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General Medicine

PREVALENCE AND PATTERN OF DYSLIPIDEMIA AND ITS ASSOCIATED FACTORS IN CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT A study of Lipid profile in CKD patient is subject of interest due to impact on the individual and society as dyslipidaemia is one of the traditional risk factors for CVD which is responsible for most of the morbidity & mortality in CKD patient. And its study can lead to therapeutical result affecting both short term and long-term outcomes. **AIMS & OBJECTIVE -** To identify and analyse lipid alteration in CKD patients and study the correlation between renal function and lipid abnormalities in CKD **METHODS –** Our study is hospital based descriptive observational study for duration of 18 months. **RESULTS –** Study included 100 patients in which mean age was 51.88 and male to female ratio of 1.5:1. Prevalence of Lipid Profile abnormalities seen as HDL decreased in 100% patient and Cholesterol, LDL, Triglyceride increased in 40%, 24%, 64% patients respectively **CONCLUSION -** Dyslipidaemia is common among patients with CKD and predominant lipid profile abnormalities were reduced HDL and elevated Triglycerides. Hence regular monitoring of lipid profile should be done in patients of CKD

KEYWORDS : chronic kidney disease (CKD), Dyslipidaemia, Cardiovascular disease (CVD)

INTRODUCTION

Cardiovascular disease (CVD) is a major cause of mortality in patients with mild to moderate chronic kidney disease (CKD) and End stage renal disease (ESRD). [1, 2] Dyslipidaemia has been established as a well-known traditional risk factor for atherosclerosis and thus for CVD development.

CKD is associated with a dyslipidaemia and its prevalence is higher than in the general population, but varies depending on the type of lipid, target population, cause of renal disease and level of renal function.[3] Disturbances in lipoprotein metabolism are evident even at early stages of CKD and usually follow a downhill course that parallels the decline of renal function.[4] Hypertriglyceridemia is most common lipid abnormality in CKD patient.

Renal Dyslipidaemia is characterized by dysregulation of the synthesis and activity of High density lipoproteins(HDL) and of the metabolism of Triglyceride(Tg) rich apo-lipoprotein(apo-B) containing lipoproteins which lead to elevated plasma levels of Tg and depressed levels of HDL,[5] a pattern similar to that in patients with nephrotic syndrome who have increased levels of VLDL and LDL as well.[6] In patients on HD, there may be lower levels of serum total cholesterol due to malnutrition and inflammation.

JUSTIFICATION OF STUDY

CKD is an independent risk factor for CVD. Another independent risk factor for CVD is dyslipidemia which is a common finding in CKD patients resulting in a high cumulative risk for CVD in these patients and mortality as high as 50% in them even before reaching end stage renal disease. As such there is need to determine the prevalence as well as pattern of dyslipidemia in the CKD population in the different stages to enable adequate and rational therapy be instituted and at the appropriate time in order to reduce cardiovascular mortality in CKD patients.

AIMS AND OBJECTIVES OF THE STUDY

1. To identify & analyse lipid alteration in CKD patients.
2. To study the correlation between renal function and lipid abnormalities in CKD

MATERIAL AND METHOD

This was a descriptive observational study of lipid profile in CKD patient. The study was conducted in Department of Medicine at SKN Medical college and General Hospital during a period of 18 months. The case record of 100 patient were reviewed who met inclusion and exclusion criteria

Inclusion criteria:

1. Patients between age group of 40 to 80 years with established CKD.
2. Patients on conservative treatment and on dialysis.

Exclusion criteria:

1. Pregnant women.
2. Patients with acute renal failure, nephrotic syndrome.
3. Who are on drugs β blockers, statins and oral contraceptive pills.
4. Patients not willing to fill consent form.

Data was recorded according to prespecified protocol. The data was registered as demographic characteristics, history regarding symptoms and duration of the kidney disease, hypertension, diabetes, smoking, alcoholism, drug intake & treatment, detailed clinical examination and diagnostic data.

Patient underwent Lipid profile estimation after 12 hours of overnight fasting. The following test were also done Fasting blood glucose and post prandial (mg/dL), HbA1c, Hemogram, RFT with electrolytes, Urine routine, Estimated Glomerular filtration rate (eGFR) as assessed by CKD-EPI, LFT with enzymes.

In this study
LDL > 130 mg/dl
HDL < 60 mg/dl
TGL > 150 mg/dl
TC > 200 mg/dl were considered abnormal

RESULTS

Study included 100 CKD patient of which age variation is 40 to 80 years and maximum number of patients were in age group of 46 to 55 years with Mean age of 51.88. In this study 60% were Male and 40% were female with Male to Female ratio is 1.5:1. Of 100 patient 22 patient were in stage 3 (egfr - 30 to 59ml/min), 56 patients were in Stage 4 (egfr - 15 to 29ml/min), 22 patients were in stage 5.

Lowest urea level found in these patients was 38 and highest was 158 and creat value ranged from 1.3 to 13.7 mg/dl.

CKD patient showed following lipid disorder

TABLE NO 1 – Sex wise distribution of Lipid abnormalities

	MALE (n = 60)		FEMALE (n = 40)		TOTAL (n = 100)	
	NO	%	NO	%	NO	%
↑ CHOLESTEROL	22	36.67	18	45	40	40
↓ HDL	60	100	40	100	100	100
↑ LDL	16	26.67	8	20	24	24
↑ TRIGLYCERIDE	22	36.67	30	75	64	64

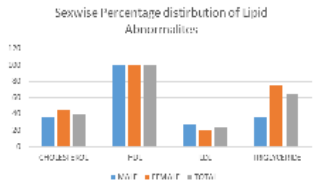

FIGURE NO – 1

TABLE NO 2 - Correlation between Lipid fraction and CKD stages

	STAGE 3	STAGE 4	STAGE 5
↑ CHOLESTEROL	6	24	10
↓ HDL	22	56	22
↑ LDL	4	12	8
↑ TRIGLYCERIDE	14	40	12

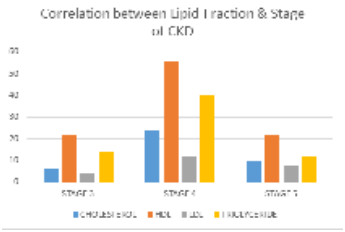

FIGURE NO – 2

DISSCUSSION

The results from the survey of 100 patients stated decreased levels of HDL in all patients and hypertriglyceridemia in significant number of patients.

DECREASED HDL LEVELS

Low levels of HDL in (<60 mg/dl) were found to be in 100% patients in this study.

The low HDL levels in patients with CKD in our study were consistent with Mikolasevic I, Žutelija M, Mavrinac V, Orlic L who studied the etiology of dyslipidaemia in CKD patients.[15] This low HDL cholesterol levels were also an independent risk factor for the development of CKD in the Framingham off spring study.

Several mechanisms may underlie these reductions in HDL cholesterol levels, which is usually an indication of impaired reverse cholesterol transport.

Apo AI, which is the activator of lecithin cholesterol acyltransferase (LACT), is reduced in CKD due to down regulation of hepatic Apo AI genes leads to decline in the activity of LACT, which causes reduced cholesterol esterification and impairment of HDL maturation. The activity of LACT is consistently diminished in CKD, so there is decrease in HDL according to Vaziri ND, Liang K, Parks JS. Down regulation of hepatic lecithin: cholesterol acyltransferase gene expression in chronic renal failure.[7]

In MDRD study LAWRENCE G. HUNSICKER et al: Predictors of the progression of renal disease in the modification of diet in renal disease study.[8] Low HDL levels in CKD patients were one of the independent risk factors for progression of kidney disease.

ELEVATED TRIGLYCERIDES

Abnormal triglyceride levels (>150 mg/dl) were found in 64 out of 100 patients Significantly elevated triglyceride levels were found in this study group attributing to the dysfunctional lipid metabolism on similar lines with the study of Alterations of Fatty Acid Profile may contribute to Dyslipidaemia in CKD by Influencing hepatocyte metabolism by Aleksandra Czumaj, Tomasz Śledziński, Juan-Jesus Carrero, Piotr Stepnowski, Malgorzata Sikorska - Wisniewska, Michal Chmielewski and Adriana Mika.[14]

The present study demonstrates that CKD is commonly accompanied by lipid abnormality in the form of hypertriglyceridemia. This is similar to the observations made in Western studies and recent Indian studies by Gupta DK, Das BS and Bagdae J. [8, 9, 10] Elevated triglyceride levels are due to impaired activity lipoprotein lipase (LPL) and direct inhibitory effect of various uremic 'toxins' on the enzymes involved in lipid metabolism represent the most important pathophysiological mechanisms underlying the development of hypertriglyceridemia in renal failure. Chan MK et al [11] also found hypertriglyceridemia was the major abnormality in their studies. Hypertriglyceridemia represents an early feature of renal failure.

Patients with CKD usually have hypertriglyceridemia due to an increased concentration of triglyceride-rich lipoproteins (VLDL, chylomicrons, and their remnants).

Hypertriglyceridemia occurs because of both the delayed catabolism and the increased hepatic production of triglyceride-rich lipoproteins. Delayed catabolism is the most prevalent mechanism responsible for an elevated triglyceride-rich lipoprotein concentration in CKD patients and occurs probably because of a decreased activity of hepatic triglyceride lipase and peripheral lipoprotein lipase. Also, the presence of lipase inhibitors may contribute to delayed triglyceride-rich lipoprotein catabolism. Apolipoprotein C-III (apoC-III) is a direct lipoprotein lipase inhibitor, and its levels are elevated in uraemia which further contributes to hypertriglyceridemia.

ELEVATED LDL

Around 24 patients showed high LDL levels in this study group. Most studies find that Uremic Patients usually have normal or slightly reduced concentrations of LDL-C levels and they exhibit important disturbance in the density distribution of LDL sub fraction that is characterized by a predominance of small dense LDL particles according to Rajman I, Harper L, McPake D, Kendall MJ, Wheeler DC.[12]

TOTAL CHOLESTEROL

Total cholesterol levels were elevated in 40 patients in our study group Heavy proteinuria alone or in combination with CKD results in acquired LDL receptor deficiency, which plays a central role in the genesis of the associated hypercholesterolemia.

In our study group, total cholesterol is even normal or low in some patient and this finding is consistent with the study of Liu Y, Coresh J, Eustace JA et al and this may be the result of an additional microinflammatory state and/or malnutrition. [13]

PCSK9 inhibitors

The PCSK9 inhibitors are a class of monoclonal antibodies which reduce LDL cholesterol by inhibiting degradation of LDL receptors resulting in more receptors recycled to the hepatocyte surface and subsequent reduction in circulating LDL cholesterol levels. The safety and clinical efficacy of the two commercially available agents has been well established in large randomized control trials There are currently two PCSK9 inhibitors available commercially, evolocumab and alirocumab.

Correlation Studies:

It was found that abnormal serum triglycerides, TC, HDL, were found to be increased significantly in the group of eGFR between15-29ml

LIMITATIONS OF THE STUDY

1. Smoking, alcoholism and diabetics may alter the lipid pattern in the body. Their influences in the study group also have to be considered.
2. Since we had not analysed the electrocardiogram & echocardiogram of the patients, the real scenario of ischemia in CKD patients was not known.
3. We had not estimated the lipid abnormalities in patients who underwent renal transplantation.
4. We had not done PCSK9 enzyme assay due to availability issue.

CONCLUSION

Major cause of mortality in end stage renal disease is CVD.
Dyslipidaemia is a major risk factor for cardiovascular morbidity and mortality and is common among patients with CKD. Predominant lipid profile abnormalities were reduced High Density Lipoprotein-Cholesterol and elevated Triglycerides. Hence it can be concluded that regular monitoring of lipid profile should be done in patients of CKD. Timely diagnosis and treatment with lipid lowering agents may help to reduce cardiovascular morbidity and mortality in patients with CKD.

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