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ORIGINAL RESEARCH

Prevalence and Antimicrobial Sensitivity Patterns of Uropathogens, in Tikur Anbessa Specialized Hospital Emergency Medicine Department Addis Ababa, Ethiopia

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Background: Empirical treatment of infections remains a major contributing factor to the emergence of pathogens that are resistant to antibiotics. The study aimed to assess the prevalence and anti-microbial sensitivity patterns of uropathogens in the Emergency Medicine Department of Tikur Anbessa Hospital, Ethiopia.

Methods: Urine sample data collected over two years from January 2015 to January 2016 at Tikur Anbessa Hospital's laboratory were retrospectively analyzed for bacterial pathogens, and their antimicrobial susceptibility. Antimicrobial sensitivity tests were done using the disc diffusion technique as per the standard of the Kirby-Bauer method.

Results: Of the total 220 samples that were collected, 50 (22.7%) were culture-positive. Male to female data ratio was 1:1.1. *Escherichia coli* was the dominant isolate (50%) followed by *Enterococcus* species (12%), *Enterobacter* species (12%), and *Klebsiella* species (8%). Overall resistance rates to Cotrimoxazole, Ampicillin, Augmentin, and Ceftriaxone were 90.4%, 88.8%, 82.5%, and 79.3%, respectively. The sensitivity rates for Chloramphenicol, Amikacin, Vancomycin, Meropenem, Cefoxitin, and Nitrofurantoin ranged from 72% to 100%. The antibiogram of isolates showed that 43 (86%) isolates were resistant to two or more antimicrobials, and 49 (98%) were resistant to at least one antibiotic.

Conclusion and Recommendation: Urinary tract infections are mostly caused by Gram-negative bacteria predominantly in females and Escherichia coli are the most common isolates. Resistance rates to Cotrimoxazole, Ampicillin, Augmentin, and Ceftriaxone were high. Chloramphenicol, Amikacin, Vancomycin, Meropenem, Cefoxitin, and Nitrofurantoin are considered appropriate antimicrobials for the empirical treatment of complicated urinary tract infections in the emergency department. Yet, using antibiotics indiscriminately for patients with complicated UTIs may increase the resistance rate and also lead to treatment failure, hence the prescriptions should be revised following the culture and sensitivity results.

Keywords: uropathogens, culture, emergency, Ethiopia

Background

Urinary tract infections (UTIs) are one of the most common types of bacterial infections in humans, occurring both in the community and in healthcare settings. UTI refers to a wide range of clinical conditions, from the asymptomatic presence of bacteria in the urine to severe kidney infection with subsequent sepsis.[1]

Females are more prone to UTIs than males, a phenomenon explained by their short urethra and its anatomical proximity to the anal orifice.[2,3] Uropathogens are simple to identify as they mainly come from colonic flora,[4] and this serves as a rationale for the empirical treatment of community acquired UTI (CA-UTI).[2,5] Empirical treatment, on the

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other hand, limits the ability to monitor antibiotic response and predisposes uropathogens that cause UTI to resistance.[5,6] Despite their use as practical methods for efficient resource use, empirical management plans must be regularly updated to account for shifting pathogen susceptibility patterns.[6] This is particularly true for developing nations, where the lack of resources for routine antibiotic sensitivity test compounds an additional challenge.[6]

In recent years, the resistance of uropathogens to previously effective antibiotics has become a global phenomenon.[7–9] Antimicrobial resistance (AMR) is currently estimated to account for more than 700,000 deaths per year worldwide.[10] If no appropriate measures are taken to halt its progress, it is projected to cost approximately 10 million lives and about US $100 trillion per year by 2050.[10] In contrast to other health issues, Anti-microbial Resistance (AMR) is a problem that concerns every country, irrespective of its level of income and development. According to the WHO report from 2014, Africa and South-East Asia are the regions with no established AMR surveillance systems.[11]

The lack of quality data is challenging, resulting in inadequate treatment guidelines for the local situation. The gap in public health capacity is also an issue given the rapidly evolving resistance mechanisms of the pathogens and the emergence of multidrug-resistant bacteria that can only be detected through systematic screening in quality-assured microbiology laboratories.[12,13] Given the widespread irrational use of antibiotics in Africa, the situation is dire[9,11] as compared to developed nations.

To design suitable interventions, it is important to understand the status of AMR and identify rollout gaps. The most recent version of the national Ethiopian treatment guideline recommends using Trimethoprim/Sulfamethoxazole (TMP-SMX) and Norfloxacin for the empirical treatment of CA-UTI in Ethiopia, one of the second-most populous regions of Africa.[14] However, we believe that there might be significant antibiotic resistance to the recommended treatments, and as a result, the likelihood of treatment failure is rising with the continued empirical use of these medications. As such, the study aimed to assess antibiotic resistance to both the suggested treatments and other drugs, as well as to identify patterns of resistance to a wide range of potentially helpful alternatives for the treatment of UTIs in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Methods

This study was conducted at Tikur Anbessa Specialized Hospital. It is the largest referral and tertiary-level teaching hospital in Ethiopia, located in the heart of Addis Ababa, the capital city.[15] The hospital is administered by Addis Ababa University and is the largest tertiary unit and the oldest teaching hospital in Ethiopia, with over 800 beds. It provides teaching for about 300 medical students and 350 residents every year and has more than 800 beds.[15] It offers diagnosis and treatment for approximately 370,000–400,000 patients a year.[15] The hospital's laboratory is one of the biggest and most advanced award-winning laboratories, providing services like culture and sensitivity, gram stain, blood chemistry, complete blood count (CBC), GeneXpert, and acid-fast bacillus (AFB) for the diagnosis of tuberculosis (TB). The hospital is also known for its multidisciplinary collaborative research with both local and international universities.

After receiving ethical approval from Addis Ababa University and a letter of support from the department of emergency medicine and critical care, a retrospective two-year record review was carried out on all UTI patients older than 14 years for whom culture and sensitivity tests were performed in the study. This review covered the period from January 2015 to December 2016. The data was retrieved and recorded in a data extraction sheet from the laboratory logbook, which contains patient age, sex, date of collection, department, isolated bacteria, and an antimicrobial susceptibility profile. The data were collected by nurses trained for this purpose. Data were cleaned, coded, and analyzed using the SPSS software program, version 21.0.

A sample taken from centrifuged urine and the sediment is evaluated for the proportion of polymorph nuclear cells (leukocytes), as >10/HPF is indicative of the presence of pathogenic bacteria. A urine sample containing less than 5 PMN cells/HPF was not cultured. The specimen is inoculated onto CLED, blood agar base, and MacConkey agar. MacConkey is to selectively grow gram-negative bacteria by discriminating between gram positives and differentiating between lactose fermenting and non-lactose fermenting gram-negative bacteria. Blood agar is a basic medium that can support both Gram-negative and Gram-positive bacteria, allowing us to cultivate a pure colony for further identification and DST testing. Colonies with a significant number (10^5 CFU/mL) from CLED Agar were subjected to Gram staining.

Antimicrobial sensitivity tests were done using the disc diffusion technique as per the standard of the Kirby-Bauer method, and CLSI criteria were used for break point.

Results

Sociodemographic Information

From January 2015 to December 2016, a total of 220 urine samples were collected and analyzed. The age of the patients ranged from 14 to 100 years, with a mean age of 32.26 (SD = 14.45) years. The mean ages of male and female patients were 35.1 (SD = 15.8) and 30.78 (SD = 12.4) years, respectively. One hundred nineteen (54%) urine samples were from females, and 101 (46%) were from male patients, with a male-to-female ratio of 1:1.17 as shown in Table 1.

Prevalence of Uropathogens

The overall prevalence of uropathogens was 22.7%. The majority of the pathogens (14%) were isolated from females. Most of the uropathogens were isolated from patients in the age range of 14 to 25 years (Table 1). *E. coli* was the most predominant pathogen (50%) isolated from urine samples (Figure 1). The gram-negative and gram-positive bacteria were responsible for 84% and 16% of the isolates, respectively.

Antibiotic Susceptibility Pattern of Uropathogens

The overall antibiotic susceptibility profiles of bacterial isolates are shown in Table 2. When the number of bacteria tested for specific antibiotics is observed, the resistance rate shows that resistance to Cotrimoxazole was the highest, with an overall resistance rate of (90.4%), followed by Ampicillin (88.8%), Augmentin (82.5%), and Ceftriaxone (79.3%). The antibiotics meropenem, amikacin, vancomycin, and cefoxitin were all found to be susceptible (Table 3). Because of the non-sustained availability of those antibiotics for which all tested etiologies are sensitive, only a few organisms were tested. *Klebsiella* species are dominant in male patients and almost resistant to all antibiotics, which shows the risk of having a resistant strain is higher in male patients. Species specific antimicrobial resistance rates are displayed in Table 3. *E. coli* showed high resistance rates to Cotrimoxazole (85.7%), Ampicillin (76.9%), and Augmentin (71.4%). The other three most common isolates exhibited resistance patterns of (80–100%) to Ampicillin, Cotrimoxazole, and Augmentin.

With no resistance rate, all (100%) E. coli isolates were susceptible to Vancomycin, Meropenem, Amikacin, and Cefoxitin. The other three common isolates were sensitive to Nitrofurantoin, Cefoxitin, Amikacin, and Vancomycin with resistance rates of 0%–17%.

Table 1 Age and Sex Distribution of Patients with Urine Culture and Sensitivity, Tikur Anbessa Specialized Hospital Emergency Department from Jan 1 2015 to Dec 30 2016, Addis Ababa Ethiopia

Socio Demographic Characteristics	Positive No (%)	No Significant Growth No (%)	Negative No (%)	Total No (%)	P value
Age (years) 14–25	17 (34%)	11 (36.7%)	47 (33.5%)	75 (34%)	P=0.34
26–35	8 (16%)	13 (43.3%)	36 (25.7%)	57 (25.9%)	
36–45	9 (18%)	2 (6.7%)	23 (16.4%)	34 (15.4%)	
46–65	15 (30%)	4 (13.3%)	34 (24.2%)	53 (24%)	
>65	1 (2%)	0	0	1 (0.45%)	
Gender Male	19 (38%)	8 (26.6%)	74 (52.8%)	101 (46%)	P=0.363
Female	31 (62%)	22 (73.3%)	66 (47.1%)	119 (54%)	
Total	50 (100%)	30 (100%)	140 (100%)	220 (100%)	

Abbreviation: No, Number.

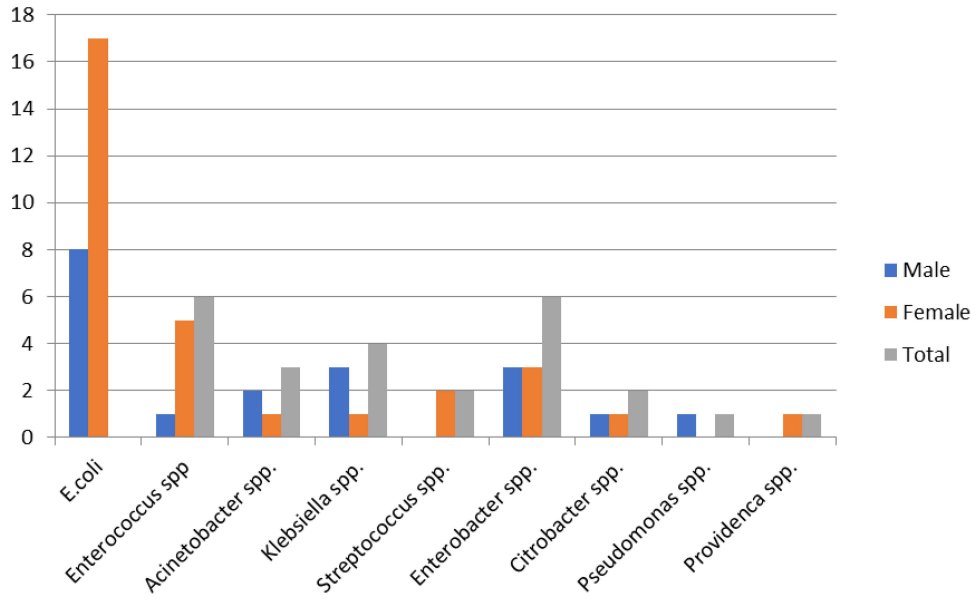

Figure 1 Bacterial isolates of patients who have urine culture and sensitivity done, Tikur Anbessa Specialized Hospital emergency department from Jan 1, 2015 to Dec 30, 2016.

Multidrug Resistance Pattern of Uropathogens

In this study, the overall resistance pattern of isolated uropathogens to more than one antimicrobial was 86%, and only 1 (2%) isolate was sensitive to all antimicrobials for which sensitivity was checked. The antimicrobial resistance rates of

Table 2 Overall Antimicrobial Susceptibility Profiles of Urine Samples from Patients Who Have Urine Culture and Sensitivity Done, Tikur Anbessa Specialized Hospital Emergency Department from, Jan 1 2015 to Dec 30 2016, Addis Ababa Ethiopia

Antimicrobial Agents	No. of Cultures Tested	Susceptibility Patterns	
		Resistant	Sensitive
		No (%)	No (%)
Gentamicin	35	19 (54.2%)	16 (45.8%)
Nalidixic acid	9	5 (55.5%)	4 (45.5%)
CAPH	21	8 (36.3%)	13 (61.9%)
Cotrimoxazole	21	19 (90.4%)	2 (9.6%)
Ampicillin	27	24 (88.8%)	3 (11.2%)
Ciprofloxacin	31	19 (61.2%)	12 (38.8%)
Nitrofurantoin	18	5 (27.8%)	13 (72.2%)
Augmentin	40	33 (82.5%)	7 (17.5%)
Ceftriaxone	29	23 (79.3%)	6 (20.7%)
Ceftazidime	23	15 (65.2%)	8 (34.8%)
Amikacin	16	0	16 (100%)
Meropenem	5	0	5 (100%)
Cefoxitin	3	0	3 (100%)
Vancomycin	7	0	7 (100%)

Abbreviation: No, Number.

Table 3 Overall Proportion of the Isolates' Resistant to All Tested Antimicrobials, Tikur Anbessa Emergency Department from, Jan 1 2015 to Dec 30 2016, Addis Ababa, Ethiopia

Isolate	Pattern	Common Antibiotics Used													
		Gentamycin	Nalidixic Acid	CAPH	Cotrimoxazole	Ampicillin	Ciprofloxacin	Nitrofurantoin	Vancomycin	Ceftriaxone	Ceftazidime	Amikacin	Meropenem	Cefoxitin	Augmentin
E. coli	T	20	7	12	14	13	14	7	2	13	13	8	4	2	21
	RNo (%)	8 (40)	3 (42.8)	3 (25)	12 (85.7)	10 (76.9)	10 (71.4)	2 (28.5)	0	9 (69.2)	9 (69.2)	0	0	0	15 (71.4)
Klebsiella	T	2	ND	1	1	2	2	ND	ND	3	3	3	ND	ND	3
	RNo (%)	2 (100)		1 (100)	1 (100)	2 (100)	1 (50)			3 (100)	3 (100)	0			3 (100)
Pseudomonas	T	1	ND	ND	ND	ND	1	1	ND	1	1	1	ND	ND	1
	RNo (%)	0					0	0		1 (100)	0	0			1 (100)
Enterococcus	T	ND	ND	ND	1	5	3	3	6	ND	ND	ND	ND	ND	2
	RNo (%)				1 (100)	4 (80)	2 (66.7)	0	1 (16.7)						2 (100)
Acineto bacter	T	2	ND	2	ND	ND	3	ND	ND	2	2	2	ND	ND	2
	RNo (%)	2 (100)		2 (100)			1 (33.3)			2 (100)	2 (100)	0			2 (100)
Enterobacter	T	5	2	3	3	3	4	3	ND	5	4	2	ND	1	5
	RNo (%)	4 (80)	2 (100)	2 (66.7)	3 (100)	3 (100)	2 (50)	1 (33.3)		4 (80)	0	0		0	5 (100)
Citrobacter	T	2	ND	2	2	1	2	1	ND	ND	1	1	ND	ND	2
	RNo (%)	0		0	2 (100)	1 (100)	1 (100)	0			0	0			1 (50)
Streptococcus	T	2	2	ND	ND	2	ND	2	ND	2	ND	ND	ND	ND	ND
	RNo (%)	1 (50)	1 (50)			1 (50)		1 (50)		1 (50)					
Providence	T	1	ND	1	ND	1	ND	ND	ND	1	ND	ND	ND	ND	1
	RNo (%)	1 (100)		0		1 (100)				1 (100)					1 (100)

Abbreviations: T, total; R, Resistant; ND, Not Done; No, Number; CAPH, Chloramphenicol.

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Table 4 Multi Drug Resistance Pattern of Isolates of Urine Culture, Tikur Anbessa Specialized Hospital Emergency Department from Jan 1 2015 to Dec 30 2016, Addis Ababa Ethiopia

Bacterial Isolates	R0 No, (%)	R1 No (%)	R2 No (%)	R3 No (%)	R4 No (%)	R5 No (%)	R6 No (%)	>R7 No (%)
E. Coli (25)	0	5 (20)	1 (4%)	4 (16)	3 (12)	6 (24)	3 (12)	3 (12)
Klebsiella (4)	0	0	0	0	0	0	3	1
Pseudomonas (1)	0	0	1 (100)	0	0	0	0	0
Entrococcus (6)	0	1 (16.7)	3 (50)	1 (16.7)	1 (16.7)	0	0	0
Acinetobacter (3)	0	0	0	0	0	0	2 (66.7)	1 (33.3)
Enterobacter (6)	0	0	1 (16.7)	1 (16.7)	2 (33.3)	0	0	2 (33.3)
Citrobacter (2)	0	0	0	0	2 (100)	0	0	0
Streptococcus (2)	1 (50)	0	0	0	1 (50)	0	0	0
Providence (1)	0	0	0	0	1 (100)	0	0	0
Total isolates	1 (2)	6 (12)	6 (12)	6 (12)	10 (20)	6 (12)	8 (16)	7 (14)

Note: R0= Sensitive to all antimicrobials tested; R1, R2, R3, R4, R5, R6, >R7= Resistant to one, two, three, four, five, six and greater than seven, respectively.
Abbreviation: No, Number.

common isolates to more than one antibiotic were 80% (*E. coli*), 83.3% (*Enterococcus*), 100% (*Enterobacter*), and 100% (*Klebsiella*) (Table 4).

Discussion

While urinary tract infections remain one of the most common disease patterns diagnosed worldwide, the management of these infections has become challenging due to the ever-rising emergence of antimicrobial drug resistance. The overall isolation rate of uropathogens in this study was found to be 22.7%, which is slightly lower than the rates reported from previous research conducted at this hospital.[17] However, the rate was similar to that of Adugna et al.[18] In this study, *E. coli* was the most predominant bacterium isolated from urine, followed by *Enterobacter* spp., *Enterococcus* spp., and *Klebsiella* spp. The isolation rates of *E. coli*, which is the most common isolate, and other pathogens in this study were comparable to the rates documented previously and also strongly agreed with similar research.[8,13,16,19]

Statistically, a significant difference was not observed between the two genders, though most pathogens were isolated from females (P = 0.34). Physiological and anatomical differences are accounted for by the differences between males and females. Females are more susceptible to infection than males, a phenomenon explained by their short urethra and its anatomical proximity to the anal orifice.[3,4]

This study showed that gram-negative bacteria were more frequent (84%) than gram-positive bacteria (16%). Similar findings have been reported by Tiruneh et al from Gondar, Ethiopia, and other studies done elsewhere.[16,19–22] Bacterial uropathogenic isolates from patients with UTIs revealed the presence of extremely high levels of single and multiple antimicrobial resistance to commonly prescribed drugs.

The most frequently isolated bacterial isolates were found to be highly resistant to ciprofloxacin but sensitive to Nitrofurantoin. This result is different from the one documented previously in this hospital,[17] in which the isolated organisms were highly sensitive to the aforementioned antimicrobials. Similar findings are reported by Gondar, including that bacterial isolates are highly resistant to CAPH.[12,16]

Enterococcus spp., *Enterobacter* spp., *and Klebsiella* spp. were found to be resistant to Ceftriaxone, Ceftazidime, Ciprofloxacin, Cotrimoxazole, Gentamicin, and Nalidixic Acid but sensitive to Nitrofurantoin, Vancomycin, and Cefoxitin. This finding is in contrast with a study done by Kibret et al,[1] in which both gram-negative and gram-positive isolates are very sensitive to Gentamicin and Ciprofloxacin. Additionally, reports from a previous study done in the same hospital[17] show that gram-negative isolates were mainly sensitive to Ciprofloxacin, Norfloxacin, and

Nitrofurantoin, a finding that is also in contrast with ours. In this study, both gram-negative and gram-positive isolates were sensitive to Vancomycin at an equal rate, which may indicate Vancomycin is covering both gram-negative and gram-positive bacteria equally in this particular study, even though it is a drug of choice to cover gram-positive bacteria.

In our study, antibiotic susceptibility data revealed that virtually all isolates (98%) were resistant to at least one antibiotic, and most of the isolates (86%) were resistant to two or more antibiotics. These findings were extremely higher than the resistance rates that were observed in other studies,[16,17] the reason for which might be the use of antibiotics and antimicrobial treatment prior to presentation to the hospital.

Conclusion and Recommendation

This study outlined that urinary tract infections are most commonly caused by Gram-negative bacteria, predominantly in females, *E. coli* is the most prevalent isolate, and the multidrug resistance of urinary tract infections was significantly high in the largest referral hospital in Ethiopia, Tikur Anbessa, with almost all bacteria tested for more than one drug resistance except for *E. coli*. Almost all bacterial isolates tested were resistant to Co-trimoxazole, Ampicillin, Augmentin, and Ceftriaxone. Most bacterial isolates were found to be sensitive to Vancomycin, Chloramphenicol, Amikacin, Meropenem, Cefoxitin, and Nitrofurantoin, indicating that these medications could be used as the first line of empirical treatment for complicated UTIs in emergency rooms. However, using antibiotics indiscriminately for patients with complicated UTIs may increase the resistance rate and lead to treatment failure, hence the prescriptions should be revised following the culture and sensitivity results.

Limitation

A limitation of this study can be understood in light of the following: Tikur Anbessa Hospital, as one of the largest tertiary units in the country, has a plethora of referral cases, the majority of which consist of debilitating comorbidities, like DM, malignancies, spinal cord injury, and septic shock, and not isolated UTO. This retrospective study is based on the results of routine microbiological tests carried out from 2015 through 2016, and so due to the nature of the retrospective analysis, tracing patients' clinical settings was challenging and beyond the scope of the study. Additionally, the practice trends in the hospital are that culture and sensitivity tests are done for inpatients and not for those seeking outpatient care, which skews the caseload towards that of a complicated UTI. Moreover, the study was done in a single center, and the sample size is also limited, so it is difficult to generalize the finding to other hospitals; however, the finding helps as a foundation for future large-scale studies.

Declarations

All authors declare that this research is entirely our own, except where clearly stated otherwise, and that it has not been submitted in whole or in part to any previous research.

Data Sharing Statement

The article and its supporting files contain the datasets that support its conclusions. Any additional material can be obtained upon reasonable request.

Ethics Consideration

Ethical approval for the study has been sought and obtained from Addis Ababa University's Ethical Review Board, and the need for individual level consent was waived as the study collects only lab results and de-identified patient information. All authors confirm that this study complies with the Declaration of Helsinki.

Consent to Publish

Informed consent was obtained from Tikur Anbessa Specialized Hospital Emergency Medicine Department and Laboratory Unit to Use secondary data recorded on the log book. Consent was not taken from the patients because we used secondary data and patients were not identified in information provided on a logbook.

Disclosure

The authors declare that they have no competing interests for this work.

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