ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 18, Issue 2, 2025

Online - 2455-3891
Print - 0974-2441

Research Article

STUDY OF CYSTATIN-C AS A CARDIOVASCULAR RISK MARKER IN PATIENTS WITH CHRONIC KIDNEY DISEASE: CROSS-SECTIONAL ANALYTICAL STUDY

HARSHAL PACHPOR[1], ARUN TADAS[2], UMESH KAWALKAR[3], AVINASH NAMDEO JADHAO[4]*

[1]Department of Biochemistry, Government Medical College and Super Speciality Hospital, Nagpur, Maharashtra, India. [2]Department of Biochemistry, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India. [3]Department of Community Medicine, Government Medical College, Akola, Maharashtra, India. [4]Department of Biochemistry, Seth GSMC and King Edward Memorial Hospital, Mumbai, Maharashtra, India.

***Corresponding author: Avinash Namdeo Jadhao; Email: avinashjadhao@kem.edu**

Received: 20 November 2024, Revised and Accepted: 04 January 2025

ABSTRACT

Objectives: The objective of this study was to evaluate the relationship between Cystatin C, lipid profile, and cardiovascular risk in patients with chronic kidney disease (CKD), particularly in a rural Indian population. The study aimed to assess whether Cystatin C could serve as a reliable biomarker for predicting cardiovascular events in CKD patients.

Methods: This cross-sectional analytical study was conducted in a tertiary care hospital in central India from September 2015 to November 2018. A total of 100 participants were enrolled, including 50 CKD patients (with GFR <60 mL/min/1.73 m^2) and 50 age- and sex-matched healthy controls. Fasting blood samples were collected to measure serum Cystatin C and lipid profile parameters (total cholesterol, triglycerides, high-density lipoprotein [HDL], low-density lipoprotein [LDL], and very low-density lipoprotein). CKD patients were followed for 6 months to monitor cardiovascular events. Statistical analyses included unpaired *t*-tests, Chi-squared tests, and correlation analysis.

Results: Serum Cystatin C levels were significantly higher in CKD patients (3.8±0.96 mg/L) compared to controls (0.76±0.11 mg/L, p<0.001). CKD patients exhibited dyslipidemia, characterized by elevated total cholesterol, LDL, and triglyceride levels, and reduced HDL levels. The LDL/HDL ratio was significantly higher in CKD patients (3.73±1.44) compared to controls (2.72±0.79, p<0.001). Among CKD patients, those who developed cardiovascular events during follow-up had significantly higher Cystatin C levels (4.9±0.91 mg/L) compared to those who did not experience cardiovascular events (3.6±0.24 mg/L, p<0.001).

Conclusion: Cystatin C is a reliable marker for renal dysfunction and an independent predictor of cardiovascular risk in CKD patients, particularly in rural populations. Elevated Cystatin C levels were closely associated with dyslipidemia and an increased risk of cardiovascular events. These findings suggest that Cystatin C could be a valuable tool for the early identification of CKD patients at high risk for cardiovascular complications. Incorporating Cystatin C into clinical practice could enhance risk stratification and improve management strategies for CKD patients.

Keywords: Chronic kidney disease, Cystatin C, Cardiovascular risk, Lipid profile, Dyslipidemia.

 DOI: http://dx.doi.org/10.22159/ajpcr.2025v18i2.53536. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Chronic kidney disease (CKD) has emerged as a major global health concern, with rising incidence and associated adverse outcomes such as cardiovascular disease (CVD) and premature death [1]. The prevalence of CKD is substantial, affecting a significant portion of the adult population [2]. CVD is a common complication of CKD, and the relationship between the two is well-established [3]. Traditional markers of kidney function, such as serum creatinine, have limitations in accurately assessing CVD risk in CKD patients [4]. Therefore, there is a need to identify novel markers that can better predict CVD risk in this population. Cystatin C, a cysteine protease inhibitor freely filtered by the glomerulus, has emerged as a promising marker for estimating glomerular filtration rate (GFR) and assessing CVD risk [5]. Several studies have demonstrated a strong association between elevated Cystatin C levels and increased CVD risk, even in individuals with normal or mildly impaired kidney function [6]. However, research investigating the relationship between Cystatin C, lipid profile, and CVD risk in CKD patients, particularly in the Indian population, is limited. This study aimed to investigate Cystatin C as a potential cardiovascular risk marker in patients with CKD by examining its association with lipid profile and cardiovascular events. The study focused on a rural population in central India, a demographic that has been underrepresented in previous research.

METHODS

This prospective analytical study was conducted in under department of biochemistry. A total of 100 study participants were included in the study. Total 50 CKD patients with GFR <60 mL/min/1.73 m^2 and 50 age- and sex-matched healthy controls. The study was conducted at a tertiary care hospital in central India from September 2015 to November 2018 after obtaining IEC approval. After obtaining informed consent, detailed medical histories were taken, and blood samples were collected after overnight fasting. Serum Cystatin C and lipid profile parameters (total cholesterol, triglycerides, high-density lipoprotein [HDL], low-density lipoprotein [LDL], and very low-density lipoprotein [VLDL]) were measured by trivitron nanolab 200 autoanalyzer. Patients were followed up every 2 months for 6 months to monitor for cardiovascular events. Statistical analysis was performed using unpaired t-tests to compare parameters between the CKD and control groups. Pearson's Chi-squared test was used to analyze categorical data. Correlation analysis was conducted to assess the relationship between Cystatin C and lipid profile parameters. p<0.05 were considered statistically significant.

RESULTS

The mean age of cases in the study was 52.58±9.7 years and in comparison, the group was 56.18±9.7 years. The mean age of the study

groups shows that the two groups in the study were comparable age wise. This shows that males is more than that of females in this study, which is found to be insignificant (p>0.05).

The cases exhibited a significantly less favorable lipid profile compared to the controls. Total cholesterol and LDL cholesterol levels were markedly elevated in the cases (209.7±75.5 mg/dL vs. 155.2±22 mg/dL and 134±66.4 mg/dL vs. 75.1±24.6 mg/dL, respectively; p<0.001 for both), while HDL cholesterol was significantly lower (39.1±7.4 mg/dL vs. 52.0±11.3 mg/dL, p<0.001). This resulted in a significantly higher LDL/HDL ratio in the cases (3.73±1.44 vs. 2.72±0.79, p<0.001), further highlighting the increased cardiovascular risk in this group. Triglyceride levels were also elevated in the cases, although this difference did not reach statistical significance. VLDL levels were numerically higher in the cases but did not differ significantly between the two groups. Cystatin C, a marker of renal function, was significantly elevated in the cases compared to the controls (3.8±0.96 mg/L vs. 0.76±0.11 mg/L, p<0.001), suggesting potential kidney dysfunction or other underlying conditions in this group.

Patients of CKD have been admitted for symptoms of a CVD (in terms of STEMI, NSTEMI, Heart Failure, etc.) in the follow-up period of 6 months, while 43 patients were without any symptoms of CVD. The mean value of serum Cystatin-C in patients of CKD with cardiovascular events in follow-up period was 4.9±0.91 and those cases of CKD without cardiovascular events was 3.6±0.24. It was found that patients who have had a cardiovascular event in the follow-up period had significantly higher levels of Serum Cystatin-C than those who did not (p<0.001).

DISCUSSION

The present study was conducted to assess the relationship between serum Cystatin-C levels and cardiovascular risk in patients with CKD by examining lipid profiles and cardiovascular events over a 6-month follow-up period. Involving 50 CKD patients with a GFR <60 mL/min/1.73 m^2 and 50 age- and sex-matched healthy controls, this study significantly contributes to understanding cardiovascular risks in the underrepresented rural population of central India. The findings revealed that the mean serum Cystatin-C level in CKD patients was significantly elevated at 3.8±0.96 mg/L compared to 0.76±0.11 mg/L in the control group (p<0.001). This result aligns with previous studies indicating that elevated Cystatin C levels are a reliable marker of renal dysfunction and are independent of factors like muscle mass and gender [7]. Randers *et al*. reported that Cystatin-C levels were significantly higher in patients with various kidney diseases and those undergoing dialysis, reinforcing its value in assessing renal impairment. Further supporting our findings, Fliser and Ritz observed that serum Cystatin-C concentrations were significantly greater in elderly subjects with impaired renal function than younger, normotensive subjects. This consistency across studies underscores the potential of Cystatin-C as a superior marker of GFR compared to serum creatinine, particularly in the context of CKD [8].

Our study also demonstrated significant dyslipidemia among CKD patients, characterized by elevated levels of total cholesterol, LDL, and triglycerides, along with a decreased HDL level, compared to healthy controls (p<0.001). These results are consistent with findings by Khatiwada *et al*., who reported a high prevalence of hypercholesterolemia, undesirable LDL, and hypertriglyceridemia in CKD patients across different stages of the disease [9]. This dyslipidemia contributes to the progression of CKD and increases cardiovascular risk, highlighting the need for comprehensive lipid management in CKD patients [9]. The observed dyslipidemia aligns with studies by Raju *et al*., who found significant increases in serum triglycerides and VLDL, along with a decrease in HDL cholesterol in CKD patients, both in non-dialysis and hemodialysis groups. This dyslipidemia in CKD is primarily due to decreased catabolism of triglycerides, influenced by factors such as diminished lipoprotein lipase activity, increased apolipoprotein C-III, and the presence of lipase inhibitors [10].

Table 1: Age distribution of cases and comparison group

Variables	Case	Control	p-value
Age (years)			
<40	2	2	0.359
40–55	29	22	
>55	19	26	
Mean±SD	52.58±9.7	56.18±9.7	>0.45
Sex			
Female	17 (34)	10 (20)	0.115 (NS)
Male	33 (66)	40 (80)	

Table 2: Statistical analysis and comparison of different parameters in cases of CKD (n=50) and comparison group (n=50)

Laboratory parameter	Cases	Control	p-value
Total cholesterol	209.7±75.5	155.2±22	<0.001
Triglyceride	183±67	140.5±30.1	<0.001
HDL	39.1±7.4	52.0±11.3	<0.001
VLDL	36.6±13.4	28.1±6	<0.001
LDL	134±66.4	75.1±24.6	<0.001
LDL/HDL	3.73±1.44	2.72±0.79	<0.001
Cystatin-C	3.8±0.96	0.76±0.11	<0.001

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein

Table 3: Comparison and statistical analysis of Cystatin-C in cases with and without cardiovascular events in follow up period

Laboratory parameter	Without cardiovascular events (n=43)	With cardiovascular events (n=7)	p-values
Cystatin-C	3.6±0.91	4.9±0.24	<0.001

During the 6-month follow-up, seven CKD patients developed cardiovascular events, and these patients had significantly higher mean serum Cystatin-C levels (4.9±0.91 mg/L) compared to those without cardiovascular events (3.6±0.24 mg/L, p<0.001). These findings are consistent with those of Keller *et al*., who demonstrated that Cystatin-C is a potent predictor of cardiovascular mortality in patients with coronary artery disease (CAD) beyond classical risk factors [11]. Keller *et al*. suggested that Cystatin-C could be particularly valuable in acute care settings, aiding in the identification of high-risk patients [11]. Similar conclusions were drawn by Astor *et al*., who found that higher concentrations of Cystatin-C were more strongly associated with mortality than creatinine-based estimates, suggesting that Cystatin-C could improve risk prediction for cardiovascular outcomes in CKD patients [12] [Tables 1-3].

The results of our study are in agreement with those of Lodh *et al*., who demonstrated that serum Cystatin-C levels are independently associated with the development of CAD. Lodh *et al.* also noted the role of Cystatin-C in inflammation and extracellular matrix regulation, which are crucial in the pathogenesis of atherosclerosis and plaque vulnerability [13]. In addition, studies by Svensson-Färbom *et al*. have established that Cystatin-C is a better risk marker for CVD morbidity and mortality than creatinine-based GFR in both middle-aged and elderly populations, further validating our findings in the context of rural India [14].

CONCLUSION

This study highlights the significance of serum Cystatin-C as a reliable marker for renal function and cardiovascular risk in CKD patients. Elevated Cystatin-C levels in CKD patients are associated with an

unfavorable lipid profile and a higher risk of cardiovascular events. These findings suggest that Cystatin-C could play a crucial role in early identification and risk stratification of CKD patients, particularly in rural settings, thereby improving patient outcomes through better management strategies.

AUTHOR'S CONTRIBUTION

Dr. Harshal Pachpor, Dr. Arun Tadas: Data analysis and draft preparation, Dr Umesh Kawalkar, Dr.Avinash Namdeo Jadhao: Data collection, compilation and statistical analysis.

CONFLICT OF INTEREST

None.

FUNDING

Nil.

REFERENCES

1. Vallianou NG, Mitesh S, Gkogkou A, Geladari E. Chronic kidney disease and cardiovascular disease: Is there any relationship? Curr Cardiol Rev. 2019;15(1):55-63. doi: 10.2174/1573403X14666180711124825, PMID 29992892
2. Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: Systematic review. BMC Public Health. 2008 Apr 11;8:117. doi: 10.1186/1471-2458-8-117, PMID 18405348
3. Said S, Hernandez GT. The link between chronic kidney disease and cardiovascular disease. J Nephropathol. 2014 Jul;3(3):99-104. doi: 10.12860/jnp.2014.19, PMID 25093157
4. Benoit SW, Ciccia EA, Devarajan P. Cystatin C as a biomarker of chronic kidney disease: Latest developments. Expert Rev Mol Diagn. 2020 Oct;20(10):1019-26. doi: 10.1080/14737159.2020.1768849, PMID 32450046
5. Dandana A, Gammoudi I, Chalghoum A, Chahed H, Addad F, Ferchichi S, *et al*. Clinical utility of serum cystatin C in predicting coronary artery disease. J Clin Lab Anal. 2014 May;28(3):191-7. doi: 10.1002/jcla.21665, PMID 24478035
6. Ix JH, Shlipak MG, Chertow GM, Whooley MA. Association of cystatin C with mortality, cardiovascular events, and incident heart failure among persons with coronary heart disease: Data from the Heart and soul study. Circulation. 2007 Jan 16;115(2):173-9. doi: 10.1161/CIRCULATIONAHA.106.644286, PMID 17190862
7. Randers E, Kristensen JH, Erlandsen EJ, Danielsen H. Serum cystatin C as a marker of the renal function. Scand J Clin Lab Investig. 1998;58(7):585-92. doi: 10.1080/00365519850186210, PMID 9890342
8. Fliser D, Ritz E. Serum cystatin C concentration as a marker of renal dysfunction in the elderly. Am J Kidney Dis. 2001 Jan;37(1):79-83. doi: 10.1053/ajkd.2001.20628, PMID 11136171
9. Khatiwada S, Rajendra KC, Gautam S, Lamsal M, Baral N. Thyroid dysfunction and dyslipidemia in chronic kidney disease patients. BMC Endocr Disord. 2015 Oct 29;15:65. doi: 10.1186/s12902-015-0063-9, PMID 26510920
10. Raju DS, Lalitha DL, Kiranmayi P. A study of lipid profile and lipid peroxidation in chronic kidney disease with special reference to hemodialysis. J Clin Res Bioeth. 2013 Dec 11;4(1):1000143. doi: 10.4172/2155-9627.1000143
11. Keller T, Messow CM, Lubos E, Nicaud V, Wild PS, Rupprecht HJ, *et al*. Cystatin C and cardiovascular mortality in patients with coronary artery disease and normal or mildly reduced kidney function: Results from the AtheroGene study. Eur Heart J. 2009 Feb;30(3):314-20. doi: 10.1093/eurheartj/ehn598, PMID 19153178
12. Astor BC, Shafi T, Hoogeveen RC, Matsushita K, Ballantyne CM, Inker LA, *et al*. Novel markers of kidney function as predictors of ESRD, cardiovascular disease, and mortality in the general population. Am J Kidney Dis. 2012 May;59(5):653-62. doi: 10.1053/j.ajkd.2011.11.042, PMID 22305758
13. Lodh M, Parida A, Sanyal J, Ganguly A. Cystatin C in acute coronary syndrome. EJIFCC. 2013 Jul 16;24(2):61-7. PMID 27683440.
14. Svensson-Färbom P, Ohlson Andersson M, Almgren P, Hedblad B, Engström G, Persson M, *et al*. Cystatin C identifies cardiovascular risk better than creatinine-based estimates of glomerular filtration in middle-aged individuals without a history of cardiovascular disease. J Intern Med. 2014 May;275(5):506-21. doi: 10.1111/joim.12169, PMID 24279862