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STUDY OF SERUM LIPID PROFILE AND LIPOPROTEIN (a) IN CHRONIC KIDNEY DISEASE

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ABSTRACT

Introduction: Chronic Kidney Disease (CKD) is a progressive loss of renal function and decline in Glomerular filtration rate . The disturbances in lipid and lipoprotein metabolism in these patients is one of the major risk factor of cardiovascular diseases. Cardiovascular diseases are the leading causes of morbidity and mortality in these patients. Lipoprotein(a) is an important atherogenic factor in the pathogenesis of cardiovascular diseases. **Aim:** To study the alteration of lipid profile and lipoprotein(a) in Chronic Kidney Disease patients not on dialysis. **Methodology:** Case control study involving 30 patients of CKD not on hemodialysis/peritoneal dialysis were taken as cases and 30 age and sex matched healthy persons were taken as controls. The cases were taken from K.P.C Medical College, Kolkata. Renal Function Test (Urea and Creatinine), Lipid profile and Lipoprotein(a) were estimated and the cardiovascular risk ratios were calculated and statistically analysed. **Results and Conclusion:** Serum Urea and Creatinine were significantly increased in cases compared to controls. Triglycerides(TGL), VLDL-C and Lipoprotein(a) were significantly increased and HDL-C was significantly decreased in cases as compared to the control group. The risk ratios: Total Cholesterol(TC)/HDL-C, TGL/HDL-C were significantly increased in cases as compared to the control group.

KEYWORDS: Chronic Kidney Disease, Lipoprotein(a), Hemodialysis, Cardiovascular diseases, Lipid Profile.

INTRODUCTION

Chronic Kidney Disease (CKD) is a world wide health problem due to its increasing incidence and prevalence, with adverse outcomes of kidney failure, cardiovascular disease (CVD) and premature death.

Based on the guidelines of the National Kidney Foundation (Kidney Disease Outcome Quality Initiative) CKD is defined as.

The presence of markers of kidney damage for more than 3 months, as defined by structural or functional abnormalities of the kidney with or without decreased Glomerulal Filtration Rate (GFR), manifest by either pathological abnormalities or markers of kidney damage including abnormalities in the composition of blood or urine or abnormalities in imaging tests Or The presence of GFR < 60ml/min/1.73m^2 for more than 3 months with or without signs of kidney damage.[1]

Globally, CKD is the 12th cause of death and the 17th cause of disability, respectively. The yearly incidence of End Stage Renal Disease in India is approximately 150-200 per million population. Patients with CKD are more likely to die of cardiovascular disease (CVD) than to reach End-Stage Renal Disease (ESRD).

Death due to cardiovascular complication is 10-200 fold higher than the general population, depending upon the stage of CKD. Dyslipidemia has been established as a well known traditional risk factor for CVD. This disturbed lipid pattern accelerates the process of atherosclerosis and impairs the blood supply, further damaging the kidneys.[2]

Lipoprotein(a) is a nontraditional, independent novel risk factor for CVD. Lipoprotein (a) (Lp(a)), for the first time described in 1963 by Berg belongs to the lipoproteins with the strongest atherogenic effect. Lp(a) is a LDL-like particle formed by the association of the highly polymorphic glycosylated apolipoprotein(a) (apo(a)) with apolipoprotein B100 (apo B100), the classic protein moiety of LDL. The apo(a) is attached to apo B100 through a single disulphide link between apo B100 Cys 4326 and apo(a) kringle(K) IV type 9 Cys4057, additional non-covalent interactions play accessory roles in promoting, mediating and reinforcing the association between the apolipoproteins[3]. In line with the fact that chronic kidney disease is associated with increased Lp(a) plasma levels, it was suggested that the kidneys may be important for Lp(a) catabolism. The identification of apo(a) fragments in urine suggest that the kidneys may actively participate in the degradation of Lp(a). Thus,

patients with primary kidney diseases usually exhibit markedly elevated concentrations of Lp(a).

Numerous epidemiological studies have shown that increased Lp(a) in plasma is a risk factor for variety of cardiovascular diseases, including silent coronary artery disease (CAD), acute myocardial infarction (AMI), asymptomatic carotid atherosclerosis, stroke and abdominal aortic aneurysm. The Framingham study reported that Lp(a) levels above 30mg/dl has similar risk to Total Cholesterol (TC) > 240 mg /dl or HDL-C< 35mg/dl.

Pathogenetic Mechanisms by which Elevated Lp(a) plasma concentration leads to an accelerated atherothrombosis[3]

❖ Easy oxidisability of Lp(a) and formation of highly atherogenic complexes with LDL in the vessel wall
❖ Enhancement of lipid uptake by macrophages
❖ Competitive inhibition of plasminogen during the binding to cellular receptors and protein binding sites
❖ Decreased thrombin formation and inhibition of fibrinolysis
❖ Inhibition of Tissue Plasminogen activator and increased formation of Plasminogen Activator-Inhibitor 1 (PAI-1)
❖ Inactivation of tissue factor pathway inhibitors
❖ Facilitation of thrombus formation at the sites of tissue lesions
❖Increase of proliferation and migration of smooth vascular muscle cells
❖Inhibition of transforming growth factor β
❖Inhibition of the formation of collateral vessels.

MATERIALS AND METHODS

Source of Data: The study comprises of 30 non dialysis dependent CKD patients as cases and 30 age and sex matched healthy persons as controls. The cases were taken from the Department of Medicine K.P.C Medical college and Hospital, Kolkata.

Method of data collection

A. Study design - Case control study

B. Sample size - 30 cases of non dialysis dependent CKD patients and 30 age and sex matched healthy controls

C. Inclusion criteria

Diagnosed cases of Non dialysis dependent CKD > 18 years.

D. Exclusion criteria

i. Patients with Diabetes Mellitus.
ii. Patients with hypertension.
iii. Patients with hypothyroidism.
iv. Patients with liver diseases.
v. Patients with cardiovascular diseases.
vi. Patients with history of familial hyperlipoproteinemia.
vii. Patients on drugs that alters the lipid profile.
viii. Obese patients (Body Mass Index ≥ 30kg/m^2).

E. Methodology

After obtaining written informed consent from cases and controls, about 5ml of fasting venous blood was obtained by venipuncture under aseptic conditions, centrifuged and the separated serum was used for the estimation of urea, creatinine, lipid profile and lipoprotein(a).

F. Parameters estimated

A) Renal Function Test includes
- Urea
- Creatinine

B) Lipid Profile which includes
- Triglycerides (TGL)
- Total Cholesterol (TC)
- Very low density lipoprotein cholesterol (VLDL-C)
- Low density lipoprotein cholesterol (LDL-C)
- High Density lipoprotein cholesterol (HDL-C)

C) Lipoprotein (a)

G. Statistical analysis

Student's t test
+ Suggestive significance (P value:0.05<P<0.10)
* Moderately significant (P value:0.01<P ≤ 0.05)
** Strongly significant (P value : P≤0.01)

RESULTS

Table. 1: Age, Body Mass Index(BMI), Serum Urea and Creatinine expressed as Mean ± Standard Deviaton (SD).

	Controls	Cases
Age (years)	42.6 ± 9.32	45.9 ± 9.64
Sex (Males %) (Females %)	60 40	62 38
BMI (kg/m^2)	22.31 ± 2.92	21.22 ± 2.36
Serum Urea (mg/dl)	27.43 ± 6.85	92.36 ± 28.21**
Serum Creatinine (mg/dl)	0.91 ± 0.22	4.52 ± 1.36**

****p < 0.001 strongly significant.**

Table. 2: Comparison of Lipid parameters in two groups studied expressed as Mean ± SD.

Lipid parameters (mg/dl)	CONTROLS	CASES
TGL	136.66±31.2	216.93±35.46**
Total cholesterol (TC)	182.22±20.62	190.05±22.34
VLDL-C	27.33±6.76	43.38±7.41**
LDL-C	110.30±11.29	109.75±12.32
HDL-C	44.6±5.65	36.9±5.92**
Lp (a)	13.26±2.92	40.67±6.62**

****p <0.001 Strongly significant.**

Table. 3: Comparison of Ratio of lipid parameters in two groups studied.

	CONTROLS	CASES
TGL/HDL-C	3.06 ± 1.32	5.8 ± 2.22**
TC/HDL-C	4.08 ± 0.35	5.15 ± 0.62**

****p <0.001 Strongly significant.**

DISCUSSION

1) Hypertriglyceridemia occurs in about 50-75% of the patients with CKD[4]

The mechanism for the cause of hypertriglyceridemia are
i) Decreased catabolism of triglycerides is the predominant mechanism.
ii) Diminished Lipoprotein lipase (LPL) activity.
iii) Disproportionate increase in plasma apolipoprotein C-III.
iv) Secondary hyperparathyroidism.

2) Serum cholesterol is not significantly altered in CKD patients as compared to the control group. This is in agreement with the study done by Vasilis et al.[5]

3) Serum VLDL-C is significantly raised in CKD patients as compared to healthy individuals, which is in agreement with Bagdade et al.[6]

Mechanism involving raised VLDL-C includes
i) Increased activity of Cholesterol Ester Transfer Protein (CETP).
ii) Increased apo C-III.

The serum LDL-C is not altered in CKD patients as compared to the control group.
This is in agreement with the study by Jain et al.[7]

4) Serum HDL-C is significantly decreased in cases than controls.

Mechanism underlying the condition are
i) Decreased apolipoproteins A-I and A-II.
ii) Diminished activity of Lecithin Cholesterol Acyl Transferase.
iii) Increased activity of CETP.

This is in accordance with the study by Das et al.[8]

5) Serum Lipoprotein(a) is increased significantly in cases as compared to the control group. The increased lipoprotein (a) is either due to its increased production or decreased catabolism by the kidney. Many studies have shown increased serum Lp(a) levels in chronic kidney disease patients, resulting in adverse cardiovascular outcomes. This is in accordance with the study by Karla et al.[9] Elevation in the ratio of TGL/HDL-C is the most powerful predictor of coronary heart disease.[10]

CONCLUSION

In this study dyslipidemia is observed in non dialysis dependent CKD patients. The alteration of cardiovascular risk ratios and increased serum Lp(a) concentration leads to accelerated atherosclerosis which favours higher incidence of cardiovascular complications as well as progression of renal damage. Moreover Lp(a) estimation is simple and relatively inexpensive, so it can be used as a biochemical parameter in CKD patients. Therefore lipid regulation must be instituted to decrease the risk of cardiovascular complications.

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