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Evaluation of lipid profile and apolipoprotein-b in CKD patient with IHD

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Abstract
Background: Cardiovascular risk in CKD patients cannot be addressed adequately with the conventional treatments including statin. To modify the residual risk of cardiovascular events in CKD patient, studies are conducted in determining the associations of different biomarkers with cardiovascular disease.
Objective: The aim of the present study was to evaluate the association of lipid profile and apolipoprotein-B (Apo-B) with ischemic heart disease (IHD) in CKD patients and to compare lipid profile and apolipoprotein-B (Apo-B) in CKD patient with IHD.
Materials and Methods: This cross-sectional study was carried out in the department of Nephrology and Cardiology of Chittagong Medical College Hospital from October 2019 to September 2020. 100 patients of CKD with IHD were included. IHD was diagnosed by reviewing the previous record and by doing ECG and echocardiography. Lipid Profile and Apo-B were assessed in each patient.
Results: Total cholesterol, triglycerides higher in CKD stage 4, Apo-B in stage 3 and LDL-C in stage 5 with IHD. Conclusion: Apo-B, total cholesterol, triglycerides and LDL-C were significantly high in CKD patients with IHD.

Keywords: Lipid profile, apolipoprotein-B, CKD, IHD

Introduction
Cardiovascular disease is the leading cause of hospitalization and mortality in patients with chronic kidney disease. More than a million of cardiovascular disease (CVD) - related death was attributable to impaired kidney function [1]. It has been acknowledged that patients with advanced CKD, stage 4 or 5, are at high risk of CVD morbidity and mortality [2]. It is nowadays being advocated that patients with earlier stages of CKD also suffer a high rate of fatal and nonfatal cardiovascular events [3]. A recent, prospective population-based cohort study concluded that patients at the early stages of CKD, even without manifestations of vascular disease, were associated with excess risk of subsequent coronary artery disease (CAD). CKD patients are more likely to die from cardiovascular events instead of developing kidney failure and ending up on renal replacement therapy [4]. Dyslipidaemia is associated with rapid decline in renal function in CKD patients [5]. Hypercholesterolaemia and hypertriglyceridaemia also cause podocyte injury and mesangial sclerosis, subsequently leading to glomerulosclerosis [6]. Higher VLDL-C and Apo-B levels, as well as lower HDL-C and Apo-AI levels, were significantly associated with increased ASCVD risk [7]. A recent meta-analysis of 13 randomized controlled trials of statins in CKD found that the response to statins diminishes in later stages of CKD, with pooled data showing that 13% of treatment groups with CKD stage 3 experienced a major cardiovascular event, 10% with stage 4, and 22% with stage 5 [8].

Materials and Methods
This descriptive cross-sectional study was carried out in Department of Nephrology and Department of Cardiology of Chittagong Medical College Hospital, Chattogram from October 2019 to September 2020. One hundred patients of CKD with IHD admitted in Nephrology and Cardiology department of Chittagong Medical College Hospital during study period were conveniently enrolled in the study according to inclusion and exclusion criteria. Inclusion criteria were patients with CKD stages 3–5D as defined by the KDIGO, age of patient 18 years

and above of either sex, and newly diagnosed or old cases of IHD patient. Exclusion criteria were patients refused to participate in the study, patients with co-morbidities such as stroke, chronic obstructive pulmonary diseases, cirrhosis of liver, active malignancy and HIV infection/AIDS, pregnancy and lactating mother, and hemoglobin level less than 7.0 g/dl. Data were collected after approval from Ethical Review Committee of Chittagong Medical College. Informed written consent was obtained from the patients or attendants after full explanation of the ultimate outcome, complications and purpose of the study. Full history taking, clinical examination and investigations including CBC, urine R/M/E, serum creatinine, fasting lipid profile, ECG, echocardiography and Apolipoprotein-B of all selected patients were done.

Statistical analysis

After completion of case record form data were entered into Microsoft Excel to generate a master sheet. Next, they were fed into SPSS (Statistical package for social science) version 23 for processing and analysis. Categorical variables of the study subjects were expressed as frequency and percentage. Continuous data were expressed either in mean (±SD). F test (Analysis of Variance –ANOVA) was used to determine the significant mean differences of different laboratory parameters among patients with different CKD stages. P values less than 0.05 was considered to be statistically significant.

Results

Table 1: Socio-demographic, clinical and laboratory characteristics of the study patients. (N=100)

Characteristics	Mean (±SD)/Frequency (%)
Age (years)	48.66 (±14.65)
Sex	
Female	34 (34.0)
Male	66 (66.0)
BMI (kg/m^2)	
18.5-22.9 kg/m^2	70 (70.0)
23.0-24.9 kg/m^2	23 (23.0)
≥25.0 kg/m^2	7 (7.0)
CKD stage	
Stage 3	16 (16.0)
Stage 4	21 (21.0)
Stage 5	30 (30.0)
Stage 5D	33 (33.0)
H/O Statin use for	
< 3 months	57 (57.0)
≥3 months	43 (43.0)
Serum creatinine, mg/dl	6.63 ± 3.36
eGFR, ml/min/1.73 m^2	13.78 ± 11.49
Total cholesterol, mg/dl	142.58 ± 45.95
Triglyceride, mg/dl	175.56 ± 69.79
LDL-C, mg/dl	99.74 ± 24.04
HDL-C, mg/dl	34.59 ± 4.69
Apo – B, g/L	2.04 ± 0.45

Mean age of the CKD patients with IHD was 48.66 years. Males were predominating (66%). Majority of the patients (70%) were normal BMI. Most of the patients were in CKD stage 5 or 5D. Mean serum creatinine, eGFR, total cholesterol, triglyceride, LDL-C, HDL-C and Apo-B were 6.63 mg/dl, 13.78 ml/min/1.73 m^2, 142.58 mg/dl, 175.56 mg/dl, 99.74 mg/dl, 34.59 mg/dl and 2.04 g/l respectively (Table I).

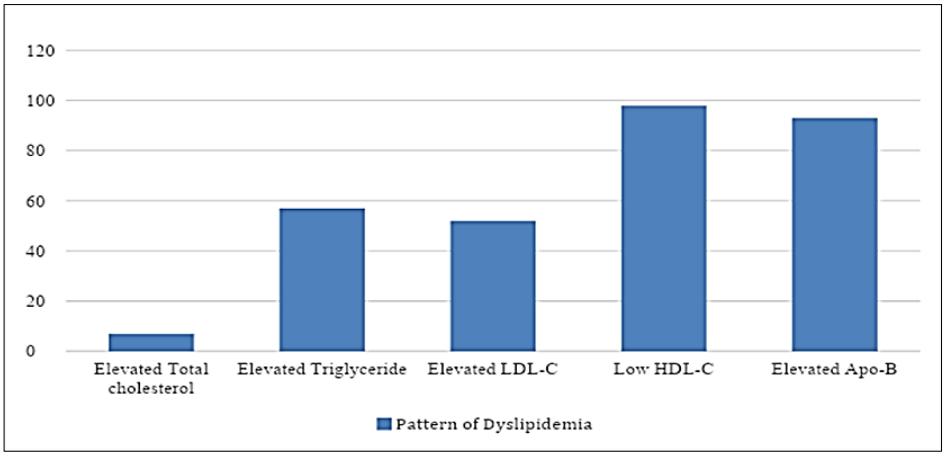

Fig 1: Pattern of dyslipidemia of study patients

The most frequent abnormality was low HDL-c (98%) followed by elevated Apo-B (93%), elevated TG (57%), elevated LDL-c (52%) and elevated total cholesterol (7%) (Figure I).

Table 2: Comparison of lipid profile and Apo-B among different stage of CKD patients. (N=100)

	CKD stage				P value
	Stage 3	Stage 4	Stage 5	Stage 5D	
Serum total cholesterol (mg/dl)	124.5±23.4	178.2±63.0	161.9±26.9	111.1±27.6	<0.001
Serum triglyceride (mg/dl)	174.2±60.6	241.4±85.9	182.4±25.9	128.1±54.0	<0.001
Serum LDL-C (mg/dl)	91.3±19.7	116.1±12.1	116.9±10.4	77.8±20.8	<0.001
Serum HDL-C (mg/dl)	35.4±3.6	35.6±3.8	32.6±4.2	36.6±5.3	0.004
Serum Apo-B (g/l)	1.8±0.4	2.2±0.4	2.3±0.4	1.8±0.4	<0.001

Data were presented as mean ±SD, *ANOVA test

The mean total cholesterol level was the highest in CKD patients with stage 4 (178.2±63.0 mg/dl) and the lowest was in CKD patients with stage 5D (111.1±27.6 mg/dl). These differences were statistically significant (p<0.001). The mean serum TG level was the highest in CKD patients with stage 4 (241.4±85.9 mg/dl) and the lowest was in CKD patients with stage 5D (128.1±54.0 mg/dl). These differences were statistically significant (p<0.001). The mean serum LDL-C level was the highest in CKD patients with stage 5 (116.9±10.4 mg/dl) and the lowest was in CKD patients with stage 5D (77.8±20.8 mg/dl). These differences were statistically significant (p<0.001). The mean serum HDL-C level was the highest in CKD patients with stage 5D (36.6±5.3 mg/dl) and the lowest was in CKD patients with stage 5 (32.6±4.2 mg/dl). These differences were statistically significant (p=0.004). The mean serum Apo-B level was the highest in CKD patients with stage 5 (2.3±0.4 g/l) and the lowest was in CKD patients with stage 3 and 5D (1.8±0.4 g/l). These differences were statistically significant (p<0.001).

Table 3: Comparison of lipid profile and Apo-B between CKD patients with statin use < 3 months and CKD patients with statin use > 3 months

Parameters	Statin use < 3 months	Statin use > 3 months	P value
	(n=32)	(n=68)	
Total cholesterol, mg/dl	173.31 ± 57.45	128.12 ± 30.40	<0.001
Triglyceride, mg/dl	245.90 ± 72.63	142.45 ± 35.80	<0.001
LDL-C, mg/dl	118.28 ±16.67	91.01 ± 22.00	0.001
HDL-C, mg/dl	33.47 ± 4.02	35.12 ± 4.91	<0.001
Apo-B, g/L	2.22 ± 0.41	1.95 ± 0.45	0.006

Study patients were categorized based on their exposure to statin therapy**.** Table 3 shows that mean (±SD) values of total cholesterol, TG, LDL-C, HDL-C and Apo-B were significantly lower in patients who received statin for more than 3 months than the patients received statin for less than 3 month's duration.

Discussion

Most common lipid abnormality in this study was low HDL levels (98%) and then elevated Apolipoprotein B (93%), hypertriglyceridemia (57%) along with a modest increase in LDL and TC. The low HDL levels in patients with CKD was consistent with Lee *et al.* and also with Moradi *et al*., 2009 [9, 10]. Decrease HDL-C might be due to the deficiency of LCAT which is essential for the esterification of cholesterol. LCAT plays an important role in HDL-mediated cholesterol uptake from the extrahepatic tissues and serves as a main determinant of HDL maturation and plasma HDL-C level. Elevated Apo-B was observed in 93% of patients which was significantly elevated in CKD stage 3 with IHD. A review by Tabas *et al*., (2007) reported that a longterm disturbance of carbohydrate metabolism can increase blood Apo-B and lipid with subendothelial accumulation of Apo-B containing lipoprotein [11]. Hypertriglyceridemia was observed in 57% of patients which was significantly elevated in CKD stage 4 with IHD. In previous studies showed that hypertriglyceridemia was the abnormality found in CKD patients [12, 13, 14]. Experimental studies revealed that accumulation of TGL-rich lipoprotein (very LDL [VLDL], chylomicrons, and their remnants) in individuals with predialysis CKD is mainly due to their decreased catabolism. Elevated LDL-C was observed in 52% of patients which was significantly elevated in CKD stage 5 with IHD. LDL-C and triglycerides were significantly higher in CKD patients showed in previous study [15]. Singh *et al*., 2019 reported that there is increase in total cholesterol, LDL-C, VLDL-C and triglycerides and decrease in HDL-C in all CKD patients compared to healthy control [16]. Their study demonstrated that there is dyslipidemia in CKD patient irrespective of mode of management but the dearrangement is much more common and significant in CKD with HD group and they are at risk of cardiovascular disease. Atherosclerosis are the byproducts of lipid metabolism, lipoproteins containing triglycerides, phospholipid and cholesterol and the changes, they undergo that eventually lead to macrophage activation, foam cell formation and other downstream atherosclerotic changes [17]. TC levels were significantly elevated in our study which was consistent with the previous study by Lee *et al*. The possible reason for the hypercholesterolemia in our study is significant elevation of cholesterol-containing lipid fractions (IDL and LDL).

Limitations

Patients were selected from a single institution; the sample size was relatively small and it was a cross-sectional design it was not possible to comment on the casualty.

Conclusion

The present study revealed that total cholesterol, triglycerides were found higher in CKD stage 4, LDL-C in stage 5 and

Apo-B in stage 3 with IHD. Total cholesterol, triglycerides and LDL-C were found lower in CKD stage 5D and Apo-B in stage 5 with IHD. Again, total cholesterol, triglycerides, LDL-C, Apo-B significantly lower in patient receiving statin more than 3 months.

Recommendations

A multicenter observational cohort study is warranted to confirm the predictive value of Apo-B for occurrence of cardiovascular events in CKD patients.

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