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Antibiotic resistance patterns in uropathogens: insights from a Nepalese tertiary care setting

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Abstract

Background: Antimicrobial resistance in uropathogens is increasing globally, particularly in resource-limited settings such as Nepal, limiting treatment options.

Objectives: This study aimed to evaluate the antimicrobial resistance patterns of uropathogens isolated from patients with urinary tract infections (UTIs) in a tertiary care hospital in central Nepal.

Design: This study utilized a retrospective study design.

Methods: We retrospectively observed medical records from August 2023 to February 2024 at Manmohan Memorial Teaching Hospital in Nepal, focusing on patients with significant bacterial growth in urine samples and antibiotic sensitivity analysis for resistance trends.

Results: *Escherichia coli* (*E. coli*) (64.7%) and *Klebsiella pneumoniae* (*K. pneumoniae*) (15.0%) were the most common uropathogens. Both showed the highest resistance to amoxicillin (>95%), while *E. coli* demonstrated the lowest resistance to gentamicin (7.4%) and nitrofurantoin (12.2%). *Klebsiella pneumoniae* also showed low resistance to gentamicin (12.0%) but higher resistance to nitrofurantoin (64.0%).

Conclusion: Empirical therapy, including nitrofurantoin and aminoglycosides, is a viable option for combating antimicrobial resistance in Nepal, necessitating region-specific surveillance and multicentre studies.

Plain language summary

Bacterial resistance to antibiotics in urinary infections: findings from a tertiary hospital of central Nepal

Antibiotic resistance is a growing problem worldwide, making it harder to treat infections. In Nepal, where healthcare resources are limited, this issue is even more challenging. This study looked at the resistance rate of bacteria that cause urinary tract infections (UTIs) among different antibiotics in a tertiary care hospital in central Nepal. We analyzed medical records from August 2023 to February 2024, focusing on patients with UTIs. The most common bacteria found was *Escherichia coli* (*E. coli*), making up nearly 65% of infections. Many of these bacteria were highly resistant to commonly used antibiotics like amoxicillin, ampicillin, and levofloxacin. However, gentamicin and nitrofurantoin were still effective against most infections. When we compared our findings with data from eastern Nepal, we found differences in the resistance rate of bacteria among various antibiotics, showing that resistance patterns vary by region. Our study suggests that nitrofurantoin and aminoglycosides could be good treatment options in Nepal, but continuous monitoring and more research across different regions and settings of hospitals are needed to guide the appropriate selection and use of the best antibiotics.

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Introduction

Antimicrobial resistance (AMR) is defined as the ability of microorganisms—such as bacteria, viruses, fungi, and parasites—to adapt and survive in the presence of medications that were once effective against them.[1] Over the past decade, there has been a significant rise in both the percentage and total number of bacterial pathogens exhibiting resistance to multiple antimicrobial medications worldwide.[2] AMR caused approximately 4.71 million deaths globally in 2021, with a projection of 8.22 million annual deaths by 2050.[3] AMR in uropathogens, particularly in urinary tract infections (UTIs), is becoming a critical global health issue. Globally, in 2019, UTIs were reported to be linked with approximately 64,890 deaths directly attributed to AMR.[4] According to a 2019 report, *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*) were responsible for over 50% of AMR-related deaths in UTIs globally, with South Asia, including Nepal, reporting the highest death counts.[4] Resistance was notably high to fluoroquinolones, carbapenems, and third-generation cephalosporins.[4] Studies have shown that the overuse of broad-spectrum antibiotics during the COVID-19 pandemic has exacerbated AMR, leading to notably higher resistance of uropathogens to fluoroquinolones.[5]

In Nepal antimicrobial resistance is a growing issue, driven by the greater prevalence of infectious disease, widespread irrational antimicrobial use in animal and agricultural products, poor healthcare infrastructure, and lack of proper infection control.[6–8] Studies revealed high resistance levels to both first and second-line antibiotics among bacterial pathogens in Nepal.[6,9,10] This situation is even worse in the case of uropathogens, where the Penicillin group (ampicillin and piperacillin) showed low antimicrobial activity (sensitive rate only $<$ 20%) against both gram-positive and gram-negative bacteria, and other groups of antibiotics also showed high resistance rate.[10,11] A 2021 study on uropathogens in Nepal revealed that 84.3% exhibited resistance to at least one antibiotic, with 53.6% classified as multidrug-resistant (MDR).[12]

In this brief report, we presented the current pattern of AMR in uropathogens from tertiary care hospitals in central Nepal and compared them with recent studies to inform effective practices aligned with the resistance trend. In addition, this report attempted to contribute to a broader discussion and understanding of the ongoing trend of antimicrobial resistance patterns in developing countries.

Method

We retrospectively reviewed medical record data of both inpatient and outpatient departments of Manmohan Memorial Teaching Hospital (MMTH) in Kathmandu, Nepal, from August 2023 to February 2024. MMTH is a 300-bed tertiary care hospital providing various services in multiple specialties based in the capital city of central Nepal.[13]

Initially, all data obtained from the medical record department of the hospital were screened, and those with provisional and final diagnoses of UTIs were segregated. A total of 2306 patients were diagnosed with UTIs. Out of all those patients whose urine samples were sent for culture and sensitivity analysis based on the clinical decision, only 167 showed significant bacterial growth and were tested for antibiotic sensitivity analysis. In all those samples, single microorganisms were found to be isolated. Culture and sensitivity tests were conducted in the hospital pathology laboratory as per the hospital's standard operating procedures and guidelines to meet the highest quality standards. So, this study included patients who underwent urine culture and sensitivity testing related to UTIs. Patients with cultures that did not yield bacterial isolation were excluded.

Descriptive statistics were employed to summarize AMR patterns and patients' sociodemographic variables. Statistical Package for Social Science (SPSS) version 26 was used for data analysis. Resistant percentages of isolated microorganisms with antimicrobials were presented in a table.

Table 1. Sociodemographic and clinical characteristics ($N = 167$).

Characteristics	Category	Frequency	%
Gender	Male	51	30.5
	Female	116	69.5
Age group	1–30	62	37.12
	31–60	72	43.11
	61–90	33	19.76
Bacteria type	Gram negative	147	88.02
	Gram positive	20	11.98

The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Supplemental Material).[14]

Result

Out of 2306 patients, only 167 patients' samples exhibited significant microbial growth. Most 31–60-year-old females had UTIs (Table 1).

Among 167 urine specimens, 12 different uropathogens were identified, where *E. coli* was the dominant one (64.7%) (Table 2).

Antimicrobial resistance pattern of central Nepal

Among the Gram-negative isolates, *E. coli* and *K. pneumoniae* were the most frequently encountered pathogens, accounting for 64.7% and 15.0% of total isolates, respectively. Notably, *E. coli* exhibited the highest resistance to amoxicillin (95.96%) and ampicillin (85.71%), whereas the lowest resistance was observed with gentamicin (7.41%) and nitrofurantoin (12.15%). Similarly, *K. pneumoniae* showed the highest resistance to amoxicillin (95.65%) and nitrofurantoin (64.00%), with relatively low resistance to gentamicin (12.00%). Resistance to third-generation cephalosporins such as cefixime and ceftriaxone remained moderately high in both species. *Citrobacter koseri* (*C. koseri*) and *Citrobacter freundii* (*C. freundii*) also demonstrated complete resistance to amoxicillin and ampicillin. Among non-fermenters, *Pseudomonas aeruginosa* (*P. aeruginosa*) was isolated in a small proportion and showed no resistance to ciprofloxacin or aminoglycosides, though data were limited. Among Gram-positive organisms, *Staphylococcus aureus* (*S. aureus*) (6%) and *Enterococcus* spp. (2.4%) were frequently isolated. *S. aureus* exhibited complete resistance to amoxicillin and high resistance to ciprofloxacin (62.5%) while showing full susceptibility to amikacin. Conversely, *Enterococcus* spp. demonstrated no resistance to nitrofurantoin and gentamicin but showed moderate resistance to ampicillin (66.67%) (Table 2).

Discussion

Consistent with global and regional trends, *E. coli* was the most prevalent uropathogen, accounting for 64.7% of isolates in Nepal, followed by *K. pneumoniae* (15.0%) and *S. aureus* (6.0%).[10,15,16] Similarly, the distribution of gender and age in UTIs observed in this study corresponds with international patterns, highlighting that females (69.5%) and those aged 31–60 years (43.11%) are the most impacted demographics.[17] This demographic pattern can be linked to anatomical and hormonal factors and behavioral differences.

High resistance rates to beta-lactams, particularly amoxicillin, were observed in this study, with *E. coli* and *K. pneumoniae* showing resistance rates of 95.96% and 95.65%, respectively. A similar resistance rate was reported in a recent eastern Nepal study (82.5%)[10] and previous studies from other regions of Nepal indicating 55.6%–79.7% resistance to amoxicillin.[12,16,18] Resistance to ampicillin was slightly lower in this study (85.71%) compared to eastern Nepal (92.5%).[10] Similarly, *K. pneumonia* demonstrated a significant resistance rate to amoxicillin (95.65%), aligning with the observations made by past studies of Nepal, Baral et al. (100%),[19] and Raya et al. (93.3%).[20] Extended-spectrum beta-lactamase was reported to be produced by 27.2%–38.9% of *E. coli* and 23.3% of *K. pneumonia* isolated in the past studies of Nepal.[20,21] Furthermore, we observed significant fluoroquinolone resistance. *E. coli* demonstrated resistance rates of 32.67% to ciprofloxacin, which is 63.9% in Eastern Nepal[10] and 35.9% in a 2012 study from central Nepal.[19] Conversely, resistance to levofloxacin was higher

Table 2. Antimicrobial resistance pattern at Manmohan Memorial Teaching Hospital, central Nepal.

Bacteria type		**Gram negative**								**Gram positive**			
Isolated bacteria	**Notation**	***Escherichia coli***	***Klebsiella pneumoniae***	***Citrobacter koseri***	***Citrobacter freundii***	***Proteus mirabilis***	***Klebsiella oxytoca***	***Pseudomonas aeruginosa***	***Providencia stuartii***	***Staphylococcus aureus***	***Staphylococcus epidermidis***	***Enterococcus spp.***	***Staphylococcus saprophyticus***
Ceftriaxone	R/T (R%)	48/104 (46.15)	10/24 (41.67)	3/4 (75.00)	1/4 (25.00)	0/1 (0.00)	0/1 (0.00)	NT	NT	4/6 (66.67)	1/4 (25.00)	NT	1/1 (100.00)
Cefixime	R/T (R%)	64/104 (61.54)	10/25 (40.00)	3/4 (75.00)	2/4 (50.00)	0/1 (0.00)	1/1 (100.00)	NT	NT	1/3 (33.33)	2/3 (66.67)	NT	1/1 (100.00)
Amoxicillin	R/T (R%)	95/99 (95.96)	22/23 (95.65)	4/4 (100.00)	3/3 (100.00)	0/1 (0.00)	1/1 (100.00)	NT	NT	3/3 (100.00)	1/1 (100.00)	NT	NT
Ampicillin	R/T (R%)	6/7 (85.71)	1/1 (100.00)	NT	1/1 (100.00)	NT	NT	NT	NT	5/7 (71.43)	1/3 (33.33)	2/3 (66.67)	0/2 (0.00)
Ciprofloxacin	R/T (R%)	33/101 (32.67)	6/18 (33.33)	4/5 (80.00)	1/4 (25.00)	0/2 (0.00)	0/1 (0.00)	0/1 (0.00)	0/1 (0.00)	5/8 (62.50)	2/4 (50.00)	2/3 (66.67)	0/2 (0.00)
Levofloxacin	R/T (R%)	5/6 (83.33)	3/3 (100.00)	1/0 (100.00)	NT	NT	NT	NT	NT	NT	NT	NT	NT
Ofloxacin	R/T (R%)	4 (57.14)	4 (57.14)	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Gentamicin	R/T (R%)	8/108 (7.41)	3/25 (12.00)	1/5 (20.00)	0/4 (0.00)	0/2 (0.00)	0/1 (0.00)	0/1 (0.00)	NT	4/10 (40.00)	2/3 (66.67)	0/1 (0.00	0/2 (0.00)
Amikacin	R/T (R%)	5/10 (50.00)	2/3 (66.67)	1/1 (100.00)	NT	NT	NT	NT	NT	0/3 (0.00)	0/1 (0.00)	NT	NT
Nitrofurantoin	R/T (R%)	13/107 (12.15)	16/25 (64.00)	1/5 (20.00)	1/4 (25.00)	1/2 (50.00)	0/1 (0.00)	NT	NT	3/10 (30.00)	0/4 (0.00)	0/3 (0.00)	0/2 (0.00)
Imipenem	R/T (R%)	2/9 (22.22)	3/3 (100.00)	1/2 (50.00)	NT	NT	NT	NT	NT	1/1 (100.00)	0/1 (0.00)	NT	NT
Meropenem	R/T (R%)	1/9 (11.11)	2/3 (66.67)	0/1 (0.00)	NT	NT	NT	NT	NT	NT	NT	1/2 (50.00)	NT
Total (%)	F (%)	108 (64.7%)	25 (15.0%)	5 (3.0%)	4 (2.4%)	2 (1.2%)	1 (0.6%)	1 (0.6%)	1 (0.6%)	10 (6.0%)	4 (2.4%)	4 (2.4%)	2 (1.2%)

F, frequency; NT, not tested; R, resistant; R%, resistance percentage; T, total.

in this study (83.33%) compared to eastern Nepal (22.1%).[10]

The resistance patterns for aminoglycosides were relatively lower, with 7.41% gentamicin resistance to *E. coli*, which is lower than previous reports (16.4%), suggesting gentamicin can be a more effective option against uropathogens in the Nepalese population.[21] Alternatively, the resistance to amikacin was notably elevated at 50.00%, which is higher than the previous study (3.9% in Raya et al. 2020),[20] potentially restricting its effectiveness as a last-resort antibiotic in certain situations. Similarly, a notable finding is the low resistance to nitrofurantoin among *E. coli* isolates (12.15%), maintaining one of the highest susceptibility rates among uropathogens. However, it is higher compared to previous studies (6.3% in Shrestha et al. 2019,[21] 5.7% in Raya et al. 2020)[20] and a recent study of eastern Nepal (30.4%), demonstrating significant regional variations.[10] The low resistance to nitrofurantoin in central Nepal makes it a viable empirical option and supports its inclusion in first-line treatment protocols for UTIs, but it is limited in the local context only due to the different resistance patterns in different regions. Nitrofurantoin has consistently demonstrated exceptional durability against resistance,[22] with previous studies confirming its low resistance rates in pediatric patients, including those with *E. coli*-induced UTIs.[23] Notably, this study highlighted its superior efficacy over ampicillin and co-trimoxazole in pediatric UTIs, reinforcing its role in empirical therapy for lower UTIs.[23] Given its affordability, accessibility, and effectiveness, nitrofurantoin remains a valuable treatment option, particularly in resource-limited settings. While its use may be limited in upper UTIs due to low renal parenchymal concentration,[23] incorporating global data—such as its low resistance in uropathogens findings from Europe[24] and the USA[25]—would further contextualize its significance in combating antimicrobial resistance.

A significant distinction between our findings and earlier studies is evident in the resistance rates observed for carbapenems. *E. coli* exhibited a relatively low resistance to imipenem (22.22%) and meropenem (11.11%). In a 2019 study by Shrestha et al. in Kathmandu, Nepal, 8.8% of *E. coli* isolates were resistant to meropenem.[21] Conversely, a recent 2023 study by Sah et al. noted that carbapenems were highly effective against multidrug-resistant (MDR) and extensively drug-resistant (XDR) uropathogens, with nearly no resistance detected.[10] The study also documented high resistance rates in less common pathogens, such as *C. koseri*, with 75% resistance to ceftriaxone and cefixime. These findings parallel the eastern Nepal study, which noted rising resistance among nondominant uropathogens such as *P. mirabilis*.[10] These results align with existing literature that has reported a rising occurrence of MDR and XDR uropathogens in Nepal.[10,26]

The comparison between central and eastern Nepal reveals both similarities and distinctions in AMR patterns. The difference in the resistance pattern might be the influence of antimicrobial usage patterns, healthcare practices, or variations in infection. However, it indicates the possibility of overuse or reduced regulation of antimicrobial utilization. The distinct resistant pattern at different regions directs the need for contextual or region-specific antimicrobial utilization guidelines. Specifically, both regions exhibit high resistance to beta-lactams and fluoroquinolones, underscoring the growing difficulties in managing UTIs. Similar to global trends,[27] the prevalent resistance pattern underscores the urgent need for enhanced antimicrobial stewardship initiatives in Nepal. Enhancing surveillance systems and executing national-level interventions is essential in reducing the effects of AMR on public health in Nepal.

Limitations and future research

The limitations of this study stem from its retrospective design and the focus on a single site, which may not adequately reflect the wider trends of AMR in Nepal. However, this study provided collective evidence on the current pattern of antimicrobial resistance, compiling recent study data. Furthermore, the representative data of Kathmandu, central Nepal, encompasses a diverse and wide range of patient groups. Second, the percentage value of resistance needs careful interpretation with viewing the number values; otherwise, it might be interpreted inappropriately because of the lower number of cultures and sensitivity tests of some pathogens. Future studies should focus on incorporating larger and multicentre datasets, including AMR patterns across different age groups and severities of UTIs, antimicrobial prescribing practices, their quality, and patient compliance, to explore the underlying factors influencing AMR.

Conclusion

This study revealed that *E. coli* and *K. pneumoniae* are the predominant uropathogens, exhibiting broad resistance, particularly to commonly used antibiotics such as penicillins and cephalosporins. While low resistance to nitrofurantoin and carbapenems presents viable treatment options, their prudent use is essential. Addressing antimicrobial resistance in Nepal requires proactive surveillance, strong stewardship programs, and evidence-based policies guided by current research.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with established ethical standards. Ethical approval was granted by the Institutional Review Committee of the Manmohan Memorial Institute of Health Sciences (MMIHS-IRC Ref. No.: NEHCO/IRC/080/24). Permission to collect data from the Manmohan Memorial Teaching Hospital (MMTH), Kathmandu, was obtained from the hospital board (Ref. No. 241). As the design was retrospective and the study did not involve the collection of identifiable personal information, the requirement for informed consent was waived by the ethics committee.

Consent for publication

Not applicable.

Author contributions

Rahi Bikram Thapa: Conceptualization; Data curation; Formal analysis; Methodology; Validation; Visualization; Writing – original draft; Writing – review & editing.

Sabin Shrestha: Conceptualization; Data curation; Methodology; Validation; Writing – review & editing.

Pharsuram Adhikari: Data curation; Formal analysis; Methodology; Validation; Writing – review & editing.

Rajeev Shrestha: Formal analysis; Investigation; Methodology; Validation; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

Data is available from the corresponding author, upon reasonable request.

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Supplemental material

Supplemental material for this article is available online.

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