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Original Research Article

Serum lipid profile among non diabetic patients with chronic kidney disease attending tertiary care hospital in West Bengal, India

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ABSTRACT

Background: Chronic kidney disease (CKD) is a major health deteriorating factor worldwide as well as in India. It encompasses various pathophysiological processes involving abnormal kidney function and thereby declination in glomerular filtration rate (GFR). CKD is known risk factor for dyslipidemia. Due to lack of studies of association between different lipid parameters and its association with severity of CKD in non-diabetic patients in Indian population, we designed a study aimed to describe the serum lipid profile in non-diabetic CKD patients.
Methods: This hospital based observational analytical was carried out in 60 subjects with CKD and non-diabetic. They were investigated for blood sugar parameters, lipid profile and renal function tests. Lipid profile was associated with different stages of CKD. Data was expressed as percentage and mean±SD.
Results: Mean BMI was found to be 21.6±2.7kg/m^2. Most common symptom encountered was H/o edema in 98% subjects. Out of total sixty subjects' maximum subjects were found to be in stage 4 (22 subjects, 36.7%). Significantly higher levels of serum creatinine ($p < 0.0001$), and serum urea ($p < 0.0001$) was observed in higher grade CKD stages in study subjects.
Conclusions: Total cholesterol (TC) and LDL were found to be significantly different amongst CKD stages having higher mean values in non-diabetic subjects. Serum TC, TG, LDL and VLDL were found to be significantly higher in subjects with advanced CKD (stage 3, stage 4). TC/HDL and LDL/HDL ratio were significantly higher in subjects with advanced CKD compared to initial stages of CKD in non-diabetic subjects.

Keywords: Chronic kidney disease, Dyslipidemia, Glomerular filtration rate, Non diabetic, Renal function

INTRODUCTION

Chronic kidney disease (CKD) is a prevalent health problem worldwide, affecting millions of people.[1] The magnitude of the problem is often failed to be described by the number of people those will initiate renal replacement therapy (haemodialysis, peritoneal dialysis and renal transplantation), as the incidence of 1- 3 per 10,000 per year in the general population may seem small.[2,3] However, owing to its cost constrains and requirement at periodic interval, renal replacement therapy ensues huge economic burden as well as dependability on the CKD patients, their family and society. Further, limitations of renal transplants such as unavailability of HLA matched donor, centre with sufficient facilities and cost of treatment renders the permanent management far from possible for many subjects.[2,4] Though there is lack of data in Indian population some isolated studies have reported stage specific prevalence of 4.2% (stage 3 and above) to 17.5%

(stage 1-5) in Indian subjects. In the wake of high prevalence of risk factors such as diabetes and hypertension, prevalence of CKD is set to rise in Indian subjects.[5]

Chronic kidney disease represents a progressive irreversible decline in the glomerular filtration rate (GFR). A common phenomenon in renal failure is progressive renal function loss, irrespective of the underlying cause of the kidney disease. Most chronic nephropathies lack a specific treatment and progress relentlessly to end stage kidney disease (ESKD) with increasing prevalence worldwide.[6]

It is characterized by a wide variety of biochemical disturbances and numerous clinical symptoms and signs.[7] The alteration includes Hematologic abnormalities, cardiovascular problems, gastrointestinal disturbances, neurologic disorder, osteodystrophy, skin disorder and altered sexual function.[8] Lipoprotein metabolism is also found to be altered in most patients with renal insufficiency.[9]

Renal disease, in early and advanced stages is associated with abnormalities in lipoprotein metabolism. Dyslipidemia appears to be independently associated with increased progression rate of CKD in patients with kidney disease, and with increased risk of graft loss after renal transplantation.[10,11] Progressive Chronic renal failure (CRF) not only leads to End stage renal disease (ESRD), but it is associated with high cardiovascular morbidity and mortality. Instead of progressing to ESRD, patients with CRF are much more likely to die.[12]

With the implication of plasma lipids in the Pathogenesis of atherosclerosis and ischemic heart disease, it becomes worthwhile to study the behavior of various lipid fractions in CRF patients.[13] In wake of thrifty phenotype and thrifty genotype in Indian population, which are significantly different compared to western countries, study about dyslipidemia risk posed by CKD in non-diabetic subjects was warranted thus explaining the independent impact of CKD on dyslipidemia. This will help to establish treatment protocol for management of evident as well as eminent dyslipidemia in subjects with CKD.

Thus, authors aimed to study serum lipid profile among non-diabetic patients with chronic kidney disease with objectives to estimate the serum level of different lipoproteins and total cholesterol among non-diabetic CKD patients, to determine the ratio of HDL and Non HDL cholesterol, to describe the influencing factors of serum lipid and find out correlation of lipid parameters with stages of CKD.

METHODS

This hospital based cross-sectional, descriptive, analytical study was performed from January 2016 to December 2017 in the Department of General Medicine, Deben Mahato Sadar Hospital, Purulia, West Bengal. The catchment area included Purulia district with nearby borders of Jharkhand. Study subjects included all subjects aged 20-80 years, diagnosed non-diabetic patients of CKD under KDIGO diagnostic criteria.14 Subjects with acute renal failure and nephrotic syndrome, who were on drugs affecting their lipid metabolism and critically ill patients were excluded from the study. With 5% type 1 error and absolute precision 5% calculated sample size came out to be 57.21 thus authors included 60 subjects in study after informed consent.

Ethical clearance and approval were obtained from the institution ethical committee of Bankura Sammilani Medical College and was performed in accordance with Declaration of Helsinki. Informed consent was obtained from all subjects. 3ml venous blood was collected from median cubital vein using standard technique of phlebotomy and tested for various biochemical parameters. The diagnosis of CKD was further established using ultrasonography and urine investigations. The lipid profile was associated with different stages of CKD. Early morning urine sample was collected for urine routine examination. Predesigned pretested interviewer administered questionnaire was done for collecting baseline information. Different laboratory tests viz. lipid profile, renal function tests, blood sugar was carried out on Erba Chem 7 semi automatic clinical chemistry analyser using manufacturer's protocol, (Erba® Diagnostics Mannhheim Germany), Ultrasonography of abdomen for evidence of CKD was performed using HD7 diagnostic Ultrasound system™ (Philips ultrasound inc.® WA USA).

Data was expressed as percentage and mean±SD. Kolmogorov-Smirnov analysis was performed for checking linearity of the data. Student's t test was used to check the significance of difference between two parameters in parametric data. ANOVA was used to test the significance of difference between more than two parameters in parametric data. Fisher's exact test or Chi square test was used to analyze the significance of difference between frequency distribution of the data. P value <0.05 was considered as statistically significant. SPSS© for windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007, Microsoft® Inc USA was used to perform the statistical analysis.

RESULTS

The general characteristics of study subjects were noted. Out of 60 subjects 21 (35%) were females and 39 (65%) were males. Subjects predominantly belonged to rural areas (34 subjects, 56.7%) (Table 1).

In present study most common symptom encountered was H/o oedema in 98% subjects to be followed by weakness in 95% subjects. Weight loss and loss of appetite was present in 85% subjects while hiccups were

present in 75% subjects. Change in bladder habits and nausea was complained by 70% and 68% subjects respectively. Forty six subjects (76.7%) had BMI 18.5-25. On examination, general condition was found to be moderate in 50 (83.3%) subjects while fair in 10 (16.7%) subjects. Pallor was present in 57 (95%) subjects and visible oedema was observed in 56 (93.3%) subjects. All subjects reported similar past event (Table 2).

Table 1: General characteristics of study subjects.

		Frequency	%
Age (years)	≤=30	7	11.7
	31-40	4	6.7
	41-50	9	15.0
	51-60	14	23.3
	>60	26	43.3
Gender	Female	21	35.0
	Male	39	65.0
Residence	Rural	34	56.7
	Semi urban	12	20.0
	Urban	14	23.3
Occupation	Business	3	5.0
	Housewife	21	35.0
	Service	4	6.7
	Skilled labourer	3	5.0
	Unskilled labourer	29	48.3

Table 2: Presenting features in study subjects.

Presenting features		No. of subjects	%
Symptoms	Weight loss	51	85.0
	Loss appetite	51	85.0
	Weakness	57	95.0
	H/o edema	59	98.3
	Nausea	41	68.3
	Hiccups	45	75.0
	Change in bladder habits	42	70.0
	Family history of kidney diseases	3	5.0
BMI (kg/m^2)	≤=18.5	5	8.3
	18.5-25	46	76.7
	25.1-30	9	15.0
General condition	Fair	10	16.7
	Moderate	50	83.3
Examination findings	Pallor	57	95.0
	Edema	56	93.3
	Past history of similar complaints	60	100.0

Vitals and laboratory findings in the study subjects were observed. RBS was found to be deranged in 1 subject (1.7%) and PPBS in 18 subjects (30%). FBS was found to be normal in all. None of the subjects were found to be frank diabetic. Serum creatinine and serum urea was seen to be raised in 57 subjects (95.0%) and 58 subjects (96.7%) respectively. Total cholesterol was found to be ≤= 200 in 95% of the subjects. LDL was noted as optimal in 63.3% subjects (Table 3).

Table 3: Vitals and laboratory findings.

Finding		Frequency	%
RBS (mg/dl)	≤=140	59	98.3
	141-200	1	1.7
PPBS (mg/dl)	≤=140	42	70.0
	141-200	18	30.0
FBS (mg/dl)	<126	60	100.0
Serum creatinine (mg/dl)	Normal	3	5.0
	Raised	57	95.0
Serum urea (mg/dl)	Normal	2	3.3
	Raised	58	96.7
Total cholesterol (mg/dl)	≤=200	57	95.0
	201-239	2	3.3
	≥=240	1	1.7
LDL (mg/dl)	Optimal (≤=100)	38	63.3
	Near optimal (101-129)	18	30.0
	Borderline high (130-159)	3	5.0
	High (160-189)	1	1.7

Table 4: Association of various factors between subjects with stages (1, 2, 3A, 3B, 4, 5) of CKD subjects.

Finding	F	P value
RBS (mg/dl)	0.421	0.832
PPBS (mg/dl)	2.159	0.072
FBS (mg/dl)	2.432	0.056
Serum creatinine (mg/dl)	33.964	<0.0001
Serum urea (mg/dl)	21.137	<0.0001
Total Cholesterol (mg/dl)	2.850	0.023
Serum Tg (mg/dl)	2.284	0.059
Serum HDL (mg/dl)	.405	0.843
LDL (mg/dl)	3.113	0.015
VLDL (mg/dl)	1.832	0.122
TC/HDL ratio	3.442	0.009
LDL/HDL ratio	3.256	0.012

The association of various factors between subjects with stages (1, 2, 3A, 3B, 4, 5) of CKD subjects were studied. No significant association of CKD was noted with RBS, PPBS, FBS, S. Tg, S. HDL, VLDL, T cholesterol, LDL, TC/HDL ratio and LDL/HDL ratio. However, significantly higher levels of Serum creatinine (p <0.0001)), and serum urea (p<0.0001) was observed in higher grade of CKD stages in study subjects (Table 4).

Comparison of various lipid profile parameters between subjects with CKD status was performed using student's test. Significantly higher levels of T. Cholesterol (p=0.004), Sr. TG (p=0.002), Sr. LDLD (p=0.003), Sr. VLDL (p=0.004), however no significant difference was

observed between two groups regarding S. HDL (p=0.197) (Figure 1).

Comparison of various lipid profile ratio between subjects with CKD status was performed between CKD status using unpaired t test. TC/HDL ratio (p<0.0001) and LDL/HDL ratio (p=0.001) was found to be significantly higher in CKD stage 4-5 compared to CKD stage 1-3 (Figure 2).

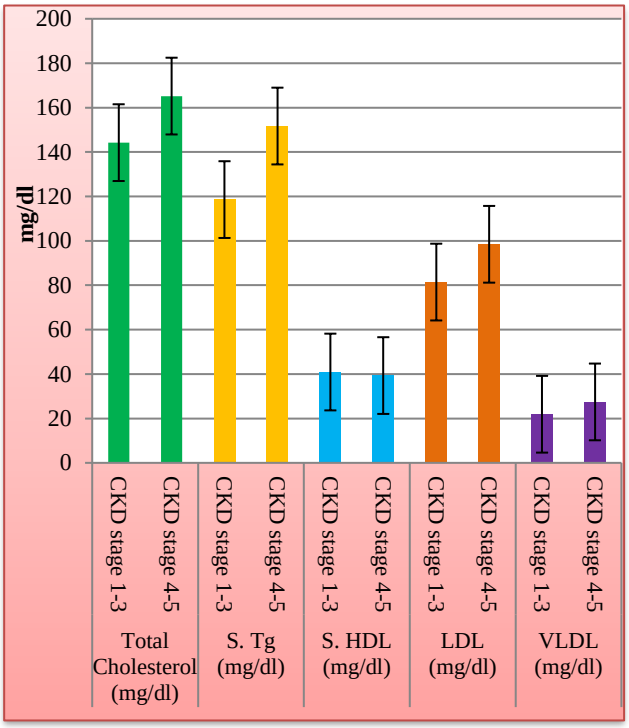

Figure 1: Comparison of various lipid profile parameters between subjects with CKD status.

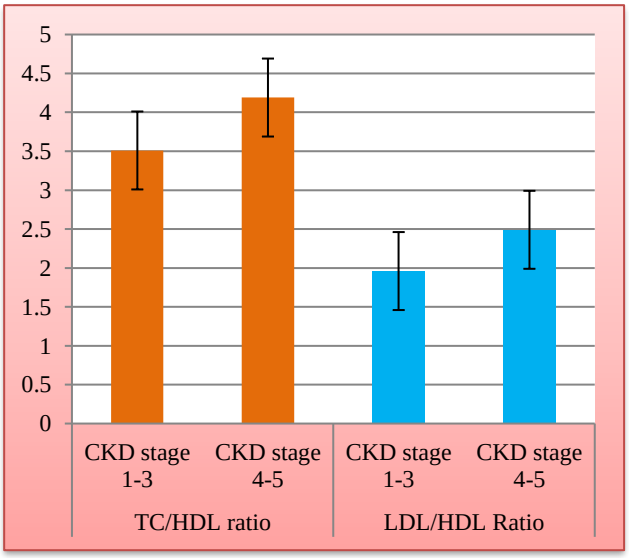

Figure 2: Association of various lipid profile ratio between subjects with CKD status.

DISCUSSION

This hospital-based study assessed the lipid profile in non diabetic subjects with CKD. Maximum subjects in our study were having normal (18.5-25kg/m^2) BMI (46 subjects, 76.7%). Nine subjects were overweight (15%) and 5 were underweight (8.3%). None were found to be obese. Mean BMI was found to be 21.6±2.7kg/m^2. Oluseyi A et al, and Magar LR et al, reported BMI to be 24.5±4.2kg/m^2 and 23.3±1.34kg/m^2 in CKD subjects respectively.[15] Gelber RP et al, have demonstrated a significant relationship between CKD and BMI in apparently healthy subjects. Physical activity did not modify the association between BMI and risk for CKD.[16] Framingham study also suggested that baseline BMI predicts subsequent kidney disease after a mean follow-up of 18.5 years.[17] Out of total sixty subjects maximum subjects were found to be in stage 4 (22 subjects, 36.7%) to be followed by 15 subjects (25%) in stage 5 and 14 (23.3%) subjects in stage 3B. Seven subjects (11.7%) were in stage 3A and one each (1.7%) in stage 1 and 2. In a study by Chen SC et al, 35.8% subjects were found to be in stage 3, 29.1% subjects were in stage 4 and 35.1% subjects were in stage 5.[18] Ganta V et al, reported 17.14% subjects to be in stage 3, 37.14% subjects to be in stage 4 and 45.71% subjects to be in stage 5. Both these studies included only non-diabetic CKD subjects similar to our study.[19]

Mean total cholesterol was found to be 157.2±28mg/dl while TG was found to be 105±60mg/dl and LDL cholesterol was 101±214mg/dl. Mohanraj et al, like in present study included only CKD subjects without diabetes. The author reported total cholesterol to be 192.24±22.55mg/dl, TG was 197.26±59.75mg/dl, HDL was 34.18±4.62mg/dl and LDL cholesterol was 118.6±21.27 mg/dl.[20]

Dyslipidemia is a common complication of CKD and lipoprotein metabolism alteration and is associated with the decline in GFR; hence, lipid profile depends on the level of kidney function and the degree of proteinuria. Patients with non-dialysis-dependent CKD and without nephrotic syndrome have low HDL and high triglycerides and normal or even low TC and LDL cholesterol, but more atherogenic profile is hidden behind this spectrum.[21-23] Besides low catabolic activity, increased hepatic production of triglyceride-rich lipoproteins contributes to increased levels of triglycerides in CKD patients. Insulin resistance, often associated with CKD, seems to be responsible for a hepatic VLDL overproduction.[23,24]

Although LDL is not usually elevated in patients with CKD, LDL particles tend to be smaller, denser, and more atherogenic in their form. Various studies have shown increased levels of small dense LDL in non-dialysis-dependent CKD patients in comparison with the healthy controls and have indicated small dense LDL as a risk factor for cardiovascular diseases (CVD)

development.[23,25,26] Patients with CKD have decreased HDL in comparison with individuals with preserved kidney function, in CKD patients, the activity of lecithin-cholesterol acyl transferase, the enzyme important for the esterification of free cholesterol in HDL, is impaired. On the other hand, the activity of cholesterol ester transfer protein (CETP), which supports the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins, is increased, responsible for the decreased serum level of HDL.[24-26]

In present study authors associated individual lipid parameters with severity of CKD and authors' observation was in coherence with observation of preceding studies additionally authors also established the association between severity of CKD and derangement of each individual parameter including the lipid ratios except for HDL cholesterol.

CONCLUSION

Authors conclude that total cholesterol, serum TG, serum LDL and serum VLDL as well as TC/HDL ratio and LDL/HDL ratio are significantly different amongst CKD stages with advanced stages having higher mean values in non-diabetic CKD subjects.

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