Original article

A retrospective study on prevalence and antimicrobial susceptibility patterns of bacterial isolates from urinary tract infections in Tikur Anbessa Specialized Teaching Hospital Addis Ababa, Ethiopia, 2011

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Abstract

Introduction: Urinary tract infection is an inflammation of the urinary tract that occurs when micro organisms, usually bacteria from digestive tract or vagina cling to the opening of the urethra and begin to multiply. An estimated 150 million urinary tract infections occur annually worldwide. Indiscriminate use of antibiotics has resulted in the emergence of drug resistant pathogens now.

Objective: To determine the prevalence and drug susceptibility patterns of bacterial pathogens involved in urinary tract infections within the last three years, January 1st 2008 to December 30th 2010 in Tikur Anbesa Specialized Teaching Hospital of Addis Ababa, Ethiopia.

Method: An institution-based retrospective cross sectional population survey was conducted in the clinical laboratory for diagnosis of patients visiting Tikur Anbessa Specialized Teaching Hospital. Collected secondary data were entered and analyzed using SPSS version 17 computer software package. Percentages and ratios were calculated in tables. P-value was used to see statistical significance ($p<0.05$).

Results: Out of 3254 recorded patient's data 3182 results were taken and analyzed. The overall prevalence of urinary tract infection was 23.32 % and the highest prevalence was obtained among age groups 21-30 years (27.16%). The bacterial pathogens isolated were predominantly, *Escherchia coli:* 361 (44.62%), followed by *Klebsella* Spp: *136* (16.81%), Coaggulase negative *Staphylococci Spp:* 49 (6.06%) and *Entrococci* Spp: 41 (5.06%). The invitro drug sensitivity testing showed that both gram negative and gram-positive organisms were extremely resistant to Ampiciline: (83.93%), Amoxicillin: (78.87%) and Tetracycline: (77.75%).

Conclusion: the prevalence of urinary tract infection was high, and the drug resistance rate was extremely high. For this reason, it is necessary to minimize the rate of urinary tract infections, and to constantly monitor susceptibility patterns of specific pathogens to commonly used antimicrobial agents before antibiotic therapy initiation. [*Ethiop. J. Health Dev.* 2013;27(2):111-117]

Introduction

Urinary tract infection (UTI) is the colonization, invasion and propagation of infectious agents in the unitary tract including the urethra, bladder, renal pelvis or renal parenchyma (1). Urinary tract infections are the second most common type of infection of the body, accounting for about 8.1 million visits to health care providers each year (2).

An infection occurs when organisms, usually bacteria from the digestive tract or vagina cling to the opening of the urethra and begins to multiply (3). Additionally, exogenous hospital acquired UTIs may occur following instrumentation of the urinary tract, mainly urinary catheterization (4). Generally, *Escherichia coli* and *Staphylococcus saprophyticus* cause approximately 80% and 15% of acute UTIs, respectively in patients without catheters, stone or other urologic abnormalities (3-4). On the other hand, organisms like *Klebsella spp, Enterobacteria spp, Proteus spp, Entrococcus, spp* and *Pseudomonas aurogenosa* assume greater importance in recurrent infections associated with urologic manipulations as in catheter associated nosocomial infection (5, 6).

In symptomatic straightforward cases, a combination of symptoms (i.e., dysuria, frequency, and absence of discharge) raised the probability of UTI to more than 90 percent. In this case, diagnosis may be made and treatment given based on symptoms alone without further laboratory investigations. However, UTIs have to be distinguished from other diseases that have similar clinical presentation. Some urinary tract infections are asymptomatic or present with atypical signs. For this reason, clinical diagnosis needs to be confirmed by laboratory tests (7). Clean catch midstream urine collected and refrigerated in a sterile container can be used within 2 hr for urinalysis test, culture and drug sensitivity test (8).

The diagnosis of urinary tract infection is based on a quantitative urine culture yielding greater than 100,000

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colony forming units per milliliter of urine, which is termed significant bacteruria. This value was chosen because of its high specificity for the diagnosis of true UTI even in asymptomatic persons (8,9).

The choice of drug and length of treatment depend on the patient's history and the urine tests that identify the offending bacteria (10). Routine uncomplicated UTIs can be treated with Nitrofurantoin, Trimethoprim-sulfamethoxazole, Fluoroquinolones (Ofloxacin, Ciprofloxacin, and Levofloxacin), Cephalosporin, Cephalexin and intravenous antibiotics for 14 days or long term low dose antibiotic treatment may be necessary in patients with frequent re-infection (11,12).

The sensitivity test is especially useful in helping the physician select drugs to treat UTIs (13). This is particularly true because of the increased incidence of antimicrobial resistance (AMR). Microbial drug resistance is how a major problem in treating infectious diseases worldwide (14). It is aggravated by the increased use of muddled empirical therapeutic treatments, mainly in economically disadvantaged countries like Ethiopia, that do not have quality microbiological laboratory facilities to isolate pathogens and determine their drug susceptibility pattern (16-17). Consequences of AMR, especially multidrug resistance include increased mortality, morbidity, and health care costs (17). For this reason, improvement of microbiological laboratory facility and laboratory professional skill in line with improving all the health care services should be enhanced across the country.

The general purpose of this study was to determine the prevalence and drug susceptibility patterns of bacterial pathogens involved in urinary tract infections in Tikur Anbesa Specialized Teaching Hospital, Addis Ababa.

Methods

Study Area

The study was done in the capital city of Ethiopia, Addis Ababa. According to the 2007 census preliminary report of the Central Statistical Authority, the total population of Addis Ababa was estimated to be 3.2 millions. Tikur Anbassa Hospital founded in 1964, is the largest and most specialized referral hospital in the country. This hospital provides health services for approximately 370,000- 400,000 patients per a year.

Source Population

All patients of this study visited Tikur Anbassa Specialized teaching Hospital from January 1st 2008 to December 30th 2010.

Study Population

All symptomatic patients sent to Tikur Anbassa Specialized teaching Hospital microbiology laboratory for diagnosis of urinary tract infections were included in the study.

Study Design and Period

An institution-based, descriptive, retrospective and cross-sectional population survey was conducted in Tikur Anbassa Specialized teaching Hospital within the three years, January 1st 2008 to December 30th 2010.

Eligibility Inclusion and Exclusion Criteria

Inclusion criteria: Data recorded have at least sex and age were included in the study.

Exclusion criteria: Data recorded with incomplete sex and age information were excluded from the study.

*Variable*s

Dependent variable

Prevalence of urinary tract infection and drug susceptibility patterns of uropathogenes.

Independent variables

Age, sex, occupation, residence, level of education, and ethnicity.

Data Collection

Urine sampling and processing

Midstream urine samples were collected from a total 3254 suspected UTI patients. Growth of 10^5 colony forming units (CFU)/mL was considered a positive urine culture (18). Uropathogens were isolated and identified according to NCCLS standard morphological, cultural and biochemical methods (19).

Determining of antimicrobial susceptibility:

Kirby-Bauer disc diffusion assay on Muller Hinton agar was carried out to determine the antimicrobial susceptibility profiles (20). The panel antimicrobials included amoxicillin: 30 mg, gentamicin: 10 mg, cefotaxime: 30 mg, nalidixic: acid 30 mg, ciprofloxacin: 5 mg, ofloxacin: 5 mg, norfloxacin: 10 mg, erythromycin: 15 mg, cloxacillin: 5 mg, vancomycin: 30 mg, nitrofurantoin: 300 mg and tetracycline: 30 mg.

Data Quality Control

Secondary data were gathered from Tikur Anbassa specialized teaching Hospital is microbiology laboratory records for processing, analyzing and determining prevalence and drug susceptibility patterns of uropathogenes. The collected data was checked for its completeness, accuracy, clarity and consistency before being entered into data entry forms. When any ambiguity or incompleteness was encountered, it were recorded and corrected immediately before proceeding to the next.

***Data Analysis*:** The collected data were sorted in the prepared format. The laboratory result of the study was categorized based on age groups and sex. Isolates prevalence rate calculations, frequency distributions, susceptibility patterns and other descriptive statistics were computed and reviewed. Percentages and ratios were calculated in tables. SPSS version 17 computer

software package was used for data analysis. P-value was used to see statistical significance (p<0.05).

Ethical Considerations

Ethically, the study was cleared and an official letter was written from Addis Ababa University (AAU) Faculty of Medicine, Department of Microbiology, Immunology and Parasitology to Tikur Anbesa Specialized Teaching Hospital. We agreed and signed the appropriate form. Given that it is a retrospective study, informed consents were not asked. The study didn't require patient's name or any personal identification details thereby assuring confidentiality of the information and privacy of the patients.

Results

Out of being the 3254 recorded patients' data, 3182 laboratory results were taken and analyzed. Because of their incomplete information about 72(2.2%) of subjects' data were excluded from the study. Females the subjects were 1827 (57.42%) and males 1355 (42.58%). The mean age of the study was 34.09 with 16.02 years SD.

The overall prevalence of urinary tract infection was 23.32 % and the highest prevalence rate was obtained from 21-30 years age group (27.16%) (Table1). UTI was relatively higher in females 428 (23.43%) than males 314 (23.17%); however this was not found to be statistically significant (p=0.89).

Table 1: **Age specific prevalence's of urinary tract infections in Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia, and January 1st 2008 to December 30th 2010**

Age group (years)	Number of study subjects	Number of positives	Age-specific prevalence (%)
< 1	176	41	23.29 %
1-10	937	208	22.19%
11-20	535	99	18.50 %
21-30	567	154	27.16 %
31-40	310	79	25.48 %
41-50	253	61	24.11%
51-60	237	58	24.47 %
≥61	167	42	25.15 %
Total	**3182**	**742**	**23.32 % (an overall prevalence)**

The bacterial pathogens isolated were predominantly, *Escherichia coli:* 361 (44.62%), followed by *Klebsella* Spp: *136* (16.81%), coaggulase negative *Staphylococcus Spp:* 49 (6.06%) and *Entrococcus* Spp: 41 (5.07%). Over all, UTI was mainly caused by gram-negative bacteria 690 (85.3%) than gram positive 119 (14.7%) (Table2). Multiple infections were observed in 67 (9.03 %) of UTI patients.

Table 2: **Distribution of isolated organisms in Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia, January 1st 2008 to December 30th 2010**

Pathogenic bacteria Isolated	No of isolates		Total Frequency	Percentage
	OPD	IPD		
Escherichia coli	137	224	361	44.63%
Klebsella species	46	90	136	16.81%
Coaggulase negative staph. spp.	23	26	49	6.06%
Enterocci species	12	29	41	5.07%
Acinetobacter species	16	23	39	4.82.%
Entrobacter species	13	16	29	3.58%
Citrobacter species	5	22	27	3.34%
Pseudomonas aerogenosa	10	17	27	3.34%
Providencia rettigeri	8	18	26	3.21%
Staphylococcus aureus	6	19	25	3.09%
Morgenella morganii	6	9	15	1.85%
Proteous vulgaris	3	7	10	1.24%
Proteous mirabilis	1	8	9	1.11%
Salmonella species	0	8	8	0.99%
Streptococcus species	0	4	4	0.49%
Serratia species	0	3	3	0.37%
Total	286	523	809	100%

Note: **OPD=Outpatient department, IPD=Inpatient department**

Organisms were isolated more frequently from inpatients (IP) than outpatients (OP) and there was a statistical significance (P=0.0005). Calculated inpatient to outpatient odds ratio of urinary tract infections was [OR= 1.35; 95%CI: 1.13-1.61; p=0.0005] (Table 3).

Table 3: **Calculated odds ratio of UTI in inpatients to outpatients in Tikur Anbessa Hospital, Addis Ababa, Ethiopia, January 1st 2008 to December 30th 2010**

Type of patient	Positive	Negative	Odds ratio
Inpatient	474	1384	**1.35** [OR= 1.35; 95% CI:1.13-1.61; p=0.0005]
Outpatient	268	1056	
Total	**742**	**2440**	

Antibiotic Susceptibility Patterns

In this study, based on the recorded data some discs such as vancomycin, cloxacilin, streptomycin, erythromycin and mithicilin for antibiotic susceptibility pattern test were used inconsistently because of blinking supply, and inappropriately against to organisms which have intrinsic resistance to that particular drug.

The gram-negative isolates were mainly sensitive to Ciprofloxacin (62.68%), Norfloxacin (61.08%) and Nitrofurantoin (50.49%) while they were resistant to most antibiotics such as Amoxicillin (85.12%), Ampcilin (81.22%) and Tetracycline (80.02%). It was observed that gram-positive isolates were relatively sensitive to Nitrofurantoin (66.30%), Chloramphinicol (60.55%) and Gentamycin (58.53%) while they were commonly resistant to Ampicilin (81.7%), Tetracycline (78.03%) and Deoxicyclin (65.87%). The in vitro sensitivity testing showed that both gram negative and gram-positive organisms were extremely resistant to Ampciline (83.93%), Amoxicillin (78.7%) and Tetracycline (77.75%).

Proteus vulgaris and *Proteus mirabilis* showed that a 100 % sensitivity to Augmentin. Complete resistance was observed in *Entrococcus Spp* and *Pseudomonas aeurogenosa* to penicillin G, *Morgenella morgenii* to Ampcilin, Tetracycline and Amoxicillin, and *Salmonella Spp* to Cefotaxim. The highest level of resistance was observed against Ampcilin. Results indicated that Nitrofurantoin was the most potent of all the antibiotics. Antibiotic susceptibility data showed that 771 (95.3%) isolates were resistant to at least one antibiotic and most of the isolates, 747 (92.34%) were resistant against two or more antibiotics (Table 4).

Table 4: **Multi-drug resistant patterns of isolates of UTI in Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia, January 1st 2008 to December 30th 2010**

Type of Isolate	R0	R1	R2	R3	R4	R5	R6	≥R7
Escherichia coli	30	10	10	19	19	35	60	178
Klebsella species	1	2	5	8	7	10	14	89
Coaggulase negative staph. spp.	2	1	0	7	5	4	5	25
Enterocci species	0	0	1	4	4	2	4	26
Acinetobacter species	0	1	0	2	2	0	1	33
Entrobacter species	1	1	0	2	0	0	6	19
Citrobacter species	0	3	0	1	0	0	5	18
Pseudomonas aerogenosa	0	1	0	0	1	2	4	19
Providencia rettigeri	0	0	1	2	0	3	6	14
Staphylococcus aureus	1	2	3	1	2	2	1	13
Morgenella morganii	0	0	0	0	0	0	3	12
Proteous vulgaris	1	0	2	0	2	1	3	1
Proteous mirabilis	0	1	0	0	1	0	2	5
Salmonella species	0	0	0	1	0	0	2	5
Streptococcus species	1	1	0	1	0	0	0	1
Serratia species	1	1	1	0	0	0	0	0

Note: R0= No resistance, R1= Resistance to one antibiotic, R2= Resistance to two antibiotics, R3= Resistance to three antibiotics, R4= Resistance to four antibiotics, R5= Resistance to five antibiotics, R6= Resistance to six antibiotics, ≥R7= Resistance to seven or more antibiotics

Discussion

In this study, of the total 3182 urine samples 742 (23.32%) gave significant growth with ≥ 10^5 cfu/ml and no bacterial growth in 2440 (76.68%). The prevalence was lower here than some other studies: 60%, in Nigeria (21), 51.1%, in South Africa (22), and 30.2%, in Ethiopia (23). The reason for this relatively lower rate of prevalence in this study might because of the fact that patients were undergoing through antibiotic treatment before coming to the hospital for diagnosis and the pathogens have been destroyed or inhibited.

On the other hand, prevalence of UTIs showed slight increment from year: to year; 2008 (22.55%), 2009: (23.04%) and 2010 (24.18%) indicating UTI remains as an important public health problem at least in the study area. Calculated odds ratio of UTI in inpatients to outpatients shows likelihood of urinary tract infection in inpatients was 1.35 times higher than in outpatients. This finding coincides with other studies and demonstrated that the most were nosocomial and infections could have been acquired through unsafe health care practices such as catheterization (4-6).

Multiple infections were observed in 67 (9.03 %) of UTI patients and prevalence of UTI was higher in females 428/1827 (23.43%) than males 314/1355 (23.17 %). These results also agree with other reports, which showed that UTIs are more common in females than in males (22-24). This is because of their short urethra allowing quick access to bladder and the near source of bacteria from the vagina and anus.

In this study age group classification was based on similar retrospective study done by Chadi et al. in Nigeria for comparison purposes. The highest age specific prevalence was found from age group of 21-30 (27.16 %) years which strongly agreed with other studies signifying that sexually active groups, particularly females, are more prone to UTIs (23, 24).

This study showed that gram-negative bacteria were more frequent (85.3%) than gram-positive bacteria (14.7%). Similar findings have been reported by Moges et al from Gondar Ethiopia and other studies done elsewhere (25-28).

According to our study *Escherichia coli* was a predominant uropathogen and this also agreed with nearly all-similar researches (22-25). This is due to the presence of a number of virulent factors specific for colonization and invasion of the urinary epithelium such as P-fimbria and S- fimbria adhesions (29).

Despite, inconsistency and some inappropriateness in testing the drug susceptibility patterns, the results were summarized and analyzed accordingly. Because of their discontinued use the pathogens susceptibility patterns to Vancomycin, Cloxacilin, Streptomycin, Erythromycin and Mithicilin were not analyzed to avoid imprecision in interpretations. Bacterial uropathogen isolates from patients with UTIs revealed the presence of extremely high levels of single and multiple antimicrobial resistances to commonly prescribed drugs (Table 4).

The gram-negative isolates were mainly sensitive to Ciprofloxacin (62.68%), Norfloxacin (61.08%) and Nitrofurantoin (50.49%) while they were commonly resistant to Amoxicillin (85.12 %), Ampicilin (81.22 %) and Tetracycline (80.02%). It was observed that gram-positive isolates were relatively sensitive to Nitrofurantoin (66.30%), Chloramphinicol (60.55%) and Gentamycin (58.53%) while they were resistant to most antibiotics such as Ampicilin (81.7 %), Tetracycline (78.03 %) and Deoxicyclin (65.87 %).

Generally, the in vitro sensitivity testing showed that both gram-negative and gram-positive organisms were extremely resistant to Ampcilin (83.93%), Amoxicillin (78.87%) and Tetracycline (77.75 %). This finding very much confers higher resistance rate than other studies (30, 31). This high level of resistance to beta lactam ring containing antibiotics (e.g., Ampcilin, Amoxicillin…) could happen because of the fact that the presence of extended spectrum β-Lactamase in these strains (32-34). Therefore, it is obvious that these antibiotics are no more useful against uropathogenes.

The drug susceptibility pattern showed that isolated organisms were relatively sensitive to Nitrofurantoin (58.09%), and Ciprofloxacilin (57.4%). Hence, these drugs could be used as the drug of choice for treatment of uncomplicated UTIs. Comparatively, the lowest level of resistance was found against Nitrofurantoin might be due to its narrow range of clinical indications, which results in less usage (35).

The highest level of resistance to common antibiotics was produced by *Morganella morganii* (76.75%), *Klebsella spp (76.63%)* and *Pseudomonas aeurogenosa* (72.81%) that demonstrated comparable finding with other studies (36). Complete resistance, was observed in *Entrococcus spp* and *Pseudomonas aeurogenosa,* to Penicillin: G, *Morgenella morgenii;* to Ampcilin: Tetracycline and Amoxicillin, and *Salmonella spp;* to Cefotaxim: The explanations could be a *blaTEM10* that encodes extended spectrum Beta lactamase (ESBL) is already isolated from *M. morganii* where as the expression of a plasmid-mediated *blaCMY-2* gene has been responsible for most Cefotaxim resistance in *Salmonella* spp (37, 38).

According to this study, antibiotic susceptibility data revealed that, virtually all isolates 771 (95.3%) were resistant to at least one antibiotic and most of the isolates, 747 (92.34%) were resistant against two or more antibiotics. These finding were extremely higher than a former done in Gondar study that showed 68% MDR, 74% conducted in Tikur Anbessa Hospital (25, 39). These might be due to the increased rate of improper self-medication and an indiscriminate use of these antibiotics in Ethiopia that allowed organisms to acquire a plasmid encoded resistance gene (40). For these organisms, expensive broad spectrum antibiotics like Oxacillin, Carbapenems (Imipenem), Lovofloxacin, Amikacine, Fosfomycin Clindamycin, Erythromycine and Cephalosporin (Ceftrazidime) should be commenced as final treatment options for life threatening cases after the sensitivity report from microbiological laboratories.

Limitations of theStudy

- Incomplete information because of the lack of quality records.
- Our findings may not be generalizable to specialized groups like HIV positive individuals, or pregnant women.

Conclusion

In conclusion, the prevalence of urinary tract infection was high, and gram-negative organisms were the most common causes of UTIs. Resistance was found to be extremely high to the commonly used antibiotics. It indicated that drug resistance is a deep-rooted problem in Ethiopia.

The development of drug resistance in uropathogens is usually, but not exclusively, the result of improper self-medication. Antibiotic resistance can also be caused by inadequate treatment regimens, insufficient patient adherence, and uncontrolled distribution and trade of drugs, as well as lack and poor quality of antibiotics. For this reason it is to minimize the prevalence of urinary tract infections, and to monitor constantly susceptibility patterns of specific pathogens to commonly used antimicrobial agents.

The most effective strategy to reduce antibiotic resistance is developing drug utilization management policies and procedures. Furthermore, there is a strong need for improving laboratory facilities and giving periodic additional training for laboratory technicians to upgrade their skill in identifying the responsible pathogenic organisms involved in urinary tract infections and to perform standardized drug susceptibility pattern tests. The hospital microbiology laboratory should produce and use standard result recording systems that may make it easy understand, analyze and interpret data. Finally, a nationwide anti-microbial resistance survey and research is mandatory to assess this devastating situation across the country and develop controlling strategies.

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