Lipoprotein(a) & Lipid profile in Chronic kidney disease. Case control study

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Abstract

Background: Chronic kidney disease (CKD) is characterized by progressive loss of renal function. These patients are at risk for adverse cardiovascular outcomes. Cardiovascular disease is the leading cause for morbidity and mortality in these patients This elevated risk is explained partially by traditional cardiovascular risk factors defined in the Framingham Cohort and other nontraditional risk factors such as lipoprotein(a) (Lp(a)) levels and apolipoprotien(a) size.

Aim of the study:

1. To estimate serum lipoprotein(a) in chronic kidney disease patients.

2. To estimate total cholesterol, HDL-Cholesterol, LDL-Cholesterol and triglyceride levels.

3. To study if there is any correlation between lipoprotein(a) and cholesterol, triglyceride, LDL-Cholesterol and HDL-Cholesterol.

Material and Methods: The study group included 30 patients with CKD selected from Nephrology department and 30 healthy control persons from hospital staffs matched for age and sex were also selected.

Results: Lp (a) levels was significantly ($p<0.05$) increased in cases compared to controls. There was increase in triglyceride and LDL-Cholesterols.

Conclusion: In our study we found high levels of lipoprotein(a) in chronic kidney disease patients. Increased levels of lipoprotein(a) can be used to assess cardiovascular outcomes in chronic kidney disease patients.

Since serum lipoprotein(a) estimation is simple and relatively inexpensive, we propose the use of lipoprotein(a) as an adjunct biochemical parameter in chronic kidney disease patients.

Introduction

Chronic Kidney Disease (CKD) is defined as either kidney damage or decreased kidney function with decreased glomerular filtration rate for more than three or more months[1]. Individuals with CKD are at an increased risk for cardiovascular disease compared to the general population [2].

Lipoprotein(a) (Lp(a)) is a cholesterol-rich particle existing in human plasma, first described by Berg in 1963 [3]. Lp(a) is made up of a low-density lipoprotein (LDL) cholesterol particle attached to apolipoprotein (a), which is a plasminogen like glycoprotein[4].

The prevalence of hyperlipidaemia or dyslipidaemia in CKD is much higher compared to the general population [5]. However, in patients with CKD, the impact of dyslipidemia on cardiovascular disease is uncertain [6].

Previous studies have shown that there was positive correlation between increased Lp(a) levels and plaque score in CKD patients[7].

Atherogenic lipid abnormalities are noticed in CKD patients. A study was done to show the impact of lipid abnormalities in patients with chronic renal failure, which revealed that there was increase in triglyceride, total cholesterol, and decrease in HDL-Cholesterol levels in chronic renal failure patients compared to controls[8].

Separate studies have shown increased Lp(a) levels and lipid abnormalities in CKD patients[7,8]. However, very few studies have been conducted to show the correlation between Lp(a) levels and lipid parameters in CKD patients. Hence the present study was undertaken to compare Lp(a) levels and lipid profile in CKD patients and normal healthy controls and also to see the correlation between the Lp(a) and lipid profile in CKD patients.

Material & Methods

The study group included 30 patients with CKD selected from Nephrology department of Jagadguru Sri Shivaratreshwar Medical College and Hospital Mysore, and 30 healthy controls from hospital staffs without renal disease matched for age and sex were selected. The study group patients with CKD were diagnosed with history of kidney damage or decreased kidney function with decreased glomerular filtration rate for more than three or more months[1]. The patients who reported with history of cigarette smoking, recent myocardial infarction and vascular diseases, history of taking lipid lowering drugs were excluded

from the study. Controls with history of cigarette smoking and chronic alcoholism were also excluded from the study. Sample size was calculated using Open Epi software, verson2:3:1. Confidence interval 95% and significance level is 95%. α =0.05 and 1-β =80%(power [9]. The study protocol was approved by the institutional ethical committee and informed consent was obtained from the subjects under study.

Under aseptic precautions 5ml of fasting venous blood was collected both from patients and controls. It was allowed to clot and serum was separated by centrifugation at 5000 rpm for 5 minutes. The following parameters were estimated.

The serum Lp(a) was estimated by immunoturbidimetric method[10]. Total cholesterol was estimated by enzymatic end point method (Cholesterol oxidase method) [11]. Serum Triglycerides by enzymatic method (GPO-PAP Method) [11]. Serum HDL-cholesterolby direct method [11]. Serum LDL-Cholesterol was calculated by Friedewald equation [11] .

All parameters were estimated using the kits provided by RX Daytona autoanalyser.

All the values are expressed in mean ± SD . Unpaired 't' test was applied. Pearson's correlation was done to see the correlation between serum Lp(a) and serum lipid parameters of CKD using SPSS(version 16.0)

Results

In the present study CKD patients and controls were 60 in number. The gender distribution was predominantly males in both groups [Table 1]. There was no significant difference with respect to body mass index and waist hip ratio in CKD patients and controls .

Lp(a) levels were significantly increased (p < 0.001) in CKD patients compared to controls. In lipid parameters only Triglycerides and LDL-Cholesterol were significantly increased (p < 0.05) in CKD patients compared to controls [Table 2]. Lp (a) showed positive correlation with both Total cholesterol and LDL-Cholesterol but was not statistically significant [Illustration 1,2].

Discussion

The principle findings of this study were high Lp(a) levels seen in chronic kidney disease patients compared to controls. Among lipid parameters , there was increase only in triglyceride and LDL-Cholesterol

levels in cases compared to controls. Lp(a) showed positive correlation with Total cholesterol and LDL-Cholesterol.

Patients with chronic renal failure (CRF) have an increased risk of cardiovascular disease (CVD). Many studies have shown serum Lp(a) levels are increased in chronic kidney disease patients, resulting in adverse cardiovascular outcomes. Study done by Baldassare et.al., showed positive relationship between levels of lipoprotein(a) and carotid intimal thickness [12].

Increased levels of Lp(a) in CKD is recognized as an independent risk factor for premature atherosclerotic coronary heart disease. The exact mechanism of Lp(a) as a cardiovascular risk factor is unknown. But it's pro-atherogenic and pro-thrombogenic effects have been hypothesized [13]. Atherosclerotic renal disease accounts for more than one third of all cases of end stage renal disease [14]. Hamid Nasri et.al., showed positive correlation between lipoprotein(a) levels and plaque score in chronic kidney disease patients, who were on hemodialysis [7].

However, CKD may lead to increased Lp(a) levels as a result of increased hepatic synthesis induced by an acute phase reaction or by protein losses from either proteinuria or peritoneal dialysis [15].

Shah B et. al., studied the impact on lipid abnormalities in patients with chronic renal failure and in renal transplants. In their study they observed increase in triglyceride levels in chronic renal failure patients compared to controls. But no change in total cholesterol, HDL and LDL level[8] **.** Patients with CKD are at an increased oxidative stress. The oxidative stress is due to dyslipidemia or accumulation of uremic toxins, as a result of deteriorated renal function. Dyslipidemia giving rise to oxidative stress includes atherogenic lipoproteins such as oxidized LDL [16]. Oxidized LDL induces endothelial injury and results in formation of atherosclerotic lesions . The oxidized LDL in particular is involved in the development of atherogenesis [17].

Atherogenic lipid abnormalities are noticed in CKD patients. The lipid abnormalities noticed are increased Lp (a), LDL-Cholesterol, triglyceride rich-VLDL and decreased HDL-Cholesterol [18]. Koch et.al., showed association between history of coronary artery stenosis and dyslipidemia in patients with CKD and observed Lp(a) levels were increased along with decreased HDL-Cholesterol, but no change in total cholesterol, LDL-Cholesterol and triglyceride levels [19]. Our results are in conformity with that of Koch et.al., who demonstrated significant increase in Lp(a) levels in CKD.

Schwaiger et.al., studied the cardiovascular events and lipid abnormalities in CKD patients. In their study the lipid abnormalities were elevated serum Lp(a) and unaltered total cholesterol, HDL-Cholesterol, LDL-Cholesterol and triglyceride levels [20]. The lipid abnormalities often accompany and aggravate the renal disease, thereby favoring the acceleration of atherogenesis and progression of cardio vascular disease [21].

However, Cheung et. al., studied on lipid abnormalities in CKD patients with previous history of cardiovascular events and showed there were no changes in the levels of Lp(a) and other lipids [22].

There are many ongoing studies relating to management of dyslipidemia in CKD. Suggestions have been made to manage patients with high Lp(a) levels in chronic kidney disease patients, as these patients are at high risk of developing adverse cardiovascular outcomes [2].

Since serum Lp(a) estimation is simple and relatively inexpensive, we propose the use of Lp(a) as an adjunct biochemical parameter in chronic kidney disease patients. However, more studies are required with a large sample size to ascertain whether serum Lp(a) can predict in hospital mortality and its patho-physiology in chronic kidney disease patient.

The principle findings of this study were high Lp(a) levels seen in chronic kidney disease patients compared to controls. Among lipid parameters , there was increase only in triglyceride and LDL-Cholesterol levels in cases compared to controls. Lp(a) showed positive correlation with Total cholesterol and LDL-Cholesterol.

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Since serum Lp(a) estimation is simple and relatively inexpensive, we propose the use of Lp(a) as an adjunct biochemical parameter in chronic kidney

disease patients. However, more studies are required with a large sample size to ascertain whether serum Lp(a) can predict in hospital mortality and its patho-physiology in chronic kidney disease patient.

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Illustrations

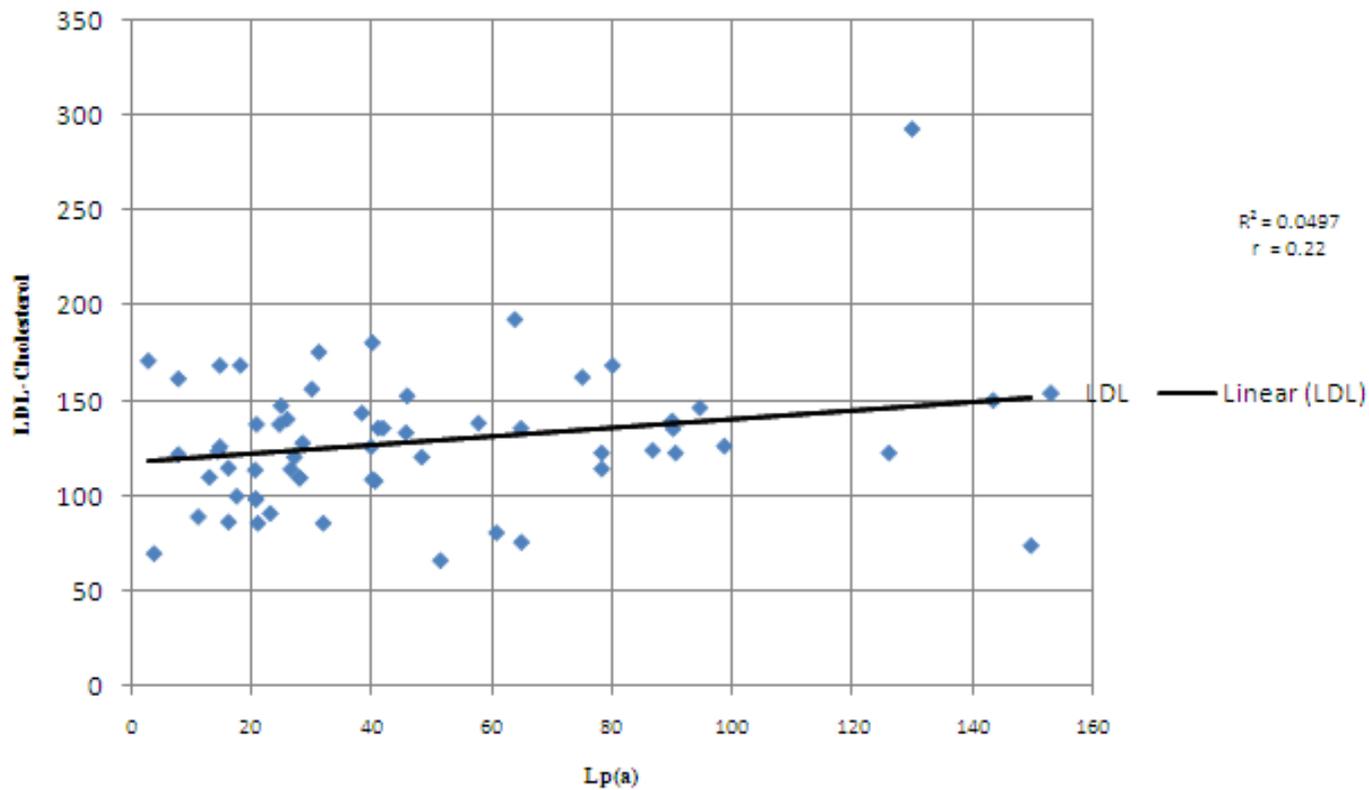## Illustration 1

Scattered graph showing positive correlation between Lp(a) and Total cholesterol

Correlation between Lp(a) and Total cholesterol

$R^2 = 0.0147$
$r = 0.118$
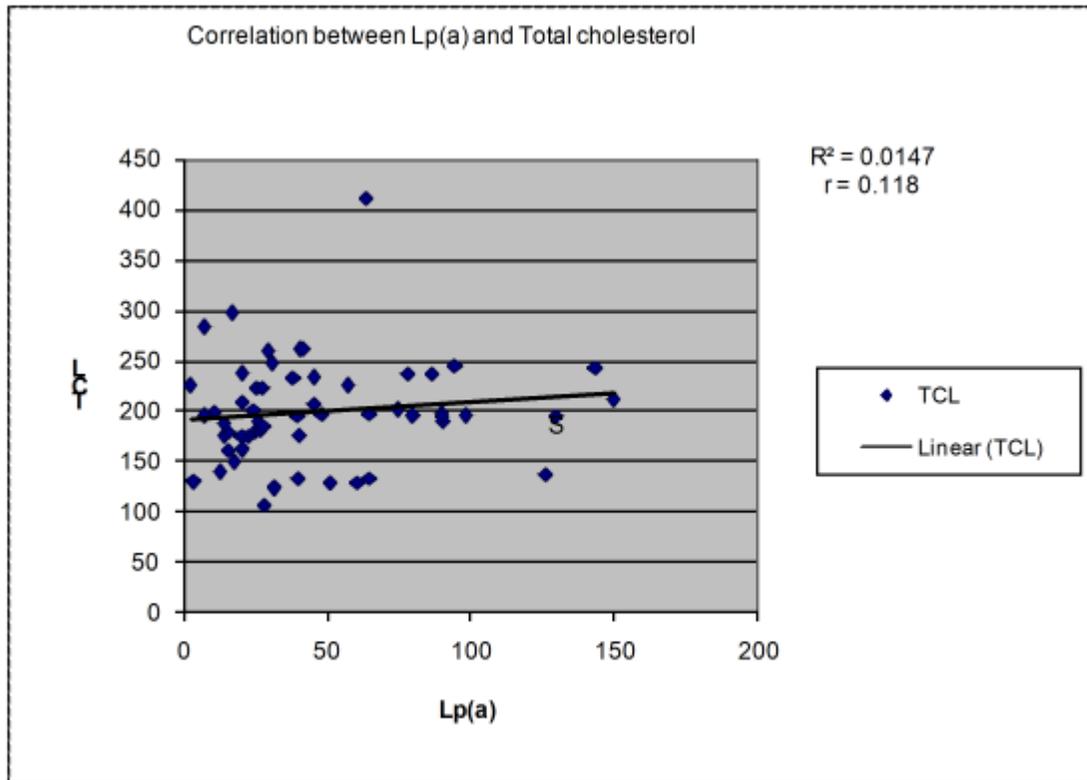
Illustration 2

Scattered graph showing correlation between Lp(a) and LDL-Cholesterol

Illustration 3

Table 1:Demographic profile in Chronic Kidney Disease patients and controls

Profile		CKD patients	Controls
Age(years)		49.50 ±10.77	49.83 ±9.40
Se x	Males	18	17
	Females	12	13
BMI(kg/mt2)		22.12 ± 1.23	22.01 ± 3.22
WHR		0.87 ± 0.07	0.77 ± 0.07

Values are mean ± SD; BMI= Body Mass Index; WHR = Waist Hip Ratio.

Illustration 4

Table 2: Comparision between Lp(a) and other Lipid parameters in CKD patients and controls

Parameters	Mean ± S.D		t	df	p
	cases	controls			
Lp(a) mg/dl	61.98 ±36.38	31.00 ± 27.42	3.72	58	0.000**
Total Cholesterol mg/dl	196.80±540.58	202.60± 470.12	- 0.441	58	0.661
Triglycerides mg/dl	187.93±60.616	153.13± 64.882	2.147	58	0.036*
HDL-Cholesterol mg/dl	38.60 ± 11.548	41.43 ± 7.780	- 1.115	58	0.270
LD – Cholesterol mg/dl	125.33±14.385	119.4 ± 09.24	0.172	57	0.024*
VLDL-Cholesterol mg/dl	34.867±11.87	40.41 ± 22.104	-1.211	58	0.231

(** very significant, * significant)   Lp(a) – Lipoprotein (a)

HDL – High Density Lipoprotein   LDL – Low Density Lipoprotein

VLDL – Very Low Density Lipoprotein   df – degrees of freedom

p - point of significance   t – students 't' test