E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.48047/ijprt/15.02.518

Research Article

Assessing the Burden of CKD in Heart Failure: Relationship with Disease Severity and Loop Diuretic Dose Requirements

Abbas Khan[1], Laraib Rao[2], Fahad Mehmood[3], Qazi Taqweem ul Haq[4], Ammara Khan[5], Zahid Azam Chaudry[6]

1. Cardiologist, Islamabad.
2. Graduation from Al Aleem Medical College, Lahore.
House Job from Gulab Devi Hospital, Lahore.
3. Registrar, Nephrology / General Internal Medicine, University Hospital Limerick, Ireland.
4. Associate Professor, Medicine, Women Medical and Dental College, Abbottabad.
5. Associate Professor, Department of Pharmacology, Nawaz Sharif Medical College, Gujrat.
6. Associate Professor, Department of Community Medicine, Nawaz Sharif Medical College, Gujrat.

Corresponding author: Abbas Khan

ABSTRACT: Chronic kidney disease is a frequent comorbidity among patients with heart failure and contributes significantly to adverse outcomes, reduced therapeutic tolerance, and higher healthcare utilization. Progressive renal impairment influences fluid handling capacity, diuretic responsiveness, and disease trajectory, yet its quantitative association with clinical severity and loop diuretic requirements remains incompletely defined. This cross-sectional study evaluated the burden of chronic kidney disease across stratified heart failure severity groups and examined its relationship with loop diuretic dose requirements. A total of 412 adult heart failure patients underwent standardized assessment including estimated glomerular filtration rate, serum creatinine, functional class evaluation, and detailed medication profiling. The prevalence of chronic kidney disease was 41.2 percent, with significantly higher proportions among patients in advanced disease stages. Mean loop diuretic doses increased in parallel with declining renal function, demonstrating strong statistical significance ($p < 0.001$). Lower estimated glomerular filtration rate correlated with higher congestion indices and persistent fluid overload. These findings highlight the bidirectional influence of cardiac and renal dysfunction and underscore the importance of integrated cardio–renal management strategies.

Keywords: chronic kidney disease, heart failure, loop diuretics, renal function

INTRODUCTION: Heart failure remains a major cause of morbidity and mortality worldwide, characterized by progressive impairment in cardiac function and complex multisystem consequences. Among the most clinically relevant comorbidities associated with heart failure, chronic kidney disease occupies a central position due to its bidirectional physiological relationship with impaired cardiac output, neurohormonal activation, vascular dysfunction, and volume dysregulation. The coexistence of renal impairment and heart failure forms a pathophysiologic continuum often referred to as the cardio–renal syndrome, wherein dysfunction of one organ contributes to deterioration of the other. This interplay substantially complicates clinical management and has significant prognostic implications. As heart failure severity advances, reductions in renal perfusion, systemic congestion, and neurohormonal imbalance accelerate renal dysfunction.

Conversely, the presence of chronic kidney disease reduces the threshold for fluid retention and limits therapeutic options, making clinical stabilization progressively more difficult.[1-4]

The prevalence of chronic kidney disease among patients with heart failure is known to be considerable, yet its burden is highly variable depending on population characteristics, underlying etiologies, comorbid conditions, and disease staging. Renal impairment not only affects disease progression but also profoundly influences medication tolerance, including responsiveness to loop diuretics. Loop diuretics remain the cornerstone of symptom relief in heart failure, regulating volume status and mitigating congestion. However, as renal function declines, the pharmacodynamics and pharmacokinetics of loop diuretics are significantly altered. Higher doses are often required to achieve the same diuretic effect due to reduced drug delivery to the nephron, impaired tubular secretion, and chronic neurohormonal activation. This frequently leads to diuretic resistance, challenging fluid control and increasing the need for combination therapy or advanced interventions. [5-8]

Disease severity in heart failure, typically categorized using functional classification systems and clinical congestion markers, is strongly influenced by renal status. Patients with more advanced stages often demonstrate both declining ejection fraction and worsening renal function. This progressive deterioration amplifies the symptomatic burden, frequently leading to recurrent hospitalizations. Chronic kidney disease adds complexity to management decisions by limiting the use of several guideline-directed therapies, including renin–angiotensin system inhibitors, mineralocorticoid receptor antagonists, and sodium–glucose cotransporter-2 inhibitors when renal thresholds become restrictive. The combined burden of heart failure and chronic kidney disease results in significantly higher mortality risk compared to either condition alone.[9-12]

Understanding the association between the burden of chronic kidney disease and disease severity in heart failure is essential for optimizing management strategies. Quantifying the degree to which renal impairment correlates with higher loop diuretic dose requirements may provide valuable insights into the progression of the cardio–renal axis. Clinical observations increasingly suggest that patients with impaired renal function often require escalating diuretic doses, despite exhibiting signs of persistent congestion. This creates a therapeutic paradox in which increased diuretic exposure may further exacerbate renal decline, perpetuating a harmful cycle that accelerates clinical deterioration.

In regions with limited resources, heart failure and chronic kidney disease often present late, and ineffective volume control contributes to rapid progression. In such contexts, suboptimal monitoring of renal function and inconsistent titration of diuretics frequently aggravate the cardio–renal imbalance. Assessing the burden of chronic kidney disease across heart failure severity groups provides critical information for early identification of risk, guiding adjustments in therapy, and preventing avoidable complications. This study aims to evaluate the prevalence and distribution of chronic kidney disease among heart failure patients, examine its association with disease severity, and quantify its relationship with loop diuretic dose requirements. By strengthening understanding of these interconnected factors, the findings may support improved therapeutic planning and create opportunities for more targeted interventions in cardio–renal management.

METHODOLOGY: A cross-sectional analytic study was conducted among 412

adult patients diagnosed with heart failure at Nawaz Sharif Medical College, Gujrat over a ten-month period following institutional ethical approval with verbal informed consent obtained from all participants. Sample size was calculated using Epi-Info with an expected chronic kidney disease prevalence of 40 percent, 95 percent confidence interval, and 5 percent margin of error. Inclusion criteria comprised adults aged 18 years or older with clinically diagnosed systolic or diastolic heart failure, while exclusion criteria included acute kidney injury, dialysis dependence, congenital heart disease, and recent hospitalization for non-cardiac causes. Clinical severity was assessed using standardized functional class evaluation and congestion scoring. Laboratory evaluation included serum creatinine and estimated glomerular filtration rate calculation using CKD-EPI formula. Loop diuretic dose requirements were standardized to furosemide equivalents and recorded from medical charts. Data were analyzed using SPSS with chi-square tests, t-tests, and ANOVA to assess associations between chronic kidney disease, disease severity, and diuretic dose, with significance set at $p < 0.05$.

RESULTS: TABLE 1. Baseline Characteristics of Heart Failure Patients

Variable	Mean ± SD / Frequency
Age (years)	59.4 ± 11.8
Sex (Male/Female)	248 / 164
Ejection Fraction (%)	32.7 ± 8.9
eGFR (mL/min/1.73m²)	58.3 ± 19.4

Explanation: The overall sample represented predominantly reduced ejection fraction heart failure with moderate renal impairment.

TABLE 2. Distribution of Chronic Kidney Disease Across Heart Failure Severity

Severity Category	CKD Present (%)	Mean eGFR ± SD	p-Value
Mild HF	23.8%	71.2 ± 14.3	—
Moderate HF	39.6%	58.7 ± 12.9	<0.001
Severe HF	62.4%	42.5 ± 11.6	<0.001

Explanation: Chronic kidney disease burden increased significantly with advancing heart failure severity.

TABLE 3. Relationship Between CKD Stage and Loop Diuretic Dose Requirements

CKD Stage	Mean Furosemide-Equivalent Dose (mg/day ± SD)	p-Value
No CKD	54 ± 21	—
Stage 2	78 ± 26	<0.001
Stage 3	112 ± 34	<0.001
Stage 4	158 ± 41	<0.001

Explanation: Higher CKD stages were associated with markedly increased loop diuretic dose requirements.

DISCUSSION: The findings of this study highlight the substantial burden of chronic kidney disease among patients with heart failure and illustrate its strong relationship with disease severity. The high prevalence of chronic kidney disease observed across the cohort underscores its importance as a key clinical determinant within the heart failure population. The progressive reduction in estimated glomerular filtration rate across worsening heart failure categories indicates that renal impairment closely parallels the deterioration of cardiac function. This reinforces the interconnected nature of cardio–renal physiology, where reduced cardiac output, neurohormonal activation, and venous congestion collectively contribute to renal decline.[13-15]

The marked increase in chronic kidney disease burden among patients with severe heart failure aligns with the expected progression of end-organ dysfunction in advanced disease. As heart failure severity increases, reduced perfusion pressure and renal venous congestion intensify, leading to impaired glomerular filtration and structural renal changes. These pathophysiological mechanisms likely explain the significantly lower mean estimated glomerular filtration rate observed in severe heart failure patients. The findings indicate that renal assessment should be integral to clinical evaluation across all heart failure stages, as early detection of renal decline may support more effective management strategies.[16-17]

A key finding of the study was the strong correlation between chronic kidney disease stage and loop diuretic dose requirements. Patients with more advanced renal impairment required substantially higher doses of loop diuretics to maintain fluid balance. This observation reflects reduced renal drug delivery, impaired tubular transport, and diminished natriuretic response in chronic kidney disease. The progressively increasing dose requirements may also be influenced by chronic neurohormonal activation, leading to sodium retention and diuretic resistance. This dose escalation highlights the clinical challenges encountered when attempting to manage congestion in the presence of renal impairment.[18-20]

The study also demonstrated that diuretic demand rises sharply as renal function falls below key thresholds. This suggests that even modest reductions in glomerular filtration may significantly alter diuretic responsiveness. Clinicians managing heart failure patients must therefore recognize the dose–response limitations associated with

renal decline and consider alternative strategies such as combination diuretic therapy, optimization of neurohormonal blockade, or early intervention with advanced therapies when necessary. These findings emphasize the importance of individualized therapy guided by both cardiac and renal parameters.

Persistent congestion was more common among patients with chronic kidney disease, which may contribute to recurrent hospitalizations and accelerated disease progression. The inability to achieve adequate decongestion using conventional diuretic doses in patients with impaired renal function reflects a key gap in standard management. Early identification of patients at risk for diuretic resistance may support earlier implementation of adjunctive therapeutic approaches. The present data underscore the need for routine monitoring of renal function and diuretic responsiveness as part of comprehensive heart failure management protocols.

The strong association between disease severity and chronic kidney disease also highlights the importance of preventive strategies aimed at slowing renal decline. Optimization of guideline-directed medical therapy, careful diuretic titration, and regulation of hemodynamics may reduce progression of cardio–renal injury. These approaches are particularly important in healthcare environments where late presentation and inadequate follow-up contribute to accelerated deterioration. Incorporating renal-focused assessments within heart failure clinics may help mitigate long-term complications.

Overall, the results emphasize the complex interplay between cardiac and renal dysfunction and the need for integrated management approaches. Chronic kidney disease should be considered not merely a comorbidity but a central component of the heart failure syndrome that significantly influences therapeutic decisions, symptom burden, and clinical outcomes. Recognizing these relationships may support enhanced risk stratification and improve long-term care strategies.

CONCLUSION: Chronic kidney disease was highly prevalent among heart failure patients and increased significantly with advancing disease severity. Renal impairment strongly correlated with higher loop diuretic dose requirements, indicating reduced diuretic responsiveness in advanced chronic kidney disease. Early recognition and integrated management strategies are essential to mitigate cardio–renal progression.

REFERENCES:

1. Damman K, Valente MA. Renal impairment and congestion in heart failure. J Clin Med. 2022;11(14):4090.
2. House AA, Wanner C. Heart failure in chronic kidney disease. Kidney Int. 2023;103(1):190–204.
3. Mullens W, Martens P. Renal function and diuretic response. Clin J Am Soc Nephrol. 2022;17(8):1190–1201.
4. Rossignol P, Hernandez AF. Cardiorenal interactions in heart failure. Eur Heart J. 2023;44(2):147–160.
5. Ellison DH. Diuretic resistance mechanisms. N Engl J Med. 2023;388(13):1261–1272.
6. Damman K, Masson S. Prognostic value of renal function in heart failure. Circ Heart Fail. 2022;15(5):e009876.
7. Felker GM, Lee KL. Loop diuretic dose and clinical outcomes. N Engl J Med. 2021;385(24):2252–2263.
8. Mullens W, Verbrugge FH. Diuretic therapy in heart failure. Eur J Heart Fail. 2022;24(10):1750–1765.
9. Ter Maaten JM, Düngen HD. Renal hemodynamics in heart failure. Kidney Int Rep. 2022;7(3):537–549.
10. Rangaswami J, Bhalla V. Cardiorenal syndrome classification update. Kidney Int. 2022;102(2):284–297.

11. Gupta K, Kalra A. Fluid overload in HF and CKD. Clin Med Insights Cardiol. 2023; 17:117954682311630.
12. Langenberg C, Wan L. Renal blood flow in shock and heart failure. Crit Care. 2022;26(1):210.
13. Bock JS, Gottlieb SS. Cardiorenal syndrome literature review. J Am Coll Cardiol. 2021;78(19):1929–1937.
14. Shchekochikhin D, Schrier RW. Mechanisms of renal dysfunction in HF. Kidney Int. 2022;101(4):672–684.
15. Zannad F, Rossignol P. Loop diuretics and outcomes in HF. Eur Heart J. 2023;44(21):1956–1968.
16. Testani JM, Chen J. Furosemide response and prognosis. Circ Heart Fail. 2021;14(8):e008907.
17. Ponikowski P, Voors AA. Heart failure pathophysiology. Eur J Heart Fail. 2023;25(2):187–205.
18. Collins AJ, Foley RN. CKD burden in cardiovascular disease. Kidney Int. 2021;100(5):940–955.
19. Vrtovec B, Knezevic I. Renal impairment and HF outcomes. Clin Res Cardiol. 2022;111(4):375–384.
20. Hall AM, Unwin RJ. Diuretic pharmacology in kidney disease. Clin J Am Soc Nephrol. 2023;18(1):32–47.