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Original Article

Biochemistry Section

Evaluation of Serum Lipoprotein (a) Levels and Novel Lipid Indices in Patients with Chronic Kidney Disease- A Case-control Study

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ABSTRACT

Introduction: Majority of Chronic Kidney Disease (CKD) patients are more likely to die of cardiovascular complications, before reaching End Stage Renal Disease (ESRD). Although there are many risk factors contributing to pathogenesis of cardiovascular disease in CKD subjects, dyslipidemia represents one of the modifiable risk factors. American Heart Association has recommended that CKD patients should be classified in the highest risk group for developing cardiovascular events. Kidney Disease: Improving Global Outcome (KDIGO) recommends, these patients should be evaluated for dyslipidemia and for treatment to reduce the risk of cardiovascular events.

Aim: To evaluate serum Lipoprotein (a) {Lp(a)} levels and assess the significance of novel lipid indices in non dialysis patients of CKD.

Materials and Methods: This analytical case-control study was conducted from January 2016 to June 2016 at Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India. It included 70 non dialysis CKD subjects and 70 healthy control subjects, adhering to inclusion and exclusion criteria. Fasting Blood Samples (FBS) were collected and analysed for: Fasting blood glucose, Fasting Lipid Profile, Serum Lp(a). Serum Lp(a) was estimated by immunoturbidimetry method and lipid profile by enzymatic method. Estimated Glomerular Filtration Rate (eGFR) was calculated using Modification of Diet in Renal Disease (MDRD) formula and staging of CKD subjects was done, based on KDIGO guidelines. Novel lipid indices were calculated using appropriate formula. Statistical analysis of the tabulated data was done using Social Sciences of the Statistical Package (SPSS) software.

Results: There were significant differences in the levels of FBS, Triglycerides (TG), Lp(a) between controls and non dialysis CKD subjects ($p<0.001$). Among Lipid Indices, Atherogenic Index of Plasma (AIP) and Lipid Tetrad Index (LTI) values were significantly higher in CKD subjects compared to controls ($p<0.001$), but no significant difference was seen in Atherogenic Coefficient (AC), Castelli's Risk Index-I (CRI-I) and CRI-II values. AIP and LTI showed significant positive correlation with Lp(a). LTI had the highest Positive Predictive Value (PPV) (77.8%) and Negative Predictive Value (NPV) (72.7%); AIP had PPV of 65.3% and NPV of 66.2%.

Conclusion: The present study concludes that, among lipid indices, AIP and LTI are the most suitable for assessment of atherogenicity in non dialysis CKD. In developing countries like India, owing to high cost of tests like Serum Lp(a), novel lipid index AIP can serve as a cost-effective screening tool for monitoring cardiovascular disease risk in CKD patients.

Keywords: Atherogenic index of plasma, Cardiovascular diseases, Estimated glomerular filtration rate, Lipid tetrad index, Renal diseases

INTRODUCTION

The CKD has become a public health problem with a prevalence of 8-16% worldwide. CKD is the 12th major cause of death and the 17th cause of disability globally [1]. A delay in recognition of various risk factors in the early stages of CKD contributes to significant mortality and morbidity. About 6% of the adult population in the United States was found to have CKD at stages 1 and 2 and the proportion of this group progressing to advanced stages of CKD is not known. About 4.5% of the US population is estimated to have Stages 3 and 4 CKD [2]. In India, diabetes and hypertension contribute to 40%-60% cases of CKD [3]. In Southern India, the major causes of CKD are diabetic nephropathy (29.6%), chronic interstitial nephritis (20.4%), chronic glomerulonephritis (17.4%) and hypertensive nephropathy (11%) [4].

In Indian population, the CKD prevalence is 13-15.04% [5]. These individuals are at a greater risk of cardiovascular disease as compared to the general population. Only a small percentage of CKD patients (0.5-1%) reach ESRD, while a major proportion of them (19-24%) die of cardiovascular complications, before reaching ESRD. Thus, cardiovascular disease is an important cause of morbidity and mortality in CKD. Past studies have clearly demonstrated an association between CKD and increased cardiovascular mortality and more so with ESRD [6-8].

Dyslipidemia is prevalent in 40-67% of CKD [9]. The prevalence of clinical Coronary Artery Disease (CAD) is 40%, in non dialysis CKD subjects, who progress to ESRD, and death due to CVD is 10-30 times higher as compared to the general population of same gender, age and race. American Heart Association has recommended that, patients with chronic impaired renal function should be categorised in the highest risk group for developing cardiovascular disease [8,9]. Although there are multiple risk factors that contribute to cardiovascular disease in CKD, a noteworthy potentially modifiable risk factor is dyslipidemia. Significant alterations in metabolism of Lps have been demonstrated in these patients, which in the advanced stages result in severe dyslipidemia [10,11].

In CKD, lipid profile parameters vary depending on the stage and associated proteinuria. In the absence of abnormal lipid profile, possibility of CAD cannot be ruled out. A widely accepted risk factor for CAD is Lp(a) [12,13]. Studies in CKD patients on dialysis have shown that different combinations of the lipid profile parameters, known as atherogenic ratios and novel lipid indices can be used to assess the total burden of dyslipidemia, as it waives the need for

various cut-off points for individual parameters in lipid profile [14]. In the present study, Serum Lp(a) levels were estimated; correlation between serum Lp(a) levels and novel lipid indices was done across stages 1-5 of CKD.

MATERIALS AND METHODS

This analytical case-control study was conducted from January 2016 to June 2016, at Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India. Institutional Ethical Committee permission was obtained before starting the study.

Sample size calculation: At Confidence Level (CI) of 95%, and prevalence of dyslipidemia in CKD being 60% [8], Sample size was estimated to be 126, using the formula:

Sample size={Z^2*p(1-p)}/e^2

Blood samples were collected from a total of 140 patients, which comprised the 70 patients, who attended Nephrology Outpatient Department (OPD) and 70 controls, at Government Stanley Medical College and Hospital, Chennai.

Inclusion criteria: Patients of both sexes, aged between 20-60 years diagnosed, as a case of CKD not on dialysis, were included in the present study.

Exclusion criteria: Patients with history of chronic smoking, Ischaemic heart disease, vascular diseases, chronic liver disease and patients taking drugs causing dyslipidemia or lipid lowering drugs, were excluded from the study.

A total of 70 cases were selected. For each case, healthy age and sex-matched control was selected. Total of 70 controls were selected.

In both cases and controls, Serum Lp(a) levels were estimated and correlated with novel lipid indices across stages 1-5 of CKD.

Study Procedure

Sample collection and preparation: After obtaining informed consent from the patients, 5 mL of fasting blood samples were collected under strict aseptic precautions in plain red capped venipuncture tubes. After the blood clotted, samples were centrifuged at 2000-2500 rpm for 15 minutes. Serum was separated, immediately from the samples and stored at -20ºC in deep freezer upto one month.

Study participants were examined and the following tests were done. Estimation of serum urea by urease coupled with glutamate dehydrogenase method, serum creatinine by Modified Jaffe's method, serum Lp(a) by Immunoturbidimetry method, Serum Total Cholesterol by Cholesterol oxidase (CHOD–PAP) method, Serum TGs by Glycero-3-phosphate oxidase (GPO-TOPS) method, Serum HDL by Direct Homogenous Assay-Modified Polyvinyl Sulfonic acid (PVS-PEGME 5thGen.) method were done using Beckman Coulter AU 480 Autoanalyser [15].

Following parameters were calculated [15].

Using Friedewald equation, Serum LDL=Total Cholesterol-HDL-(TG/5)

Non HDL=Total Cholesterol-HDL

Serum VLDL=TGs/5

MDRD formula was used to calculate eGFR. CKD subjects were classified into five stages according to KDIGO 2012 [16]:

Stage G1 CKD: eGFR 90 mL/min/1.732 m^2 or higher

Stage G2 CKD: eGFR 60-89 mL/min/1.732 m^2

Stage G3a and G3b CKD: eGFR 30-59 mL/min/1.732 m^2

Stage G4 CKD: eGFR 15-29 mL/min/1.732 m^2

Stage G5 CKD: eGFR less than 15 mL/min/1.732 m^2

Lipid Indices were calculated using following formulas:

1. AIP=log10 (TGs/HDL) [17]
   In which concentrations of TGs and HDL are expressed in molar concentrations
2. LTI=(Total Cholesterol*TGs*Lp(a))/HDL [18]
3. CRI-I=TC/HDL [19]
4. CRI-II=LDL/HDL [19]
5. AC=(TC–HDL)/HDL [20]

STATISTICAL ANALYSIS

Statistical analysis has been carried out using SPSS software version 16.0. To compare the means between two independent groups, Student's unpaired t-test was used. F test was applied between the study variables to know whether t-test can be applied to study the parameters and also, which type of t-test, either equal variance or separate variance unpaired t-test can be applied in the present study. Pearson's coefficient of correlation was used to estimate the degree of association between two quantitative variables. A p-value of <0.05 was considered as statistically significant.

RESULTS

[Table/Fig-1] depicts the baseline characteristics between controls and CKD subjects. The data suggests that there exists significant difference in blood glucose, urea, creatinine, eGFR values between controls and CKD subjects.

Parameters	Mean±SD		't' value*	p-value
	Controls (n=70)	Cases (n=70)		
Age (in years)	44.23±9.97	48.19±9.24	2.44	<0.001**
Glucose (mg/dL)	108.39±51.33	140.34±72.36	3.01	<0.001**
Urea (mg/dL)	24.96±6.65	53.74±27.00	8.66	<0.001**
Creatinine (mg/dL)	0.78±0.13	2.46±1.69	8.29	<0.001**
eGFR (mL/min/1.73m^2)	105.80±17.06	34.72±16.70	24.91	<0.001**

[Table/Fig-1]: Baseline characteristics of the study population.
(*Unpaired t-test; **p<0.05-Statistically significant)
eGFR: Estimated glomerular filtration rate

[Table/Fig-2] shows the distribution of male and female subjects among controls and CKD subjects. The distribution of both sexes is more or less equal within CKD subjects. [Table/Fig-3] shows the comparison of various lipid profile parameters between controls and CKD subjects. The data indicates that statistically significant differences exist in TG, VLDL and Lp(a) values. No statistically significant difference is observed between total cholesterol, LDL, HDL

Gender	Controls	Cases
Males	42 (60%)	31 (44.3%)
Females	28 (40%)	39 (55.7%)
Total	70 (100%)	70 (100%)

[Table/Fig-2]: Gender distribution among controls and CKD subjects.

Lipid profile parameters	Mean±SD		't' value*	p-value
	Controls (n=70)	Cases (n=70)		
Total cholesterol (mg/dL)	184.26±30.7	191.28±53.62	0.951	0.34
TG (mg/dL)	156.31±28.28	227.41±109.95	5.239	<0.001**
VLDL (mg/dL)	31.26±5.66	45.48±21.99	5.239	<0.001**
LDL (mg/dL)	111.61±25.11	105.62±39.76	1.066	0.29
HDL (mg/dL)	41.39±6.18	40.18±7.57	1.036	0.30
Lp(a) (mg/dL)	17.88±14.5	53.26±39.56	7.023	<0.001**
Non HDL (mg/dL)	142.87±26.68	151.10±48.64	1.241	0.2

[Table/Fig-3]: Comparison of lipid profile parameters between controls and CKD subjects.
(*Unpaired t-test; **p<0.05-Statistically Significant)
TG: Triglycerides; VLDL: Very low density lipoprotein; LDL: Low density lipoprotein; HDL: High density lipoprotein; Lp(a): Lipoprotein(a); Non HDL: Non high density lipoprotein

values between controls and CKD subjects. [Table/Fig-4] depicts the prevalence of dyslipidemia among controls and CKD subjects. The prevalence rates are higher for hypertriglyceridemia (74.3%) in CKD subjects compared to controls. No significant difference is observed in the prevalence rates of increased total cholesterol and increased LDL values between cases and controls. The prevalence rates of raised serum Lp(a) levels and low HDL levels are 48.6% and 65.7%, respectively, in cases, which are higher compared to controls. [Table/Fig-5] shows the comparison of various lipid Indices between controls and CKD subjects. The data demonstrates extremely significant differences in the values of AIP, LTI between controls and CKD subjects, whereas no significant difference in the values of AC, CRI-I and CRI-II between controls and CKD subjects is observed. [Table/Fig-6] explains the classification of CKD subjects into five stages, based on their eGFR (MDRD formula). A 43% of patients were in stage 3 and no patients in stage 1, stages 2, 4 and 5 have 10%, 36% and 11% patients, respectively.

Lipid profile parameters	Controls (n=70)	Cases (n=70)
Total cholesterol (>200 mg/dL)	21 (30%)	27 (38.6%)
Triglycerides (>150 mg/dL)	43 (61.4%)	52 (74.3%)
Low density lipoprotein (>130 mg/dL)	17 (24.3%)	16 (22.9%)
Lipoprotein(a) (>30 mg/dL)	25 (35.7%)	34 (48.6%)
High density lipoprotein (<40 mg/dL)	10 (14.3%)	46 (65.7%)

[Table/Fig-4]: Prevalence of dyslipidemia in controls and CKD subjects.

Lipid indices	Mean±SD		't' value*	p-value
	Controls	Cases		
Atherogenic Index of Plasma (AIP)	0.21±0.09	0.35±0.19	5.571	<0.001*
Lipid Tetrad Index (LTI)	12712.65±10790.82	73532.92±98208.05	5.150	<0.001*
Atherogenic Coefficient (AC)	3.48±0.64	3.77±1.15	1.843	0.06
Castelli's Risk Index-I (CRI-I)	4.48±0.64	4.77±1016	1.831	0.07
Castelli's Risk Index-II (CRI-II)	2.72±0.60	2.64±1.02	0.565	0.57

[Table/Fig-5]: Comparison of novel lipid indices between controls and CKD subjects. (*Unpaired t-test; **p<0.05; statistically significant)

Stages of CKD	eGFR (mL/min/1.73 m²)	No. of cases	Percentage of cases (%)
Stage G1	>90	0	0
Stage G2	60-89	7	10
Stage G3a and G3b	30-59	30	42.86
Stage G4	15-29	25	35.71
Stage G5	<15	8	11.43

[Table/Fig-6]: Staging of CKD in cases.

[Table/Fig-7] demonstrates that the most prevalent quantitative lipid abnormality is hypertriglyceridemia (85.7% in stage 2 and 84% in stage 4), followed by increased serum Lp(a) levels (75% in stage 5 and 71% in stage 2) and reduced HDL levels (75% in stage 5 and 57.1% in stage 2).

Lipid profile parameters	Stage 2 (n=7)	Stage 3 (n=30)	Stage 4 (n=25)	Stage 5 (n=8)
Total cholesterol (>200 mg/dL)	4 (57.1%)	11 (36.7%)	12 (48%)	0
Triglycerides (>150 mg/dL)	6 (85.7%)	21 (70%)	21 (84%)	4 (50%)
Low density lipoprotein (>130 mg/dL)	4 (57.1%)	6 (20%)	6 (24%)	0
Lipoprotein (a) (>30 mg/dL)	5 (71.4%)	19 (63.3%)	16 (64%)	6 (75%)
High density lipoprotein (<40 mg/dL)	4 (57.1%)	15 (50%)	9 (36%)	6 (75%)

[Table/Fig-7]: Prevalence of dyslipidemia across different stages of CKD subjects.

[Table/Fig-8] demonstrates that in CKD subjects there is a moderate positive correlation between serum Lp(a) and AIP (r=0.388), Non HDL (r=0.41). A strong positive correlation exists between serum Lp(a) and LTI (r=0.799). A weaker positive correlation is observed between serum Lp(a) and CRI-I (r=0.17). [Table/Fig-9] shows that, by using AIP (AIP >0.1), the prevalence of CKD subjects at high risk for CAD stratified are 85.7%, 63.3%, 72%, 50% in stages 2,3,4,5 of CKD, respectively. [Table/Fig-10] shows that the prevalence of CKD subjects at high risk for CAD stratified by using LTI >20,000 are 100%, 63.3%, 72%, 62.5% in Stages 2,3,4,5 of CKD, respectively. [Table/Fig-11] depicts the prevalence of CKD subjects at high risk, stratified using the independent CAD risk factor Lp(a) are 71.4%, 63.3%, 64%, 75% in stages 2,3,4,5 of CKD, respectively. [Table/Fig-12] compares the prevalence rates of CKD subjects stratified as high risk for CAD by AIP and LTI across various stages of CKD with the prevalence rate of increased serum Lp(a) levels, which is a standard risk factor for CAD. High risk subjects predicted by AIP and LTI, as evident by respective prevalence rates are equal and comparable to serum Lp(a) in Stage 3 (63.33%). The prevalence rates of increased AIP and LTI values are equal in stage 4 (72%) and higher than serum Lp(a) (64%). The prevalence rate of raised serum Lp(a) levels in stage 5 (75%) is higher than that of AIP (50%) and LTI (62.5%). [Table/Fig-13] indicates that Serum Lp(a) has the highest PPV (83.6%). Among the lipid indices, LTI has the highest PPV (77.8%) and the highest NPV (72.7%), followed by AIP with PPV (65.3%) and NPV (66.2%). [Table/Fig-14] shows the unpaired t-test between different analytes in CKD patients. The t-test between AIP, LTI, AC, CRI-I and CRI-II, non HDL, eGFR and Lp(a) shows significant differences between them, thereby implying that these variables are not independent of each other.

S. No.	Analytes	Pearson's correlation coefficient ('r-value')	Significance
1.	Lp(a) vs AIP	0.388	Positive correlation
2.	Lp(a) vs LTI	0.799	Positive correlation
3.	Lp(a) vs AC	0.327	Positive correlation
4.	Lp(a) vs CRI-I	0.327	Positive correlation
5.	Lp(a) vs CRI-II	0.171	Positive correlation
6.	Lp(a) vs non HDL	0.410	Positive correlation
7.	Lp(a) vs eGFR	0.071	Postive correlation

[Table/Fig-8]: Pearson's correlation between serum Lp(a) and lipid indices in CKD patients.
Lp(a): Lipoprotein(a); AIP: Atherogenic index of plasma; LTI: Lipid tetrad index; AC: Atherogenic coefficient; CRI-I: Castelli's risk index I; CRI-II: Castelli's risk index; Non HDL: Non high density lipoprotein; eGFR: Estimated glomerular filtration rate

Risk stratification using AIP	Stage 2	Stage 3	Stage 4	Stage 5
High Risk (AIP <0.1)	85.71%	63.33%	72%	50%
Low Risk (AIP >0.1)	14.29%	36.67%	28%	50%

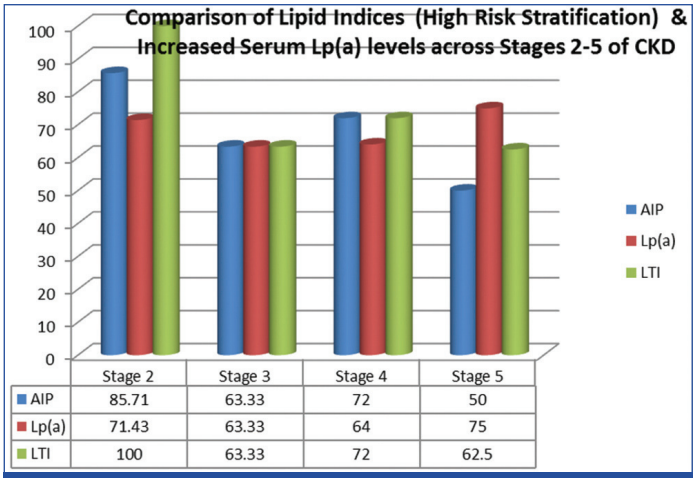
[Table/Fig-9]: Risk stratification using Atherogenic Index of Plasma (AIP) across stages 2-5 in CKD subjects.

Risk stratification using LTI	Stage 2	Stage 3	Stage 4	Stage 5
High risk (LTI >20000)	100%	63.33%	72%	62.5%
Low risk (LTI <20000)	0	36.67%	28%	37.5%

[Table/Fig-10]: Risk stratification using Lipid Tetrad Index (LTI) across stages 2-5 in CKD subjects.

Risk stratificationusing Lp(a)	Stage 2	Stage 3	Stage 4	Stage 5
High risk {Lp(a) >30 mg/dL}	71.4%	63.3%	64%	75%
Low risk {Lp(a) <30 mg/dL}	28.6%	36.7%	36%	25%

[Table/Fig-11]: Risk stratification using lipoprotein(a) across stages 2-5 in CKD subjects.



	Stage 2	Stage 3	Stage 4	Stage 5
AIP	85.71	63.33	72	50
Lp(a)	71.43	63.33	64	75
LTI	100	63.33	72	62.5

[Table/Fig-12]: Comparison of lipid indices (high risk stratification) and increased serum Lp(a) levels across stages 2-5 of CKD.
Lp(a): Lipoprotein(a); AIP: Atherogenic index of plasma; LTI: Lipid tetrad index

Parameters	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
Serum Lp(a)	83.6%	71.8%
AIP	65.3%	66.2%
LTI	77.8%	72.7%
AC	49.5%	48.9%
CRI-I	73.7%	53.7%
CRI-II	50%	50%

[Table/Fig-13]: Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of Lipid Indices and Serum Lp(a) in the study population.
Lp(a): Lipoprotein(a); AIP: Atherogenic index of plasma; LTI: Lipid tetrad index; AC: Atherogenic coefficient; CRI-I: Castelli's risk index I; CRI-II: Castelli's risk index

Parameters	t-value*	p-value
AIP Vs Lp(a)	11.19	<0.001**
LTI Vs Lp(a)	10.46	<0.001**
AC Vs Lp(a)	6.26	<0.001**
CRI-I Vs Lp(a)	10.25	<0.001**
CRI-II Vs Lp(a)	10.70	<0.001**
Non HDL Vs Lp(a)	13.05	<0.001**
eGFR Vs Lp(a)	3.61	<0.001**

[Table/Fig-14]: Unpaired t-test between different analytes among CKD subjects.
(*Unpaired t-test; **p<0.05-statistically significant)
Lp(a): Lipoprotein(a); AIP: Atherogenic index of plasma; LTI: Lipid tetrad index; AC: Atherogenic coefficient; CRI-I: Castelli's risk index I; CRI-II: Castelli's risk index; Non HDL: Non high density lipoprotein; eGFR: estimated Glomerular filtration rate

DISCUSSION

The present study examined the prevalence of dyslipidemia and evaluated serum Lp(a) levels across all stages of CKD subjects. Novel lipid indices, namely, AIP, LTI, AC, CRI-I and CRI-II were calculated and correlated with serum Lp(a) levels, which is a recognised independent risk factor for CAD. In the present study, the risk of CAD among non dialysis CKD subjects was assessed using lipid indices.

In the present study, the major causes of renal disease were diabetes mellitus and hypertension, accounting for 51.4%, 67.1%, respectively. CKD subjects were classified into five stages according to KDIGO 2012 [16]. Cases were 10%, 42.86%, 35.71% and 11.43% in stages 2, 3, 4, 5, respectively. A large proportion of cases belonged to stages 3 and 4 and no cases in stage 0 and 1, implying a delay in seeking medical opinion and thereby patients presenting in advanced stages to the OPD. Derangements of all classes of Lps were evident in all of the stages of CKD with progression of disease, which concurs with the study by Tsimihodimos V et al., [9].

In the present study, the most common lipid abnormality observed in CKD subjects was hypertriglyceridemia. The prevalence of hypertriglyceridemia was 74.3%, which is significantly higher than that of previous studies by Mikolasevic I and Zutelija M, and Choudhary N which reported the prevalence of hypertriglyceridemia to be 60% and 67%, respectively [21,22]. This might be due to a larger proportion of diabetics among the CKD subjects as compared with the controls. Vaziri ND and Moradi H study has shown that, it indicates an early feature of renal failure, the major mechanism is delayed clearance of ApoB containing Lps [23].

The difference in non HDL cholesterol values was not statistically significant {p-value=0.2, (>0.001)} between cases and controls which is similar to the studies by Mannangi NB and Jayaram S and Heon S et al., thus non HDL may not be an appropriate marker for cardiovascular risk assessment among CKD patients [14,24].

Mannangi NB and Jayaram S reported a statistically significant difference in serum Lp(a) levels (p<0.001) between cases (mean=61.98 mg/dL) and controls (mean 31.00 mg/dL). Similar results were observed in the present study which showed statistically significant difference (p-value <0.001) cases (mean=53.26 mg/dL) and controls (mean 17.8 mg/dL) in serum Lp(a) between levels. Of all lipid indices, statistically significant difference (p-value <0.001) were evident for AIP and Lipid Tedrad Index (LTI) which concurs with Mannangi NB and Jayaram S [14].

Cabarkapa V et al., reported AIP >0.11 in 56% of non dialysis subjects, whereas studies of Dobiasova M, Cai G et al., Hang F et al., also have shown that AIP is a strong predictor of the incidence of infarction [25-28]. Cai G et al., demonstrated that AIP levels were much higher in CAD group than in control subjects (0.17 vs 0.12) [27]. Hang F et al., showed that AIP quartile was associated with increased risk of major adverse cardiovascular outcomes [28]. Thus, AIP can serve as a diagnostic alternative, in subjects with normal serum TG and/or Serum HDL levels which concurs with Nwagha UI et al., [29]. As described in the study by Enas EA and Das S et al., LTI is a novel way to assess the cardiovascular disease risk [30,31]. It incorporates the product of three risk factors of atherogenesis namely, serum total cholesterol, serum TGs and serum Lp(a) and relates this product to non atherogenic protective HDL particle; thus reflects the overall lipid profile of patients. Statistically differences were not significant for other lipid indices-AC, CRI-I, CRI-II, which concords with Mannangi NB and Jayaram S [14].

Pearson's correlation was studied between serum Lp(a) and lipid indices in CKD subjects. A strong positive correlation (r=0.799, p<0.001) was observed between serum Lp(a) and LTI, which is concordant with study by Mannangi NB and Jayaram S, followed by AIP (r=0.388, p<0.001) [14]. Between serum Lp(a) and lipid indices namely, AC and CRI-I, moderate positive correlation was observed. A weak correlation exists between serum Lp(a) and CRI-II.

Individuals were stratified as high risk and low risk for CAD by using AIP and LTI, and the prevalence rates for high CAD risk in stage 3 was 63.3%, which is equal to the prevalence rate of raised serum Lp(a) levels. In the other stages of CKD, the prevalence rates of increased values of AIP and LTI were similar to that of serum Lp(a) values, implying that these indices are comparable in assessing CAD risk, as with serum Lp(a). Other Indices such as AC, CRI-I and CRI-II are not comparable with serum Lp(a) in risk assessment, as the prevalence rates of increased values of AC, CRI-I and CRI-II are much lower than that of serum Lp(a).

In the present study, among the lipid indices, LTI has the highest PPV (77.8%); AIP has PPV of 65.3%, concordant with study by Patil M et al., [12]. In the early stages of CKD, there is a higher prevalence of dyslipidemia and increased serum Lp(a) levels. The novel lipid indices LTI and AIP correlated strongly with serum Lp(a) levels, a widely accepted independent risk factor for CAD, and therefore can be used as screening tools for cardiovascular disease risk assessment stages 2 to 5 CKD subjects, whereas lipid indices namely, AC, CRI-I and CRI-II may not be appropriate for assessment of risk in CKD.

Limitation(s)

Robust multivariate analyses to determine independent association between various isoforms of Lp(a) in CKD, Lp measures, novel lipid indices and cardiovascular outcomes are required with larger sample size with a longer period of follow-up, to improvise and better reflection of the study results, across all stages of CKD.

CONCLUSION(S)

Dyslipidemia was evident in all the stages of CKD, with hypertriglyceridemia being the most common lipid abnormality. Dyslipidemia in CKD actively participates in the pathogenesis of cardiovascular disease. Plasma lipids, apoproteins alone as individual predictors of CAD risk, will be inadequate, especially in the early stages of kidney disease. Among the lipid indices, only AIP and LTI showed significant contribution in high risk prediction, when compared with serum Lp(a) levels. Out of which, AIP is preferred because it is the best cost-effective marker and it's increased pathological values act as an indirect indicator of small dense LDL particles, which are relatively more atherogenic. These novel lipid indices can be valuable screening tools, for monitoring cardiovascular disease risk in non dialysis CKD subjects.

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