

Effects of Haemodialysis on Serum Lipid Profile in Patients with Chronic Kidney Disease

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ABSTRACT

Objective: To compare the lipid parameters in Chronic Kidney disease patients undergoing haemodialysis with those on conservative management.

Study Design: Comparative cross sectional study.

Place and Duration of Study: Chemical Pathology and Endocrinology Department, Armed Forces Institute of Pathology, Rawalpindi, Pakistan from Jul to Dec 2023.

Methodology: The study was conducted on Chronic Kidney disease (CKD) patients. Blood sample was collected in gel bottles and centrifuged at 3000 revolution per minute for 5 minutes. The lipid profile and Renal Function Tests (RFTs) were analyzed on clinical chemistry auto-analyzer.

Results: A total of 257 patients of CKD, 147 on conservative management (Group A) and 110 on hemodialysis (Group B) were selected. Patients on hemodialysis with advance CKD, displayed significantly elevated median Total Cholesterol (4.67mmol/L versus 3.48mmol/L), LDL-Cholesterol (2.53mmol/L versus 1.80mmol/L), Non-HDL Cholesterol (3.71mmol/L versus 2.48mmol/L), Non-HDL to HDL-Cholesterol ratio (3.99mmol/L versus 2.36mmol/L) and Triglyceride (1.98mmol/L versus 1.54mmol/L) ($p<0.05$), while HDL-Cholesterol (0.81mmol/L versus 1.01mmol/L) was significantly lower ($p<0.001$) as compared to conservative managed patients. Total Cholesterol, LDL-Cholesterol, Non-HDL-Cholesterol, and Non-HDL to HDL-Cholesterol ratio showed significant positive association with serum creatinine, while HDL-Cholesterol exhibited a negative correlation with serum creatinine ($p<0.05$).

Conclusion: The progression of dyslipidemia is directly related to the stages of CKD. Therefore, early monitoring of lipid profiles in patients on hemodialysis with advance CKD is crucial to decrease risk which may reduce mortality and morbidity associated with cardiovascular disease among these patients.

Keywords: Chronic Kidney disease, Conservative management, Hemodialysis, Lipid parameters.

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INTRODUCTION

Chronic kidney disease (CKD) is characterized by a decline in the glomerular filtration rate (GFR) to below 60 mL/min per 1.73 m² persisting for a minimum of three months, irrespective of the underlying cause.^{1,2,3} Advanced CKD stages may require kidney replacement therapy. The disease affects plasma lipid levels, causing dyslipidemia and contributing to elevated risk of cardiovascular disease (CVD) mortality.⁴ Patients with End Stage Kidney Disease (ESKD) exhibit altered lipid profiles, emphasizing the intricate relationship between CKD and cardiovascular health.^{5,6} This involves an atypical distribution of Apo-C-III and Apo E, in High Density Lipoproteins (HDL), decline in lipoprotein lipase function, reducing the conversion of VLDL to LDL and leading to low HDL-cholesterol and Hypertriglyceridemia. These changes are documented in individuals with GFR of ≤ 50 mL/min/1.73m².⁷

Non-HDL cholesterol which is the cholesterol contained in all cholesterol-carrying particles except HDL-C, emerged as a more reliable predictor of CVD risk compared to LDL-C.⁸ Hemodialysis patients as patients with advance CKD, face factors promoting atherosclerosis, including increased triglyceride-rich particles, elevated susceptibility to LDL oxidation, and reduced protective effects of HDL-C. Lipid profiles vary among dialysis patients, emphasizing the need for individualized assessments.^{2,9}

The reported CKD prevalence rate ranges from 12.5% to 29.9%, in Pakistan with an average prevalence rate of 21.2%.¹⁰ Despite the rise in CKD patients and its established risk for cardiovascular disease, comprehensive research comparing cardiovascular disease risk in CKD patients under conservative management versus those undergoing dialysis with advance CKD is lacking. The primary goal of this study was to analyze and compare various lipid parameters among CKD patients in early stages managed with conservative treatment and advance disease on dialysis potentially identifying specific

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dyslipidemic risk factors and developing targeted interventions to alleviate cardiovascular disease risk in this population.

METHODOLOGY

This comparative cross-sectional study was conducted at the Chemical Pathology and Endocrinology Department of the Armed Forces Institute of Pathology in Rawalpindi, in collaboration with the Nephrology ward of the Armed Forces Institute of Urology. Study was conducted from July 2023 to December 2023, after approval from the Institutional Review Board with certificate number BSAHS/CHP-2/IRB/24/2264.

Inclusion Criteria: Both male and female subjects aged 17 years and older participated in the study.

Exclusion Criteria: Patients with history of pre-existing cardiovascular disease, smoking, or those on lipid-lowering drugs were excluded.

Informed consent was obtained after explaining the nature of the study to the patients. A total of 257 diagnosed CKD patients were included, comprising 147 patients under conservative management and 110 patients undergoing hemodialysis. The sample size was determined using the WHO formula, considering a CKD prevalence of 21.2%,¹¹ a margin error of 5%, and a confidence interval of 95%. Non-probability convenient sampling was employed, and samples were collected at the Armed Forces Institute of Urology.

After obtaining written informed consent, a detailed medical history was taken and approximately 5mL blood samples were collected in gel tube from each participant and centrifuged at 3000 RPM for 5 minutes. Total Cholesterol, HDL-Cholesterol, Triglyceride, Urea and Creatinine levels were analyzed on automated chemistry analyzer (Cobas-Pro) using respective enzymatic colorimetric kits with quality assurance protocols. LDL cholesterol levels were determined using the Friedwald equation: $\text{LDL cholesterol (mmol/L)} = \text{Total Cholesterol} - \text{HDL Cholesterol} - (\text{Triglyceride}/2.2)$. Non-HDL cholesterol was calculated as follows: $\text{Non-HDL cholesterol (mmol/L)} = \text{Total Cholesterol} - \text{HDL Cholesterol}$. The Non-HDL Ratio was obtained using the formula: $\text{Non-HDL Ratio} = \text{Non-HDL Cholesterol}/\text{HDL Cholesterol}$.

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics, including frequencies and percentages for qualitative variables and median values for

quantitative variables, were estimated. The Shapiro-wilks test was applied to check the data distribution, which revealed non-parametric distribution. The Independent-Samples Mann-Whitney U test was used to compare lipid profile parameters (Total Cholesterol, LDL-Cholesterol, HDL-Cholesterol, VLDL-Cholesterol, Triglycerides, and Non-HDL cholesterol) between patients under conservative management (early stage CKD) and those undergoing hemodialysis (Advance CKD). Spearman's Rank Correlation and Linear Regression Analysis were used to correlate lipid profile derangement among conservative group (Group A) and hemodialysis group (Group B). The p -value ≤ 0.05 was considered statistically significant.

RESULTS

Out of 357 individuals 127(49.4%) were males and 130(50.6%) were females. The mean age of patients was 53.18 ± 12.20 years, with mean age for CKD patients on conservative treatment was 52.86 ± 12.35 years, while for those on hemodialysis, and it was 53.61 ± 12.04 years.

Descriptive statistics, including the median and inter-quartile range (IQR), for various Lipid Profile parameters and RFTs in Group A and Group B were calculated. A non-parametric Mann-Whitney U-test was conducted to compare lipid profile patterns and RFTs between two groups. Results revealed that in Group B, (Advance CKD patients undergoing hemodialysis) median and IQR values for Total Cholesterol, Triglycerides, LDL-Cholesterol, VLDL-Cholesterol, Non-HDL-Cholesterol, Non-HDL/HDL-Cholesterol ratio, Serum Urea, and Serum Creatinine were significantly higher while HDL-Cholesterol was lower than Group A (Early stage CKD on Conservative management) p -value < 0.05 as shown in Table-I and Figure-1. All lipid parameters were higher in group B, while HDL-Cholesterol was the only lipoprotein found to be lower in Group B than in Group A.

Total Cholesterol, Triglycerides, LDL-Cholesterol, VLDL-Cholesterol, Non-HDL-Cholesterol and Non-HDL/HDL-Cholesterol ratio displayed significant positive correlations with Serum Creatinine, only HDL-Cholesterol exhibited a negative correlation with serum creatinine ($p < 0.05$). Notably, Triglyceride did not show a significant correlation with serum creatinine ($p = 0.056$) as shown in Table-II and Figure-2.

Table-I: Comparison of Median and IQR across Hemodialysis and Conservative Treatment Group (n=357)

Parameters	Comparison Groups	Median (IQR)	p- value
Total Cholesterol	Dialysis	4.67 mg/dl(2.34%)	<0.001
	Conservative	3.48 mg/dl(1.50%)	
Triglycerides	Dialysis	1.98 mg/dl(1.25%)	0.036
	Conservative	1.54 mg/dl(0.74%)	
LDL- Cholesterol	Dialysis	2.53 mg/dl(2.17%)	<0.001
	Conservative	1.80 mg/dl(1.19%)	
HDL- Cholesterol	Dialysis	0.81 mg/dl(0.39%)	<0.001
	Conservative	1.01 mg/dl(0.47%)	
VLDL Cholesterol	Dialysis	0.51 mg/dl(0.56%)	0.002
	Conservative	0.39 mg/dl(0.52%)	
Non - HDL Cholesterol	Dialysis	3.71 mg/dl(2.42%)	<0.001
	Conservative	2.48 mg/dl(1.19%)	
Non - HDL:HDLRatio	Dialysis	3.99 mg/dl(4.38%)	<0.001
	Conservative	2.36 mg/dl(1.78%)	
Serum Urea	Dialysis	17.0 mg/dl(9.7%)	<0.001
	Conservative	11.0 mg/dl(8.3%)	
Serum Creatinine	Dialysis	534.0 mg/dl(316%)	<0.001
	Conservative	197.0 mg/dl(99%)	

HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, VLDL : Very-Low-Density Lipoprotein

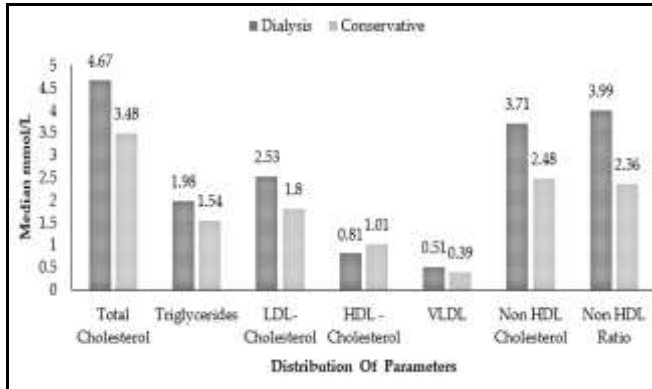


Figure-1: Graphical Comparison of Lipid Profile in Both Treatment Groups (n=357)

Table II: Spearman Correlation of Lipid Profile Parameters with Renal Function Tests (n=357)

Parameters	Correlation Variable	Spearman's Rho	p- value
Total Cholesterol	Serum Urea	0.124	0.047
	Serum Creatinine	0.215	<0.001
Triglycerides	Serum Urea	0.064	0.309
	Serum Creatinine	0.119	0.056
LDL - Cholesterol	Serum Urea	0.126	0.044
	Serum Creatinine	0.242	<0.001
HDL - Cholesterol	Serum Urea	-0.208	<0.001
	Serum Creatinine	-0.418	<0.001
VLDL Cholesterol	Serum Urea	0.057	0.359
	Serum Creatinine	0.205	<0.001
Non HDL - Cholesterol	Serum Urea	0.145	0.020
	Serum Creatinine	0.291	<0.001
Non HDL:HDL Ratio	Serum Urea	0.189	0.002
	Serum Creatinine	0.407	<0.001

HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, VLDL : Very-Low-Density Lipoprotein

DISCUSSION

CVD are the leading cause of hospitalization and mortality in CKD patients. Dyslipidemia, a well-established cardiovascular risk factor, is frequently encountered in CKD patients and is closely associated with deterioration in renal function and the initiation of renal replacement therapy (RRT).^{12,13} This study was

aimed to examine lipid profile patterns in two groups of patients: those under conservative management with early stages of CKD (Group A) and those receiving hemodialysis with advanced stages of CKD (Group B) to determine risk for CVD.

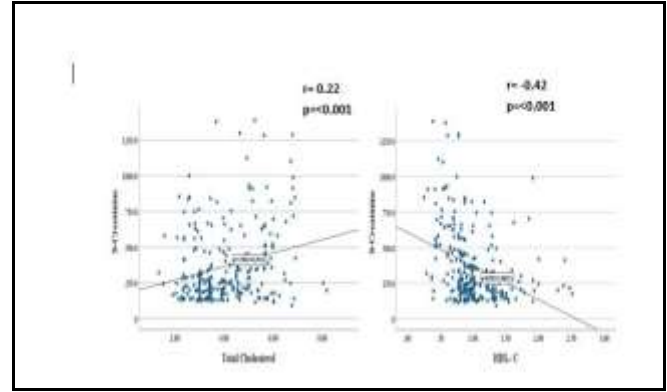


Figure-2: Linear Regression Analysis between Lipid Profile variables with Renal Function Test

In our study, hemodialysis patients (Group B) exhibited increased levels of total cholesterol (TC), low-density lipoprotein Cholesterol (LDL-C), triglycerides (TGs), very-low-density lipoprotein Cholesterol (VLDL-C), Non high-density lipoprotein Cholesterol (Non HDLC)- and Non HDLC- to HDL-C ratio, while high-density lipoprotein Cholesterol(HDL-C) levels were lower compared to patients on conservative management (Group A). These findings are consistent with Choudhary study (2019),¹² who reported that in patients with CKD lipid profiles showed significant rise in TC, LDL-C and TG levels, with significant decrease in HDL-C, overall frequency of dyslipidemia was 82.6% in these patients. This upward trend in Total Cholesterol, TG, Low density lipoprotein-Cholesterol, and Very Low-Density Lipoprotein-Cholesterol was more prominent with the progression of CKD stages, particularly in End-Stage Renal Disease (ESRD) patients. Saini and colleague (2022)² also reported a significant decrease HDL-C, increase TC, LDL-C, TG and VLDL-C levels in CKD patients on hemodialysis as compared patients on conservative management (p -value <0.05). Singh *et al.* in 2019,¹³ reported that TC, LDL-C,VLDL-C) and (TG) were significantly higher while HDL-C was significantly lower in CKD patients as compared to healthy controls (p -value for each variable was <0.001). They also noted that dyslipidemia was present in CKD patients irrespective of type of management protocol, but this derangement was

much more significant in CKD with hemodialysis patients as noted in our results. Muhammad *et al.* (2019),¹⁴ in a study regarding dyslipidemia in CKD patients on Haemodialysis/Conservative management with Control Population reported elevated levels of TC, TG, LDL-C and low levels of HDL-C in CKD patients. Monitoring and treatment of dyslipidemia helps to decrease mortality in CKD patients. Elevated TC levels in CKD patients undergoing hemodialysis were also noted by Kumari & Srinivas (2018).¹⁵ These results were consistent to our results. One of the reasons these findings may be that most of the patients on haemodialysis were with advanced renal failure than on conservative management.

Ganta *et al.* (2016),¹⁶ reported prevalence of dyslipidemia in CKD patients of about 65% and HDL-C was significantly lower while TG and TC were significantly higher in the hemodialysis group; our results also noted lower HDL-C levels in advanced CKD patients. These findings were also supported by Barbagallo *et al.* (2021),¹⁷ and Meena BS *co.*¹⁸ They recommended that lipid lowering treatments may change the natural history of CVD in advance CKD patients and may be an important management protocol for these patients. Enzymes and proteins involved in different metabolism pathways in lipoprotein metabolism are impaired in CKD. The reduced HDL-C levels in uremic patients, may be due to decreased levels of apolipoprotein A along with diminished activity of lecithin-cholesterol acetyltransferase (LCAT), facilitating the transfer of cholesterol esters from HDL to TG-rich lipoproteins. Elevated levels of apo C-III, apo B- lipoproteins and decrease apo A- lipoproteins may be responsible to alter lipoprotein metabolism, and accumulation of atherogenic particles characterized by raised TG, Lp(a), dense LDL and low HDL-C.¹⁷ Kazi *et al.* (2022),¹⁹ noted that Plasma TG and VLDL-C fraction were significantly elevated, while HDL-C significantly decreased in CKD patients compared to controls ($p < 0.001$), but there was no significant difference in TC and LDL-C in two groups. Anwar S and colleagues (2021),²⁰ reported, lower TC levels in 61.4% and increased levels in 2.9% of patients with CKD on hemodialysis. Both of these studies reported different results regarding TC as compared to our results, although they reported raised TG and low HDL-C similar to our study. The difference regarding cholesterol may be due to sample size as only 30 patients were included by Kazi D *et al.* and 70 patients by Anwar S, in contrast we selected 257 diagnosed

CKD patients (147 patients under conservative management and 110 patients undergoing hemodialysis) in our study.

Current evidence indicates that decreasing LDL-C is beneficial for preventing major CVD events in CKD patients. Lipid lowering treatment is recommended in all patients with stage 3 or worse CKD, independent of baseline LDL-C or TC levels.²¹ Lifestyle modifications, careful selection of drugs and statin therapy are key components in managing dyslipidemia in renal transplant and other solid organ transplant patients to prevent CVD.²²

Our study observed a strong positive correlation among lipid parameters, including TC, LDL, Non-HDL-C and the Non-HDL-C to HDL-C ratio, while HDL-C showed negative correlation in relation to Serum Urea and Serum Creatinine with Urea levels. Notably, there was no significant correlation found between TGs and VLDL with S. Urea and S. Creatinine. These findings differ from those reported by Baqi and K. Rostam⁴ and Liao *et al.*²³ and who observed a significant correlation between blood urea and TGs levels. Reported difference may be due to sample size, variation in population and methodologies used for analysis and selection of patients. Non-HDL-C and Non-HDL-C to HDL-C ratio is a potentially better marker for identification of CVD risk as it reflects the total atherogenic and antiatherogenic particles. Our study observed a significant increase in Non-HDL-C and Non-HDL-C to HDL-C ratio among hemodialysis patients compared to those on conservative management, highlighting its role as a crucial predictive marker for CVD risk. Liao *et al.*²³ also reported similar results emphasizing the role of elevated Non-HDL-C to HDL-C ratio for increased morbidity in CKD patients. Early identification and treatment may be important for individuals, who are at high risk of CVD like CKD.

LIMITATION OF STUDY

The limitations of our study were; it was a single center study and we did not follow individuals for long term effects. Multicenter studies with longitudinal follow up to check the long term effects of dyslipidemia in CKD patients may be more beneficial to establish cause effect relationship.

CONCLUSION

The study reveals significant dyslipidemia in CKD patients, particularly those having advanced disease undergoing hemodialysis, increasing the risk of atherosclerosis and CVD. Early identification and lipid-lowering interventions by drugs or life style changes are

crucial for effective disease management and reduce CVD risk in CKD patients.

Conflict of Interest: None.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

SK & MA: Conception, study design, drafting the manuscript, approval of the final version to be published.

MQAK & MY: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SS & AA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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