

Antibiotics Sensitivity of Bacteria Associated with Urinary Tract Infection of Outpatients in Sirte City (Libya).

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Abstract

Urinary tract infection (UTI) is one of the most common bacterial infections in humans and a major cause of morbidity among male and female. The pathogens traditionally associated with UTI and their antibiotic sensitivity patterns are changing from time to time and across different environment. Knowledge of the antibiotic resistance is an important factor for choosing an appropriate empirical antimicrobial treatment.

Study was designed to find the prevalence of UTI among patients complaining of UTI symptoms, to determine the causative organism (s) of UTI, and also to measure the antibiotic sensitivity of microbial agents isolated.

Urine samples collected were cultured on Agar media; strains isolated were identified using standard microbiological methods and tested for antimicrobial susceptibility via the disc diffusion method.

A total of 266 samples of outpatients, (156 female and 110 male). *E. coli* was the most common 130(48.9%) organism isolated, followed by *Proteus mirabilis* 61(22.9%), *Klebsiella pneumonia* 44(16.5%), *Enterococcus faecalis* 13(4.8%), *S. aureus* 11(4.1%), and *Pseudomonas aeruginosa* 7(2.6%). Imipenem, Augmentin and ciprofloxacin were found the most susceptible drug against isolated uropathogens, the resistance rate of isolates were more common in Clarithromycin, Ampicillin and Doxycycline.

Study notes increasing of antibiotics resistance among Uropathogenic isolates to most common drugs recommended. Therefore the antibiotics management's plane should be developed locally in accordance with the susceptibility pattern of the uropathogens to avoid further resistance as well as morbidity of the patient.

Keywords: *Urinary tract infection (UTI), E. coli, Antibiotics sensitivity.*

1. Introduction

Urinary tract infection (UTI) is one of the most common infection diagnoses today among adults and children, Urinary tract infections most commonly affect women, but men and children can get

them too, which can cause a lot of pain and irritation if not treated early, UTI infection easy to treat with antibiotics if diagnosed correctly, UTI is much more common in women than in men due to anatomical and physiological reason; by virtue of its position.^{4,16,17}

Urogenital tract is more vulnerable to bacterial infections caused by both internal and external flora.³⁴ A UTI is an infection that occurs anywhere along the urinary tract, which includes the kidneys, ureters, bladder and urethra.¹³ Most UTIs are caused by bacteria. Common symptoms include burning with urination, pain in the bladder area and frequent urination. But UTI symptoms can vary depending on where the infection is located.^{4,16,23}

Most UTIs occur when bacteria get into the urethra and spread to the bladder. Sometimes the body can get rid of the bacteria on its own. If it can't, an infection sets in. Left untreated, the infection can spread to the ureters and kidneys and cause serious infections difficult to treated.^{16,7}

E.coli are known the most commonly isolated from UTI patients, and other bacteria can be involved such as *Proteus mirabilis*, *Klebsiella pneumonia*, *Enterococcus spp*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Variations in microbial spectrum and susceptibility patterns may occur in different regions of these bacteria isolates.^{1,15,20,27}

The diagnoses of UTI usually carried out by checking the presence of bacteria in the urine, usually based on a clean midstream urine sample, cultured on laboratory media to check the growth of causative organisms on media beside the patient compiling symptoms, but the culture remains the gold standard for diagnosis of urinary tract infection.^{7,35,37}

The use of antimicrobial therapy has contributed a great deal to the management of UTI. However, accumulated evidence shows that treatment of these infections is increasingly becoming difficult due to the rapid emergence of antimicrobial resistance in hospitals and the community worldwide.^{7,9,31}

On UTI studies have shown increased resistance to commonly used antimicrobials. Besides, knowledge of the resistance pattern of uropathogens is important in guiding optimal antimicrobial choice in the initial approach of the patient.^{9,15}

The aim of this study was to describe to investigate antibiotics susceptibility and resistant pattern in isolates obtained from UTI patients. This would be helpful to clinicians to make new choices of antibiotic therapy for the management of UTI.

2. Materials And Methods

A total of 266 midstream urine samples of outpatients suspected for UTI, (156 female and 110 male) of different age groups, they were between ages 10 to 71, attended to clinical Laboratory for urine analysis and had clinical evidence of urinary tract infection. The study was carried out during Eight months period between October 1st, 2019 and May 30th, 2020, in the microbiology laboratory at the Department of Microbiology, Faculty of Medicine, Sirte University.

Bacterial identification:

All samples were collected as mid-stream urine sample in wide-mouthed sterile containers were cultured on Nutrient agar, MacConkey agar and 5% sheep Blood-agar, which performed to support growth most Gram negative bacteria and *Staphylococcus*.

After overnight incubation at 37 °C for 24–48 hours colonies were identified and characterized using colony characteristics, gram reaction of the organisms and biochemical test following standard procedure.⁸

Antibiotics sensitivity test:

The antimicrobial susceptibility testing of all isolates was done by the standard Kirby-Bauer disk diffusion method by using Mueller Hinton agar plates.⁵ Discs containing the following antibacterial agents were used: Ofloxacin 5 µg, Doxycycline 30 µg, Amoxicillin/Clavulanate 30 µg, Ampicillin 10 µg, Ciprofloxacin 5 µg, Gentamicin 10 µg, Nitrofurantoin 30 µg, Erythromycin 5 µg, Cephalexin 30 µg, Cefoxitin 30 µg, Norfloxacin 10 µg, Cefotaxime 30 µg, Ceftriaxone 30 µg, Clarithromycin 10 µg, Cefixime 30 µg, Levofloxacin 10 µg, Cefuroxime 30 µg.

The plates were incubated at 37 C for 24 hours after which the zones of inhibition were measured in millimetre. Using the interpretative chart derived from the zones of inhibition of Standard organisms according to the Clinical Laboratory Science Institute (CLSI), the zone size of each antimicrobial agent was interpreted.

3. Results And Discussion

A total of 266 samples were collected over a period of 6 months with symptomatic and documented urinary tract infection according to the detailed analysis of urine. In this study, female represent 156 (58.6%), has a larger risk of UTI whereas the male represent 110 (41.3%) among age groups. Most of individuals with positive UTI were patients with age between 40 -70 years old most of them are females as shown in (table 2).

Table 3 and figure 2 illustrate that the *Escherichia Coli* 130 (48.9%) was found to be the commonest microbial agent identified leading to UTI followed by *proteus mirabilis* 61 (22.9%), *Klebsiella pneumonia* 44 (16.5%), *Enterococcus faecalis* 13 (4.8%), *Staphylococcus aureus* 11 (4.1%), and *Pseudomonas aeruginosa* 7(2.6%).

The highest sensitivity of *E. coli* was found for Imipenem (95%), Augmentin (83%), Ciprofloxacin (57%), Cephalexin (52%) and Nitrofurantoin (50%). *E. coli* were resistant to Erythromycin (95%), Cefoxitin (90%), Clarithromycin (90%) and Ampicillin (87%). *Proteus mirabilis* was highly sensitive to Imipenem (95%) Cephalexin (74%) and Ampicillin (69%), whereas highly resistant to Clarithromycin (95%) and Cefoxitin (95%). *Klebsiella* was found to be sensitive to Imipenem (60%), and Ceftriaxone (53%)., while are highly resistant to Doxycycline (100%), and Erythromycin (100%). *Enterococcus faecalis* are sensitive to Imipenem (95%), and rates of resistance are high the most antibiotics used Clarithromycin (100%), and Ampicillin (96%), *Staphylococcus aureus* was sensitive to Imipenem (98%), Norfloxacin (82%), and Augmentin (77%), highly resistant to Clarithromycin (95%), Doxycycline (95%), *Pseudomonas aeruginosa* found to be sensitive to Imipenem (95%),and highly resistant to most Antibiotics used in this study table 4.

The results of this study showed that Most of the uropathogens are sensitive to Imipenem, and highly resistance against Clarithromycin, Doxycycline and Erythromycin used in this study as shown in table 4.

Table 1. Samples of UTI Cases in Different Gender Group:

Sex	No. (%) of samples	No. (%) positive cases
Male	110	41.3%
Female	156	58.6%
Total	266	100%

Table 2. Age and gender distribution of UTI patients:

Gender	Total (%)		Total (%)
	Male (%)	Female (%)	
< 10 years	6 (5.5%)	9 (5.8%)	15 (5.6%)
11-20 years	8 (7.2%)	13 (8.3%)	21 (7.9%)
21-30 years	5 (4.5%)	8 (5.1%)	13 (4.9%)
31-40 years	13 (11.8%)	18 (11.5%)	31 (11.7%)
41-50 years	22 (20%)	27 (17.3%)	49 (18.4%)
51-60 years	20 (18.1%)	31 (19.9%)	51 (19.2%)
61-70 years	23 (20.9%)	29 (18.6%)	52 (19.5%)
>71 years	13 (11.8%)	21 (13.5%)	34 (12.8%)
Total	110 (41.4%)	156 (58.6%)	266 (100%)

Table 3. Bacteria isolated from urine culture:

Bacteria isolated from urine culture.	Total (%)
<i>E. coli</i>	130 (48.9%)
<i>Proteus</i>	61 (22.9%)
<i>Klebsiella</i>	44 (16.5%)
<i>Enterococcus spp</i>	13 (4.8%)
<i>S. aureus</i>	11 (4.1%)
<i>Pseudomonas</i>	7 (2.6%)
Total	(100%)

Table 4. Bacterial isolates with their sensitivity to various antibiotics:

Types of isolates	No of isolates	Sensitivity to different antibiotics (%)																	
		AMC	AMP	CFM	CFU	FOX	CTX	CRO	CFX	CIP	CLR	DOX	ERY	GM	IMP	LV	NI	NOR	OF
<i>E.coli</i>	130	83	13	23	32	10	37	40	52	57	10	20	05	42	95	38	50	19	25
<i>P. mirabilis</i>	61	66	11	62	43	05	10	25	74	37	05	15	10	40	95	35	45	50	13
<i>K. pneumonia</i>	44	47	09	44	50	10	49	53	50	40	05	00	00	30	70	10	29	20	44
<i>E. faecalis</i>	13	12	04	15	34	20	18	26	32	20	00	05	33	56	98	40	10	40	12
<i>S. aureus</i>	11	77	10	30	68	12	72	59	61	34	05	05	33	56	98	40	82	45	38
<i>P. aeruginosa</i>	07	10	05	05	05	00	45	00	00	22	00	00	00	10	96	43	20	40	13

Different antibiotic discs used in sensitivity tests (quantity/disc) are: Amoxicillin/Clavulanate 30 µg (AMC), Ampicillin 10 µg (AMP), Cefixime 30 µg, (CFM), Cefuroxime 30 µg (CU), Cefoxitin 30 µg (FOX), Cefotaxime 30 µg (CTX), Ceftriaxone 30 µg (CRO), Cephalexin 30 µg (CFX), Ciprofloxacin 5 µg (CIP), Clarithromycin 10 µg (CLR), Doxycycline 30 µg (DO), Erythromycin 5 µg (ERY), Gentamicin 10 µg (GM), Imipenem 10 µg (IMP) Levofloxacin 10 µg (LV), Nitrofurantoin 300 µg (NI), Norfloxacin 10 µg (NOR), Ofloxacin 5 µg (OF).

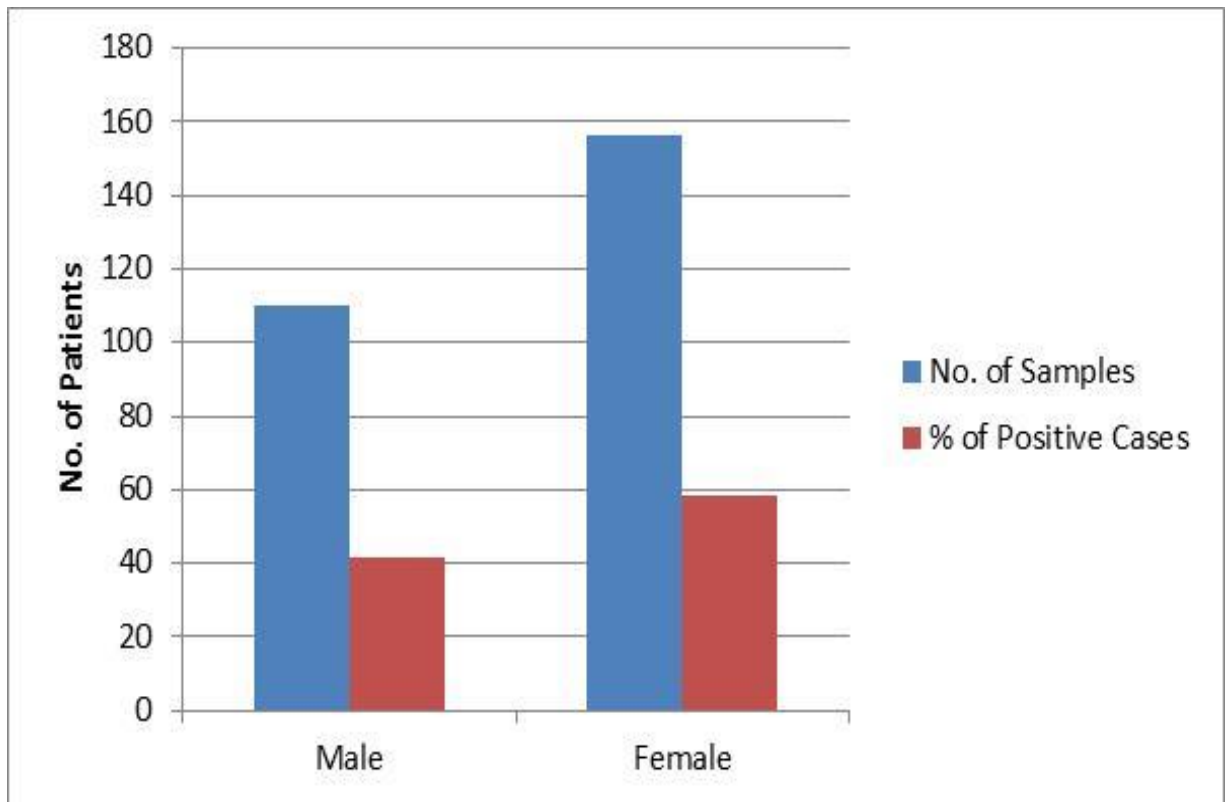


Figure 1. Samples of UTI Cases in Different Gender Group

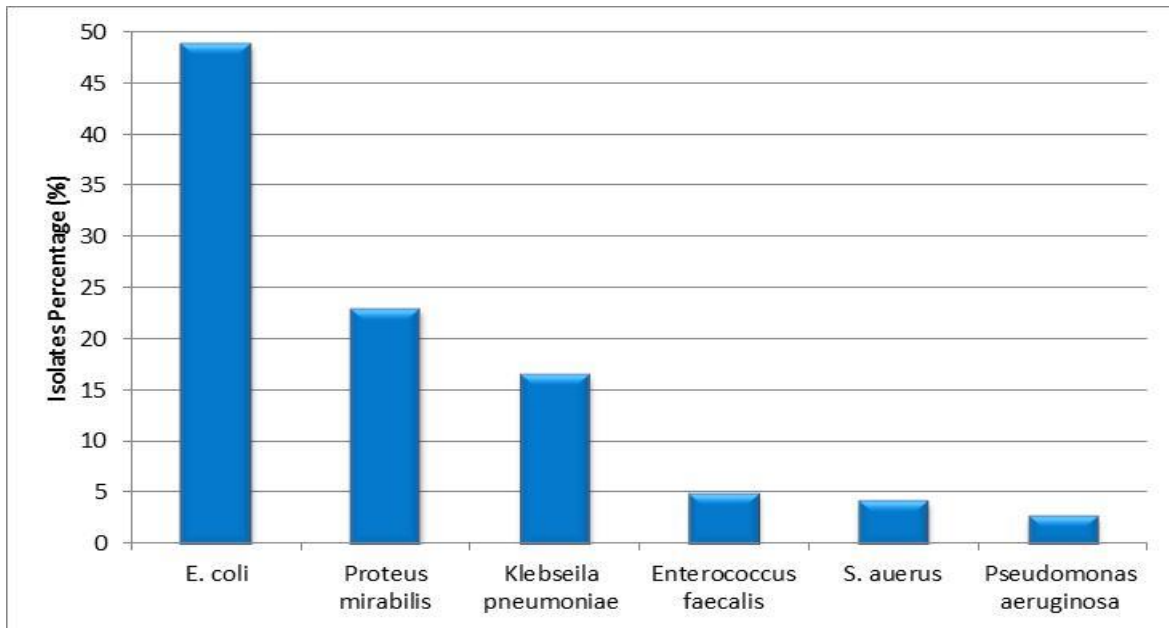


Figure 2. Bacteria isolated from urine culture

Discussion: On base of gender the study shows female at high risk of UTI more than male (table 1 and figure 1); the higher prevalence rate recorded in females could be due to the proximity of the urethral meatus to the anus, shorter urethra, contraception, and pregnancy.¹⁵ Among age groups above 30 more susceptible to UTI than other age groups may be due to increase sexual activity and progenies.³³ Our study found that *E. coli* is still the most common etiological agent of UTI, accounting for 48.9% of the cases, followed by *proteus mirabilis*, *Klebsiella pneumonia*, *Enterococcus faecalis*, *S. aureus* and *Pseudomonas aeruginosa*. Most cases of UTI are treated empirically, especially in third world countries, where patients often cannot afford to consult a physician or have a laboratory analysis made. Consequently, when urine samples are collected for laboratory tests, there may be an overrepresentation of microorganisms that do not respond to treatment.¹²

This study presents the microbiological examination of urine samples of 266 outpatients that between the age group of 10 to above 70 years (table 2). The most predominant bacterial isolate from the urine samples is *Escherichia coli* (48.9 %), followed by next leading microbes as *Proteus mirabilis* (22.9%), *Klebsiella pneumoniae* (16.5 %), *Enterococcus faecalis* (4.8%) *Staphylococcus aureus* (4.1%), *Pseudomonas aeruginosa* (2.6 %) (table 3). This finding is similar to previous

reports in Tobruk, Sobrata, Almel Cities and Tripoli In Libya,^{6,11,18} also other reports worldwide shown that similar organisms to our finding were the most common organisms associated with UTI for both community acquired and hospitalized cases.^{14,24,25,30}

Antibiotic sensitivity test is necessary to be conducted because sensitivity test is one method to determine bacteria vulnerability to the antibiotic.¹⁵ In this study from the results of antibiotics sensitivity were found, the most effective antibiotic, in vitro was Imipenem, Ciprofloxacin, and cefotaxime respectively, for both Gram Positive and Gram-Negative isolates, these results similar to study in Bangladesh by Aktar et al.,³ Were all isolates shown high level of resistance in both gram-positive and gram negative bacteria responsible of UTI in community isolates in this study to Ampicillin, cefoxitin and Doxycycline Similar to results found in Tripoli –Libya by Ben Ashur et al.,⁶ The reason may be due to the continuous use of these drugs for many years, easily availability, self-prescription, the tendency of patients using relatively cheaper antibiotics for all types of infection, and misuse.²⁶

As in Table 4 results show, Imipenem (95%), Augmentin (83%), and ciprofloxacin (57%) found to be the best performance against *E. coli*. This finding was almost similar with the findings reported,¹³ and also high rates of resistance to Erythromycin (95%), Cefoxitin, clarithromycin (90%), Ampicillin (87%) have been noted.

The susceptibility test of *Proteus mirabilis* shows that high sensitive to Imipenem (95%), cephalexin (74%), and Ampicillin (69%) similar to other study by wang et al.,³⁶ found to be highly resistant to cefoxitin (95%), cefotaxime and Erythromycin (90%). While the susceptibility test for *Klebsiella pneumonia* found to be sensitive to Imipenem (70%), and completely resistant to Doxycycline and Erythromycin (100%), and highly resistant to Clarithromycin (95%) which is similar results found in other studies by Cristea et al. and Saha et al.,^{10,32}

Pseudomonas was completely resistant to cefoxitin, ceftriaxone, cephalexin, clarithromycin, Doxycycline and Erythromycin (100%) and found high resistant to Ampicillin (98%) similar results found in similar study in Tobrouk, Libya by Dabobash et al.,¹¹ and also found to be highly resistant to cefixime, cefuroxime (95%), Gentamycin (90%) and Ofloxacin (87%) these results seems to agree with previous studies by Khan et al., and Ezenobi et al.,^{19,13} Higher resistance pattern of *Pseudomonas* as described here was not observed earlier. But increasing resistance to different drugs by the most common pathogens causing UTI is alarming and indicates the

treatment failure by these antibiotics become major problem for treatment such infections. On the other hand, Imipenem, Ciprofloxacin and Cefotaxime seemed to be more effective with higher sensitivity for most microbes causes UTI.²²

All Gram-positive isolates found in this study *S. aureus* and *Enterococcus faecalis* showed highly similarity sensitivity to imipenem (98%) and resistance to Clarithromycin and Ampicillin. A similar result was reported.^{21,29} *S. aureus* found to be also highly sensitive to imipenem (95%), and sensitive to Augmentin (83%) similar results founded elsewhere,¹³ and most of species resistant to Erythromycin (95%), Cefoxitin and Clarithromycin (90%), also the study found *Enterococcus faecalis* sensitive to Imipenem (98%) and completely resistant to Clarithromycin (100%) and highly resistant Ampicillin (96%) similar to prewise results found in Tobruk Libya,¹¹ and also found to be resistant to doxycycline (95%) and resistant to Nitrofurantoin (90%), Augmentin, and Ofloxacin (88%). This might be due to the abuse of these drugs leading to mutations which may be transferred though bacteriophage or plasmid thereby promoting resistance. The availability of drugs over the counter without the need of a prescription encourages the abuse of drugs. In addition, the use of fake and substandard drugs in world-wide may also be a contributory factor to the emergence of resistant strains.^{13,25}

From the comparative data, it is also clear that the bacteria representing as the predominant causes of UTI are becoming resistant to the most commonly used antibiotics for UTI treatment. These data provide information on antimicrobial resistance pattern among pathogens currently causing UTI in Sirte city. Since the resistance pattern of pathogens are ever changing and continuous, dealing with a limited number of samples the present study emphasizes on the necessity of a broad-based study that can reflect the authentic data and reliable information as treatment guidelines for UTIs.

The emergences of resistant strains among uropathogens are alarmingly increasing with different resistance patterns.² Acquisition of resistance might be either mutational by changing the target site of a bacteria within its genetic material or acquisition of new genetic material from other bacteria. This problem is also magnified by an irrational use and poor administration of drugs. Once a patient acquires resistant strain bacteria, then it transfers antibiotic resistance genes to other bacteria.²⁸

Conclusions

The From our results we notes that Gram-negative bacteria are the most common cause of urinary tract infections in about 90% of cases, while gram-positive bacteria are the cause in only 10%, *E. coli* was the most frequent causative agent in UTI. Higher prevalence cases of UTI was seen in females 156 (58.6%) rather than males 110 (41.4%). The study highlights that *E. coli* contributes to the majority of the urinary tract infections diagnosed in Sirte city.

Uropathogens showed resistant to commonly used antibiotics like Ceftriaxone, Cefepime, Cefrioxneand, Norfloxacin. On the basis of this study we can conclude that the resistance of commonly used antibiotics is very crucial. The antibiotic treatment should be limited to symptomatic UTIs to prevent emergency of resistance to antibiotics.

Based on the study results about the antibiotic sensitivity to the patients with UTI in Sirte city, it can be concluded as follows:

1. The study found *E.coli* the most common agent of UTI, beside some other gram negative and gram positive bacteria common causes of community-acquired UTI in Sirte.
2. The most widely used antibiotic Augmentin and some other Antibiotics listed in table 4.
3. The most effective antibiotic is Imipenem, which found to be (98%) to the *Enterococcus faecalis* and *S. aureus*, (96%) to *Pseudomonas aeruginosa*, (95%) to *E. coli*, and *proteus mirabilis*, and (60%) to *Klebsiella pneumonia*.
4. The most resistance antibiotic is ampicillin, Erythromycin and Doxycycline to most isolated strains isolated from UTI patients in this study.
5. In this study, UTI was found to be more prevalent in females than males, and in age group between 30 to 70.
6. Diagnosis, treatment, and the prevention of UTIs is a good example of the need for close cooperation between the clinician and the microbiologist.

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