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Original Article

Antibiotic sensitivity patterns of uropathogens in hospitalized patients at Teaching Hospital Jaffna

[1]Thilukshikka K, [1]Anuruddha AN, [1]Spelman Croos MV, [1]Erandi R, [1]Pravina S, [1]Kumar R, [1]Balagobi B, [2]Rajanthi R, [2]Ambalavanar V

[1]Faculty of Medicine, University of Jaffna,

[2]Teaching Hospital Jaffna

Abstract

Indiscriminate use of antibiotics has led to the emergence of antibiotic resistance in hospital settings. Awareness of local antimicrobial resistance patterns is essential for prudent empirical therapy of urinary tract infections.

This study describes the uropathogens isolated, their antibiotic sensitivity patterns and associated factors in adult inpatients with a positive urine culture at Teaching Hospital Jaffna.

All positive urine culture reports and relevant request forms of adult inpatients (≥18years) investigated at the Microbiological Unit of Teaching Hospital Jaffna during a three-month period (October 1st to December 31st 2020) were analyzed retrospectively with SPSS v27. Standard descriptive statistics and the chi square test were used (critical value 0.05).

Data were extracted from 426 culture reports. Mean age of the sample was 53.2 years (SD 19.9); 47.2% (n=201) of the reports belonged to patients ≥60 years and 60.1% (n=256) were of females. Antibiotics prescribed prior to culture were documented in 183 (43%) reports. The most commonly prescribed empirical antibiotic was co-amoxiclav (24%, n=183). Coliforms were the commonest isolate (63.4%, n=270) and showed resistance to several commonly prescribed antibiotics; antibiotic sensitivity was relatively low to ampicillin (9.5%), ceftriaxone (40%) and amoxicillin (48.1%); highest susceptibility was to meropenem (87.6%). Age group and gender were significantly associated with the type of uropathogen isolated ($p \leq 0.05$).

Prior antibiotic therapy was common among inpatients with urinary tract infection at the Teaching Hospital Jaffna. Sensitivity patterns suggest that antibiotic resistance is a major concern. Empirical therapy needs to be guided by institutional policies and local sensitivity patterns.

Keywords: Uropathogens, Urinary tract infection, Antimicrobial resistance, Antibiotic therapy, Coliforms

Introduction

Urinary tract infection (UTI), which refers to the invasion and growth of microorganisms in the urinary tract, is a common problem in clinical practice (1) The most common uropathogens are *Escherichia coli*. Other common causative organisms include *Enterococcus* spp., *Klebsiella* spp., *Proteus* spp., *Staphylococcus aureus* and *Staphylococcus saprophyticus* (2).

In Sri Lanka, nitrofurantoin, norfloxacin, cefuroxime, co-trimoxazole, and co-amoxiclav are recommended as empirical antibiotics for uncomplicated UTIs in adults. For complicated UTIs, such as UTIs in men/pyelonephritis, intravenous antibiotics like co-amoxiclav, ceftriaxone, ceftazidime, meropenem, or piperacillin-tazobactam are usually recommended (3).

A urine culture should be performed before commencing antibiotic treatment, and continuing antibiotic therapy should be based on an antibiotic sensitivity test (ABST) (4, 5). An ABST can identify the effective antibiotic(s) against specific uropathogens and guide the prescription of the most appropriate antibiotic (5,6).

Inappropriate antibiotic therapy has led to the emergence and spread of antimicrobial resistance (AMR) throughout the world, including in Sri Lanka(1) antibiotic susceptibility rates, association between(7).

Corresponding author: K. Thilukshikka, email: kthilu03@gmail.com, ORCID 0009-0004-6015-616X, Submitted June 2024 Accepted October 2024

Though AMR is a concern in community-acquired UTIs, it is especially worrying in hospital settings where UTI is a common hospital-acquired infection(8). Although retrospective studies have described antibiotic sensitivity patterns of uropathogens in several outpatient settings in Sri Lanka. Less is known about the problem among hospitalized patients, particularly in Jaffna. (9,10).

Teaching Hospital Jaffna is the biggest tertiary care centre in the Northern Province serving a population of about 1.2 million. The hospital has a Microbiology Unit operating under a Consultant Microbiologist. Although healthcare facilities should have their own antibiotic policies based on the local sensitivity patterns (11). Such policies are yet to be developed for the Teaching Hospital Jaffna.

This study aims to describe the uropathogens isolated, their antibiotic sensitivity patterns and associated factors among adult inpatients (≥18 years) with a positive urine culture investigated at the Microbiology Unit of the Teaching Hospital Jaffna.

Methods

This institution-based cross-sectional study based on secondary data was carried out at the Microbiology Unit of Teaching Hospital Jaffna**.** Data were extracted from all positive urine culture reports and relevant request forms of adult inward patients (≥18 years) investigated at the Microbiology Unit between October 1, 2020 and December 31, 2020. Data were analyzed with the Statistical Package for Social Sciences (SPSS v27). Standard descriptive statistics were used to describe patient characteristics, uropathogens and antibiotic sensitivity patterns. The association between age and sex and the type of uropathogen was determined using chi square test with the critical level set at 0.05.

Ethics approval for this study was obtained from the Ethics Review Committee, Faculty of Medicine, University of Jaffna.

Results

Data were extracted from a total of 426 positive urine culture reports and relevant request forms. The mean age of the patients was 53.2 years (SD 19.9) with a median of 58 years (IQR 35-70). Just under half the reports belonged to patients who were 60 years of age or above (47.2%, n=201), and the majority were females (60.1%, n=256; Table 1).

Table 1. Age and sex distribution of patients with a positive urine culture (n=426)

Demographic details		**n**	**%**
Age (years)	<40	132	31.0
	40-59	93	21.8
	≥60	201	47.2
Gender	Male	170	39.9
	Female	256	60.1
Total		426	100.0

Table 2 describes the uropathogens documented in positive urine culture reports of inpatients. Coliforms were the most common (63.4%, n=270) followed by *Candida* spp. (19.2%, n=82), *Pseudomonas* spp. (8.2%, n=35), *Acinetobacter* spp. (4.2%, n=18) and *Enterococcus* spp. (4.2%, n=18). *Staphylococcus aureus* was the least common (0.7%, n=3).

Table 2. Uropathogens isolated from positive urine cultures (n=426)

Uropathogen	**n**	**%**
Coliforms	270	63.4
Candida spp	82	19.2
Pseudomonas spp.	35	8.2
Acinetobacter spp.	18	4.2
Enterococcus spp.	18	4.2
Staphylococcus aureus	3	0.7
Total	426	100.0

Antibiotic therapy given before culture was documented in 183 (43%) inpatients. Details of prior antibiotic therapy were not documented in 36 request forms (8.5%) whereas the remainder (48.5%, n=207) had not received prior antibiotic therapy. Based on documented prior antibiotic therapy among 183 patients, the most commonly prescribed antibiotic was co-amoxiclav (24%, n=44), followed by ceftriaxone (19.7%, n=36), and ciprofloxacin (15.8%, n=29) (Figure 1).

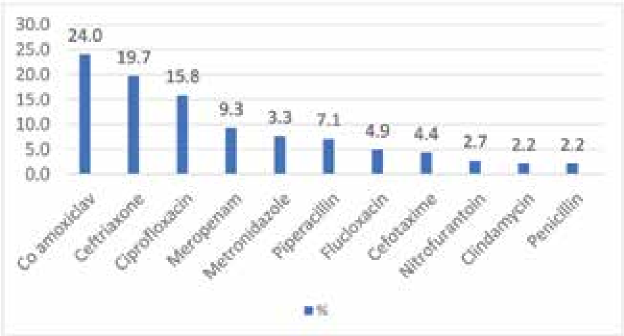

Figure 1. Antibiotic used prior to culture (n=183)

Our analysis of antibiotic sensitivity patterns showed that a large proportion of coliform isolates showed resistance to ampicillin (90.5%), ceftriaxone (60%), amoxicillin (41.1%), norfloxacin (42.8%), and ciprofloxacin (39.9%), while comparatively greater proportion of coliform isolates showed susceptibility to amikacin (83.1%), gentamicin (77.6%) and nitrofurantoin (76.3%). Meropenem resistance was seen in 9.3 % of the coliforms (Table 3).

Table 3. Antibiotic sensitivity patterns of uropathogens

Antibiotics	CF			PA			EC			A			SA		
	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R
Meropenem	87.6	3.1	9.3	66.7	0	33.3	-	-	-	75	0	25	-	-	-
Amikacin	83.1	4.2	12.7	70	0	30.0	-	-	-	23.1	0	76.9	-	-	-
Gentamicin	77.6	1.6	20.8	69.7	0	30.3	-	-	-	44.4	0	55.6	-	-	-
Nitrofurantoin	76.3	10.5	13.2	-	-	-	88.9	0	11.1	0	0	100	100	0	0
Piperacillin Tazobactam	66.7	1.6	31.7	40	10	50.0	-	-	-	36.4	0	63.6	-	-	-
Cotrimoxazole	58.5	0.6	40.9	50	0	50.0	0	0	100	57.1	14.3	28.6	100	0	0
Ciprofloxacin	58.5	1.6	39.9	67.6	0	32.4	50	0	50	35.3	0	64.7	0	50	50
Cefotaxime	58.5	1.7	39.8	-	-	-	-	-	-	0	0	100	-	-	-
Norfloxacin	56.4	0.8	42.8	67.7	0	32.3	18.2	18.2	63.6	21.6	0	78.4	0	0	100
Cefuroxime	53.7	2.5	43.8	-	-	-	-	-	-	33.3	0	66.7	-	-	-
Cephalexin	48.2	1.2	50.6	-	-	-	-	-	-	0	0	100	-	-	-
Amoxicillin	45.1	13.8	41.1	0	0	100	-	-	-	0	50	50	-	-	-
Nalidixic acid	44	0	56	100	0	0	50	0	50	66.7	0	33.3	-	-	-
Ceftriaxone	40	0	60	-	-	-	-	-	-	-	-	-	-	-	-
Ceftazidime	33.3	0	66.7	78.8	3	18.2	-	-	-	40	13.3	46.7	-	-	-
Aztreonam	26.5	7.1	66.4	33.3	11.1	55.6	-	-	-	100	0	0	-	-	-
Ticarcillin Clavulanic acid	11.1	0	88.9	-	-	-	-	-	-	-	-	-	-	-	-
Ampicillin	9.5	0	90.5	-	-	-	38.9	0	61.1	-	-	-	0	0	100
Imipenem	0	0	100	66.7	0	33.3	-	-	-	36.4	0	63.6	-	-	-
Vancomycin	-	-	-	-	-	-	23.1	15.4	61.5	-	-	-	100	0	0

CF- Coliforms, PA- Pseudomonas aeruginosa, A-Acinetobacter, EC-Enterococcus, SA- Staphylococcus aureus, S- Sensitive, I-Intermediate, R- Resistant

A comparatively higher proportion of *Pseudomonas* isolates were sensitive to ceftazidime (78.8%), amikacin (70%) and gentamicin (69.7%), while only 40% were sensitive to piperacillin-tazobactam. Meropenem resistance was seen in 33.3% of the *Pseudomonas* isolates. Only 23.1% of *Acinetobacter* isolates were sensitive to amikacin and 36.4% to piperacillin-tazobactam. Meropenem sensitivity was seen in 75% of the *Acinetobacter* isolates. *Enterococcus* isolates showed good sensitivity to nitrofurantoin (88.9%) with a lower proportion showing sensitivity to ampicillin (38.9%) and norfloxacin (18.2%). Only 23.1% of the Enterococci were sensitive to vancomycin. *Staphylococcus aureus* showed 100% sensitivity to nitrofurantoin, cotrimoxazole and vancomycin, while 50 % of the isolates showed resistance to ciprofloxacin (Table 3).

Overall, 75.7% of all isolates were susceptible to nitrofurantoin. Overall susceptibility of uropathogens to ciprofloxacin was 57.8 % and to ceftriaxone 40% and meropenem 87.2%.

We found evidence of an association between the uropathogen isolated and age (X^2=18.89, df=10, p value=0.042) and sex (X^2=12.35, df=5, p value=0.030) of the patients (Table 4).

Table 4: Association of age and sex with uropathogen isolated

		n	CF	PA	A	EC	C	SA	p value
Age	<40	132	84 63.6%	12 9.1%	11 8.3%	4 3.0%	20 15.2%	1 0.8%	0.042
	40-59	93	63 67.7%	6 6.5%	4 4.3%	4 4.3%	14 15.1%	2 2.2%	
	≥60	201	123 61.2%	17 8.5%	3 1.5%	10 5.0%	48 23.9%	0 0%	
Sex	Male	170	102 60%	21 12.4%	3 1.8%	10 5.9%	33 19.4%	1 0.6%	0.03
	Fe-male	256	168 65.6%	14 5.5%	15 5.9%	8 3.1%	49 19.1%	2 0.8%	

CF- *Coliforms*, PA- *Pseudomonas aeruginosa*, A-*Acinetobacter*, EC-*Enterococcus*, C- *Candida* spp, SA- *Staphylococcus aureus*

Discussion

Among the organisms causing UTI in the present study, coliforms (63.5%) stand at the top of the list as has been previously described in several studies (1,2,6,13) followed by *Candida* spp., *Pseudomonas* spp., *Enterococcus* spp. (4.2%), *Acinetobacter* spp. and *Staphylococcus aureus*. The high percentage of *Candida* isolated in the present study indicates the need to consider whether they are an important cause of UTI among inpatients in our settings. This high proportion may be due to poorly controlled diabetes and/or immunocompromised status(12), given the high community prevalence of type 2 diabetes mellitus in Jaffna(13). However, another reason for *Candida* in urine could be contamination of urine samples due to indwelling catheters (14).

A substantial proportion of hospitalized patients with UTI had received antibiotics prior to culture, perhaps because the study focused on inpatients who are more likely to have been treated prior to admission. It is noteworthy that whether antibiotics were given prior to culture was not documented in 8.5% of the request forms, signaling the need for improved investigation requisition practices in ward settings.

The most commonly prescribed antibiotic in the present study was co-amoxiclav, followed by ceftriaxone, ciprofloxacin and meropenem (Figure 1). It is encouraging to know that the most commonly prescribed antibiotic for inpatients with UTI was co-amoxiclav in our study as it is the recommended first-choice antibiotic for complicated UTIs and pyelonephritis. However, we could not describe its sensitivity pattern from the data available owing to the unavailability of co-amoxiclav discs at the Microbiology Unit during the period under study. Parenteral antibiotics such as ceftriaxone and meropenem may have been prescribed before culture to these patients because they had recurrent UTI with pathogens resistant to oral antibiotics or because they were treated for acute pyelonephritis/complicated UTI. This pattern of prescription differs from that described in a study among inpatients at Colombo North Teaching Hospital, where the most frequently prescribed empirical antimicrobial was ciprofloxacin (54.6%), followed by cefuroxime (12.3%) and nitrofurantoin (9.2%)(1). This difference might be due to the varying spectrum of clinical conditions for which antibiotics were prescribed in the two studies which we cannot confirm in our study as the indication for antibiotic prescription was not documented in the request forms.

The sensitivity pattern of coliforms to nitrofurantoin (76.3%) in our study was similar to that of a Colombo North Teaching Hospital study (74.8%), whereas a higher percentage of susceptibility was seen in India (90%) and in the United Kingdom (93.9%)(1) In the present study, coliforms had higher resistance to antibiotics such as co-trimoxazole (40.9%) and norfloxacin (42.8%), which can be used in the empirical treatment of uncomplicated cystitis than the Colombo North Teaching Hospital study (1). The large proportion of coliform isolates resistant to amoxicillin (41.1%), ceftriaxone (60%) and ceftazidime (66.7%)—the latter which is recommended in the treatment of complicated UTI and pyelonephritis(4)(5)—is comparable to that of the Colombo North study(1). Though sensitivity of coliform isolates to ciprofloxacin, the third most commonly prescribed empirical antibiotic in the present study, was only 58%, susceptibility was notably greater than that reported in the Colombo North Teaching Hospital study where only 37.7% of coliform isolates were susceptible to ciprofloxacin(1). A higher proportion of coliforms were sensitive to amikacin in Colombo North Teaching Hospital study (93.1%) compared to that of ours (83.1%). However, gentamicin sensitivity to coliforms was higher (77.6%) in the present study than in the Colombo North Teaching Hospital study (63.0%).

We found a higher percentage of coliforms (9.3%) in the present study showed resistance to meropenem, an antibiotic that has been the ultimate option for several drug resistant uropathogens, including extended spectrum beta-lactamase (ESBL) producers. This result is similar to that of the study carried out at Colombo North Teaching Hospital (10.4%). According to the authors of the latter study, the ampicillin susceptibility reported in their study (13.4%) was one of the lowest reported in the literature (1). However, our study elicited an even lower susceptibility to ampicillin (9.5%).

More than 65% of the Pseudomonas isolates were sensitive to ciprofloxacin, gentamicin and ceftazidime in our study which is higher than the sensitivity pattern seen in the Colombo North study(1). although susceptibility to amikacin and meropenem was comparatively lower in our study. It is noteworthy that a high percentage of resistance (50%) was seen to piperacillin-tazobactam among Pseudomonas isolates and an even higher percentage of resistance (63.6%) to piperacillin-tazobactam among *Acinetobacter* isolates in the current study. Indeed, more than 60% of Acinetobacter in our study showed resistance to most of the antibiotics tested, including amikacin (76.9%) and a quarter were resistant to meropenem.

Enterococcus spp. showed higher resistance to norfloxacin (63.6%), vancomycin (61.5%) and ampicillin (61.1%) and good sensitivity to nitrofurantoin (88.9%). The high percentage of vancomycin-resistant Enterococci seen in our study is of great concern. It is much higher than the colonization seen in ICU patients at the National Hospital of Sri Lanka in 2012 (18). All *Staphylococcus aureus* in our study were resistant to ciprofloxacin, whereas around 40% were sensitive in the Colombo North study.

According to a recent study in China by Wei Zhang *et al*, piperacillin-tazobactam is an effective, safe, and definite treatment option for complicated UTIs by ESBL-producing Enterobacteriaceae (19). However, piperacillin-tazobactam resistance was high among the uropathogens documented in our study, with resistance among *Pseudomonas spp*, 50%, *Acinetobacter* spp., 63.6% and even coliforms, 31.7%. These findings question its use in the empirical treatment of complicated UTI in patients exposed to antibiotics or hospitalized recently.

In our study, *Pseudomonas* and *Enterococcus* isolates were seen more in male patients, while females had more *Acinetobacter*. *Candida* and *Enterococcus* were isolated more in the age group of more than 60 years, whereas *Acinetobacter* was isolated among the younger group of less than 40 years. These results are consistent with the Colombo North study, which found that Pseudomonas and *Candida* isolates were seen more in male patients and elderly patients, respectively (1). In a China study, *Pseudomonas*, *Enterococcus* and *Acinetobacter* isolates were seen more in female patients and *Enterococcus* and *Acinetobacter* displayed an age-related increase in prevalence.(20).

High resistance among the uropathogens seen in our study to most antibiotics tested, including empirical antibiotics, can lead to treatment failure and possible sepsis. Further, it will demand the use of more toxic and expensive antibiotics and more hospital admissions. These findings highlight the need for urgent measures to address antimicrobial resistance in the hospital setting. An initial step would be to develop and implement an institutional policy to ensure the collection of urine samples for culture prior to empirical therapy and to continue antibiotic therapy according to local sensitivity patterns(21). Of course, it is essential to ensure education and pre- and in-service training regarding the basics of urine collection and catheter care for healthcare professionals and adherence to infection prevention and control measures during urine collection for culture (22). As irrational use of antibiotics is a major contributor to antibiotic resistance (23), measures to incentivise adherence to institutional guidelines on antibiotic therapy and strict infection control measures are needed.

This study has some limitations. We relied solely on the request forms and culture and ABST reports for data. Therefore, we were unable to find adequate clinical data and the type of UTI, which are likely to be important factors associated with the uropathogens isolated from inpatients with UTI. Further, although co-amoxiclav was the most commonly prescribed empirical antibiotic, we could not describe the sensitivity patterns of uropathogens to co-amoxiclav due to the unavailability of discs at the Microbiology Unit during the period under study.

Conclusion

A high proportion of isolates from adult inpatients at Teaching Hospital Jaffna were found to be resistant to several commonly prescribed antibiotics. These findings indicate the need for regular surveillance of uropathogens and their antibiotic sensitivity patterns, institutional policies to guide antibiotic prescription, and in-service training on strict infection prevention and control measures. Efforts should be made to perform co-amoxiclav sensitivity tests on uropathogens as it is the recommended first-choice antibiotic for complicated UTIs and pyelonephritis. The prevalence of vancomycin-resistant enterococci (VRE) in our setup should be studied further. Piperacillin-tazobactam should be used with caution as an empirical antibiotic for complicated UTI in our setting. A substantial proportion of hospitalized patients with UTI received antibiotics prior to culture, and a sizeable proportion of urine culture request forms did not contain details of prior antibiotic therapy. Therefore, improved investigation requisition practices in ward settings should be encouraged.

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Conflicts of interest

The authors have no conflicts of interests to declare.

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