ejpmr, 2022,9(1), 248-252

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

AN EVALUATION OF DYSLIPIDEMIA IN CHRONIC KIDNEY DISEASE AND ITS CORELATION TO STAGES OF CHRONIC KIDNEY DISEASE

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Article Received on 10/11/2021 **Article Revised on 30/11/2021** **Article Accepted on 20/12/2021**

BACKGROUND

In Osmania General Hospital, Lipid analysis is done in fasting state mainly for patients having risk of poor cardiovascular outcome. Experimental and clinical studies have suggested a correlation between the progression of renal disease and dyslipidemia. High Plasma cholesterol, LDL and Triglyceride level and low HDL level have been demonstrated to be independent risk factors for progression of renal disease from CKD stages 1-5 in humans. We conducted this study to evaluate the lipid abnormalities in various stages of chronic kidney disease on the background of these references. We used CKD -EPI formula to calculate the predicted creatinine clearance which is a rough estimation of G.F.R. in staging of Kidney disease.

KEYWORDS: Chronic Kidney Disease, Low Density Lipoprotein, High Density Lipoprotein, Triglycerides, Diabetes Mellitus.

INTRODUCTION

Cardiovascular disease is a major cause of mortality in patients with mild to moderate kidney disease and end stage renal disease [ESRD]. Chronic kidney disease (CKD) is associated with a dyslipidemia comprising high triglycerides, low HDL-cholesterol and altered lipoprotein composition. The principal reason to evaluate dyslipidemias in patients with chronic kidney disease is to detect abnormalities that may be treated to reduce the incidence of cardiovascular disease.[1]

Since chronic Kidney disease is a progressive disease, the various lipid abnormalities vary from CKD stages 1-5. So it is prudent to look into various lipid abnormalities attributed to each stages of kidney disease.[2]

In our hospital, there are many patients admitted last year fulfilling the criteria for chronic kidney disease and treated as inpatient or outpatient.

At present the medical treatment for kidney disease is improving and patients long term survival is improving. Peritoneal dialysis, hemodialysis and transplantation have revolutioned the prognosis of chronic kidney disease in recent time. Although there is still controversy whether CKD represents an independent risk factor for incident cardiovascular disease, accumulating evidence over the last decade marks out cardiovascular disease as major cause of mortality in patients with mild to moderate CKD or ESRD.[3]

Dyslipidemia has been established as a well known traditional risk factor for cardiovascular disease in the General Population and large scale observational studies have shown that patients with impaired renal function exhibit significant alterations in lipoprotein metabolism, which in their most advanced form may result in the development of severe Dyslipidemia.[4]

The Study mainly focuses on the lipid abnormalities attributed to different stages of chronic kidney disease

Aim of the Study

1. To analyze the lipid abnormalities in Patients with Non Diabetic Chronic Kidney Disease.
2. To find the correlation in various stages of Chronic Kidney disease with Lipid abnormalities.
3. To find which lipid abnormalities is more common in the study group.

MATERIAL AND METHODS

This study was conducted in Osmania General Hospital. Hyderabad Patients are selected from all medical wards. By applying the inclusion and exclusion criteria, we selected 50 patients for our study among them.

Inclusion criteria

1. All newly detected Non diabetic Chronic kidney disease from Sep 2017-2020
2. Age Group 15-65yrs.
3. Elevated Renal Parameters with Urea: Creatinine ratio <20.

4. Stable creatinine values taken 4 days apart with variation less than20 %.
5. Ultrasonographic evidence of Chronic Kidney Disease with kidney size less or equal to 9cm.
6. Normal Values of LDL< 100mg/dl, HDL <40 [M]<50[F]mg/dl;
7. T. Chol<200mg/dl,TGL-150 mg/dl has been taken cut- off range for this study.

Exclusion Criteria

1. Patients with known h/o diabetes mellitus and patients with Diabetic kidney. disease, with elevated random blood sugar values of >200mg% were excluded.
2. Ischemic heart disease on treatment already were excluded
3. Severe Comorbid conditions like pneumonia, alcoholic Liver disease and hypotension.
4. Those who are taking Beta blocker and thiazide diuretics at time of study were excluded.
5. Patients with H/o intake of anti cholestrelomic agents.
6. H/O cigarette smoking.
7. Patients with the features of hypothyroidism and obstructiveLiver disease.
8. Patients with previous H/o hemodialysis and peritoneal dialysis

RESULTS

Table-1: Percentage distribution of sex wise study subjects according to their age.

Age group (yrs)	Male		Female		Total	
	No	%	No	%	No	%
15 – 29	1	2.0	3	6.0	4	8.0
30 – 44	8	16.0	3	6.0	11	22.0
45 – 59	16	32.0	6	12.0	22	44.0
60 and above	8	16.0	5	10.0	13	26.0
Total	33	66.0	17	34.0	50	100. 0

Table 2: Sex wise percentage distribution of hypertensive changes in fundus.

Funds Changes	Male		Female		Significance	Total	
	N o	%	No	%		No	%
Normal	7	31.8	3	33.3	P>0.05	10	32.3
Grade I	9	40.9	3	33.3	P>0.05	12	38.7
Grade II	6	27.3	3	33.3	P>0.05	9	29.0
Grade III	Nil	-	Nil	-			
Papilledema	Nil	-	Nil	-			
Total	22	100.0	9	100.0		31	100.0

Table 3: Percentage distribution of E.C.G. classification according to their sex.

ECG	Male		Female		Significance	Total	
	No	%	No	%		No	%
Normal	21	63.6	10	58.8	P>0.05	31	62.0
LVH	7	21.2	5	29.4	P>0.05	12	24.0
Hyperakalemi a (Tall T waves)	5	15.2	2	11.8	P>0.05	7	14.0
Total	33	100.0	17	100.0		50	100.0

Table 4: Sex wise classification and analysis of creatinine clearance.

Creatinine Clearance	Male		Female		Significance	Total	
	No	%	No	%		No	%
<10	12	36.4	6	35.3	P>0.05	18	36.0
10 - 20	4	12.1	6	35.3	P>0.05	10	20.0
20 - 30	8	24.2	4	23.5	P>0.05	12	24.0
30 - 40	9	27.3	1	5.9	P<0.05	10	20.0
40 and above	Nil	-	Nil	Nil	-	Nil	Nil
Total	33	100.0	17	100.0	-	50	100.0

Table 5: Sex wise percentage distribution of staging of kidney diseases.

Stages of Kidney disease	Male		Female		Significance	Total	
	No	%	No	%		N o	%
Stage - III	9	27.3	1	5.8	P<0.05	10	20.0
Stage - IV	11	33.3	8	47.1	P>0.05	19	38.0
Stage - V	13	39.4	8	47.1	P>0.05	21	42.0
Total	33	100.0	17	100.0		50	100.0

Table -6: Decreased level HDL among the study subjects according to their sex and stage.

Stages	Male		Female		Significance	Total	
	No	%	No	%		No	%
III	5	22.7	1	7.7	P>0.05	6	17.1
IV	8	36.4	7	53.8	P>0.05	15	42.9
V	9	40.9	5	38.5	P>0.05	14	40.0
Total	22	100.0	13	100.0	-	35	100.0

Table 7: Analysis and assessment of sex wise and stage wise LDL level in CKD cases.

Stage	Male			Female			Mean difference	Signi-ficance	Total	
	n	Mean	S.D	n	Mean	S.D			Mean	S.D
III	9	100.6	37.1	1	59.0	0.0	41.6	P<0.01	96.4	37.4
IV	11	103.7	56.4	8	124.6	54.8	20.9	P>0.05	112.5	55.2
V	13	118.3	31.9	8	106.9	49.8	11.4	P>0.05	114.0	38.9
Total	**33**	**108.6**	**42.2**	**17**	**112.4**	**51.7**	**3.8**	**P>0.05**	**109.9**	**45.2**

Table 8: Analysis and assessment of TGL in stage wise and sex wise.

Stage	Male			Female			Mean difference	Signi Ficanc e	Total	
	n	Mean	S.D	N	Mean	S.D			Mean	S.D
III	9	133.2	62.1	1	102.0	0.0	31.2	P<0.01	130.1	59.4
IV	11	141.0	55.3	8	148.8	67.2	7.8	P>0.05	144.3	58.9
V	13	162.4	69.4	8	129.5	40.7	32.9	P>0.05	149.8	61.1
Total	33	147.3	62.4	17	136.9	53.6	10.4	P>0.05	143.8	59.2

Table 9: Analyses and assessment of HDL level among the CKD cases sex wise and stage wise.

Stage	Male			Female			Mean differenc e	Signi ficanc e	Total	
	n	Mean	S.D	N	Mean	S.D			Mean	S.D
III	9	40.2	8.2	1	30.0	0.0	10.2	P>0.01	39.2	8.4
IV	11	36.2	7.5	8	39.1	7.5	2.9	P>0.05	37.4	7.4
V	13	36.0	5.2	8	46.0	9.1	10.0	P<0.05	39.8	8.6
Total	33	37.2	7.1	17	41.8	9.0	4.6	P>0.05	38.8	8.0

Table 10: Stage wise comparison of lipid abnormalities.

Lipids	Stage	III n=10	Stage IV n=19		Stage V n=2[g]		Anov a F	Significan t
	Mean	S.D	Mea n	S.D	Mean	S.D		
HDL	39.2	8.4	37.4	7.4	39.8	8.6	0.464	P>0.05
TGL	130.1	59.4	144.3	58.9	149.8	61.1	0.369	P>0.05
LDL	96.4	37.4	112.5	55.2	114.0	38.9	0.553	P>0.05

DISCUSSION

Chronic kidney disease (CKD) results in profound dysregulation of several key enzymes and metabolic pathways that eventually contributes to disordered high-density lipoprotein (HDL) cholesterol and triglyceride-rich lipoproteins. With the progression of CKD, these metabolic derangements may be further worsened and participate in atherogenic diathesis and possibly renal functional progression itself. Published data regarding the relationship between dyslipidemia and renal outcomes in moderate to advanced CKD stages are limited.[5]

In our study had taken the study population from the low socio economic status group. After satisfying the inclusion and exclusion criteria we analysed the lipid abnormalities in all stages of chronic kidney disease, since. We have no study group fits into stage I and II kidney disease, we analyze the other 3 stages of CKD. The decrease in HDL was found to be present in stage III, IV and V stages of CKD amounting to 70% of total. The decrease in HDL observed in 3 group (mean 39.2,

37.4, 39.8) respectively are not statistically significant in severity when compared with stages (P>0.05). Similarly rise in TGL observed in III IV and V stage of CKD having mean value (130.1, 144.3, 149.8) respectively are not statistically significant in severity when compared with stages (P>0.05). The increase in TGL in all stages of CKD amounting to 36% total. The rise in LDL obtained in III, IV and Vth stages of CKD having mean value (96.4, 112.5, 114.0) respectively, on comparison are not statistically significant (P>0.05). We found lipid abnormalities in form of increased TGL, increased LDL and decreased HDL in study group in all stage of CKD.

Similar studies were done by Choudhary N. et al in a total of 100 patients which had results showing TC, TG, LDL-C and VLDL-C in increasing trend with progression of CKD stages (3 to 5), while HDL value was in decreasing trend.[6]

In Indian studies, there is no evidence of hypercholesteremia in earlier stages but in ESRD, cholesterol is either normal or reduced whereas western studies have reported hypercholesteremia to be present predominantly in all CKD groups. This could be due to difference in dietary habits[7]. In our study there were no patients in the stage 1 & 2 reflecting results of previous studies. This trend suggests that majority of patients in our setup present with advanced disease.

Rao et al studied pattern of lipoprotein abnormalities in ckd patients. He also showed that in non-dialyzed patients with CKD serum levels are significantly high in triglycerides, VLDL cholesterol, Lp(a), apo B and low in apo A at all the stages. However, HDL cholesterol level was reduced in all the groups but statistically not significant. This study reflects same results as our study.[7]

Statins are medications that are very often prescribed for lipid lowering in the general population, and various large, randomized, prospective studies have shown that their use leads to significant decrease in cardiovascular events. KDIGO guidelines recommend treatment with a statin or statin/ezetimibe combination in adults aged >50 years with eGFR <60 mL/min/1.73 m^2 who are not treated with chronic dialysis or kidney transplantation (GFR categories G3a-G5).[8]

A cross sectional study in China in 2000 patients by Wang et al showed aprogressive increase in serum triglyceride levels with increase in stage of ckd. These results were consistent with our study showing increase in TG levels although rise is not significant.[9]

Zubovic et al studied variation of triglycerides in various stages of ckd. Average cholesterol levels does not statistically significantly change with progression of chronic renal disease. Triglyceride levels in serum begins to increase in the early stage of chronic renal disease and reach the peak in stage IV. But in our study we have maximum increase in TG levels in stage V in men and stage IV in women. Triglyceride levels in serum begins to increase in the early stages of chronic kidney disease, and the highest value are achieved in stages IV and V.[10]

Kim et al studied on total cholesterol and CKD relation either ways. His experience showed total cholesterol variability is a risk factor for ESRD as well as for myocardial infarction, stroke, and all-cause mortality. A significant relationship was observed between TC variability and progression to ESRD. He also quoted that lipid variability accelerates renal disease progression or that renal disease increases lipid variability. Patients with impaired renal function exhibit increased concentrations of triglycerides, even when their serum creatinine levels are within normal limits. People with more significant renal disease might have greater TC variability because of changes in their lipid metabolism.[11]

Our study showed that with increase in stage HDL levels gradually decrease although this decrease is not significant statistically, it can be observed this is the most common abnormality in our study, Studies clearly indicate that HDL particles can lose their normal biological activities and acquire impaired properties as a result of perturbations in metabolism and composition. These alterations in HDL structure are characteristic for CKD and other pathological conditions associated with inflammation, infection or oxidative stress. Chronic kidney disease, especially in advanced stages, affects the ability of HDL to accept free cholesterol and phospholipids from peripheral tissues, to control inflammation and oxidation, and to support the endothelium.[12,13]

Maofi et al conducted a study in children aimed at evaluating the serum lipid profile in apparently healthy children and adolescents to find whether there is a relation between dyslipidemia and changes in GFR. The findings showed that increased TC, TG, and LDL-C are the strong negative determinants of eGFR after adjustment for age, gender, weight, BMI, blood glucose and systolic pressure. This study gives some evidence how the reciprocal relationship of ckd and dyslipidemia exit.[14]

Chen et al in his paper quoted that plasma levels of saturated fatty acids including tetracosanoic acid, octadecanamide, palmitic amide and palmitoylcarnitine were significantly increased, whereas polyunsaturated fatty acids (PUFA), including docosatrienoic acid level, were significantly decreased in CKD rats. This is consistent with earlier studies that have shown marked elevation of plasma free fatty acids and saturated fatty acids in the pre-hemodialysis blood samples from end-stage renal disease patients compared with controls. In fact, blood level of saturated fatty acids has been shown to be associated with the odds of sudden cardiac death in patients maintained on hemodialysis. *In vitro* experiments they found that inhibition of fatty acid

oxidation in cultured renal tubular epithelial cells caused ATP depletion, cell death, dedifferentiation and intracellular lipid deposition, phenotypes observed in fibrosis. In contrast, restoration of fatty acid metabolism by genetic or pharmacological methods protected mice from tubulointerstitial fibrosis.

So overall with the progression to higher stage of CKD there is increase in the severity of lipid abnormalities although some of them are not statistically not significant still we need explore the biochemical mechanisms of these molecules in causing atherogenic vascular disease and significant mortality and morbidity.

CONCLUSION

1. The lipid abnormalities are found to occur in all stages of chronic kidney disease.
2. The Reduction in HDL is the most observed lipid abnormality.
3. The lipid abnormalities started to occur even in the earlier stages of chronic kidney disease.
4. However the severity of chronic kidney disease did not correlate with the severity of lipid abnormalities and it was found to be statistically insignificant.

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