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ORIGINAL ARTICLE

Correlation of fasting lipid profile in non-diabetic CKD patients on conservative management

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Abstract

Background- Chronic kidney disease is emerging as a major chronic disease worldwide. There is surge in incidence of CKD in developing countries that is likely to pose a major problem in both health and economic sector. Ultimately, ESRD occurs due to progressive and unrelenting loss of nephron function.

Aim- This study aims to investigate the potential correlation between fasting lipid profile and carotid intimal thickness in non-diabetic CKD patients who are undergoing conservative management.

Discussion- CKD comprises of a spectrum of disease processes which results in metabolic, excretory, and synthetic failure culminating into the buildup of non-protein nitrogenous compounds and presents with numerous clinical features.

Conclusion- The findings of this study indicate a significant correlation between fasting lipid profile in CKD patients who are non-diabetic and undergoing conservative management.

Keywords- CKD, Fasting lipid profile, Carotid intimal thickness, HDL, LDL, VLDL

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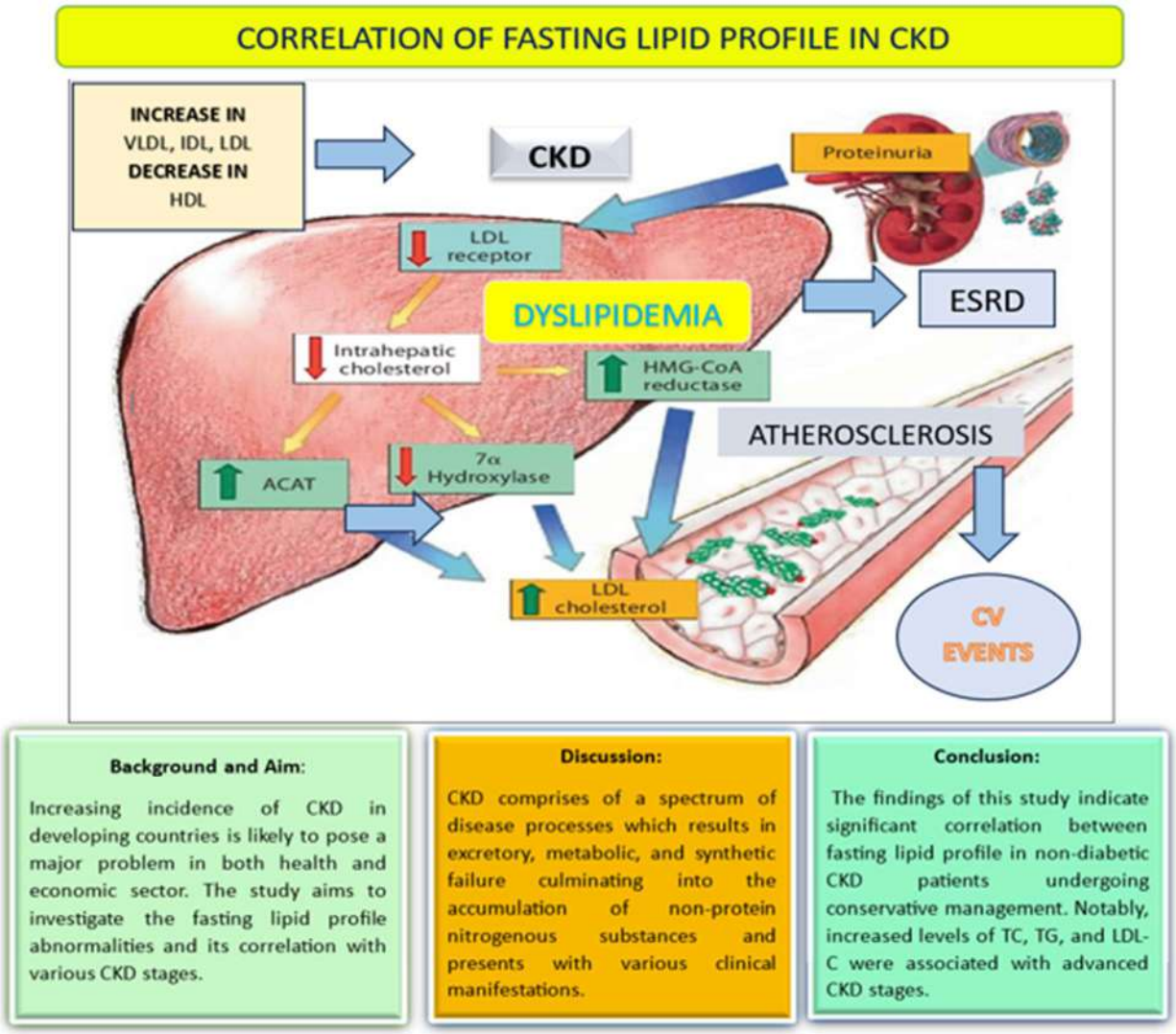
Graphical Abstract



Abbreviations-

CKD	:	Chronic Kidney Disease
ACAT	:	Acyl-Coenzyme A Cholesterol Acyltransferase
FGF-23	:	Fibroblast Growth Factor
GFR	:	Glomerular Filtration Rate
HMG CoA	:	Hydroxymethyl Glutaryl Coenzyme A
HDL	:	High Density Lipoprotein
ESRD	:	End Stage Renal Disease
LCAT	:	Lecithin Cholesterol Acyltransferase
TG	:	Triglycerides
LPL	:	Lipoprotein Lipase
LDL	:	Low Density Lipoprotein
VLDL	:	Very Low-Density Lipoprotein

Introduction

CKD is a globally recognized chronic condition that is rapidly increasing in prevalence, particularly in developing countries. This upward trend in CKD incidence presents significant challenges in both the healthcare and economic sectors. The etiology of CKD varies, with hypertension, diabetic nephropathy, glomerulonephritis, and nephrosclerosis being the most prevalent underlying causes. CKD is characterized by a decline in GFR and nephron population reduction on histology. The clinical course typically follows a progressive and relentless pattern, leading to ESRD with a complete loss of nephron function. ESRD, the final common pathway of various kidney injuries, manifests as renal bone disease, hypertension, anemia, nutritional impairment, neuropathy, reduced quality of life, and decreased life expectancy [1].

CKD Pathophysiology

CKD encompasses a diverse range of pathological processes that result in impaired excretory, metabolic, and synthetic functions, leading to the buildup of non-protein nitrogenous compounds and manifesting in various clinical features. The fundamental pathology of CKD is attributed to injury, inflammation, or hypertensive scarring, which ultimately leads to the loss of functional nephrons and progressive mechanisms resulting from long-term reduction in renal mass. This reduction is often due to increased glomerular capillary pressure and flow, leading to hyperfiltration and subsequent hypertrophy [2]. Moreover, it has been proposed that hyperfiltration and the reabsorption of proteins by the kidneys activate inflammatory responses mediated by vasoactive molecules such as cytokines and growth factors, ultimately leading to glomerular scarring [3]. Factors such as proteinuria, endothelial dysfunction, low-grade inflammation, dyslipidemia, and hypertension play prominent roles in CKD pathogenesis. Endothelial dysfunction, in particular, plays a pivotal role in initiating renal damage, leading to glomerulosclerosis and eventual renal failure [4].

CKD and dyslipidemia

In CKD, dyslipidemia acts as an independent risk factor contributing to disease progression. Several mechanisms are implicated in the development of kidney damage induced by lipid abnormalities. In renal failure, the concentration of lipoproteins may increase due to enhanced synthesis, reduced catabolism, or a combination of both processes. Among the lipid abnormalities commonly observed in CKD, hypertriglyceridemia and decreased HDL concentration are frequently noted [5].

In patients with CKD, there is an observable qualitative change in LDL particles. Specifically, there is a bigger proportion of highly atherogenic small density LDL (sdLDL). Certain modified LDL particles, such as Malondialdehyde-modified LDL and oxidized LDL (ox-LDL) have an affinity for binding to scavenger receptors on the surface of macrophages. This binding leads to cholesterol accumulation within macrophages, causing their evolution into foam cells within the vascular wall. Such processes contribute to the occurrence of atherosclerosis. Additionally, patients with

CKD exhibit significantly higher levels of lipoproteins, further correlating with an increased risk of atherogenesis and cardiovascular mortality [6].

Hypertriglyceridemia is commonly observed in patients with renal failure. One of the primary mechanisms contributing to this abnormality is the impaired activity of lipoprotein lipase, an enzyme involved in lipid metabolism. Additionally, various uremic toxins produced in renal failure directly inhibit the enzymes responsible for lipid metabolism [7].

In patients undergoing hemodialysis, triglyceride levels are typically elevated compared to those who are not undergoing dialysis. This elevation can be attributed to procedure of hemodialysis where heparin is used which have an inhibitory effect on lipoprotein lipase responsible for hydrolysis of TG's. Therefore, hypertriglyceridemia is considered an early characteristic of renal failure [8].

In CKD, there is a delay in the catabolism of VLDL leading to a rise in its concentration. Uremia is linked with depleted levels of apolipoprotein C-II and a decreased cholesterol content in high-density lipoprotein (HDL). Apo C-II is shifted from HDL to VLDL, and reduced levels of Apo C-II result in reduced metabolism of VLDL and triglycerides [9].

Multiple mechanisms contribute to the impaired reverse cholesterol transport resulting in reduction in cholesterol levels, which is often indicative Apolipoprotein AI (Apo AI), the activator of LCAT, is depleted in CKD due to downregulation of hepatic Apo AI genes.

As a result, the activity of LCAT, which is responsible for the esterification of cholesterol, is reduced, leading to faulty maturation of HDL. The function of LCAT constantly diminishes in CKD, resulting in lower levels of HDL [10].

CKD and Cardiovascular correlation

CKD is a significant predictor of atherosclerotic CVD and remains the leading cause of mortality and morbidity. The pathogenesis of atherosclerosis in CKD involves oxidative stress, where an imbalance between prooxidant and antioxidant systems contributes to an increased burden of atherosclerosis [11].

Increased levels of FGF-23, phosphate, anemia, and hyperparathyroidism, which are associated with CKD, play a substantial role in the development of occlusive coronary, cerebrovascular, and peripheral vascular diseases. Vascular remodeling is a characteristic feature of CKD, affecting both small and large arteries like aorta and coronary vessels. This remodeling is driven by medial calcification, which diminishes arterial compliance and leads to a rise in pulse pressure and systolic hypertension [12].

Consequently, this process causes aortic stiffness, left ventricular hypertrophy, and ultimately leading to myocardial infarction.

Methods

To achieve this objective, a cross-sectional study was conducted on a cohort of non-diabetic CKD patients receiving conservative management. The study involved measuring the fasting lipid profile

parameters, including total cholesterol, very low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, and low-density lipoprotein cholesterol (LDL-C). In early morning, a 12-hour fasting venous sample was collected in plain vial to measure the fasting lipid profile. The sample was allowed to clot and then centrifuged at 3000 RPM to separate the serum, which was subsequently sent for analysis. The lipid profile analysis was performed using the following principles:

1. Serum cholesterol was measured using the Triden method [13].
2. Serum HDL cholesterol was measured using the HDL-HDL Dimer Method [14].
3. Serum triglycerides were measured using the glycerophosphate oxidase method [15].
4. Serum LDL cholesterol was estimated using the Friedewald formula [16].
5. Serum VLDL cholesterol level equals to plasma triglyceride level divided by 5, representing the cholesterol-to-triglyceride ratio in VLDL particles.

Table 1. Distribution of laboratory parameters among study participants

Parameter	N	Mean	Standard Deviation	Minimum	Maximum
HB	90	8.18	2.26	3.40	15.20
TLC	90	9571.77	4849.22	1009.00	31400.00
PLT	90	227.94	102.93	60.00	542.00
B UREA	90	108.94	59.11	26.70	320.00
CREATININE	90	3.33	1.53	1.60	8.74
GFR	90	23.51	10.94	5.00	52.00
S ALBUMIN	90	2.99	.68	1.45	4.78
TOTAL CHOL	90	176.02	64.72	52.00	476.00
TG	90	178.06	69.02	50.87	405.90
HDL	90	39.31	12.67	17.00	102.00
LDL	90	101.32	53.43	11.80	388.40
VLDL	90	35.52	13.66	10.17	81.20
HbA1c	90	5.30	.34	4.20	5.80

Results

The study was conducted at GMSH-16 in Chandigarh and included 90 participants. The mean age of study participants was 54.01 ± 12.73 years, with the highest number of participants (31, 34.4%) falling in the age group of 51-60 years. The mean BMI of the study participants were 24.98 ± 3.38 kg/m². The mean systolic and diastolic blood pressure was 141.22 mmHg

and 83.76 mmHg respectively. The mean estimated glomerular filtration rate (GFR) was found to be 23.51 in the 90 cases.

In the present study, several parameters were evaluated, and it was observed that mean hemoglobin, GFR, and serum albumin levels were low, while serum creatinine and blood urea levels were high, as shown in Table 1.

The correlation between individual parameters of the lipid profile and the stage of chronic kidney disease is presented in Tables 2, 3, 4, 5, and 6.

Table 2. Correlation of Total Cholesterol with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
TOTAL CHOL	N	27	39	24	5.648	.005**
	Mean	151.63	172.53	209.13		
	SD	81.89	53.50	45.11		

Table 3. Correlation of Triglyceride level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
TG	N	27	39	24	3.948	.023*
	Mean	149.68	183.82	200.64		
	SD	58.73	68.87	71.86		

Table 4. Correlation of LDL level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
LDL	N	27	39	24	4.753	.011*
	Mean	84.56	96.73	127.64		
	SD	73.55	42.09	30.28		

Statistical analysis using Pearson's correlation coefficient was performed to assess the association between lipid profile parameters and CKD stages. The mean LDL ($p<0.011$), total cholesterol ($p<0.005$), VLDL ($p<0.022$), and triglyceride level ($p<0.023$) showed a significant increase as CKD stages progressed from 3 to 5. Additionally, the mean HDL cholesterol level decreased in stage 3 CKD patients.

Table 5. Correlation of VLDL level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
VLDL	N	27	39	24	4.013	.022*
	Mean	29.86	36.67	40.02		
	SD	11.68	13.74	13.98		

Table 6. Correlation of HDL level with CKD stages

		CKD STAGE			F-value	p-value
		3rd	4th	5th		
HDL	N	27	39	24	.467	.629
	Mean	37.98	38.98	41.35		
	SD	11.22	10.51	17.03		

Conclusion

This study's findings indicate a significant correlation between fasting lipid profile in non-diabetic CKD patients undergoing conservative management. Notably, increased levels of total cholesterol, triglycerides, and LDL-C were found to be linked with progression of CKD stages, while lower levels of HDL-C were also linked to with progression of CKD stages.

Future scope

The correlation between fasting lipid profile and carotid intimal thickness in non-diabetic CKD patients undergoing conservative management has emerged as an intriguing area of research. With the well-established link between lipid abnormalities and atherosclerosis progression, understanding the specific association between these two factors holds great potential for risk assessment, therapeutic strategies, and improved patient outcomes. Several promising avenues can be explored to expand our knowledge of this correlation:

- Conducting longitudinal studies will be crucial to establish a cause-and-effect relationship.
- Further investigation is warranted for prognostic value of fasting lipid profile and carotid intimal thickness allowing for more targeted interventions and improved management in non-diabetic CKD patients.
- Future research should focus on assessing the impact of lipid-lowering therapies, lifestyle modifications.
- Investigation of biomarkers of oxidative stress, inflammation, and endothelial dysfunction associated with carotid intimal thickness can contribute to a comprehensive understanding of the disease process.

These efforts will ultimately lead to improved patient outcomes and personalized care, effectively reducing the burden of cardiovascular disease in CKD patients.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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