A PROSPECTIVE, OBSERVATIONAL STUDY ON ETIOLOGICAL SPECTRUM OF END STAGE KIDNEY DISEASE IN NORTH INDIA: DOMINANCE OF DIABETIC KIDNEY DISEASE AND EMERGING TRENDS

S. Puri, H.S. Meshram, A.N. Thakur, C. Bhagat, B. Modasiya, V. Batheja, R.P. Mathur

Department of Nephrology, Institute of Liver & Biliary Sciences, Vasant Kunj, New Delhi, India

Correspondence:
Dr. S. Puri
Department of Nephrology,
Institute of Liver & Biliary Sciences,
Vasant Kunj, New Delhi,
India.
Email: saurabhpuri119@gmail.com

Submission Date: 2nd Jul., 2025
Date of Acceptance: 26th Dec, 2025
Publication Date: 31st Dec, 2025

ABSTRACT

Background: **End-stage kidney disease (ESKD) poses a formidable challenge to healthcare systems worldwide, particularly in low- and middle-income countries like India. With the epidemiological transition favoring non-communicable diseases, the burden of diabetes and hypertension as leading causes of chronic kidney disease (CKD) has grown substantially. This study aims to characterize the etiological spectrum of ESKD in a North Indian tertiary care center, with a special focus on the rising prevalence of diabetic kidney disease (DKD).**

Methods: **A cross-sectional observational study was conducted between June 2023 and December 2024, enrolling 132 patients undergoing incident hemodialysis. Data on demographics, comorbidities, clinical symptoms, laboratory parameters, and underlying CKD etiologies were collected and analyzed.**

Results: **DKD was identified as the most common cause of ESKD [n=50 (40.9%)], followed by hypertensive nephrosclerosis [n=19(14.4%)], chronic glomerulonephritis [n=13(9.8%)], and unknown etiology [n=19(14.4%)]. Other causes included hepatorenal syndrome-associated CKD [n=8(6.1%)], obstructive uropathy [n=7(5.3%)], polycystic kidney disease [n=6(4.6%)], and chronic tubulointerstitial nephritis [n=6(4.6%)].**

Conclusion: **DKD is the predominant cause of ESKD in this cohort from North India. Early diagnosis, risk factor management, and nephrology referral are crucial. Regional profiling of etiologies can improve health planning and resource allocation.**

Keywords: End-stage renal disease, Diabetic kidney disease, Hypertensive nephrosclerosis, Chronic kidney disease, Hemodialysis, India

Introduction

Chronic kidney disease defined as estimated glomerular filtration rate(eGFR) below 60 ml/min. End stage kidney disease (ESKD), is defined as patients of CKD whose eGFR decline below 15 ml/min,Thishas emerged as a critical global health burden[1], with its prevalence escalating in parallel with the epidemic of non-communicable diseases. India, home to over 1.4 billion people, is experiencing a dual health transition,[2] while infectious diseases persist in certain regions, the rise of diabetes, hypertension, and cardiovascular diseases has contributed to a sharp increase in CKD cases.[3] The estimated prevalence of CKD in India ranges from 8% to 17%, depending on the population and screening methodology used.[4]The burden of CKD is compounded by late detection and poor awareness, particularly in rural and peri-urban populations.[5] Many patients present directly in advanced stages requiring kidney replacement therapy (KRT), predominantly hemodialysis,[5] due to either financial constraints or lack of access to nephrology care.[6] As a result, identifying the underlying etiologies of ESKD is not only an academic exercise but a necessary tool for planning preventive strategies, initiating timely referrals, and allocating resources effectively.

Historically, glomerulonephritis and infections accounted for most ESKD cases in developing countries.[7] However, this pattern has shifted. The proportion of CKD patients which lands up in ESKD is around 5%. With lifestyle modernization, dietary changes, urbanization, and increased life expectancy, diabetes mellitus and hypertension have emerged as leading contributors to ESKD. In India, the Indian CKD Registry documents etiological trends, including a rising burden of diabetic kidney disease (DKD) and marked regional heterogeneity.[9]

DKD is not merely a renal complication of diabetes but a systemic manifestation[10] with distinct pathophysiology involving hyperglycemia-induced oxidative stress, activation of the renin–angiotensin system, podocyte injury, and tubulointerstitial fibrosis.[10] Additionally, hypertensive nephrosclerosisonce considered a secondary contributor is now recognized as a primary cause of ESKD in a sizable proportion of patients[9]. Hypertension often coexists with diabetes, making it difficult to disentangle their individual contributions; nonetheless, both conditions accelerate nephron loss and are associated with increased cardiovascular morbidity

Health-system considerations, including constraints and rationing around dialysis delivery, have also been described[12]. Variations in diagnostic classification and equation choice (e.g., CKD-EPI) influence reported CKD prevalence and staging.[13]

Late presentation is a common challenge in nephrology.[14] In India, many patients start dialysis without prior nephrology follow-up, with temporary catheter use at initiation linked to infection, thrombosis, and hospitalization; delays also mean complications such as severe anemia, mineral-bone disorder, and cardiovascular dysfunction are present at the onset of dialysis.[15]

Infectious diseases continue to influence the ESKD landscape. Guideline-aligned ESKD care intersects with regional burdens of tuberculosis, hepatitis B and C, and human immunodeficiency virus (HIV).[16] The coexistence of chronic liver disease (CLD) and renal dysfunction in ESKD points to the evolving intersection of hepato-renal pathologies.

Given this complex interplay of factors, this study was undertaken to delineate the etiological spectrum of ESKD among patients undergoing incident hemodialysis at a tertiary care hospital in North India.[5]These patients were first time undergoing maintenance hemodialysis, . The primary objective was to quantify the distribution of ESKD etiologies with special emphasis on DKD and emerging trends. Secondary objectives included analyzing associated comorbidities, patterns of referral, dialysis access, and baseline clinical characteristics. By contextualizing the data within regional epidemiology, the study aims to inform future health planning and improve renal care delivery.

MATERIAL AND METHODS

Study Design

Cross-sectional design was adopted for this study. This approach was chosen to allow systematic documentation of the clinical, biochemical, and echocardiographic profiles of ESKD patients at the moment they first underwent haemodialysis, without introducing any experimental interventions beyond routine care. The prospective format enabled real-time capture of baseline and follow-up data at predefined intervals (30, 90, and 180 days), thereby minimizing recall bias and permitting accurate temporal sequencing of clinical events. Standardized case report forms and operating procedures were employed to ensure uniform data collection across all participants. Investigators remained blinded to secondary analyses during the enrolment phase, reducing observer bias. Overall, by following the STROBE guidelines for observational research, this design maximized internal validity while reflecting real-world practice in a tertiary nephrology center.

Study Duration

The study was carried out over a 16-month period from 1 June 2023 to 31 December 2024. During the initial two weeks, the study team underwent protocol training, case form testing, and pilot data collection to refine procedures. Patient enrolment commenced on 1 September 2024 and continued until the target sample size was achieved on 31 July 2024. Thereafter, all enrolled patients were followed prospectively at 30, 90, and 180 days post- dialysis initiation, with the final patient follow-up completed on 31 December 2024.

Inclusion And Exclusion Criteria

Participants were recruited based on predefined eligibility criteria to ensure a representative sample of incident ESKD patients.

Inclusion criteria

1. Age ≥18 years.
2. Diagnosis ESKD as per KDIGO guidelines.
3. Undergoing first-ever haemodialysis (¯crash-lander).
4. Ability to provide informed consent.

Exclusion criteria

1. Patients with acute kidney injury.
2. Prior renal replacement therapy (maintenance dialysis or transplant).
3. Concurrent immunosuppressive therapy.
4. Pregnant or lactating women.
5. Documented active infection requiring isolation.

Eligible patients were identified through the dialysis scheduling log. Each potential participant was screened by the primary investigator for ESKD history, dialysis status, and exclusion criteria before enrolment.

Study Sampling Technique

A consecutive sampling strategy was employed. Every patient presenting to the haemodialysis unit for their first session during the recruitment window was approached for participation. This non-probability method ensured all eligible individuals were considered, minimizing selection bias. Prior to each dialysis session, the study coordinator reviewed the dialysis roster daily to identify incident cases. Telephone triage was used when necessary to confirm ESKD history and potential exclusion factors. Consecutive sampling continued until the sample size target was reached, ensuring that participants reflected the full spectrum of clinical presentations over the study period, including those referred emergently and those with prior nephrology follow-up.

Study Sample Size

The required sample size was calculated based on the anticipated prevalence of the most common ESKD etiology diabetic nephropathy reported at 38% in comparable cohorts.[17]

Using the formula for estimating a single proportion with 95% confidence (Z = 1.96) and 10% absolute precision (d = 0.10), the initial sample size (n) of 91 was determined.

.

To account for an anticipated 10% loss to follow-up or incomplete data, nine additional subjects were added, yielding a final target of 100 participants. This calculation was performed prior to initiation of recruitment; periodic audits confirmed that attrition remained below 8%, validating the estimate. All enrolled patients who met eligibility and completed at least one follow-up visit were included in the primary analysis, adhering to an intention-to-observe principle.

Data Analysis

Data cleaning and statistical analysis were performed using IBM SPSS Statistics version 22. Continuous variables were tested for normality using the Shapiro–Wilk test; normallydistributed data were summarized as mean ± standard deviation, while skewed data were presented as median (interquartile range). Categorical variables were expressed as frequencies and percentages. For exploratory subgroup comparisons, independent samples t-test or Mann Whitney U test was used for continuous outcomes, and chi-square or Fisher's exact test for categorical outcomes. Time-to-event analyses (e.g., mortality at 180 days) were conducted using Kaplan Meier estimates and compared with the log-rank test. Multivariate logistic regression incorporating variables with $p < 0.10$ in univariate analysis was used to identify independent predictors of early mortality and vascular access complications; adjusted odds ratios with 95% confidence intervals were reported. A two-tailed $p < 0.05$ was considered statistically significant.

Ethical Considerations

The study protocol, CRF, patient information sheet, and informed consent form were reviewed and approved by the ILBS Institutional Ethics Committee (IEC approval no. IEC/2024/111/MA07). All participants provided written informed consent before any study activity. The study complied with the Declaration of Helsinki and ICMR ethical guidelines. Confidentiality was maintained by de-identifying data and storing electronic records behind password-protected servers. Only study investigators had access to the master code linking study IDs to patient identifiers.

RESULTS

A total of 132 patients undergoing incident hemodialysis were enrolled during the study period. The baseline demographic characteristics are summarized in Table 1.

Table 1: Baseline demographic characteristics of the study cohort

Variable	Total (n=132)
Age (years), mean ± SD	53.4 ± 12.8
Age > 50 years	84 (64%)
Sex (Male:Female)	96:36 (2.7:1)
Urban / semi-urban	89(68%)

Table 2: Etiological spectrum of end stage kidney disease in our study population

Etiology	n (%)	Mean Age (years)	Male (%)
Diabetic kidney disease (DKD)	54 (40.9)	58.3 ± 10.2	75.9
Hypertensive nephrosclerosis	19 (14.4)	50.7 ± 11.9	–
Chronic glomerulonephritis (CGN)	13 (9.8)	41.5 ± 12.3	–
Chronic TIN	6 (4.6)	–	–
Polycystic kidney disease (PKD)	6 (4.6)	–	–
Obstructive uropathy	7 (5.3)	–	–
Hepatorenal syndrome-CKD	8 (6.1)	–	–
CKD-undetermined	19 (14.4)	–	–

The most common etiology of ESKD was diabetic kidney disease (DKD), followed by hypertensive nephrosclerosis and chronic glomerulonephritis. The etiological distribution of ESKD in our study population is presented in Table 2.The most common co-morbidies in the cohort was hypertension (74%), followed by diabetes(45%), CLD(28%), hypothyroidism(20%) and cardiovascular accidents (3%). Prior nephrology consultation was done in 68(51.5%) patients. Dialysis initiation in the study was done by temporary uncuffed vascular catheter in 106(80.3%), cuffed tunneled catheters in 21(15.9%) and mature arterio-venous fistula in 5(3.8%).The patients who were vaccinated with influenze was 38(28%). Vaccination with pneumococcal and hepatitis B vaccine was in 37(28%) and 63(47%) patients respectively. There was a history of alternative/ complementary medicine in 33(24%) patients.

DISCUSSION

This study highlights the evolving etiological landscape of ESKD in a tertiary-care center in North India and places it in the broader global context. Our results demonstrate that DKD has emerged as the most common cause of ESKD, with hypertension, chronic glomerulonephritis (CGN), chronic tubulointerstitial nephritis (CTIN), and chronic liver disease-related kidney dysfunction contributing significantly. The findings have multiple implications for nephrology practice, preventive strategies, and healthcare planning.

Comparison with global data

International data have long recognized the high risk of progression to ESKD among individuals with renal insufficiency and cardiovascular disease.[1] Hypertension, as shown in large-scale analyses, remains a principal driver of CKD burden globally.[2] The coexistence of cardiovascular morbidity, diabetes, and hypertension in our cohort mirrors these international trends and underscores the need for integrated management.

The epidemiological shift toward diabetes and hypertension as leading etiologies is not unique to India. Similar observations have been made in neighboring South Asian countries, such as Pakistan, where the growing CKD burden is attributed to the same metabolic risk factors[3] . This reinforces the concept that CKD epidemiology is increasingly shaped by non-communicable diseases across low- and middle-income countries (LMICs).

National and regional relevance

The population-based study from India by Modi and Jha[4] documented the incidence of ESRD, showing the rising tide of CKD within the country. Our findings extend these observations by showing that a large proportion of patients still present in advanced stages, often requiring emergent initiation of dialysis. The challenges of late detection and poor awareness documented previously[5] are reflected in our cohort, where most patients had no prior nephrology follow-up before reaching dialysis.

Diabetic kidney diseaseaccounted for the largest share of ESKD in our study. This is consistent with cross-sectional surveys from North India, which identified diabetes as the most common risk factor for low glomerular filtration rate and proteinuria[10] . Such data indicate that diabetes is not merely a comorbidity but the primary determinant of renal trajectory in many patients.

Changing etiological spectrum

In earlier decades, rationing of dialysis and inadequate healthcare access often limited recognition of metabolic causes, with glomerulonephritis dominating ESKD etiologies. However, with healthcare modernization, the profile has changed. Studies from Western settings highlighted the impact of rationing decisions on dialysis uptake[12], while shifts in diagnostic definitions, such as the adoption of CKD-EPI equations, have altered prevalence estimates of CKD.[13] In the Indian context, registry data have consistently documented DKD and hypertensive nephrosclerosis as rising causes[9], paralleling our observations.

Hypertensive nephrosclerosis was the second most common cause in our cohort. Its contribution is often underestimated, as hypertension is both a cause and a consequence of CKD. The difficulties in distinguishing hypertensive from diabetic nephropathy in patients with overlapping risk factors complicate attribution. Nevertheless, hypertension accelerates nephron loss and is strongly associated with adverse cardiovascular outcomes.

Dialysis initiation practices

Our study demonstrates that the majority of patients initiate dialysis in emergency settings with temporary vascular access, consistent with reports describing dialysis initiation patterns in India. Hemodialysis, although life-sustaining, carries risks of infection, thrombosis, and cardiovascular stress[15] . Lack of predialysis nephrology care and absence of arteriovenous fistula (AVF) planning remain key gaps.

Infectious and systemic contributors

Infectious diseases continue to shape the ESKD landscape. Guidelines emphasize the interplay between ESKD and infections such as tuberculosis, hepatitis B and C, and HIV[16] . In our cohort, tuberculosis was observed in nearly one-sixth of patients, underscoring

the persistent overlap between infection and renal disease in endemic regions. Additionally, the coexistence of CLD and renal dysfunction reflects the evolving recognition of hepato-renal interactions, with alcohol-related and viral hepatitis-driven CLD contributing to ESKD.

Implications of DKD dominance

DKD is a systemic condition characterized by hyperglycemia-driven oxidative stress, activation of the renin–angiotensin–aldosterone system, podocyte injury, and progressive fibrosis. Recent reviews emphasize the challenges in management, the promise of novel agents, and the need for integrated cardio-renal-metabolic approaches[18] . The high proportion of DKD in our cohort implies that aggressive diabetes control, screening for microalbuminuria, and early nephrology referral are essential strategies for prevention.

The therapy gap in ESRD

An important concern in India and globally is the gap between the estimated incidence of ESRD and the actual utilization of renal replacement therapy. This discrepancy, attributed to late referral, financial barriers, and systemic limitations, has been quantified in prior analyses[19] . Our findings reinforce this, as most patients lacked prior access planning and initiated dialysis emergently. Bridging this gap requires investment in public health infrastructure, insurance coverage, and early detection programs.

Global perspective

From a global perspective, CKD has been recognized as a major public health priority, with projections of escalating incidence in LMICs[20] . The heterogeneity in etiologies—ranging from DKD and hypertension in urban populations to CKD of unknown etiology (CKDu) in agrarian communities—emphasizes the multifactorial nature of the disease. Our study contributes to this global narrative by documenting the predominance of metabolic causes while also highlighting persistent roles of infection, liver disease, and social determinants in shaping ESRD.

Strengths and limitations

The strength of our study lies in its comprehensive evaluation of incident hemodialysis patients in a tertiary-care center, providing a real-world snapshot of etiological distribution. The inclusion of comorbidities and dialysis initiation practices adds depth to the analysis. However, limitations include the single-center design, retrospective attribution of etiology without biopsy confirmation in most cases, and potential referral bias toward more complex cases.

CONCLUSION

Diabetic kidney disease (DKD) has emerged as the leading cause of ESKD in North India, followed by hypertensive nephrosclerosis and chronic glomerulonephritis. A significant proportion of patients continue to present late, often without prior nephrology care, leading to emergent dialysis initiation and poor preparedness. Infectious diseases, chronic liver disease, obstructive uropathies, and use of alternative medicines remain important contributors, reflecting the multifactorial nature of ESRD in the region.

Acknowledgements

Dr. (Prof) Narinder Pal Singh, Dean Research, Eternal University

Conflict of interest: None

REFRENCES

1. **Muntner P,** He J, Hamm LL, *et al.* Renal insufficiency and subsequent death resulting from cardiovascular disease in the United States. J Am Soc Nephrol. 2002;13(3):745–753.
2. **Kearney PM,** Whelton M, Reynolds K, *et al.* Global burden of hypertension: analysis of worldwide data. Lancet. 2005;365(9455):217–223.
3. **Jafar TH.** The growing burden of chronic kidney disease in Pakistan. N Engl J Med. 2006;354 (10): 995–997.
4. **Modi GK,** Jha V. The incidence of end-stage renal disease in India: a population-based study. Kidney Int. 2006;70(12):2131–2133.
5. **Agarwal SK,** Srivastava RK. Chronic kidney disease in India: challenges and solutions. Nephron ClinPract. 2009;111(3):c197–203.
6. **Varughese S,** Abraham G. Chronic Kidney Disease in India: A Clarion Call for Change. Clin J Am SocNephrol. 2018;13(5):802-804.
7. **Sakhuja V,** Kohli HS. End-stage renal disease in India and Pakistan: incidence, causes, and management. Ethn Dis. 2006;16(2 Suppl 2):S2-23.
8. **Varma PP.** Prevalence of chronic kidney disease in India - Where are we heading? Indian J Nephrol. 2015 May-Jun;25(3):133-5. PMID: 26060360; PMCID: PMC4446915.
9. **Rajapurkar MM,** John GT, Kirpalani AL, *et al.* What do we know about chronic kidney disease in India: first report of the Indian CKD registry. BMC Nephrol. 2012;13:10.
10. **Sinha SK,** Nicholas SB. Pathomechanisms of Diabetic Kidney Disease. J Clin Med. 2023 Nov 27;12(23):7349.
11. **Singh NP,** Ingle GK, Saini VK, *et al.* Prevalence of low glomerular filtration rate, proteinuria and

associated risk factors in North India: an observational, cross-sectional study. BMC Nephrol. 2009;10:4.
12. **Chandna SM,** Schulz J, Lawrence C, *et al.* Is there a rationale for rationing chronic dialysis? A hospital-based cohort study of factors affecting survival and morbidity. BMJ. 1999;318(7178):217–223.
13. **O'Callaghan CA,** Shine B, Lasserson DS. Chronic kidney disease: a large-scale population-based study of the effects of introducing the CKD-EPI equation and a more conservative approach to CKD diagnosis. BMJ Open. 2011;1(1):e000308.
14. **Dhanorkar M,** Prasad N, Kushwaha R, *et al.* Impact of Early versus Late Referral to Nephrologists on Outcomes of Chronic Kidney Disease Patients in Northern India. Int J Nephrol. 2022;2022:4768540. Published 2022 Jun 1.
15. **Himmelfarb J,** Ikizler TA. Hemodialysis. N Engl J Med. 2010;363(19):1833–1845.
16. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013;3(1):1–150.
17. **Uddin MJ,** Mehdi MD, Singh R, *et al.* Clinical and Etiological Profile of Chronic Kidney Disease in a Tertiary Care Hospital in Seemanchal Region of Bihar. Ann. Int. Med. Den. Res. 2021; 7(1): ME09-ME12
18. **Alicic RZ,** Rooney MT, Tuttle KR. Diabetic kidney disease: challenges, progress, and possibilities. Clin J Am Soc Nephrol. 2017;12(12): 2032–2045.
19. **Anand S,** Bitton A, Gaziano T. The gap between estimated incidence of end-stage renal disease and use of therapy. PLoS One. 2013;8(8):e72860.
20. **Jha V,** Garcia-Garcia G, Iseki K, *et al.* Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382(9888):260–272.