Open Access

Original Article

Association of Dyslipidemia with Chronic Kidney Disease in Patients Requiring Renal Replacement Therapy

Muhammad Ansar, Malik Nadeem Azam Khan, Asif Farooq, Hafiz Asad Saeed*, Falak Naz Alvi, Haider Rana

Department of Medicine, Combined Military Hospital, Kharian/National University of Medical Sciences (NUMS) Pakistan, *Department of Medicine, Combined Military Hospital, Nowshera /National University of Medical Sciences (NUMS) Pakistan,

ABSTRACT

Objective: To highlight the association of dyslipidemia in patients of Chronic Kidney Disease requiring Hemodialysis (CKD-5D) at a tertiary care hospital.

Study Design: Comparative cross-sectional study

Place and Study of Duration: Department of Nephrology, Combined Military Hospital, Kharian, Pakistan, Jan to Jun 2023.

Methodology: Using consecutive sampling, CKD patients of either gender with age > 20 years, both dialysis dependent (CKD-5D) and non-dialysis (CKD-5ND) were included and divided into two Groups of 50 patients each. Serum cholesterol, triglycerides (TGs), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) levels in both Group patients were assessed and analyzed. Measures of association like odds ratio and prevalence ratio were calculated.

Results: Diabetes Mellitus was the most common cause of CKD in both groups. Majority of Group A patients 20(40.0%) had CKD-5 for 3-5 years as compared to majority of Group B patients 22(44.0%) who had CKD-5 for > 5 years with dialysis dependency for at-least 1 year (p=0.805). LDL-C levels comparison in both groups showed hyper-LDL-cholesterolemia in 30(60.0%) vs 37(74.0%) of Group A (CKD-5ND) and Group B (CKD-5D) patients, respectively (p=0.109). Odds ratio (OR) and prevalence ratio (PR) were > 1 indicating there were higher odds and higher prevalence of raised LDL levels in CKD-5D (OR=1.89 [95% CI 0.812 - 4.431], p=0.069, PR = 1.23).

Conclusion: There is high prevalence of dyslipidemia in advancing CKD patients and with declining eGFR dyslipidemia risk increases leading to increased incidence of fatal events.

Keywords: Chronic Kidney Disease, Cholesterol, Dyslipidemia, Hemodialysis, Renal Replacement therapy

How to Cite This Article: *Ansar M, Khan MNA, Farooq A, Saeed HAS, Alvi FN, Rana H. Association of Dyslipidemia with Chronic Kidney Disease in Patients Requiring Renal Replacement Therapy. Pak Armed Forces Med J 2025; 75(5): 965-968. DOI: https://doi.org/10.51253/pafmj.v75i4.10845*

INTRODUCTION

Chronic Kidney Disease (CKD) has a projected prevalence of 13.4% globally, with patients needing hemodialysis (CKD-5D) estimated to be between 4.9-7.1 million.[1] In 2019, 1.4 million deaths were secondary to CKD.[2] Dyslipidemia, characterized by high levels of Low Density Lipoprotein (LDL) and low levels of High Density Lipoprotein (HDL),[3] is caused by genetic predisposition, unhealthy diet, sedentary lifestyle, obesity, diabetes mellitus, thyroid disease and CKD, is a risk factor for cardiovascular diseases, leading to myocardial ischemia, infarction and stroke.[4] CKD causes down regulation of lipoprotein lipase and LDL receptor leading to increased cholesterol and TGs, decreased activity of lecithin-cholesterol acyltransferase (LCAT) and increased activity of cholesteryl ester transferase protein (CETP).[5] Increased requirement of lipid lowering drugs from 18.1% in CKD-1 to 44.7% in CKD-4 is noted among patients.[6] Dyslipidemia in CKD-5ND patients is characterized by raised levels of LDL-C and TG, and low levels of HDL-C, wile dyslipidemia in dialysis dependent CKD patients is usually more severe and characterized by raised levels of LDL-C, TC, and TG, and low levels of HDL-C.[7] Dyslipidemia in CKD patients on hemodialysis is a common occurrence primarily due to deterioration of renal function and reduced glomerular filtration.[8] Dyslipidemia in the background of CKD is linked to risk of cardiovascular event, which is the leading cause of death among patients on hemodialysis (HD).[9] Furthermore, increased LDL-C is associated with a rapid progression of CKD. Studies have shown an inverse association between HDL-C and CVD in these patients.[10] The purpose of this study was to assess and compare the association and incidence of dyslipidemia in CKD patients with hemodialysis (HD) dependency and without hemodialysis dependency.

Correspondence: Dr Muhammad Ansar, Department of Medicine, Combined Military Hospital, Kharian Pakistan

Received: 08 Sep 2023; revision received: 16 Jan 2024; accepted: 09 Feb 2024

METHODOLOGY

Following approval of Institutional Ethics Committee (IEC: 17/03Jul23), this study was

conducted at Department of Nephrology and Dialysis Unit, Combined Military Hospital (CMH), Kharian, Pakistan, over a period of 6 months from January to June 2023. Sample size of n= 92 was calculated using online sample size calculator keeping in view the estimated population of End Stage Renal Disease (ESRD) in CKD requiring hemodialysis to be 3 million with 13.4% prevalence of ESRD in CKD.[11] and 45.5% prevalence of dyslipidemia in CKD,[6] with confidence interval of 95% and margin of error 5%. However, a total of 112 patients of CKD-5 were enrolled using consecutive, non-probability sampling technique after obtaining informed consent.

Inclusion Criteria: Patients of either gender, age > 20 years with CKD-5 (e-GFR < 15 mL/min/1.73m2), on hemodialysis (CKD-5D) for at least 1 year and without hemodialysis dependency (CKD-5ND).

Exclusion Criteria: Patients who had a genetic factor leading to dyslipidemia, previous history of use of lipid lowering agents or on peritoneal dialysis with BMI > 25, thyroid disease and having any tumor or malignancy were excluded.

All patients were advised fasting lipid profile and results were recorded. Duration of RRT (Hemodialysis in this study) along with per week hemodialysis dependency, adequacy and compliance to HD were also noted as contributing factors for dyslipidemia. Association of dyslipidemia in CKD-5 patients were observed and compared between CKD-5D and CKD-5ND patients with measures of association including Odds ratio (OR) and prevalence ratio (PR). The routine diet of the patients was also inquired by thorough history from patients as well as their attendants. Out of total patients, 4 patients were lost to follow up after investigations,[8] patients expired before follow-up due to cardiovascular events secondary to CKD-5 so 100 patients with 50 patients in each group were included in final analysis. All patients age, gender, duration of CKD and the cause of CKD were assessed, and the data was summarized as mean, frequency, and percentage and analyzed via Statistical Package for the Social Sciences (SPSS) version 23.0. Odds ratio and prevalence ratio was also calculated and Chi-square was applied with *p*-value ≤ 0.05 taken as statistically significant.

RESULTS

Among 100 patients analyzed, the mean age of Group A was 53.58±9.75 years and 51.23±9.71 years of Group B patients (*p*=0.148). There were 29(58.0%) males and 21(42.0%) females with CKD-5ND in the Group A and 22(44.0%) males and 28(56.0%) female patients of CKD-5D in Group B (*p*=0.181). The underlying cause of CKD was also inquired and Diabetes Mellitus was the most common cause of CKD in both groups, 22(44.0%) versus 18(36.0%) in Group A and Group B, respectively. In Group A, 20(40.0%) patients had CKD-5 for 3-5 years as compared to majority of Group B patients 22(44.0%) who had CKD-5 for > 5 years with dialysis dependency for at least 1 year (*p*=0.805). Out of total 50 CKD-5D patients in Group B, 11(22.0%) were on once weekly maintenance HD, 24 (48.0%) were on twice weekly and 15(30.0%) were undergoing HD thrice weekly, as illustrated by Figure-1. There were statistically no significant differences between high fat diet consumption between both groups 23(46.0%) vs 21(58.0%) respectively (*p*=0.261). Table-I shows all parameters that were studied in both groups.

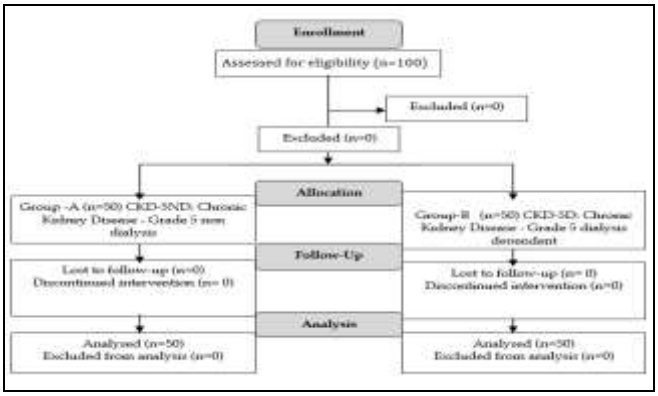

Figure: Patient Flow Diagram (n=100)

Table-I: Studied Parameters of patients in both Groups (n=100)

Variable		Group A CKD-5ND (n=50)	Group B CKD-5D (n=50)	*p*-value (≤0.05)
Age (years)	(Mean±SD)	53.58±9.75	51.23±9.71	0.148
Gender	Male	29(58.0%)	22(44.0%)	0.181
	Female	21(42.0%)	28(56.0%)	
CKD Duration (years)	1 - 3	13(26.0%)	16(32.0%)	0.805
	3 - 5	20(40.0%)	12(24.0%)	
	>5	17(34.0%)	22(44.0%)	
Diet	Normal Fat (20-35%)	27(54.0%)	29(42.0%)	0.261
	High Fat (> 35%)	23(46.0%)	21(58.0%)	

**SD: Standard Deviation, CKD-5ND: Chronic Kidney Disease - Grade 5 non dialysis, CKD-5D: Chronic Kidney Disease - Grade 5 dialysis dependent*

Total cholesterol (TC), Triglycerides (TGs), Low density lipoprotein cholesterol (LDL-c) and High density lipoprotein (HDL-c) levels were checked and compared between both groups for incidence and severity of dyslipidemia as shown in Table-II. LDL-C levels were compared in both groups which showed

hyper-LDL-cholesterolemia in 30 (60.0%) compared to 37(74.0%) patients of Group A (CKD-5ND) and Group B (CKD-5D) respectively (p=0.109).

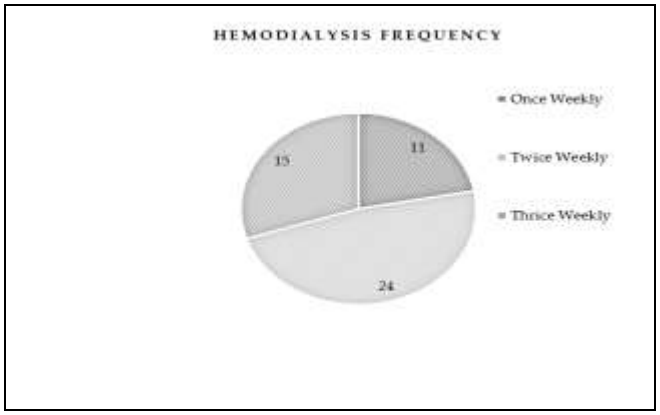

Figure-1: Frequency of Hemodialysis in CKD-5D patients, (n=100)

Table-II: Comparison of Dyslipidemia in Both Groups (n=100)

Variable		Group A CKD-5ND (n=50)	Group B CKD-5D (n=50)	p-value (≤0.05)
Total Cholesterol (TC)	Normal < 5.2 mmol/L)	28(56.0%)	21(42.0%)	0.109
	High > 5.2 mmol/L	22(44.0%)	29(58.0%)	
Triglycerides (TGs)	Normal (70 - 150 mg/dL)	21(42.0%)	16(32.0%)	0.255
	High (> 150 mg/dL)	29(58.0%)	34(68.0%)	
LDL	Normal (< 2.6 mmol/L)	20(40.0%)	13(26.0%)	0.109
	High (> 2.6 mmol/L)	30 (60.0%)	37 (74.0%)	
HDL	Normal (< 0.8 - 1.8 mmol/L)	29(58.0%)	18(36.0%)	0.047
	Low (< 0.9 mmol/L)	21(42.0%)	32(64.0%)	

**CKD-5ND: Chronic Kidney Disease - Grade 5 non dialysis, CKD-5D: Chronic Kidney Disease - Grade 5 dialysis dependent, LDL: Low density lipoprotein, HDL: High density lipoprotein*

Odds ratio (OR) and prevalence ratio (PR) were calculated for association of increased LDL levels with hemodialysis. Both odds ratio (OR) and prevalence ratio (PR) were > 1 indicating there were higher odds and higher prevalence of raised LDL levels in patients with CKD-5D (OR=1.89 [95% CI 0.812 - 4.431], p=0.069, PR = 1.23 as shown in Table-III.

DISCUSSION

Dyslipidemia is common in patients with CKD along with hyperuricemia as TG and LDL levels are generally relatively near normal or marginally raised with raised triglycerides in patients with CKD without HD dependency.[12] In one study, it was concluded that according to K/DOQI guidelines on dyslipidemia in CKD patients, 55.7% patients on HD dependency have LDL levels > 100mg/dL as compared to non-HD dependent patients in which LDL relatively near normal or marginally raised.[13] While pathophysiology and management of dyslipidemia in early CKD is quite similar to normal individuals, dyslipidemia incidence is disproportionately increased in advancing as well as end stage CKD leading to ineffectiveness to lipid lowering therapy, and highest risk of cardiovascular fatal events.[14] One study concluded that overall mortality in CKD patients on dialysis was 18.4% out of which 43% died of cardiovascular complications secondary to dyslipidemia.[15] Similarly, in another study, the hazard ratio of dyslipidemia between CKD and non-CKD patients was calculated which revealed that the incidence of high TG, high cholesterol, high LDL were 64.4/1000 person-years, 83.1/1000 person-years and 14.5/1000 person-years respectively.[16] In one study, stage 4 target LDL-cholesterol (LDL-C) was 55mg/dL or less with recommended LDL-C reduction of 50% from baseline and in stage 3, LDL-C target was 70 mg/dL or less with recommended 50% reduction from baseline.[17] Similar to our study, another author also concluded that advanced stage CKD patients were more likely to have hypertriglyceridemia and hypo-HDL-cholesterolemia.[18] As dyslipidemia is a risk factor for cardiovascular events, it was noted to be even higher and more severe in the background of CKD, it was explained in association of non-HDL cholesterol and mortality in CKD patients undergoing dialysis.[19]

Table-III: Measures of Association of High LDL with Hemodialysis (n=100)

		Hemodialysis		Total
		Yes	No	
High LDL	Yes	37 (55.2%)	30 (44.8%)	67
	No	13 (39.3%)	20 (60.7%)	33
Total		50	50	100

Odds of High LDL in Hemodialysis = (37/13) = 2.84
Odds of High LDL in Non-Hemodialysis = (30/20) = 1.50
Odds Ratio (OR) = Odds in Hemodialysis / Odds in Non-Hemodialysis
OR = 2.84/1.50 = 1.89 [95% CI 0.812 - 4.431], p=0.069

Prevalence of High LDL in Hemodialysis: 37/50 = 0.74
Prevalence of High LDL in Non-Hemodialysis: 30/50 = 0.60
Prevalence Ratio (PR): Prevalence of Hyperlipidemia in Hemodialysis/Prevalence of Hyperlipidemia in Non-Hemodialysis:
PR: 0.74/0.60 = 1.23

LIMITATION OF STUDY

This study was conducted in a single health care setup within a limited time duration and small sample size, hence it does not represent the exact number of the individuals with dyslipidemia in background of CKD-5. Peritoneal

dialysis is also an important confounding factor in association of dyslipidemia, but patients on peritoneal dialysis were not studied. Therefore, further studies including randomized controlled trails (RCTs) with larger sample size are needed for more accurate results before implementing on general population.

CONCLUSION

The prevalence of dyslipidemia is high in both HD dependent and non-HD dependent CKD patients but is more pronounced and severe in dialysis dependent CKD patients, needing lipid lowering therapy. Hence, regular lipid profiling, dietary modifications and appropriate lipid lowering medications are required to manage dyslipidemia and prevent cardiovascular events.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

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

MA & MNAK: Data acquisition, data analysis, critical review, approval of the final version to be published.

AF & HAS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

FNA & HR: 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.

REFERENCES

1. Lv JC, Zhang LX. Prevalence and Disease Burden of Chronic Kidney Disease. In: Liu BC, Lan HY, Lv LL, editors. Renal Fibrosis: Mechanisms and Therapies; 2019. p. 3–15. (Advances in Experimental Medicine and Biology; vol. 1165). https://doi.org/10.1007/978-981-13-8871-2_1
2. Shrestha N, Gautam S, Mishra SR, Virani SS, Dhungana RR. Burden of chronic kidney disease in the general population and high-risk Groups in South Asia: A systematic review and meta-analysis. PLoS One 2021; 16(10): e0258494. https://doi.org/10.1371/journal.pone.0258494
3. Pappan N, Rehman A. Dyslipidemia. In: StatPearls: StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560891/
4. Hager MR, Narla AD, Tannock LR. Dyslipidemia in patients with chronic kidney disease. Rev Endocr Metab Disord 2017; 18(1): 29–40. https://doi.org/10.1007/s11154-016-9402-z
5. Kopin L, Lowenstein CJ. Dyslipidemia. Ann Intern Med 2017; 167(11): ITC81–96. https://doi.org/10.7326/AITC201712050
6. Rosenstein K, Tannock LR. Dyslipidemia in Chronic Kidney Disease. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext: MDText.com, Inc.; 2000. Available from: https://www.ncbi.nlm.nih.gov/books/NBK305899/
7. Reule S, Ishani A, Goldsmith D. Dyslipidemia and Chronic Kidney Disease. In: Chronic Renal Disease. 2nd ed. Elsevier; 2020. p. 1093–101. https://doi.org/10.1016/B978-0-12-815876-0.00066-8
8. Pontremoli R, Bellizzi V, Bianchi S, Bigazzi R, Cernaro V, Del Vecchio L, et al. Management of dyslipidaemia in patients with chronic kidney disease: a position paper endorsed by the Italian Society of Nephrology. J Nephrol 2020; 33(3): 417–430. https://doi.org/10.1007/s40620-020-00736-x
9. Kochan Z, Szupryczynska N, Malgorzewicz S, Karbowska J. Dietary Lipids and Dyslipidemia in Chronic Kidney Disease. Nutrients 2021; 13(9): 3138. https://doi.org/10.3390/nu13093138
10. Theofilis P, Vordoni A, Koukoulaki M, Vlachopanos G, Kalaitzidis RG. Dyslipidemia in Chronic Kidney Disease: Contemporary Concepts and Future Therapeutic Perspectives. Am J Nephrol 2021; 52(9): 693–701. https://doi.org/10.1159/000518650
11. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular Disease in Chronic Kidney Disease: Pathophysiological Insights and Therapeutic Options. Circulation 2021; 143(11): 1157–1172. https://doi.org/10.1161/CIRCULATIONAHA.120.050686
12. Ferro CJ, Mark PB, Kanbay M, Sarafidis P, Heine GH, Rossignol P, et al. Lipid management in patients with chronic kidney disease. Nat Rev Nephrol 2018; 14(12): 727–749. https://doi.org/10.1038/s41581-018-0072-9
13. Mikolasevic I, Žutelija M, Mavrinac V, Orlic L. Dyslipidemia in patients with chronic kidney disease: etiology and management. Int J Nephrol Renovasc Dis 2017; 10: 35–45. https://doi.org/10.2147/IJNRD.S101808
14. Tunbridge MJ, Jardine AG. Atherosclerotic Vascular Disease Associated with Chronic Kidney Disease. Cardiol Clin 2021; 39(3): 403–414. https://doi.org/10.1016/j.ccl.2021.04.009
15. Dušejovská M, Vecka M, Rychlík I, Žák A. Dyslipidemia in patients with chronic kidney disease: etiology and management. Vnitr Lek 2020; 66(5): 275–281.
16. Kosugi T, Eriguchi M, Yoshida H, Tasaki H, Fukata F, Nishimoto M, et al. Association between chronic kidney disease and new-onset dyslipidemia: The Japan Specific Health Checkups (J-SHC) study. Atherosclerosis 2021; 332: 24–32. https://doi.org/10.1016/j.atherosclerosis.2021.07.008
17. Carmena R, Ascaso JF, Redon J. Chronic kidney disease as a cardiovascular risk factor. J Hypertens 2020; 38(11): 2110–2121. https://doi.org/10.1097/HJH.0000000000002553
18. Nakano T, Tanaka S, Tsuruya K, Kitazono T. Relationship between serum lipid concentrations and impaired renal function in patients with chronic kidney disease: the Fukuoka Kidney Disease Registry Study. Clin Exp Nephrol 2021; 25(4): 385–393. https://doi.org/10.1007/s10157-020-01996-4
19. Chang TI, Streja E, Ko GJ, Naderi N, Rhee CM, Kovesdy CP, et al. Inverse Association Between Serum Non–High-Density Lipoprotein Cholesterol Levels and Mortality in Patients Undergoing Incident Hemodialysis. J Am Heart Assoc 2018; 7(12): e009096. https://doi.org/10.1161/JAHA.118.009096