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Short Communication **Open Access**

Spectrum of bacterial uropathogens and their antibiotic susceptibility among patients with chronic kidney disease in a tertiary hospital, northcentral Nigeria

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Abstract:

Background: Chronic kidney disease (CKD) is increasingly recognized as a global public health problem. CKD patients are prone to comorbidities, such as diabetes mellitus, urinary tract infection (UTI), hypertension, immune-suppression, anaemia, malnutrition, inflammation, and vitamin deficiencies. However, UTI is known to be the most significant cause of morbidity and mortality in CKD patients. Therefore, this study aimed to identify the spectrum of uropathogenic bacteria in patients with CKD at the University of Ilorin Teaching Hospital (UITH), Ilorin, and determine their susceptibility to selected antibiotics.
Methodology: The study is a descriptive cross-sectional design conducted among 157 patients with CKD recruited from the renal clinic of UITH between January and June, 2024. Clean-catch voided midstream urine samples were collected for culture on CLED and blood agar plates and incubated at 37°C for 24 hours. Microbial identification and antimicrobial susceptibility were performed on the pure colonies of isolated bacteria using the VITEK 2 Compact system. The data were analyzed for descriptive statistics.
Results: This study reported 22.9% (n=36) prevalence of bacterial uropathogens, with *Escherichia coli* (22.2%, n=8) being the most frequently isolated pathogen among the CKD patients. Antimicrobial susceptibility of the Gram-negative isolates showed high sensitivity to imipenem (85.7%, n=24), ceftazidime (64.3%, n=18), ceftriaxone (63.0%, n=17), piperacillin-tazobactam (57.1%, n=16), and nitrofurantoin (55.6%, n=15), but high resistance to gentamicin (53.6%, n=15), augmentin (51.9%, n=14), and ciprofloxacin (50.0%, n=14). Antimicrobial susceptibility of the Gram-positive isolates showed 100% sensitivity to linezolid and vancomycin, but high resistance to cefoxitin (60.0%, n=3) and clindamycin (42.9%, n=3).
Conclusion: This study showed a relatively high prevalence of UTI among CKD patients, and the implicated uropathogens show high susceptibility to the common antibiotics that are clinically accessible.

Keywords: Chronic Kidney Disease, Urinary Tract Infection, Uropathogens, Antimicrobials

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Spectre des uropathogènes bactériens et leur sensibilité aux antibiotiques chez les patients atteints d'insuffisance rénale chronique dans un hôpital de référence du centre-nord du Nigéria

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Résumé:

Contexte: L'insuffisance rénale chronique (IRC) est de plus en plus reconnue comme un problème de santé publique

mondial. Les patients atteints d'insuffisance rénale chronique (IRC) sont sujets à des comorbidités telles que le diabète, les infections urinaires, l'hypertension, l'immunosuppression, l'anémie, la malnutrition, l'inflammation et les carences vitaminiques. Cependant, les infections urinaires constituent la principale cause de morbidité et de mortalité chez ces patients. Cette étude visait donc à identifier le spectre des bactéries uropathogènes chez les patients atteints d'IRC au Centre hospitalier universitaire d'Ilorin (UITH) et à déterminer leur sensibilité à certains antibiotiques.
Méthodologie: Il s'agit d'une étude descriptive transversale menée auprès de 157 patients atteints d'IRC recrutés à la clinique de néphrologie de l'UITH entre janvier et juin 2024. Des échantillons d'urine du milieu de jet, recueillis par la méthode du jet moyen, ont été mis en culture sur gélose CLED et gélose au sang, puis incubés à 37 °C pendant 24 heures. L'identification microbienne et l'antibiogramme ont été réalisés sur les colonies pures de bactéries isolées à l'aide du système VITEK 2 Compact. Les données ont été analysées statistiquement.
Résultats: Cette étude a rapporté une prévalence de 22,9% (n=36) d'uropathogènes bactériens, *Escherichia coli* (22,2%, n=8) étant le pathogène le plus fréquemment isolé chez les patients atteints d'IRC. La sensibilité aux antimicrobiens des isolats à Gram négatif a montré une forte sensibilité à l'imipénem (85,7%, n=24), à la ceftazidime (64,3%, n=18), à la ceftriaxone (63,0%, n=17), à la pipéracilline-tazobactam (57,1%, n=16) et à la nitrofurantoïne (55,6%, n=15), mais une forte résistance à la gentamicine (53,6%, n=15), à l'augmentin (51,9%, n=14) et à la ciprofloxacine (50,0%, n=14). L'étude de la sensibilité aux antimicrobiens des isolats à Gram positif a révélé une sensibilité de 100.0% au linézolide et à la vancomycine, mais une forte résistance à la céfoxitine (60,0%, n=3) et à la clindamycine (42,9%, n=3).
Conclusion: Cette étude a mis en évidence une prévalence relativement élevée d'infections urinaires chez les patients atteints d'insuffisance rénale chronique, et les uropathogènes impliqués présentent une forte sensibilité aux antibiotiques couramment utilisés en pratique clinique.

Mots-clés: Insuffisance rénale chronique, Infection urinaire, Uropathogènes, Antimicrobiens

Introduction:

The prevalence of CKD is estimated to be 13.4%, resulting in a major global health concern (1,2). Its rise to prominence as a significant global cause of disease and mortality underscores the importance of thorough study and intervention across populations (1,3). Diabetes mellitus, hypertension, obesity, and an aging population are all contributing causes to the global increase in CKD (4). However, there are regional differences in the frequency of CKD, with certain factors, including exposure to environmental chemicals and infections, playing a role (5).

According to recent comprehensive evaluations, the prevalence in sub-Saharan Africa (SSA) was between 10.1% and 13.9% (6,7). Additionally, West Africa was found to have the highest pooled frequency on the continent, at 16% (8). In Africa, CKD is typified by young patients, high morbidity, and early mortality. Ninety percent of CKD patients pass away within ninety days after beginning dialysis. Nigeria has a population of 180 million, yet little is known about the epidemiology of CKD in the general population (8). However, the prevalence of CKD in Nigeria varied from 2.5 to 26%, indicating a high prevalence of CKD overall and the need for additional research to determine the actual burden of CKD in Nigerians (8,9).

Nevertheless, due to the lack of affordability of the life-saving treatments of renal replacement therapies, which have been available for the past thirty years, the disease is silently killing a large number of Nigerians (10). Meanwhile, the majority of patients with CKD arrive late to nephrologists in Nigeria, already uremic and in need of renal replacement therapy (RRT) (11).

Similar to patients with other acquired immune deficits or those receiving immunosuppressive medication, patients with CKD and renal failure are at increased risk for infectious complications (12). Because metabolic diseases cause secondary immunological changes that impact numerous resistance components, chronic renal failure is therefore a risk factor for urinary tract infections (UTIs) (13,14). Haemodialysis may also weaken the immune system of CKD patients, leaving them more susceptible to illnesses like UTIs. Consequently, this could result in recurrent UTIs and kidney infections in the past (13,14).

Therefore, CKD could be a risk factor for UTIs, which can manifest as asymptomatic bacteriuria or symptomatic infection that requires treatment. A study in Nepal reported the prevalence of bacteria causing UTIs among CKD patients to be 15.8%, which was significantly high in the setting (15). UTI in CKD patients can occur as a mild case of cystitis, which can be treated with oral antibiotics, or a serious case of sepsis and multiple organ failures, and usually severe or potentially fatal infections manifest as complex UTI cases (16). If left undiagnosed or untreated, a UTI could result in significant deterioration in renal function with progress to advanced stages of CKD and death (15).

The prevalence of CKD in Nigeria is an indication for the investigation of UTI as a complication associated with CKD, in order to improve the quality of life of CKD patients. With paucity of data on the distribution of bacterial uropathogens and their susceptibility to commonly used antimicrobials among CKD patients

in Nigeria, this study aimed to determine the spectrum of bacterial uropathogens and their antibiotic susceptibility among CKD patients attending the University of Ilorin Teaching Hospital, Ilorin, Nigeria.

Materials and method:

Study setting:

The study was conducted at the University of Ilorin Teaching Hospital (UITH). The hospital was selected because it is the only tertiary healthcare facility in Ilorin serving large population with advanced health challenges and a referral centre for hospitals in Kwara, Oyo, Osun, Niger, Kogi, and Ekiti States in Nigeria.

Study design, sample size, and method of sampling:

The study was a descriptive cross-sectional design to determine the prevalence of bacterial uropathogens among patients with CKD and determine their antibiotic susceptibility. To determine the sample size, the prevalence of 10.1% of CKD reported in a study conducted in Sub-Saharan Africa (7) was incorporated into the formula (17); $N=Z^2 PQ(1-P)/d^2$, where N = minimum desired sample size, Z= normal standard deviation at 95% confidence interval (= 1.96), Q = 1-P, and d= precision (allowable error) of 5% (0.05), which gave a sample size of 138.

However, a total of 157 CKD patients were selected using consecutive sampling technique to recruit patients who satisfied the inclusion criteria and showed signs of a UTI during the period of January and June 2024, whether they were hospitalized in the nephrology unit or attended the renal clinic.

Inclusion and exclusion criteria:

Consenting CKD patients who willingly provided their urine samples and who had not been placed on antibiotics were included in the study. Patients' prescription history was assessed, and information on patients' medication history were further obtained to identify those who have not been on antibiotics. However, patients who have not been clinically diagnosed with CKD, CKD patients on antibiotics, and those who did not give consent to participate were excluded from the study.

Ethical consideration:

Ethical approval was obtained from the University of Ilorin Teaching Hospital Ethical Review Committee with the ERC approval number of ERC PAN/2023/05/0361 before commencing the project. All participants were informed about the purpose of the research, benefits, and risks, with certainty that their participation was voluntary and guaranteeing the confidentiality of data and their right to partake or withdraw from the study. All participants included in the study provided written informed consent to participate in the study.

Sample and data collection:

A midstream voided urine specimen of each CKD patient was collected into a sterile leak-proof universal bottle. Patients were properly instructed on how to collect clean catch urine. Samples were transported immediately for processing and analysis. Bio data of the sample, including specimen types, clinical diagnosis, gender, hospital unit, and age, was recorded in a format created especially for the research.

Laboratory analysis of urine samples:

Each urine sample was properly mixed and aseptically inoculated onto the CLED and blood agar plates to aid the growth of bacteria owing to the availability of the nutrient on the media. The inoculated agar plates were incubated at 37°C for 24 hours. Bacterial growth colonies were Gram-stained following standard procedure (18), and microbial identification and antimicrobial susceptibility testing were performed using the VITEK 2 Compact system.

Data analysis:

Data were analyzed using SPSS version 25.0. Descriptive statistics (chart, frequency, and percentage) were used to summarize the data.

Results:

Demographic characteristics of the participants:

Majority of the participants were females (54.8%, n=86), and in the age group above 60 years (37.6%, n=59), while the age group 1-10 years (1.3%, n=2) was the least frequent (Table 1).

Table 1: Socio-demographic characteristics of patients with chronic kidney disease in UITH Ilorin

Variables	Frequency	Percentage
Gender		
Male	71	45.2
Female	86	54.8
Age group (years)		
1-10	2	1.3
11-20	8	5.1
21-30	16	10.2
31-40	17	10.8
41-50	23	14.6
51-60	32	20.4
Above 60	59	37.6
Total	**157**	**100.00**

Prevalence of bacterial pathogens:

Of the total samples from 157 CKD participants, a prevalence of 22.9% (n=36) of bacterial uropathogens was reported (Fig 1). *Escherichia coli* was the most frequently isolated bacterium among the participants (22.2%, n=8), followed by *Klebsiella pneumoniae* (19.4%, n=7). *Staphylococcus lentus*, *Staphylococcus lugdunensis*, *Streptococcus mutans*, *Acinetobacter* species, and *Enterococcus faecalis* were the least frequently isolated pathogens, with 2.8% (n=1) each (Table 2).

Antimicrobial susceptibility of bacterial uropathogens:

The antimicrobial susceptibility of the Gram-positive isolates showed 100% sensitivity to linezolid and vancomycin, but high resistance of 60.0% (n=3) and 42.9% (n=3) to cefoxitin and clindamycin, respectively (Table 3). The antimicrobial susceptibility of the Gram-negative bacteria showed sensitivity to imipenem (85.7%, n=24), ceftazidime (64.3%, n=18), ceftriaxone (63.0%, n=17), piperacillin-tazobactam (57.1%, n=16), and nitrofurantoin (55.6%, n=15), but the isolates were resistant to gentamicin (53.6%, n=15), augmentin (51.9%, n=14), and ciprofloxacin (50.0%, n=14) (Table 4).

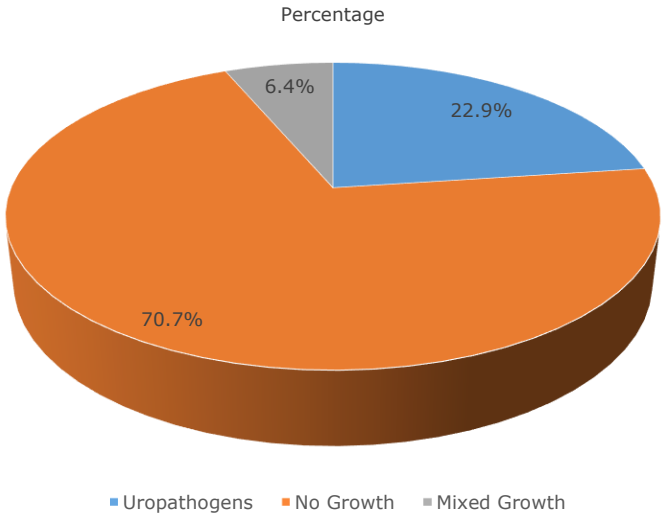

Fig 1: Prevalence of uropathogens among patients with chronic kidney disease in UITH Ilorin

Table 2: Frequency Distribution of bacterial uropathogens isolated from patients with chronic kidney disease in UITH Ilorin

Bacterial isolates	Frequency	Percentage
Gram-negative	**29**	**82.6**
Escherichia coli	8	22.2
Klebsiella pneumoniae	7	19.4
Klebsiella oxytoca	3	8.3
Enterobacter cloacae	3	8.3
Proteus mirabilis	3	8.3
Serratia ficaria	2	5.6
Pseudomonas aeruginosa	2	5.6
Acinetobacter specie	1	2.8
Gram-positive	**7**	**17.4**
Staphylococcus saprophyticus	2	5.6
Staphylococcus lugdunensis	1	2.8
Staphylococcus hominis	1	2.8
Staphylococcus lentus	1	2.8
Streptococcus mutans	1	2.8
Enterococcus faecalis	1	2.8
Total	**36**	**100.0**

Table 3: Antimicrobial susceptibility of Gram-positive isolates from patients with chronic kidney disease in UITH Ilorin

Antibiotics	No of isolates tested	No sensitive (%)	No intermediate (%)	No resistant (%)
Cefoxitin	5	2 (40)	0	3 (60)
Linezolid	7	7 (100)	0	0
Erythromycin	7	4 (57.1)	2 (28.6)	1 (14.3)
Clindamycin	7	4 (57.1)	0	3 (42.9)
Gentamicin	5	3 (60)	1 (20)	1 (20)
Tetracycline	5	4 (80)	0	1 (20)
Levofloxacin	5	3 (60)	2 (40)	0
Nitrofurantoin	7	6 (85.7)	0	1 (14.3)
Vancomycin	7	7 (100)	0	0

Table 4: Antimicrobial susceptibility of Gram-negative bacterial isolates from patients with chronic kidney disease in UITH Ilorin

Antibiotics	No of isolates tested	No sensitive (%)	No intermediate (%)	No resistant (%)
Ceftazidime	28	18 (64.3)	2 (7.1)	8 (28.6)
Augmentin	27	10 (37.0)	3 (11.1)	14 (51.9)
Ceftriaxone	27	17 (63.0)	0	10 (37.0)
Piperacillin-Tazobactam	28	16 (57.1)	0	12 (42.9)
Gentamicin	28	12 (42.9)	1 (3.6)	15 (53.6)
Ciprofloxacin	28	13 (46.4)	1 (3.6)	14 (50)
Imipenem	28	24 (85.7)	1 (3.6)	3 (10.7)
Nitrofurantoin	27	15 (55.6)	5 (18.5)	7 (25.9)

Discussion:

This study reported the prevalence of bacterial uropathogens to be 22.9%, which agrees with 26% rate reported by Chaudary et al., (19) but contrast the 70.6% rate reported by Raphael and Udo (20). This difference in rates may be due to differences in the regions and hospital settings of the studies. In patients with CKD, infectious complications are much higher, similar to individuals on immunosuppressive medications or those with other forms of acquired immune deficiency (12). The risk of infection in CKD patients has been reported to be three times higher than the general population (21). Also, the vulnerability of CKD patients to diseases such as UTI is due to prolonged haemodialysis, compromising their immune system function, resulting in recurrent UTIs and ascending renal infection. More so, chronic renal failure serves as a contributing factor for the development of UTIs due to secondary immunological changes brought on by metabolic diseases that impact several resistance components (13,14).

In this study, *E. coli* is the most frequently isolated bacterium in the CKD patients, contributing to about 22.2% of the total isolates, followed by *K. pneumoniae* (19.4%) and *K. oxytoca* (8.3%). This is similar to the studies of Pugalendhi et al., (22) and Shankar et al., (23), who both reported *E. coli* (47.7%) and *K. pneumoniae* (15.4%), and *E. coli* (61.8%) and *K. pneumoniae* (13.7%), respectively, as the most frequent bacterial isolates with a lower frequency of other bacteria uropathogen in CKD patients. This finding may be because *E. coli* is a ubiquitous bacterium and is the most predominant bacterium in UTI, hence a high tendency for *E. coli* to be reported in CKD patients. Also, numerous virulence factors, such as flagella, lipopolysaccharides, toxins, surface vesicles, polysaccharide capsules, fimbrial and non-fimbrial adhesins, and iron acquisition system, enable *E. coli* to survive and cause infection in the urinary tract. Thus, *E. coli* frequently targets the urethra, bladder, and kidneys (24).

Assessing the antibiotic susceptibility of the bacterial uropathogens, Gram-positive bacteria had higher susceptibility to linezolid and vancomycin compared to other antibiotics, while 60% and 42.9% of the isolates were resistant to cefoxitin and clindamycin, respectively. This finding is similar to that reported by Shankar et al., (23), with higher susceptibility of Gram-positive cocci to linezolid and vancomycin. This indicates the continued efficacy of these antibiotics against Gram-positive bacteria. This may partly be because these drugs cannot be bought easily over the counter, as they are mainly used in hospitals.

In this study, most of the Gram-negative bacteria showed high sensitivity to ceftazidime, ceftriaxone, piperacillin-tazobactam, imipenem, and nitrofurantoin, but were resistant to augmentin, gentamicin, and ciprofloxacin. This finding contrast that of Thapa et al., (25), who reported higher resistance of Gram-negative bacteria to ceftazidime and ceftriaxone, but agrees with their findings of high susceptibility to meropenem and nitrofurantoin. Our study rep-

ort absence of multi-drug resistance among the uropathogens from the CKD patients, which may be an important factor in management of the patients, with potential improved outcomes as resistance appears not to be a challenge.

This study has some limitations. We could not determine the distribution of isolated bacterial pathogens across the 5 stages of CKD, which would be beneficial in determining the stages that are most at risk of UTI. Additionally, the study did not take into account the risk factors that influence the prevalence of UTI. However, the study leverages the strength of the automated method (Vitek 2 system) used for bacteria identification and susceptibility testing.

Conclusion:

This study reported 22.9% prevalence of uropathogenic bacteria, with *E. coli* being the predominant pathogen among CKD patients. Bacterial uropathogens isolated from CKD patients in this study show high susceptibility to the common antibiotics that are clinically accessible, indicating that antimicrobial resistance is not significantly high among CKD patients. Future research should explore the association between the stages of CKD and UTIs, and other risk factors should be considered.

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Contributions of authors:

AJA conceptualized the idea and designed the study, and was involved in data acquisition, interpretation and writing of the manuscript; KAB was involved in data interpretation, validation and writing of the manuscript; TJO was involved in data analysis and interpretation, writing, revising and proofreading of the manuscript; DSO was involved in data interpretation and validation, reviewing and proofreading of the manuscript and AAAII supervised the study and was involved in conceptualization, design, data acquisition and interpretation, reviewing and proofreading of the manuscript. All authors approved the final version of the manuscript submitted for publication.

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Authors declare no conflict of interest

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