ORIGINAL ARTICLE

NOVEL LIPID INDICES IN CHRONIC KIDNEY DISEASE

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ABSTRACT

Objectives: To Evaluate and compare lipoprotein(a) [Lp(a)], lipid profile and novel lipid indices in chronic kidney disease(CKD) patients undergoing hemodialysis with healthy controls. To find the correlation between Lp(a) with novel lipid indices.

Methodology: The study group included 30 patients with CKD andage and sex matched 30 healthy controls were selected for the study. Lp(a) was estimated by immunoturbidimetric method. Lipid profile by enzymatic method. Lipid indices were calculated using appropriate formula.

Results: There was significant increase in Lp (a)($p<0.000$), triglyceride($p<0.05$) and LDL-Cholesterol levels in cases compared to controls. Atherogenic index of plasma (AIP), Lipid tetrad index (LTI), Castellis risk index–2(CRI2) and Atherogenic co-efficient were also significantly increased in cases compared to controls but there was no significant increase in Castellis risk index – 1(CRI1). AIP showed significant positive correlation with Lp(a).

Conclusion: The present study concludes that AIP is the better novel lipid index for assessing atherogenecity in CKD patients compared to other indices as it doesn't require special investigation.

Keywords: Lipoprotein (a), Lipid profile, Lipid indices (AIP, LTI, CRI-I, CRI-II, Atherogenic Coefficient), Chronic kidney disease.

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]

In the absence of an abnormal lipid profile the possibility of CAD cannot be ruled out. It has been suggested that the different combinations of the lipid profile parameters can be used to identify such high risk individuals. These are the calculated fractions which can be used in the clinical setting for assessing the risk of cardiovascular disease beyond the routinely done lipid profile.

The retention of lipoproteinparticles of modified structure and size occurs alreadyin the early, predialysis stage, before the elevationof plasma lipids, and persists even after successful transplantation.[7] Plasma lipids and apolipoproteins may hencebe unreliable predictors of the cardiovascular risk in CRFinduceddyslipidemia, especially in the early stages ofkidney disease.

For such patient populations calculations of novelbioindices have recently been proposed, such as lipid tetradindex (LTI)[8], lipid pentad index (LPI)[9] and atherogenic index of plasma (AIP)[10], whose formulas comprise severallipid parameters (total cholesterol, triglycerides, HDL-C, apoA, apo

B and Lp(a)). In addition, AIP is an indirect indicatorof sdLDL levels.[10]

Thus, the present study was conducted with the objective of assessing the significance of lipid indices like Atherogenic Index of Plasma (AIP), Lipid Tetrad Index (LTI), Castellis Risk Index (CRI) and Atherogenic Coefficient (AC), in CKD patients who are at risk for coronary artery disease(CAD) beyond the routinely done lipid profile especially in insufficient resource situations.

MATERIAL AND METHODS

The study group included 30 patients with CKD and 30 healthy controls 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. 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.The cases were selected on the basis of simple random sampling method. The study was conducted from February 2014- September 2014. The study protocol was approved by the institutional ethical committee and informed consent was obtained from the subjects under study.

The serum Lp(a) was estimated by immunoturbidimetric method.[11] Total cholesterol was estimated by enzymatic end point method (Cholesterol oxidase method).[12] Serum Triglycerides by enzymatic method (GPO-PAP Method).[12] Serum HDL-cholesterolby direct method.[21] Serum LDL-Cholesterol was calculated by Friedewaldequation.[12]

All parameters were estimated using the kits provided by RX Daytona autoanalyser. Lipid indices were calculated using appropriate formulas. Following are the lipid indices:

1. Atherogenic Index of Plasma (AIP) = log TG/HDLc
2. Lipid Tetrad Index(LTI)= [TotalcholesterolxTtriglycerides x Lipoprotein(a) / HDL]
3. Castelli's Risk Index (CRI-I) = TC/HDLc
4. Castelli's Risk Index (CRI-II) = LDLc/HDLc
5. Atherogenic Coefficient (AC) = (TC– HDLc)/HDLc

Statistics: 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 30 in number each. 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.

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
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.

Lp(a) levels were significantly increased($p < 0.001$) in CKD patients compared to controls. In lipid parameters Triglycerides and LDL-Cholesterol were significantly increased ($p < 0.05$) in CKD patients compared to controls [Table 2].

Among lipid indices, AIP, LTI & CRI-II showed statistically significant ($p< 0.05$) in cases compared to controls. When Lp(a) single variable was correlated with other lipid indices it showed significant and positive correlation with AIP, & LTI.

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

Parameters	Mean ± S.D		p-Value
	Cases	Controls	
Lp(a) mg/dl	61.98 ±36.38	31.00 ± 27.42	0.000**
Total Cholesterol mg/dl	196.80±540.58	202.60± 470.12	0.661
Triglycerides mg/dl	187.93±60.616	153.13± 64.88	0.036*
HDL-Cholesterol mg/dl	38.60 ± 11.55	41.43 ± 7.78	0.270
LD – Cholesterol mg/dl	125.33±14.38	119.4 ± 09.24	0.024*
VLDL-Cholesterol mg/dl	34.867±11.87	40.41 ± 22.10	0.231

** very significant, * significant, Lp(a) – Lipoprotein (a), HDL – High Density Lipoprotein, LDL – Low Density Lipoprotein, VLDL – Very Low Density Lipoprotein

Table 3: Lipid indices in cases and controls

Lipid Indices	Cases	Controls	p-Value
AIP	0.32±0.19	0.17±0.21	<0.01
LTI	60.483.16±42.543	28.534±4.577.6	<0.0001
CRI1	5.3327±1.471	4.9336±1.452	<0.294
CRI2	3.834±1.384	2.9605±0.8314	<0.004
AC	4.3327±1.471	3.9334±1.452	<0.2944
Non-HDL Cholesterol	158.2±51.8	161.6±48.04	0.81

Table 4: Correlation between Lp(a) and other lipid variables

Variable Lp(a)	R	p-Value
TCl	0.118	>0.05
LDL	0.22	0.0503
AIP	0.00	<0.001
CRI1	0.7775	0.5561
CRI2	0.08837	0.5020
LTI	0.8199	<0.001
AC	0.5024	<0.6175

DISCUSSION

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 Baldassareet.al.,showed positive relationship between levels of lipoprotein(a) and carotid intimalthickness.[13]

Increased levels of Lp(a) in CKD is 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.[14] Atherosclerotic renal disease accounts for more than one third of all cases of end stage renal disease.[15] 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.[16]

AIP is an indirect indicator of small dense LDL levels . The value of AIP indicates a balance between the actual concentration of plasma TG and HDL-c, which predetermine the direction of the cholesterol transport in the intravascular pool (i.e the flux of newly produced cholesteryl esters by lecithin cholesterol acyltransferase) toward atherogenic LDL-c or beneficial HDL-c.[17] Clinical studies have shown that AIP predicts cardiovascular risk and that it is an easily available risk marker and a useful measure of the response to treatment.[18] Atherogenic lipoprotein phenotype is characterised by high TG, low HDLc and rise in small dense LDLc.[19] In such a scenario, it is essential to go beyond the routinely done lipid profile; especially, in centres with insufficient resources and owing to high cost of mostly available tests, these lipid ratios may prove a boon in the patient management.

On evaluation of lipid ratios, in the current study, we observed that Atherogenic Index of Plasma (AIP) was significantly higher in cases as compared to controls ($p < 0.001$). AIP is a ratio calculated as (logTG)/HDLc. Studies have shown an inverse relationship that exist between TG and HDLc and that the ratio of TG to HDLc is a strong predictor of infarction.[20] AIP is being used by some practitioners as a significant predictor of atherosclerosis. Moreover, studies have shown that in situations where other atherogenic risk parameters like TG and HDLc appear normal, AIP may be the diagnostic alternative.[21]

Studies have shown its role in predicting cardiovascular risk and effectiveness of therapy.[22] LTI was described by Enas et al as a new way to assesscardiovascular risk. Characterized by the multiplication ofthree atherogenic particles, which are total cholesterol,triglycerides and Lp (a), and the division of this productby the non-atherogenic HDL particle, the index describesthe overall lipid profile of patients.[23] Castelli's Risk Ratio (CRI) is based on three important lipid profile parameters i.e. TC, LDLc and HDLc. CRI-I calculated as the ratio of {TC/HDLc} and CRI-II as {LDLc/HDLc}[24], was found to be significantly higher in cases compared to controls ($p<0.001$).

CONCLUSION

From the present study we observed that only three indices viz- AIP, LTI, CRI-2 were significantly increased in cases compared to controls. When these three indices were compared with Lp(a) only AIP & LTI showed significant quantribution. Out of which AIP is the best and preferred indice because it doesn't require any special investigation. The aforementioned observations suggest that lipid ratios like Atherogenic Index of

Plasma, Castelli risk index and LTI could be used for identifying individuals at higher risk of cardiovascular disease in Indian population in the clinical setting especially when the absolute values of individual lipoproteins seem normal and in individuals with elevated TG concentrations. These can be easily calculated from the routinely done lipid profile parameters especially in centres where new tests are not possible due to cost factor. Thus, the use of these indexes should be encouraged to complement the existing profile of tests for identifying high risk individuals for CAD and effective drug management.

The increased pathological values of AIP suggestthat this index may have a potential application in routineclinical practice as an indirect indicator of sdLDL levels.

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