

Original Research Article

Dyslipidemia in chronic kidney disease excluding diabetic and nephrotic aetiology

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ABSTRACT

Background: Dyslipidemia is hypothesized as one of the risk factor of chronic kidney disease and plays an important role in the progression of renal failure. The present study was conducted to assess the association between ratio of TG/HDL-C and CKD and other abnormalities in the lipid profile in CKD patients.

Methods: This case-control study was conducted in Government General Hospital from July 2013 to November 2013. 100 patients with CKD were included as study cases. 100 healthy patients from the same hospital, who came with different illness other than the study disease were included as controls. Fasting lipid profile was done – total cholesterol, triglycerides and high-density lipoproteins (HDL) were measured and low-density lipoproteins, & TG/HDL ratio were calculated. Comparison of lipid parameters among study and control groups was done. P value <0.05 was considered as statistically significant.

Results: Majority of the study patients were under the age group of 40-50 years. Male dominance (86%) was seen in the study group. The association of HDL, LDL, TGL, TGL/HDL, TC parameters and stages of CKD was observed and found to be statistically significant (p value <0.0001 and <0.05). Comparison of lipid parameters among study and control groups were done and difference was found to be statistically significant (p value <0.0001).

Conclusions: Dyslipidemia should be treated in early stages of CKD to prevent secondary complications.

Keywords: Cardiovascular disease, Chronic Kidney disease, Lipid abnormalities

INTRODUCTION

Chronic kidney disease (CKD) is defined as “decline in renal function attributed to changes either in the structure of kidney or its function as evident by imaging or biochemistry respectively, in a person for more than 90 days duration” with its implications for health.¹ In CKD, not only there is decline in excretory function, as the disease process affects the kidney as a whole which is evident by decline in other functions like endocrine functions (decreased erythropoietin production), metabolic functions (acid base balance). According to WHO, CKD is one among the major causes leading to mortality (12th major cause) and morbidity (17th major

cause).² Detection of new cases of stage 5 CKD is increasing at a rate of 8% per year.³

Hypertension and diabetes are the major forerunners of CKD. India is one of the leading nations in terms of prevalence of diabetes and hypertension. So naturally ESRD burden will be increasing at an alarming pace. In 2030, India will have a prevalence of 79.4million cases.⁴

One of the leading cause for death in stage 5 CKD patients is secondary cardio vascular problems associated with natural history of disease process. Relative risk of CVD in patients with CKD ranges between 10-200. This implies the chance of developing cardiovascular event is

10 to 200 times higher in CKD patients when compared to the control group of same age and sex.

The most common dyslipidemia seen in CKD patients are elevated triglycerides (TGL) and low high density lipoproteins (HDL). This change seen in CKD patients highly favours and accelerates the process of atherosclerosis.⁵ Dyslipidemia is a marker of disease progression per se regardless of the cause and contributes to high risk of cardiovascular disease (CVD).^{6,7} Increased levels of lipoprotein (a) are also common in CKD.⁸

In CKD there is progressive increase in levels of TGL and decrease in HDL levels. The TG/HDL-C ratio is a far better indicator of insulin resistance and adverse cardiovascular events than the other lipid parameters including low density lipoproteins (LDL)-C, TG or the ratio of total cholesterol (TC) to HDL-C. Further, the ratio of TG/HDL-C correlates very well with concentration of small, dense LDL-C particles, which are more prone to oxidization and are highly atherogenic. Thus, it is conceivable that elevated TG/HDL-C ratio may also indicate the progression and development of CKD, since similar pathogenic mechanisms are involved in both atherosclerosis and glomerulosclerosis.

This case-control was conducted to assess the association between ratio of TG/HDL-C and CKD and other abnormalities in the lipid profile in CKD patients.

METHODS

This was a case control study conducted in Government General Hospital from July 2013 to November 2013. Study population includes 100 patients with chronic kidney disease (CKD). Controls include age & sex matched 100 normal healthy controls from the same hospital, who came with different illness other than the study disease.

Selection criteria for cases

Inclusion criteria

CKD patients in stage III-V, irrespective of aetiology except nephrotic proteinuria and diabetes mellitus on conservative management were included in the study.

Exclusion criteria for both cases and controls

Patients who are obese, with diabetes mellitus, those on beta-blockers and oral contraceptive pills, pregnant patients, renal transplant patients, patients on dialysis, patients with nephrotic proteinuria were excluded from the study.

In the proforma, detailed history regarding the presenting symptoms like fatigue, weakness, pruritis, anorexia, nausea, vomiting, nocturia, polyuria, oliguria, insomnia, oedema, difficulty in breathing, etc., was noted. Past

history and history of dialysis was obtained. General examination including pallor, pulse rate, blood pressure, height and weight were noted, and BMI calculated. Cardiovascular system, respiratory system, per abdomen examination and central nervous system examination including fundus examination was done.

The following laboratory investigations were done; haemoglobin (g/dl), blood sugar – fasting & post prandial (mg/dl), urea (mg/dl), creatinine (mg/dl), electrolytes – sodium, potassium, chloride and bicarbonate (mEq/L). Creatinine clearance was calculated. Ultrasonography of the abdomen was done to measure the kidney size. Fasting lipid profile was done, total cholesterol, triglycerides and high-density lipoproteins (HDL) were measured and low-density lipoproteins, and TG/HDL ratio were calculated. Electrocardiogram, urine analysis and spot urine protein creatinine ratio were also done.

Statistical analysis

All the data collected were analysed using SPSS (Statistical Package for the Social Science) system. For analysing statistical significance in study group, inferential statistics was employed. Test used is chi-square test. For analysing statistical significance of study group in comparison to control group, descriptive statistics was used. Test employed is Unpaired t test/ independent t test. P value of <0.05 was considered significant.

RESULTS

In our study group of 100 patients, clustering of cases was observed between the age group 30-50 years (60%). Of this, 40-50 years had maximum percentage (33%) in our study population. Association between age group and stage of CKD was statistically significant (p= 0.004). Males are more affected (86%) than females (14%). It appears as if there was a considerable gender prevalence among CKD patients. But the association between gender and prevalence of CKD was statistically not significant (p value =0.977) as shown in Table 1.

Table 1: Age distribution versus stages of CKD.

Age group (yrs)	Stages of CKD			Total
	3	4	5	
<30	3	2	5	10
30-40	12	7	8	27
40-50	11	17	5	33
50-60	2	13	7	22
>60	0	2	6	8
Sex				
Male	24	35	27	86
Female	4	6	4	14

Figure 1 shows the distribution of different stages of CKD among males and females. Even though the majority of patients in our study group belonged to the

male sex, but no difference in gross variability was observed.

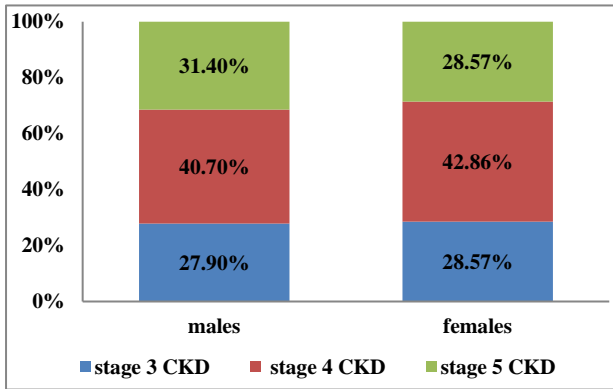


Figure 1: Distribution of different stages of CKD among males and females.

Table 2: Distribution of abnormal lipid parameters among study groups.

Parameters	Stages of CKD			Total	P value
	3	4	5		
LDL (mg/dl)					
<100	17	11	5	33	<0.001
100-129	2	0	0	2	
130-159	9	0	0	9	
>159	0	30	26	56	
TGL (mg/dl)					
<150	19	11	5	35	<0.001
150-199	9	30	12	51	
>200	0	0	14	14	
TC (mg/dl)					
<200	19	11	5	35	<0.001
200-240	9	10	0	19	
>240	0	20	26	46	
HDL (mg/dl)					
>40	19	11	5	35	<0.001
<40	9	30	26	65	
TGL/HDL ratio					
<2.00	17	11	5	33	<0.001
2 - 3.5	2	0	0	2	
3.5 - 5	9	11	0	20	
>5	0	19	26	45	
Lipid profile					
Normal	19	11	5	35	<0.05
Abnormal	9	30	26	65	

Table 2 presents the distribution of LDL, TG, TC, HDL and lipid profile among study groups. 33 % of patients had normal values of LDL. About 56 % had abnormally high values of LDL >159 mg/dl. 65% of patients had TGL levels more than 150 mg/dl. Of this, 14 cases had TGL values more than 200 mg/dl, interestingly all those were stage 5 CKD patients. 65 Patients out of 100 had abnormal levels of total cholesterol more than 200 mg/dl. Levels more than 240 mg/dl was seen in stages 4 and 5 of

CKD (n=46). Decreased levels of HDL (<40 mg/dl) was observed in stages 3, 4 and 5 of CKD patients. 65% of patients had values <40mg/dl. In our study group, 20 patients had TGL/HDL ratio 3.5-5, 45 patients had TGL/HDL ratio >5. 65 patients had abnormality in lipid profile. Of this, most of the cases were in the stage 4 (n=30) and stage 5 CKD (n=26). The association of all the above estimated parameters and stages of CKD was statistically significant (p value <0.0001 and <0.05). Comparison of lipid parameters among study and control groups was given in Table 3. In the study group, there was an increase in LDL, TGL, TGL/HDL, TC and decrease in HDL when compared with the control and difference was found to be statistically significant (p value <0.0001).

Table 3: Comparison of lipid parameters among study and control groups.

Lipid parameters	Groups	N	Mean	Std. deviation	P value
LDL	Study	100	134.674	55.6159	<0.001
	Control	100	131.304	0.827	
HDL	Study	100	41.53	12.176	<0.001
	Control	100	51.31	7.484	
TGL	Study	100	154.93	45.128	<0.001
	Control	100	108.23	19.357	
TGL/HDL ratio	Study	100	4.3095	2.10460	<0.001
	Control	100	2.2156	0.82329	
TC	Study	100	207	53.30	<0.001
	Control	100	178	46.79	

DISCUSSION

Dyslipidemia is a significant risk factor in cardiovascular diseases in rural population and in patients with CKD, alterations in lipoprotein metabolism may result in development of severe dyslipidemia.⁹ This study was hence undertaken to look, whether chronic kidney disease per se, possess a risk of dyslipidemia (without the above secondary causes of dyslipidemia) by excluding obesity, diabetes, patients with nephrotic range of proteinuria, those on beta-blockers, & OCPs, pregnant patients, renal transplant patients and CKD patients on HD.

The fact that ratio of triglyceride/high density lipoprotein is a surrogate marker of insulin resistance and its elevation in diabetic patients is well known. This ratio represents the concentration of highly atherogenic small density LDL in the body. This study was conducted to assess the association between the ratio of triglyceride/high density lipoprotein in non-diabetic CKD patients.

In the present study, 100 CKD patients were selected (who satisfied the above exclusion and inclusion criteria) and 100 age and sex matched, hospital based controls were also chosen and lipid profile was done on a fasting sample.

In our study group of 100 patients, clustering of cases was observed between the age group 30-60 years (82%).

Of this, 40-50 years had maximum number of cases. Male dominance was observed in the study (86%). Similar observation was made by Bhargavi in her study in which majority of the males were in the age group of 60-79 years, and females were in the age group of 50-69 years.¹⁰

In our study, the LDL values were 134.67±55.61 mg/dl. About 56 % had abnormally high values of LDL >159 mg/dl. The association between rise in serum LDL levels and stages of CKD was statistically significant (p value <0.001). In controls, the mean and SD were 131.30 and 157.054 respectively and P value was statistically significant when compared with controls. This shows that the LDL levels are significantly elevated in CKD patients compared to the control group. This result was in accordance with the observations of Ljutfi et al.¹¹

In study group, 65% of patients had TGL levels more than 150 mg/dl. Of this, 14 cases had TGL values more than 200 mg/dl. Mean and standard deviation was 154.93 and 45.128 respectively. In controls, the mean and standard deviation were 108.23 and 19.357 and a significant P value was observed between the two groups. Shah et al demonstrated that hypertriglyceridemia was the abnormality found in CKD patients.¹² Similar findings were seen in the studies of Gupta et al, Das et al.^{13,14} They found that hypertriglyceridemia was the major abnormality in their studies.

In the study group, 65 Patients out of 100 had abnormal levels of total cholesterol more than 200 mg/dl. Levels more than 240 mg/dl was seen in stages 4 and 5 of CKD (n=46). This association between the elevation of LDL and progression of CKD was found to be statistically significant (p value < 0.001). Similar elevation in cholesterol was found in study conducted by Diana M Lee et al.¹¹ In another study, rise in TC levels and proteinuria had positive cholesterol with severity of CKD.¹⁵ But most studies state that hypercholesterolemia is not a common feature of CKD. It is commonly found in nephrotic syndrome.

In the study population, decreased levels of HDL (<40 mg/dl) was observed in all stages of CKD. 65% of patients had values <40 mg/dl. The association between decreasing HDL levels and the progression in stage of CKD was statistically significant (p value <0.001). In control group the mean was 51.31 and standard deviation was 7.484 with p value <0.001. This shows that there was a significant reduction in HDL-C levels in patients with CKD than that of controls. Similar findings were found in the conducted by Diana M Lee et al. and MDRD study.^{11,16}

Increasing TGL levels and decreasing HDL levels in CKD patients are reflected as rising TGL/ HDL ratio with progression of the severity of CKD from stage 3 to stage 5. In our study group, 35% had ratios less than 3.5. About 20 patients had TGL/HDL ratio in the range of 3.5-5, 45 patients had TGL/HDL ratio >5. This association

between the rise in TGL/HDL ratio and progression of CKD was found to be statistically significant (p value <0.0001). In control group the mean was 2.215 and standard deviation was 0.823 and the difference was (P<0.0001) was statistically significant. This shows that the TGL/HDL ratio was significantly elevated in CKD patients when compared with the control group. Studies have shown that this ratio was significantly associated with the prevalence of CKD and its rise correlates with the severity of CKD.¹⁷

CONCLUSION

The results of the present study conclude that CKD patients with lipid abnormalities are more prone to higher risk of cardiovascular events. Hence, it is essential to treat dyslipidemia in early stages CKD to prevent secondary complications.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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