)	Dyslipidemia (D=27)(54%)	Normal (M=23)(46%)	P-Value
Age	<35	6(12%)	3(50%)	3(50%)	0.70
	35-60	35(70%)	18(51.4%)	17(48.6%)	
	>60	9(18%)	6(66.6%)	3(33.3%)	
Sex	M	32(64%)	18(56.2%)	14(43.8%)	0.67
	F	18(36%)	9(50%)	9(50%)	
Locality	U	16(32%)	10(62.5%)	6(37.5%)	0.40
	R	34(68%)	17(50%)	17(50%)	
Bmi	<25	49(98%)	22(44.9%)	27(55.1%)	0.27
	25-30	1(2%)	0	1(100%)	
	>30	0	0	0	
Hypertension	YES	32(64%)	16(50%)	16(50%)	0.44
	NO	18(36%)	11(61.1%)	7(38.9%)	
Dm	YES	13(26%)	9(69.2%)	4(30.8%)	0.20
	NO	37(74%)	18(48.6%)	17(51.4%)	
Addiction	Smoker	17	9(52.9%)	8(47.1%)	0.91
	Alcoholic	12	7(58.3%)	5(41.6%)	0.73

Table No.4 Mean values of Different Lipids in all three groups.

LIPIDS	**Normal Values (mg/dl)**	**TOTAL (mg/dl) N=50**	**Dylipidemia (mg/dl) D=27**	**Normal (mg/dl) M=23**	**P- value (95%-CI)**
Cholesterol	<200	149.66± 34.76	159.04± 40.75	138.65± 22.22	0.037
Triglycerides	60-160	129.10± 65.51	157.00± 77.87	96.35± 17.79	0.001
Hdl	30-60	39.76± 10.02	37.81± 11.18	42.04± 8.12	0.139
Ldl	UP TO 110	81.14± 25.83	84.83± 31.68	76.81± 16.22	0.278
Vldl	UP TO 32	28.18± 13.19	34.28± 15.01	21.01± 4.67	<0.001
Ldl/Hdl	UP TO 4	2.18± 0.93	2.40± 1.10	1.92± 0.62	0.072
Chol: Hdl	UP TO 6	3.99± 1.33	4.47± 1.46	3.43± 0.89	0.004

Figure No.1: Pattern of dyslipidemia.

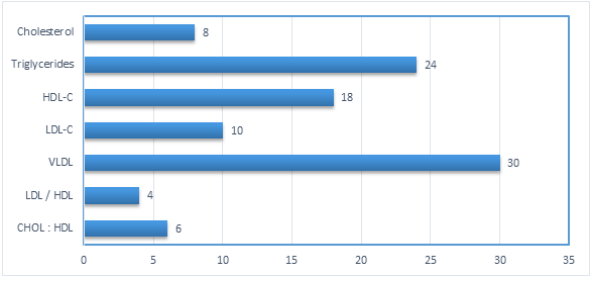
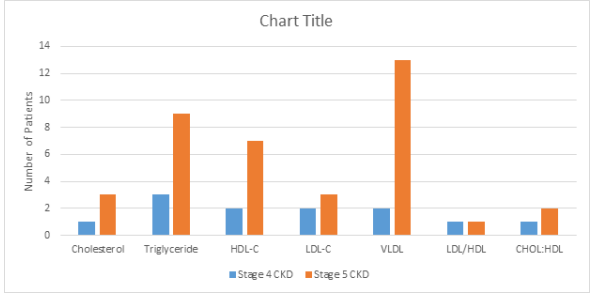


Figure No.2: Lipid components according to stages of CKD.



The prevalence of dyslipidemia in CKD patients is 54% in my study. Mean value of all lipid components were higher though within normal range in dyslipidemic group in comparison to non-dyslipidemic group. This difference is statistically significant for Serum cholesterol, triglyceride, VLDL, LDL/HDL, Cholesterol: HDL. (P-value = 0.03, 0.001, <0.001, 0.07, 0.004 respectively). (Table No.4). On analysis of different patterns of dyslipidemia, Increased VLDL is the most common type of dyslipidemia (30%), followed by increased triglyceride (24%), Decreased HDL (18%), Increased LDL (10%) respectively. Increased Serum cholesterol (8%) is the least observed abnormality in lipids in our CKD patients. (Figure No.1). Mix dyslipidemia also observed in many patients. Hypertriglyceridemia with Increase VLDL was most common (25.9%) followed by hypercholesterolemia with Increase VLDL has 7.49%. (Figure No.1). All study patients were either in stage 4 (20%) or in stage 5 (80%). Out of the stage 4 patients, 40% patients were having dyslipidemia. While 57.5% stage-5 CKD patients were having dyslipidemia. Increased VLDL and triglyceride levels were again found to have more derangement in severest form of CKD.

Discussion

Cardiovascular disease is a major cause of morbidity & mortality in patients with Chronic Kidney Disease. The prevalence of clinical coronary heart disease in CKD patients is 40% and CVD mortality is 10-30 times more than in the general population of the same

gender, age and race.[3] Patients with deranged renal function exhibit significant alteration in lipid metabolism, which involve all lipoprotein classes. Dyslipidemia is also been found to cause microscopic kidney damage & play an important role in progression of renal failure. In my study prevalence of dyslipidemia in CKD patients is 54%. Non-modifiable risk factors like age and gender were not found to be associated with occurrence of dyslipidemia in CKD in our study. Similar results were noted in *Gaurav G et al*[4] *& D.S.S.K. Raju et al*[5]. *Modifiable* risk factors like obesity, hypertension, and addiction like smoking and alcohol were not found to be more prevalence in CKD with dyslipidemia. Diabetic CKD patients were having high prevalence of dyslipidemia comparatively. It is a known fact that dyslipidemia is very common finding in type-2 diabetes, study done by *Hetal Pandya et al.*[6] in the same region had shown very high prevalence (82.4%) of diabetic dyslipidemia. Implications of dyslipidemia in diabetic CKD needs further large-scale study.

Most common lipid abnormality observed was increase in serum VLDL levels (30%) followed by Hypertriglyceridemia (24%). Hypertriglyceridemia is the most common documented quantitative lipid abnormality observed in CKD. Many studies had already demonstrated this findings[7,8,9]. It occurs due to increased synthesis and/or diminished clearance from the circulation. The concentrations of triglyceride-rich lipoproteins (VLDL, chylomicrons and their remnants) start to increase in early stages of CKD and show the highest values in nephrotic syndrome and in dialysis patients.[10] the predominant mechanism responsible for hypertriglyceridemia is defective metabolism of TG rich lipoproteins by lipoprotein lipase (LPL) and hepatic lipase. The decrease in enzyme activity may be due to down regulation of enzyme gene and presence of circulating inhibitors of lipolytic enzymes like pre βHDL in uremia and changes in concentration of apolipoprotein C-II (activator of LPL) and apolipoprotein C-III (inhibitor of LPL) with a decrease in apolipoprotein C-II/C-III ratio due to a disproportionate increase in plasma apolipoprotein C-III.[11] VLDL is one of the triglyceride rich lipoprotein. CKD is associated with impaired clearance of VLDL and chylomicrons too. This is due to dysregulation of Lipoprotein Lipase (LPL), hepatic lipase, VLDL receptor and impaired HDL metabolism leading to increased levels of VLDL-C. CKD is also associated with hepatic lipase deficiency, which appears to be caused by secondary hyperparathyroidism and dysregulation of cytosolic calcium leading to decreased VLDL clearance.[12] *Bagade et al.*[13] also had reported similar high prevalence of VLDL as in our study.

The mean value of serum cholesterol was 149.66±34.76 mg/dl in my study, which is within normal range for serum cholesterol according to NCEP-ATP III guidelines for dyslipidemia. Only 8% of our patients had hypercholesterolemia. Hypercholesterolemia in CKD is due to associated proteinuria and renal insufficiency per se. Most of previous studies like Attman et al.[14] and Tsumura et al.[15] had also shown only marginally increase level of serum cholesterol in CKD patients. Mean LDL-C of total patients was 81.14±25.83 mg/dl, which was again in normal range as per NCEP-ATP III guidelines. *Gaurav G et al*[4] & Bhagwat et al.[7] has shown marginal increase in LDL-C levels. However Ljulfi Z[16] and Bagade et al.[13] in their studies showed significant increase in LDL-C levels in CKD patients. In uremia there is decrease in catabolism of IDL and LDL leading to their increased plasma residence time. This reduced catabolism, however, is masked by the decreased production of LDL; resulting in near normal plasma levels of LDL in patients of CKD.[17]Mean HDL-C value in our study population was 39.76±10.02 mg/dl, which at lower normal range. This was in concordance with the results obtained by Bhagwat R[18] Massy et al[19] and Morena M et al.[20] Patients with CKD generally have reduced plasma HDL-C because they usually exhibit decreased levels of apolipoproteins A-I and A-II (the main protein constituents of HDL)21, diminished activity of Lecithin cholesterol acyltransferase (LCAT; the enzyme responsible for the esterification of free cholesterol in HDL particles)[21], as well as increased activity of cholesteryl ester transfer protein (CETP) that facilitates the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins thus reducing the serum concentrations of HDL-C.

Limitation of the study

All participants were having sevre renal impairment. Therefore It was very difficult to compare severity and pattern of dyslipidemia with severity of renal impairment.

Conclusion

Patients with CKD are subjected to accelerated atherosclerosis leading to increased cardiovascular complications. Several factors contribute to atherogenesis, most notable among which is dyslipidemia. This study confirms the presence of atherogenic lipid profile in patients of CKD which can lead to increased morbidity and mortality due to additional cardiovascular risks. Hence maintenance of desired lipid levels either through diet or early initiation of lipid lowering drugs can be helpful in decreasing the risk of cardiovascular complications in these patients.

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