ORIGINAL ARTICLE

Characteristics and Prognosis of Infectious Disease Emergencies in Patients with Chronic Kidney Disease in India

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Received on: 23 April 2024; *Accepted on:* 20 May 2024; *Published on:* 31 May 2024

Abstract

Objectives: Chronic kidney disease (CKD) significantly increases the risk of infectious diseases (IDs), leading to heightened morbidity and mortality. However, there remains a lack of detailed, region-specific studies. This study investigates the clinical spectrum, etiologies, outcomes, and baseline predictors of mortality of ID emergencies in CKD patients in North India.

Methods: This retrospective study was conducted at the Postgraduate Institute of Medical Education and Research, Chandigarh, from January 2021 to December 2022. It included patients aged ≥13 years with CKD and IDs admitted to the Acute Care and Emergency Medicine Unit.

Results: We enrolled 248 patients (mean age 50 years, 58.1% males). About 60% had CKD stage 5, and 46% were on maintenance hemodialysis. Diabetic kidney disease was the predominant etiology (38.7%). The principal IDs were pneumonia (27.4%), urinary tract infection (UTI) (21.4%), sepsis of unknown primary focus (15.7%), tuberculosis (8.1%), and multisite infections (7.7%). Patients commonly have atypical clinical presentation, e.g., absence of fever and nonspecific symptoms such as shortness of breath and altered mental status. An emergence of multidrug-resistant organisms, e.g., *Enterococcus faecium* for UTI and *Stenotrophomonas maltophilia* for catheter-related bloodstream infections, was noted.

In-hospital mortality rate was 33.5%, higher with multisite infections (58%) and pneumonia (47%). A low baseline Glasgow coma scale (GCS) was an independent predictor of mortality [odds ratio (OR) 0.786, 95% confidence interval (CI) 0.693–0.891, *p*-value <0.001].

Conclusion: Effective management and early intervention are needed to improve outcomes in CKD patients with ID emergencies, given the high mortality and atypical clinical presentations.

Keywords: Chronic kidney disease, Emergency, Hemodialysis, Infections, Mortality, Pneumonia, Urinary tract infection.

Indian Journal of Critical Care Medicine (2024): 10.5005/jp-journals-10071-24731

Highlights of the Study

This study underscores the diagnostic and treatment challenges of infectious disease emergencies in patients with chronic kidney disease, marked by atypical presentations, high mortality, and emergence of multidrug-resistant bacteria.

The most common infections were pneumonia and urinary tract infections, with mortality often associated with multisite infections and lower Glasgow coma scale (GCS).

Introduction

Infectious diseases (IDs) are a significant cause of hospitalization among patients with chronic kidney disease (CKD), markedly contributing to increased morbidity and mortality in these patients.[1–5] The increased susceptibility to infections in CKD and subsequent complications are multifactorial and complex. Progressive renal dysfunction alters almost all aspects of innate and adaptive immunity.[6,7] Along with this, the uremic milieu increases the proinflammatory state by increasing the production of cytokines and reducing their clearance.[6,7] Other key factors include coexisting comorbidities such as diabetes mellitus and malnutrition, diminished response to vaccinations, immunosuppressive treatments, and complications related to dialysis treatment, including vascular access and repeated exposure to nosocomial pathogens.[1–4,6–8]

Common IDs requiring hospitalization in patients with CKD include pneumonia, sepsis, catheter-related bloodstream infection (CRBSI), complicated urinary tract infection (UTI), and skin and soft-tissue infection.[1–5,9–11] Additionally, CKD patients are often highly susceptible to specific infections, notably *Staphylococcus aureus* and tuberculosis (TB).[1–3,10–12] Infections are a significant cause of Emergency Department (ED) visits in CKD patients globally, with a particularly high impact in low- and middle-income countries.[13–15]

Although infections are frequently reported in CKD, there remains a need for more detailed and region-specific studies to optimize clinical practices, improve patient outcomes, and shape healthcare policies specifically designed for this vulnerable population. This study aims to investigate the clinical spectrum, etiologies, and outcomes of ID emergencies in CKD patients in North India.

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How to cite this article: Prabhahar A, Vijaykumar NA, Selvam S, Ramchandran R, Sethi J, Pannu AK, *et al*. Characteristics and Prognosis of Infectious Disease Emergencies in Patients with Chronic Kidney Disease in India. Indian J Crit Care Med 2024;28(6):601–606.

Source of support: Nil

Conflict of interest: None

Materials and Methods

Study Design and Population

This hospital-based retrospective study was conducted at the Acute Care and Emergency Medicine Unit, Department of Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India. We reviewed the case records of all patients aged ≥13 years with CKD and IDs admitted to ED between January 2021 and December 2022. The Institutional Ethics Committee approved the study (No.: INT/IEC/2021/SPL-1062, date 8 August 2021).

Case Definitions

Chronic kidney disease was diagnosed and classified following the Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines.[15] It was defined by a persistently reduced estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 for >3 months and classification based on the etiologies and eGFR category, ranging from stage 1 to 5.

Infectious diseases were diagnosed using a comprehensive approach that included clinical features, radiological characteristics, and microbiological or molecular investigations in accordance with established standard definitions and guidelines. Pneumonia was clinically diagnosed based on clinical features such as fever and respiratory symptoms, along with lung parenchymal abnormalities evident on chest radiology.[16] Microbiological confirmation was established by identifying microorganisms from culture or microscopy of respiratory samples and blood cultures. The UTI was diagnosed with clinical features such as fever, dysuria, or suprapubic or flank tenderness, the presence of pyuria (i.e., >10 white blood cells per high-power field) on urine microscopy and/or renal imaging characteristics (cystitis, pyelonephritis, or renal abscess).[17] Microbiological confirmation was obtained through urine or blood culture.

Sepsis diagnosis was based on the Surviving Sepsis Campaign guidelines of 2021, with the exclusion of alternative diagnoses.[18] The CRBSI was defined by clinical features of infection such as fever, leukocytosis, and erythema or exudate at the catheter exit site and positive blood culture in patients with a central venous catheter in place for >48 hours and no apparent alternative source of infection.[19] Empyema was diagnosed by the presence of gross pus in the pleural space or a positive Gram stain or culture of pleural fluid. Skin and soft-tissue infections included erysipelas, cellulitis, and necrotizing fasciitis. The diagnosis of TB, including its classification into pulmonary and extra-pulmonary forms, adhered to national TB guidelines.[20] Meningitis or encephalitis was diagnosed by clinical features, neuroimaging characteristics, and cerebrospinal fluid analysis.[21]

The shock was defined with systolic blood pressure <90 mm Hg, mean arterial pressure <70 mm Hg, or the requirement of vasopressor therapy to maintain the blood pressure.[22] The quick sequential organ failure assessment (qSOFA) was calculated at baseline as a prognostic tool for severe infections. It comprises systolic blood pressure ≤100 mm Hg, a respiratory rate ≥22 breaths per minute, and a score on the Glasgow coma scale (GCS) <15, with ≥2 criteria indicating a severe infection.[18] Leukocytosis was defined as a white blood cell count >11,000 per µL.

Data Collection and Analysis

Clinical details and laboratory data were obtained from the Central Record Department, with a focus on microbiological and molecular testing for IDs. In-hospital outcomes, including mortality, survival (planned discharge) or leave against medical advice, and length of hospital stay, were recorded. Statistical analysis was conducted using Statistical Package for the Social Sciences, version 25.0. For descriptive statistics, categorical variables were presented as frequency and percentage (*n* or %), while continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range (IQR) based on the normality of data distribution. The normality was assessed using the Kolmogorov–Smirnov test and visual examination of quantile–quantile plots. Comparative analyses involved using the Chi-square test or Fisher's exact test for categorical variables, and the Students' unpaired *t*-test or Mann–Whitney *U*-test for continuous variables, tailored to their respective data characteristics. A multivariate logistic regression analysis was employed to predict in-hospital mortality, calculating the odds ratio (OR) and a 95% confidence interval (CI). The level of statistical significance was set at a *p*-value threshold of <0.05 for all tests.

Results

We enrolled a total of 248 cases with CKD and ID emergencies. The mean age was 50 ± 15.6 years, ranging from 13 to 84 years, with males constituting 58.1% (*n* = 144) of the cohort. The predominant etiological categories of CKD included diabetic kidney disease (*n* = 96, 38.7%), hypertension-associated (*n* = 10, 4.0%), renal stone disease (*n* = 10, 4.0%), glomerulonephritis (*n* = 8, 3.2%), autosomal dominant polycystic kidney disease (*n* = 6, 2.4%), and congenital anomalies of the kidney and urinary tract (*n* = 6, 2.4%). In 96 cases (38.7%), the underlying cause of CKD was unknown. 60.1% (*n* = 149) had CKD stage 5 at baseline, and 46.0% (*n* = 114) were on maintenance hemodialysis prior to their current ED admission.

The predominant ID emergencies identified in our cohort were pneumonia and related complications (*n* = 68, 27.4%), complicated UTI (*n* = 53), sepsis of unknown primary focus (*n* = 39), multisite infections (*n* = 19), TB (*n* = 20), CRBSI (*n* = 12), and empyema (*n* = 10). Of the total cases, 102 (41.1%) were confirmed through microbiological testing, as detailed in Table 1. UTI cases had a higher rate of microbiological confirmation compared with pneumonia (66.0 vs 36.8%). Notably, emphysematous pyelonephritis was diagnosed in six out of the 53 UTIs. Extrapulmonary TB was more prevalent than pulmonary TB, with pleural involvement being the most common site (9 out of 17 cases). In the context of CRBSI, Gram-negative bacilli were identified as the primary causative agents in 83.3% (10 out of 12) of the cases.

In our cohort study, the most common presenting complaints were fever (*n* = 112, 45.2%) and shortness of breath (*n* = 109, 44.0%), followed by altered mental status (*n* = 72, 29.0%). Among the patients diagnosed with pneumonia (*n* = 68), the predominant symptoms included shortness of breath (*n* = 47, 69.1%), fever (*n* = 28, 41.2%), altered mental status (*n* = 21, 30.9%), and cough with or without expectoration (*n* = 4, 5.8%). For UTI cases, the usual symptoms were fever (*n* = 20, 37.7%), altered mental status (*n* = 13, 24.5%), reduced urine output (*n* = 11, 20.8%), dysuria (*n* = 6, 11.3%), flank pain (*n* = 4, 7.5%), and abdominal pain (*n* = 4, 7.5%).

Septic shock at admission was present in 50 patients (20.2%), occurring more frequently in cases with multisite infections (*n* = 7/19, 36.8%), TB (*n* = 6/20, 30.0%), UTI (*n* = 11/53, 20.8%), and sepsis of unknown source (*n* = 8/39, 20.5%), compared with pneumonia (*n* = 8/68, 11.8%) and CRBSI (*n* = 2/12, 16.7%).

Principal microbiological investigations included blood cultures (*n* = 144), urine cultures (*n* = 111), and testing of other body fluids or purulent secretions (*n* = 143). Diagnostic yield from

Table 1: Etiology of infectious disease emergencies in patients with chronic kidney disease ($n = 248$)

Infections	*Total cases (n = 248)*	*Microbiologically confirmed cases*	
		(n = 102)	*Causative organisms*
Pneumonia and complications	68 (27.4%)	25	*SARS-CoV*-2 (15), *Klebsiella pneumoniae* (2), *Escherichia coli* (2), *Pseudomonas aeruginosa* (1), *Pseudomonas putida* (1), *Staphylococcus aureus* (1), *Acinetobacter baumannii* (1), combined *SARS-CoV*-2 and *E. coli* (1), and combined *SARS-CoV*-2, *Streptococcus pneumoniae* and *Serratia marcescens* (1)
UTI	53 (21.4%)	35	*E. coli* (20), *Enterococcus faecium* (4), *A. baumannii* (2), *E. faecalis* (1), *K. pneumoniae* (1), *Burkholderia cepacia* (1), *S. aureus* (1), *Candida* spp. (1), combined *E. coli* and *Candida* spp. (1), combined *E. coli* and *E. faecium* (1), combined *K. pneumoniae* and *S. aureus* (1), and combined *E. coli, K. pneumoniae* and *E. faecium* (1)
Sepsis of unknown primary focus	39 (15.7%)	–	–
TB	20 (8.1%)	3	*Mycobacterium tuberculosis* (3)
Extrapulmonary	13 (5.2%)	1	
Both pulmonary and extrapulmonary	4 (1.6%)	2	
Pulmonary	3 (1.2%)	0	
CRBSI	12 (4.8%)	12	*Stenotrophomonas maltophilia* (3), *P. aeruginosa* (2), *Enterobacter cloacae* (2), *K. pneumoniae* (1), *B. cepacia* (1), *S. aureus* (1), *Trichosporon asahii* (1), combined *S. maltophilia* and *P. aeruginosa* (1)
Empyema	10 (4.0%)	4	*S. pneumoniae* (2), *P. aeruginosa* (1), combined *E. faecium* and *Providencia stuartii* (1),
Skin and soft-tissue infection	6 (2.4%)	2	*Candida* spp. (1), and combined *E. coli* and *Proteus mirabilis* (1)
Viral encephalitis	5 (2.0%)	1	Herpes simplex (1)
Infectious diarrhea	5 (2.0%)	1	SARS-CoV-2 (1)
Dengue	3 (1.2%)	3	Dengue (3)
Miscellaneous[a]	9 (3.6%)	0	
Multisite infections	19 (7.7%)	(16)	
Pneumonia and UTI	5 (2.0%)	5	*SARS-CoV*-2 and *K. pneumoniae* (2), *SARS-CoV*-2 and *E. coli* (1), *SARS-CoV*-2 and *P. aeruginosa* (1), and combined *Aspergillus* spp., *K. pneumoniae, E. coli,* and *P. otitidis* (1)
Pneumonia and pulmonary TB	4 (1.6%)	3	*K. pneumoniae* (1), *S. aureus* (1), and *A. baumannii* (1)
UTI and skin and soft-tissue infection	3 (1.2%)	1	*K. pneumoniae* and *E. cloacae* (1)
UTI and bacteremia of unknown primary focus	1 (0.4%)	1	*K. pneumoniae* and *Salmonella* spp. (1)
UTI and CRBSI	1 (0.4%)	1	*S. aureus* and *Delftia acidovorans* (1)
UTI and disseminated histoplasmosis	1 (0.4%)	1	*E. coli* and *Histoplasma* spp. (1)
Infective endocarditis and pulmonary TB	1 (0.4%)	1	*S. aureus* (1)
Pneumonia, pulmonary TB and UTI	1 (0.4%)	1	*E. coli* (1)
Pneumonia, pulmonary TB and skin and soft-tissue infection	1 (0.4%)	1	*E. cloacae* and *S. aureus* (1)
Pneumonia and candidemia of unknown primary focus	1 (0.4%)	1	*S. maltophilia* and *Candida* spp. (1)

[a]Miscellaneous included bacterial meningitis (2), septic arthritis (1), liver abscess (1), splenic abscess (1), infective endocarditis (1), enteric fever (1), endophthalmitis (1), and peritonitis (1). CRBSI, Catheter-related bloodstream infection; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TB, tuberculosis; UTI, urinary tract infection

these tests were 19.4% ($n = 28$), 43.2% ($n = 48$), and 42.7% ($n = 61$) cases, respectively.

The in-hospital survival (planned discharge) was 58.5% ($n = 145$) and mortality was 33.5% ($n = 83$). Additionally, 8.1% ($n = 20$) of patients left the hospital against medical advice. Univariate analysis identified several baseline parameters associated with increased mortality, including higher mean age, diabetic kidney disease, fever, shock, multisite infections, low GCS, qSOFA ≥ 2, lower

Table 2: Univariate analysis for predictors of mortality in infectious disease emergencies in patients with chronic kidney disease

Parameters	*Survived (n = 145)*	*Died (n = 83)*	*p-value*
Age (years), mean ± SD	47.7 ± 16.1	52.9 ± 14.5	0.016
Male gender, *n* (%)	88 (60.7%)	45 (54.2%)	0.340
Diabetic kidney disease, *n* (%)	49 (33.8%)	41 (49.4%)	0.020
Chronic kidney disease stage 5, *n* (%)	89 (61.4%)	83 (57.8%)	0.599
Fever, *n* (%)	75 (51.7%)	30 (36.2%)	0.023
Glasgow coma scale, median (IQR)	15 (15–15)	8 (13–15)	<0.001
Systolic blood pressure (mm Hg), mean ± SD	128.4 ± 32.1	121.5 ± 31.9	0.120
Diastolic blood pressure (mm Hg), mean ± SD	77.1 ± 19.0	71.4 ± 24.4	0.053
Shock, *n* (%)	21 (14.5%)	23 (27.7%)	0.015
qSOFA score ≥2, *n* (%)	98 (67.6%)	36 (43.4%)	<0.001
Hemoglobin (gm/dL), mean ± SD	7.5 ± 2.2	8.2 ± 2.1	0.023
Total leukocyte count (per µL), median (IQR)	14,300 (9,800–18,500)	15,200 (9,000–20,500)	0.756
Leukocytosis, *n* (%)	100 (69.0%)	54 (65.1%)	0.545
Neutrophils (%), median (IQR)	85.0 (80.0–89.0)	87 (78.5–90.0)	0.374
Platelets ($\times 10^3$ per µL), median (IQR)	188 (113–265)	149 (77–233)	0.038
Serum sodium (mEq/L), mean ± SD	133.1 ± 7.0	135.6 ± 8.1	0.016
Serum potassium (mEq/L), mean ± SD	5.0 ± 1.1	5.0 ± 1.0	0.854
Blood urea (mg/dL), median (IQR)	151.0 (101.0–207.0)	161 (102.0–222.0)	0.397
Serum creatinine (mg/dL), median (IQR)	7.5 (5.7–9.9)	6.0 (4.6–8.6)	0.004
Serum albumin (gm/dL), mean ± SD	2.9 ± 0.6	2.7 ± 0.7	0.051
Infectious disease, *n* (%)			
Pneumonia	32 (53.3%)	28 (46.7%)	0.054
Urinary tract infection	36 (78.3%)	10 (21.7%)	0.021
Sepsis of unknown primary focus	27 (73.0%)	10 (27.0%)	0.195
Tuberculosis	12 (60.0%)	8 (40.0%)	0.726
Multisite (>1 site) infections	8 (42.1%)	11 (57.9%)	0.042
Catheter-related bloodstream infection	10 (83.3%)	2 (16.7%)	0.144

qSOFA, quick sequential organ failure assessment

Table 3: Multivariate analysis for predictive factors of mortality in infectious disease emergencies in patients with chronic kidney disease

Parameters	*OR (95% CI)*	*p-value*
Age (years)	1.017 (0.995–1.039)	0.129
Diabetic kidney disease	0.626 (0.331–1.186)	0.151
Glasgow coma scale	0.786 (0.693–0.891)	<0.001
Shock	1.297 (0.541–3.111)	0.560
qSOFA score ≥2	1.242 (0.514–3.002)	0.631
Serum albumin	0.700 (0.436–1.123)	0.139

qSOFA, quick sequential organ failure assessment

platelet count, higher sodium, lower creatinine, and lower albumin (Table 2). However, multivariate analysis revealed that a low GCS was the only independent predictor of mortality ($p = <0.001$) (Table 3). The median length of hospital stay was 5 days (IQR 3–8, range 0–94 days).

Discussion

This retrospective study provides significant insights into the epidemiology of IDs requiring ED admissions in CKD patients in India. The majority of these patients had advanced CKD, with nearly half undergoing maintenance hemodialysis. About half of the IDs were pneumonia and UTI. Over one-third of the patients died, particularly those with multisite infections and pneumonia. Notably, a low GCS score at admission strongly predicted in-hospital mortality.

In contrast to other recent hospital-based studies in India, our adult CKD cohort showed a higher proportion of diabetic kidney disease, CKD stage 5, and patients on maintenance hemodialysis.[23] This highlights the significant role of diabetes, advanced azotemia, and hemodialysis-related factors in predisposing CKD patients to severe infections. Our findings underscore the importance of integrated diabetes and early stage CKD management and comprehensive vaccination strategies to prevent infectious complications in this vulnerable population.[15]

The clinical features of the IDs in our CKD cohort were often atypical. More than half of the patients demonstrated a lack of fever response. Nonspecific symptoms such as shortness of breath, altered mental status, and reduced urine output were more common than typical symptoms of various IDs (e.g., cough in pneumonia and dysuria in UTI). These findings highlight the need for heightened clinical vigilance and comprehensive laboratory investigations to enable prompt management of common ID emergencies in CKD patients.

Consistent with existing literature, our study identified pneumonia and UTI as the predominant ID emergencies in CKD patients, with the prevalence of pneumonia partly elevated due to the coronavirus disease pandemic.[9,10,24,25] Many of these infections, particularly pneumonia and sepsis, were not microbiologically confirmed, underscoring the diagnostic challenges and highlighting the need for advanced laboratory testing in CKD patients. The absence of pathogen-directed therapy may have contributed to the poor outcomes observed in such cases. Although many UTI cases had microbiological diagnosis, with common urinary pathogens identified, the frequency of *Enterococcus faecium* infection was notably higher compared with earlier studies.[10] Additionally, *Stenotrophomonas maltophilia* was attributed to one-fourth of CRBSI cases in our CKD cohort. The emergence of these multidrug-resistant organisms is alarming, posing further treatment challenges in this vulnerable population.[26]

Given the association of advanced CKD with a heightened risk of TB, its prevalence remained notable in our cohort.[12] Extrapulmonary TB, particularly pleural TB, was more frequently observed. This increased frequency might stem from delayed diagnoses, often due to overlapping features of extrapulmonary TB and CKD (e.g., anorexia, shortness of breath, and pleural effusion) or the low sensitivity of microbiological tests for extrapulmonary TB.[12,27,28] Furthermore, the similar frequency of pleural TB and bacterial empyema in our cohort underscores the necessity of detailed investigations in CKD patients with suspected pleural infections.

A substantial proportion of IDs in our study involved multi-site infections and multiple causative organisms, notably higher frequency than what has been observed in the diabetes population with ID emergencies.[28,29] This finding underscores the significant immunodeficient state associated with advanced CKD. Multi-site infections frequently led to shock and were correlated with the highest mortality among all IDs in our cohort. This could be attributed to delays in recognizing all sources of infection.

Alarmingly, more than one-third of CKD patients with infections died, a rate higher than the overall in-hospital mortality for ID emergencies at our ED.[13] A low baseline GCS score was a significant predictor of mortality, emphasizing the critical need for early detection of altered mental status and subsequent intensive management in this patient group.[30]

Limitation

Our study faces several limitations that affect the generalizability of our results, including single-center data, a retrospective design, and a referral bias of a tertiary-care hospital. The study predominantly included patients on hemodialysis, limiting the applicability of our findings to those on peritoneal dialysis. Additionally, due to the study design and limited available data, we could not determine the vaccination status of our study population. Another significant limitation is the lack of data on empirical antimicrobial agents used and detailed antimicrobial susceptibility testing for the isolated organisms, which precluded their inclusion in our analysis.

Conclusion

This study highlights the challenges in the diagnosis and treatment of ID emergencies in CKD patients, characterized by atypical presentations, high mortality, and the emergence of multidrug-resistant bacteria. It underscores the need for integrated diabetes and early stage CKD management, combined with increased clinical vigilance and advanced diagnostic testing for infections.

Author Contributions

- Prabhahar A is responsible for data curation (lead) and writing-original draft (lead).
- Vijaykumar NA is responsible for data curation (supporting) and writing-original draft (supporting).
- Selvam S is responsible for writing-original draft (supporting).
- Ramchandran R, Sethi J, and Sharma N are responsible for writing-review and editing (supporting).
- Pannu AK is responsible for conceptualization (lead); methodology (lead); formal analysis (lead); writing-original draft (supporting), writing-review and editing (lead).

The corresponding author is responsible for ensuring that the descriptions are accurate and agreed upon by all authors.

Ethical Approval

The Institutional Ethics Committee of Postgraduate Institute of Medical Education and Research, Chandigarh (India) approved the study (No.: INT/IEC/2021/SPL-1062, date 8 August 2021).

Acknowledgment

The authors thank Mrs Sunaina Verma for help in statistics.

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