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ORIGINAL RESEARCH

Prevalence and antibiogram of uropathogens isolated in a South Indian government hospital: A cross-sectional study

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ABSTRACT

Background: Urinary tract infections are among the most common bacterial infections that are largely treated using empirical antibiotic therapy. Due to the prevailing antibiotic resistance trends, treatment may be inadequate or overzealous. This study was undertaken with the objectives of:i)determining the prevalence of uropathogens, and ii) preparing a hospital antibiogram so as to facilitate better decision-making.**Methods:** A cross-sectional study was undertaken at a government hospital in Chikkamagaluru district of Karnataka, India, using secondary data of bacterial isolates in urine cultures from July 2022 to December 2023. Data entry and analyses were performed using Microsoft Excel. The prevalence of specific causative organisms and antibiotic susceptibility were presented as percentages and graphs. An antibiogram was prepared from the analysed data.**Results:** The study population was evenly distributed across adult and paediatric age groups. Bacterial isolates from 674 urine samples were subjected to culture and sensitivity testing. 71.9% of all culture-confirmed urinary tract infections were observed in female patients. The overall prevalence of urinary tract infection was 19% (128/674), of which 93.7% were gram-negative infections. *E. coli* was the most commonly isolated organism (84.4%). On antimicrobial susceptibility testing, uropathogens exhibited maximum sensitivity to meropenem (98.3%), imipenem (98.1%), amikacin (95.3%) and gentamicin (91.3%), while being most resistant to amoxicillin and ampicillin.**Conclusion:** Most commonly encountered uropathogens were *E. coli* and *Klebsiella* that responded maximally to carbapenems and aminoglycosides while showing greatest resistance to penicillins. The antibiogram constructed based on the results of this study can be used to guide empirical therapy in the affiliated hospital.

Key words: Urinary tract infections, prevalence, uropathogens, antibiotics, antibiogram

INTRODUCTION

Urinary tract infections (UTIs) are defined as a spectrum of infectious syndromes that affect the urinary tract, *i.e.*, any site between the urethra and the kidneys.[1]Being among the most common bacterial infections worldwide, they pose a significant treatment challenge due to widespread antibiotic resistance and the emergence of multi-drug resistant pathogens.[2]UTIs are commonly associated with symptoms including increased urinary frequency, urgency, burning or painful micturition, and suprapubic discomfort. A diagnosis of UTI is made from both clinical history and urine analysis with gold standard confirmation being through urine culture.[3]

Empirical antibiotic therapy is administered when a UTI is suspected but the specific causative organism and its susceptibility pattern have not yet been ascertained by culture and sensitivity testing. Most antibiotic use for UTIs is empirical because definitive identification of the infective pathogen typically takes 24–48 hours. Such delay would be detrimental, more so in the case of acute severe infections in patients with greater morbidity or compromised immunity[4],while early containment of infection would prevent its spread to the kidneys and the associated complications.[3]Thus, antibiotics are promptly initiated based on the most likely infectious agent and local epidemiology after collection of the diagnostic samples. In several cases, a combination of antibiotics is used in order to achieve an adequate spectrum of activity against the likely pathogens. However, once the culture and sensitivity results become available, definitive therapy should be started, typically as monotherapy to minimize toxicity and the development of multi-drug resistance.[4]

Antibiotic resistance has been largely attributed to antibiotic misuse that includes self-medication and nonadherence, bacterial transmission of drug resistance genes, and human consumption of antibiotic-treated animal products.[5]Increased resistance rates not only adversely affect patient health by prolonging illness and extending morbidity but also increase the financial burden borne by doubling treatment costs.[6]Shifting resistance patterns have been particularly discernible among the widely isolated uropathogens due to the indiscriminate use of empirical antibiotics.[7]With the rising trends of antibiotic resistance, regular surveillance programs are intended to throw light on microbial drug sensitivity so as to help steer empirical therapy towards better treatment outcomes while upholding the principal tenets of antimicrobial stewardship.[8]

An antibiogram is a summary of antibiotic susceptibility patterns for select bacterial pathogens tested against specific antibiotics.[9]Studying the prevalence and susceptibility patterns of uropathogens can aid the construction of a hospital antibiogram according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, that would in turn serve as a decision-making tool for empirical therapy. Further, preparing an antibiogram is the first step of framing an antibiotic policy which is one of the mandatory requirements for institutional accreditation.[10]
The aim of this study was to assess the prevalence and antibiotic susceptibility of urinary pathogens in order to generate an antibiogram for UTIs in the district.

METHODS

This cross-sectional study was conducted at Aralaguppe Mallegowda District Government Hospital, Chikkamagaluru from July 2022 to December 2023. Permission from the concerned authorities was obtained in order to access secondary data from the 'Urine Culture and Sensitivity' registers maintained in the Microbiology laboratory affiliated with the hospital. The first instance of all urine samples sent to the laboratory from the outpatient department (OPD), inpatient (IP) wards and intensive care units (ICUs) of the hospital were included in the study irrespective of the patient's age and sex. We excluded subsequent samples from individuals whose data were collected for the study to ensure equal contribution from every subject in devising the hospital antibiogram.

Bacterial isolation and identification: Mid-stream urine samples of patients with clinically suspected UTIs were centrifuged and inoculated onto Blood agar and MacConkey agar, and then incubated at 37ºC overnight. A colony count of $>10^5$ CFU/mL was considered as significant bacteriuria. Bacterial species were identified based on colony appearance, Gram staining and biochemical reactions.

Antimicrobial susceptibility testing: Antimicrobial susceptibility test was performed using Kirby Bauer disc diffusion method on Mueller-Hinton agar as per CLSI guidelines.[11]The susceptibility of sample strains to various drugs was determined by observing and measuring the diameter of the zone of inhibition. The following antibiotic discs (drug concentrations in µg) were used: amikacin (30), gentamicin (10), amoxicillin (25), cefuroxime (30), norfloxacin (5) and cotrimoxazole (25) as broad-spectrum agents; piperacillin-tazobactam (30/6), ampicillin (30), imipenem (10), meropenem (10), ceftazidime (10), ceftazidime-clavulanic acid (30/10), cefotaxime (10), ceftriaxone (30), cefepime (10) and nitrofurantoin (300) for Gram-negative organisms; and cefoxitin (30), ciprofloxacin (5), doxycycline (30), vancomycin (30), linezolid (30), clindamycin (2) and erythromycin (15) for Gram-positive organisms.

Data collection and analysis: (i) Demographic data of patients with suspected UTIs, as well as (ii) causative organisms and antibiotic susceptibility in confirmed UTI cases were collected fromMicrobiologylaboratory registers maintained from July 2022 through December 2023.Microsoft Excel® 2021 software was used for data entry and analysis. The ensuing results regarding baseline patient characteristics, microbial prevalence and antibiotic susceptibility were presented as graphs and percentages.

RESULTS

Patient characteristics:A total of 674 urine samples were processed between July 2022 and December 2023, of which 454 (67.4%) were collected from female patients and 220 (32.6%) were from male patients. The study population was almost evenly distributed between adult and paediatric age groups with 342 (50.7%) subjects aged ≥18 years, and 332 (49.3%) being children. Mean ages of adults and children were 43 ± 18.2 and 7 ± 4.2 years respectively. The age and sex distribution of the study population across the three major hospital wings, viz., OPD, IP wards and ICUs, is illustrated below [Fig. 1]. Among the adult population, the majority of the samples were sent from the OPD (59.1%) while most paediatric samples were collected from the IP wards (49.7%). The most common presenting complaints which prompted culture orders were those of fever, burning micturition, polyuria, and abdominal or groin pain.

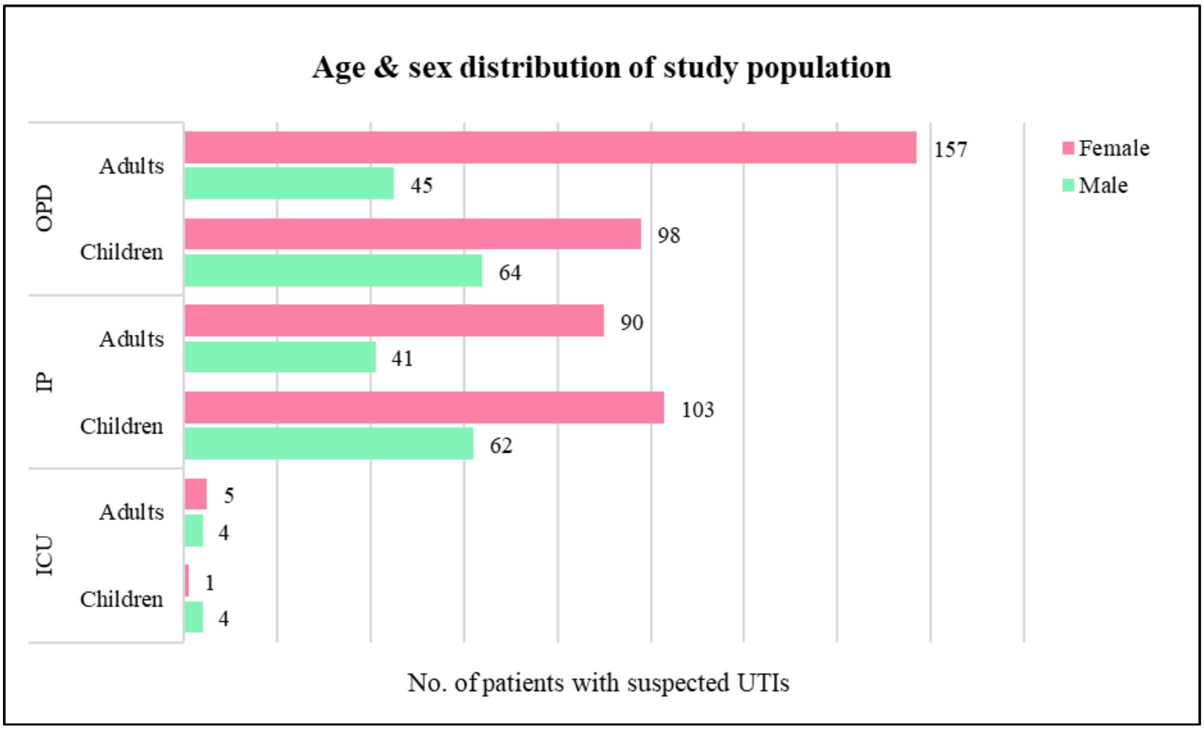

Figure 1: Age and sex distribution of suspected UTI patients across OPDs, IP wards and ICUs

Prevalence ofUTI: Significant bacterial growth was noted in 128 urine sample cultures accounting for an overall UTI prevalence of 19%, which can be further specified based on age group as 19.9% (68/342) prevalence among adults and 18.1% (60/332) in children. Among the positive cultures, 71.9% (92/128) were from female patients, and 46.9% (60/128) were of the paediatric age group with one-quarter of all UTI cases (25.8%, 33/128) being recorded among children aged 6-12 years [see *Fig. 2*]. In the adult population, the highest prevalence of UTI (35.3%, 24/68) was seen among patients aged 45–64 years. At 61.7% (79/128), the majority of confirmed UTIs were from samples collected on an OP basis, followed by 35.9% (46/128) from the IP wards, and 2.3% (3/128) from ICUs.

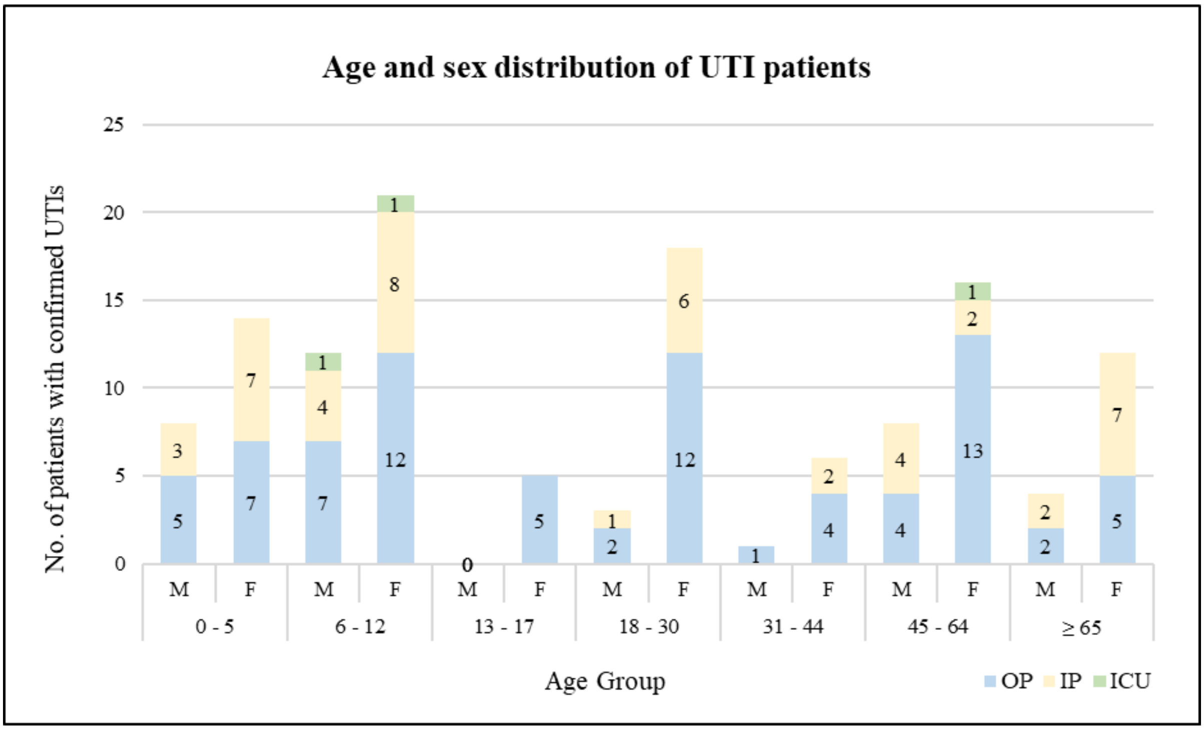

Figure 2: Age and sex distribution of confirmed UTIs

Microbial prevalence: Of the isolates obtained from the 128 positive cultures, 120 (93.7%) revealed Gram-negative bacteria while only 8 (6.3%) were Gram-positive. The bacterial pathogen encountered in the majority of cases was *Escherichia coli* (108/128), accounting for 84.4% of all confirmed UTIs. Less commonly, *Klebsiella* spp. (9.4%), *Staphylococcus aureus* (5.5%) and *Streptococcus* (0.8%) strains were isolated in culture. The sunburst chart depicted below in *Fig. 3* is a visual representation of the prevalence of individual uropathogens across male and female patients as well as adult and child populations.

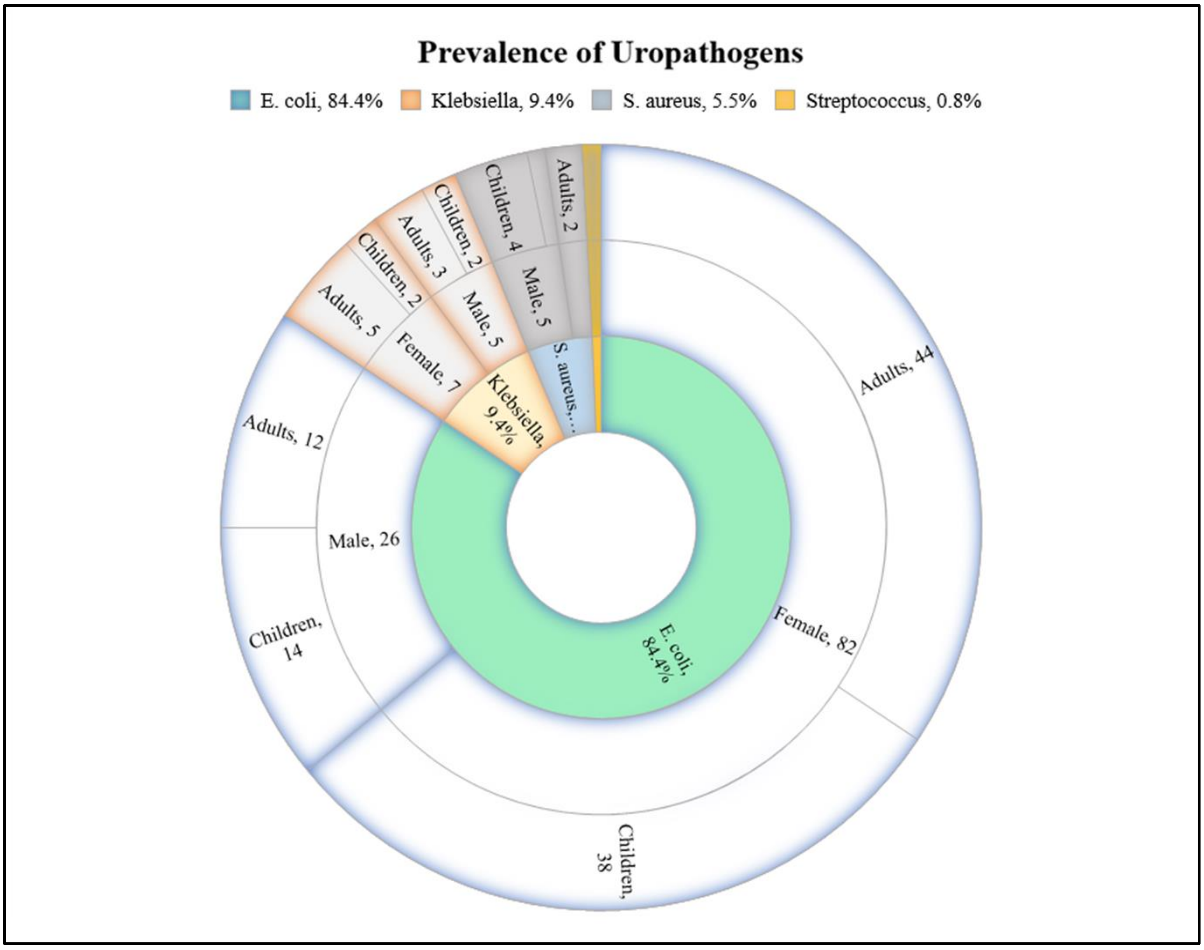

Figure 3: Prevalence of uropathogens

Antibiotic susceptibility: The results of antimicrobial susceptibility testing revealed that of all the samples tested against broad-spectrum antibiotic drugs, the vast majority were sensitive to aminoglycosides amikacin (95.3%) and gentamicin (91.3%), whereas, a mere 2.4% were sensitive to amoxicillin [see *Table 1*]. The assessment of susceptibility trends indicated that sensitivity to first-line agent cotrimoxazole was only 62%.

The highly prevalent gram-negative uropathogens showed greatest sensitivity to meropenem (98.3%), imipenem (98.1%) and piperacillin-tazobactam (87%). Moderate sensitivity was observed for third and fourth generation cephalosporins such as ceftazidime (63.8%) and cefepime (68.3%), with only 50% of strains being sensitive to the first-line drug nitrofurantoin. Greater resistance rates (>75%) were noted with ceftriaxone and cefotaxime. 100% resistance to ampicillin was observed with *E. coli*.

On the other hand, gram-positive strains showed maximum sensitivity to doxycycline (100%) followed by 87.5% sensitivity to the reserve antibiotics vancomycin and linezolid. Half of these strains were resistant to cefoxitin and clindamycin. Maximum resistance was seen for the macrolide antibiotic erythromycin.

Antibiogram: A hospital antibiogram prepared from the culture and sensitivity results is depicted in *Fig. 4*. The first column of the antibiogram lists the microbial organisms that were isolated from urine cultures, separately categorized as Gram-negative and Gram-positive bacteria. The second column indicates the number of positive patient samples included in the antibiogram. The subsequent columns show the antibiotics that were tested and the uropathogens'susceptibility to them.

Table 1: Antimicrobial susceptibility profiles of bacterial isolates from patients with confirmed UTI [in decreasing order of sensitivity]

Antimicrobial agents	No. of sensitivity tests	Susceptibility patterns		Antimicrobial agents	No. of sensitivity tests	Susceptibility patterns	
		Sensitive n (%)	Resistant n (%)			Sensitive n (%)	Resistant n (%)
Broad-spectrum agents				Cefepime	104	71 (68.3)	33 (31.7)
Amikacin	127	121 (95.3)	6 (4.7)	Ceftazidime	105	67 (63.8)	38 (36.2)
Gentamicin	127	116 (91.3)	11 (8.7)	Nitrofurantoin	108	54 (50)	54 (50)
Cotrimoxazole	108	67 (62)	41 (38)	Cefotaxime	118	26 (22)	92 (78)
Norfloxacin	101	39 (38.6)	62 (61.4)	Ceftriaxone	118	23 (19.5)	95 (80.5)
Cefuroxime	29	5 (17.2)	24 (82.8)	Ampicillin	2	0	2 (100)
Amoxicillin	124	3 (2.4)	121 (97.6)	**Gram-positive agents**			
Gram-negative agents				Doxycycline	5	5 (100)	0
Meropenem	118	116 (98.3)	2 (1.7)	Vancomycin	8	7 (87.5)	1 (12.5)
Imipenem	105	103 (98.1)	2 (1.9)	Linezolid	8	7 (87.5)	1 (12.5)
Piperacillin-Tazobactam	108	94 (87)	14 (13)	Ciprofloxacin	8	5 (62.5)	3 (37.5)
				Cefoxitin	8	4 (50)	4 (50)
Ceftazidime-Clavulanic acid	8	6 (75)	2 (25)	Clindamycin	2	1 (50)	1 (50)
				Erythromycin	3	0	3 (100)

Hospital Antibiogram *Period*: 01.07.2022 – 31.12.2023 Gram (-)ve organisms	TOTAL ISOLATES	Aminoglycosides		β-lactams					Cephalosporins						Quinolones	Others	
		Amikacin	Gentamicin	Piperacillin-Tazobactam	Amoxicillin	Ampicillin	Imipenem	Meropenem	Cefuroxime	Ceftazidime	Ceftazidime-Clavulanic acid	Cefotaxime	Ceftriaxone	Cefepime	Norfloxacin	Nitrofurantoin	Cotrimoxazole
Escherichia coli	108	97.2	92.5	89.8	1.9	0	98.9	98.1	13.6	66	71.4	21.7	18.9	71	33.7	50	61.4
Klebsiella spp	12*	100	100	80	8.3		91.7	100	0	45.5		25	25	45.5	72.7		72.7

Gram (+)ve organisms	TOTAL ISOLATES	Aminoglycosides		Penicillins	Cephalosporins		Quinolones		Others					
		Amikacin	Gentamicin	Amoxicillin	Cefoxitin	Cefuroxime	Ciprofloxacin	Norfloxacin	Doxycycline	Vancomycin	Linezolid	Cotrimoxazole	Clindamycin	Erythromycin
Staph. aureus	7*	83.3	85.7	0	42.9	40	71.4	66.7	100	85.7	85.7	57.1	50	0
Streptococcus	1*	0	0	0	100	0	0	0		100	100	0		

*Results based on fewer than 20 isolates (highlighted in yellow) are less reliable and should be interpreted with caution.

Figure 4: Antibiogram of urinary pathogens

DISCUSSION

This study was conducted over a period of 18 months and provided practical information regarding the prevalence and antibiotic susceptibility of uropathogens isolated in the district. Of the total number of urine samples sent to the laboratory for culture, nearly two-thirds (67.4%) were collected from female patients, of which 20.3% (92/454) were positively confirmed for UTI. This finding that is reflected in similar studies[6,12,13],corroborates the general understanding that women have a greater predisposition for developing UTIs over men as pathogens from the perineum and rectum ascend into the periurethral area more readily, and the female urethra is much shorter compared to that of the opposite sex.[3]

UTIs in children present a significant challenge to clinicians due to the high incidence, associated morbidity, tendency to relapse, and difficulty in procuring uncontaminated samples.[14] At 18.1%, the overall prevalence of UTIs among the children included in our study was far less than the 31.8% prevalence seen among African children aged 6 ± 0.91 years in a 2023 study that found *E. coli* and *S. aureus* to be the most implicated uropathogens.[15] Even so, school-going children aged 6–12 years were found to have the highest prevalence of UTIs (25.8%) in our study, which may be a reflection of poor hygiene and sanitation practices.

Data obtained from adult patients were categorized according to the four stages of adulthood described by Medley *et al.*[16], *i.e.*, early adulthood (18–30 years), early middle age (31–44 years), late middle age (45–64 years) and late adulthood (≥ 65 years) as seen in *Fig. 2*. The age-specific prevalence of UTI was as high as 35.3% in late middle age, and only 10.3% in the early middle age group. Similarly, a 2022 study by Utami *et al.* found the highest prevalence of UTI among patients aged over 59 years at 41.4%, and the least prevalence of 7.4% among those in their thirties.[17] A Maharashtrian study conducted by Pardeshi *et al*. reported higher UTI prevalences of 49.1% and 34.2% in the late and early middle ages respectively.[18]

UTIs are among the three most common nosocomial infections that are monitored as infection control indicators in the ICU, the other two being ventilator-associated pneumonia and blood stream infections.[19] The low UTI prevalence reported from our ICUs (2.3%) is a good indicator of healthcare quality and patient safety in the hospital.[20]

Highest antibiotic susceptibility was seen for aminoglycosides, carbapenems and tetracyclines. Tano *et al*.[13] reported high sensitivity of uropathogens to amikacin (99.7%), meropenem (99.6%) and gentamicin (94.2%) which is similar to our findings. In contrast, a 2023 Lahore study reported sensitivity to amikacin and gentamicin as being only 61.9% and 43.7%.[6] This may be owing to the overuse of aminoglycosides to treat UTIs in the region.

The apparent resistance to penicillins and cephalosporins is presumably due to the bacterial production of extended spectrum beta-lactamases (ESBL). In a 2022 Brazilian study that reported an overall prevalence of ESBL-producing strains of 4.7%, that nearly doubled to 8.3% among those aged ≥60 years, resistance to ampicillin and cephalothin was 45.7% and 48.5% respectively. In the same study, *E. coli* resistance to first-line agent cotrimoxazole was greater than 30% across all age groups[13] which is comparable to the 32% cotrimoxazole resistance reported by John *et al.* in Mangalore[21] as well as the 38% resistance noted in the present study. A 2018 study conducted by Naik *et al*.[12] in the state of Karnataka revealed that the vast majority of bacterial isolates (93.9%) were sensitive to nitrofurantoin.

Another study from Karnataka conducted in 2019 by Prasada *et al.* placed nitrofurantoin at 86.7% susceptibility[22], whereas, our study showed that sensitivity to the same drug has further reduced to a mere 50% over a 5-year period. This steady but precipitous decline in susceptibility to nitrofurantoin that is still recommended as the first-line empirical agent for uncomplicated UTIs[13, 23] can most likely also be attributed to the development of resistance secondary to overuse.

While most susceptibility results from this study are in line with general trends in the subcontinent, the results of the antibiogram must be interpreted with caution owing to the fact that some conclusions were drawn from less than twenty isolates. This limitation could be justified by the fact that a greater number of UTIs encountered in the study population were of the ascending variety, and hence produced a larger number of Gram-negative cultures as opposed to Gram-positive isolates that are more commonly associated with descending UTIs. Another limitation of this study was that anaerobic bacteria were not accounted for due to shortage in culture conditions.

As this is the first antibiogram study done in the district, it is meant to be built upon and furthered so that changing susceptibility trends can be tracked over a longer period of time. Evidence from the study would also encourage a greater focus on antibiotic stewardship in the future.

CONCLUSION

The study revealed that *E. coli* and *Klebsiella* spp. were the most commonly encountered pathogens causing UTIs in the region. Both organisms responded maximally to carbapenems and aminoglycosides while exhibiting the highest resistance to penicillins, second and third generation cephalosporins, and fluoroquinolones in that order. The antibiogram developed from the study will be used to guide empirical therapy for UTIs in the District Hospital.

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AUTHORS' CONTRIBUTIONS

PR was responsible for data collection, analysis, interpretation and drafting the manuscript. SR contributed to data analysis and critical revision of the manuscript. LJ was responsible for study conception and design, as well as critical revision and final approval of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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