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ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF PATHOGENIC BACTERIA CAUSING URINARY TRACT INFECTIONS AT AZADI HOSPITAL IN DUHOK CITY, KURDISTAN REGION, IRAQ.

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ABSTRACT:
Urinary tract infections is one of the most common diseases encountered in medical practice affecting people of all ages from the neonate to the geriatric age group. The aim of this study was to determine and evaluate the antimicrobial susceptibility patterns for most common strains of bacterial urine isolates taken from patients at Azadi teaching hospital laboratories in Duhok city, Kurdistan Region, Iraq; during 2014-2015. A retrospective survey study was conducted and 1003 data of urine culture sensitivity test were collected from recorded archives of the Azadi hospital. The study included all recorded positive urine samples cultures isolated from inpatients and outpatients. Results revealed that the female to male ratio for urinary tract infection was 2.7:1 and the most common microorganisms isolated were *Escherichia coli* (52%), *Staphylococcus aureus* (11%), *Staphylococcus haemolyticus* (9.6%) and *Klebsiella pneumoniae* (8.1%). In general, maximum sensitivity was seen for meropenem (94.9%), followed by imipenem (89.7%) and ertapenem (88.7%). The maximum resistance was seen against cefazolin (79.7%) and amoxicillin/clavulanic acid (77.5%). The antibiotic sensitivity pattern of *E. coli* reveals that the maximum sensitivity was seen for meropenem (97.3%) and imipenem (95.6%). The maximum resistance was seen against amoxicillin/clavulanic acid (83.1%). The resistance against many commonly used antibiotics have been increased which limit the options for treating urinary tract infection. This is resulted from uncontrolled use of the antibiotics and lack of policies and guidelines for their use in public health.

KEYWORDS: Antimicrobial, Urinary Tract Infections, Susceptibility, Iraq.

1. INTRODUCTION

Urinary tract infections (UTIs) are one of the most main infectious diseases with an extensive financial burden on society. UTI is a bacterial infection of the urinary bladder, kidney, or collecting system. It may be either acute or chronic, and may affect any part of the upper or lower urinary system (Abrams *et al.*, 2002). UTI classified into either complicated or uncomplicated based upon patient's characteristics and on the clinical setting in which the infection is acquired (community acquired verses healthcare acquired) (Lin, 2014).

A major worldwide problem nowadays is the resistance of the invading microorganisms to the treatment; resistant organisms have emerged due to several factors related to the genetic nature of the organisms and selective antimicrobial pressure in humans (Saffar *et al*., 2008; Habeeb *et al*., 2014; Hussein *et al*., 2017). Globally UTIs area serious health problem which affects millions of peoples every year (Mahmood, 2011).Worldwide, UTI is identified in about 150 million people annually (Gupta *et al*., 2001). About 40% of all hospital acquired infections are due to UTIs which are catheter associated (Ruden *et al*., 1997).About 25% of patients who subjected to urinary catheter for one week or more developed bacteriuria with a daily risk of 5-7% (Maki and Tambyah, 2001).

Antibiotic resistance in the treatment of UTIs is a serious public health issue, especially in the developing world. A recent WHO report showed a high level of obvious resistance of common bacteria to antibiotics in many parts of the world. With an increase of the resistance to major antibiotics of common bacteria such as *Escherichia coli* which accounts the higher percentage among isolated uropathogen (Carlet *et al.*, 2011).

The presence of extended-spectrumβ-lactamase (ESBLs) producing bacteria showing resistance to most antibiotics is gradually increasing in the society. The aim of this study was to determine the antimicrobial susceptibility patterns for most common isolated bacteria from urine for patients at Azadi teaching hospital laboratories Duhok city, Kurdistan region, Iraq, during 2014-2015and to evaluate the results.

2. MATERIALS AND METHOD

2.1 Study setting

This study was conducted in the Department of Microbiology in Azadi teaching hospital laboratories in Duhok city, Kurdistan Region, Iraq. Number of daily patients visits the hospital was about 875 patients, about 120 of them requiring general urine analysis and about 25 of them urine culture on a daily basis.

2.2 Study design

This is a retrospective survey study of sensitive cultures records for a period 2014 and 2015; at Azadi hospital. The study included all recorded positive urine samples cultures isolated from inpatients and outpatients. All the patients symptomatic of UTI were included irrespective of their co-morbidities. Negative growth cultures and cultures with candida growth were excluded from this analysis. Patients with recurrent UTI and failure of treatment met the basic criteria for doing culture sensitivity test.

2.3 Data Collection

The data of this study have been obtained from the records of clinical microbiology. 1003 patient culture sensitivity results were recorded during study period; 306 from 2014 and 697 from 2015.Cultures were done by BD Phoenix 100 instrument and antibiotic sensitivity further cheeked manually. Urine was collected by midstream-clean catch method and from catheters of the catheterized patients. During the study period the laboratories

was visited once weekly and all patients lab results were recorded which were registered by laboratory staff.

2.4 Antimicrobial susceptibility test

The sensitivity of isolated bacteria to commonly used antimicrobial agents from different groups was determined. Antimicrobial susceptibility testing was performed on Mueller-Hinton agar using disk diffusion for gram negative and gram positive bacteria except *Streptococcus* spp which was done on Mueller Hinton agar with Blood. Each sample was inoculated and incubated at 37ºC for 24 hours. The antibiotic discs were beta-lactams –penicillins (ampicillin /sulbactam, amoxicillin/clavulanic acid, piperacillin /tazobactam), cephalosporins (cefoxitin, cefuroxime, cefazolin, ceftazidime, ceftriaxone, cefepime, cefoperazone /sulbactam), monobactam (aztreonam), aminoglycosides (amikacin, gentamicin), quinolones (ciprofloxacin, levofloxacin, norfloxacin), carbapenems (ertapenem, imipenem, meropenem), glycopeptides (vancomycin), nitrofurantine and trimethiprim/ sulfamethoxazole.

2.5 Statistical analysis

The collected data was coded, computerized and analyzed by SPSS for Windows, version 20, identified by frequencies and percentages.

3. RESULTS

From the recorded data of archives in Azadi hospital, a total of 1003 positive urine cultures were taken; 268 (26.7 %) were from male and 735 (73.3%) from female patients. Female to male ratio was 2.7:1. Out of total number of patients, 306 were from 2014 and 697 from 2015. The data reveals that *Escherichia coli* (52%) were the leading uropathogen followed by *S. aureus* (11%), *S. haemolyticus* (9.6%) and *K. Pneumonia* (8.1%) respectively (Figure 1).Regarding gender distribution, the commonest isolated microorganism was *E. coli* in both gender, followed by *S. aureus* in females and *S. haemolyticus* in male (Table 1).

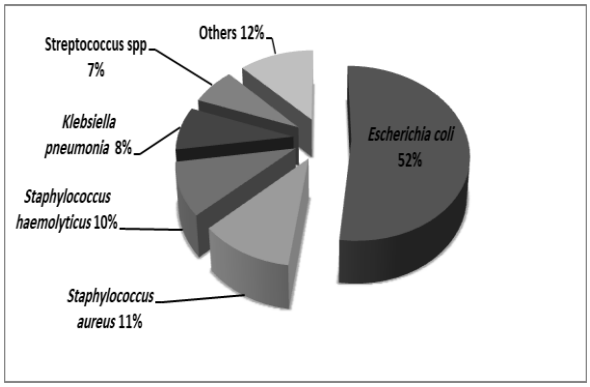

Figure 1. Frequency of isolated uropathogenic bacteria

Table 1. Gender wise Distribution of Isolated Bacteria in Urine Samples

Microorganism		Male No. (%)	Female No. (%)	Total No. (%)
Gram negative	*Escherichia coli*	141(14.1)	381(38)	522(52.1)
	Klebsiella pneumonia	22(2.2)	59(5.8)	81(8)
	Pseudomonas aeruginosa	18(1.7)	14(1.4)	32(3.1)
	Proteus mirabilis	2(0.2)	14(1.4)	16(1.6)
	Burkholderia cepacia	4(0.4)	2(0.2)	6(0.6)
	Morganella morganii	0(0)	3(0.3)	3(0.3)
	Citrobacter freundii	0(0)	1(0.1)	1(0.1)
	Pantoea agglomerans	1(0.1)	0(0)	1(0.1)
Gram positive	*Staphylococcus aureus*	24(2.4)	86(8.6)	110(11)
	Staphylococcus haemolyticus	25(2.5)	71(7.1)	96(9.6)
	Streptococcus species	13(1.3)	59(5.9)	72(7.2)
	Enterococcus faecalis	11(1.1)	19(1.9)	30(3)
	Staphylococcus saprophyticus	4(0.4)	15(1.5)	19(1.9)
	Staphylococcus epidermids	1(0.1)	9(0.9)	10(1)
	Staphylococcus hominis	2(0.2)	2(0.2)	4(0.4)
Total		268(26.7)	735(73.3)	1003(100)

In 2014, *E. coli* (42.8%) was the leading uropathogen followed by *K. pneumoniae* (15.7%), *S. aureus* (15.7%), *S. haemolyticus* (8.8%) and *Streptococcus spp* (7.5%). In 2015, again *E. coli* (55.1%) was the leading uropathogen followed by *S. haemolyticus* (8.8%), *S. aureus* (8.9%), *K. pneumoniae* (7%), and *Streptococcus spp* (7%). Other bacteria were responsible in total for only (9.5%) and (13.2%) of positive urine cultures in 2014 and 2015 respectively (Table 2).

The maximum antibiotic sensitivity pattern of the uropathogen was seen for meropenem (94.9%), followed by imipenem (89.7%), ertapenem (88.7%), vancomycin (87.7%), piperacillin/tazobactam (79.9%) and amikacin (74.3%). the maximum resistance was seen against cefazolin (79.7%), amoxicillin /clavulanic acid (77.5%), cefuroxime (72.3%), ceftriaxone (63.7%), aztreonam (61.5%) and ceftazidime (60.4%) (Figure 2). *E. coli* were the commonest isolated microorganisms accounting for 52% of the uropathogens isolated in 522 out of total number of patients. The antibiotic sensitivity pattern of *E. coli* reveals that the maximum sensitivity was seen for meropenem (97.3%) followed by imipenem (95.6%), ertapenem (95.4%), cefoxitin (81.9%), and amikacin (80.8%). The maximum resistance was seen against amoxicillin/clavulanic acid (83.1%), followed by cefazolin (77.3%), cefuroxime (76.9%), ceftazidime (68.3), and ceftriaxone (68.3%) (Figure 3). The resistance pattern of *E. coli* to ceftriaxone, cefuroxime, aztreonam and norfloxacin were more in 2015 than 2014 (Figure 4).

Table 2. Frequency and percentage of bacterial urinary tract infections from patients at Azadi Teaching Hospital in Duhok city during 2014-2015

Microorganism		2014	2015
Gram negative	*Escherichia coli*	131 (42.8)	384 (55.1)
	Klebsiella pneumonia	33(10.7)	48 (7.1)
	Pseudomonas aeruginosa	8(2.7)	24 (3.4)
	Proteus mirabilis	3(1)	13(1.9)
	Burkholderia cepacia	1(0.3)	5(0.7)
	Morganella morganii	0(0)	3(0.4)
	Citrobacter freundii	0(0)	1(0.1)
	Pantoea agglomerans	0(0)	1(0.1)
Gram positive	*Staphylococcus aureus*	48 (15.7)	62(8.9)
	Staphylococcus haemolyticus	27(8.8)	69(9.9)
	Streptococcus species	23(7.5)	49(7)
	Enterococcus faecalis	11 (3.6)	26(3.7)
	Staphylococcus saprophyticus	18(5.9)	1(0.1)
	Staphylococcus epidermids	3(1)	7(1)
	Staphylococcus hominis	0(0)	4(0.6)
Total		306(100)	697(100)

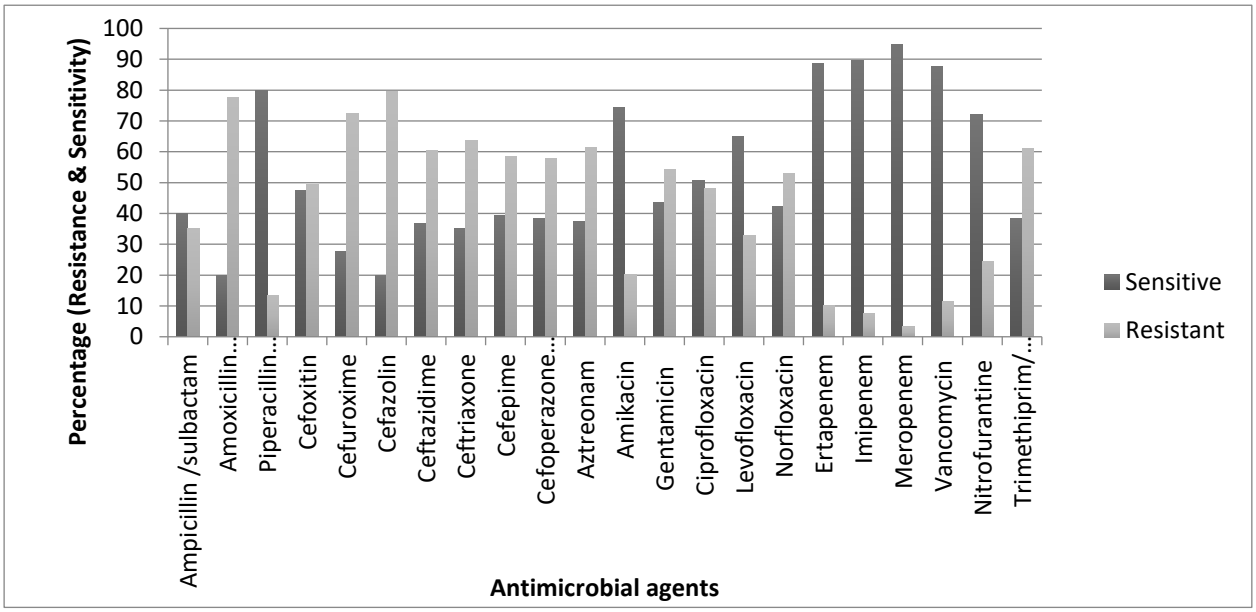

Figure 2. Antimicrobial resistance and sensitivity pattern of uropathogen

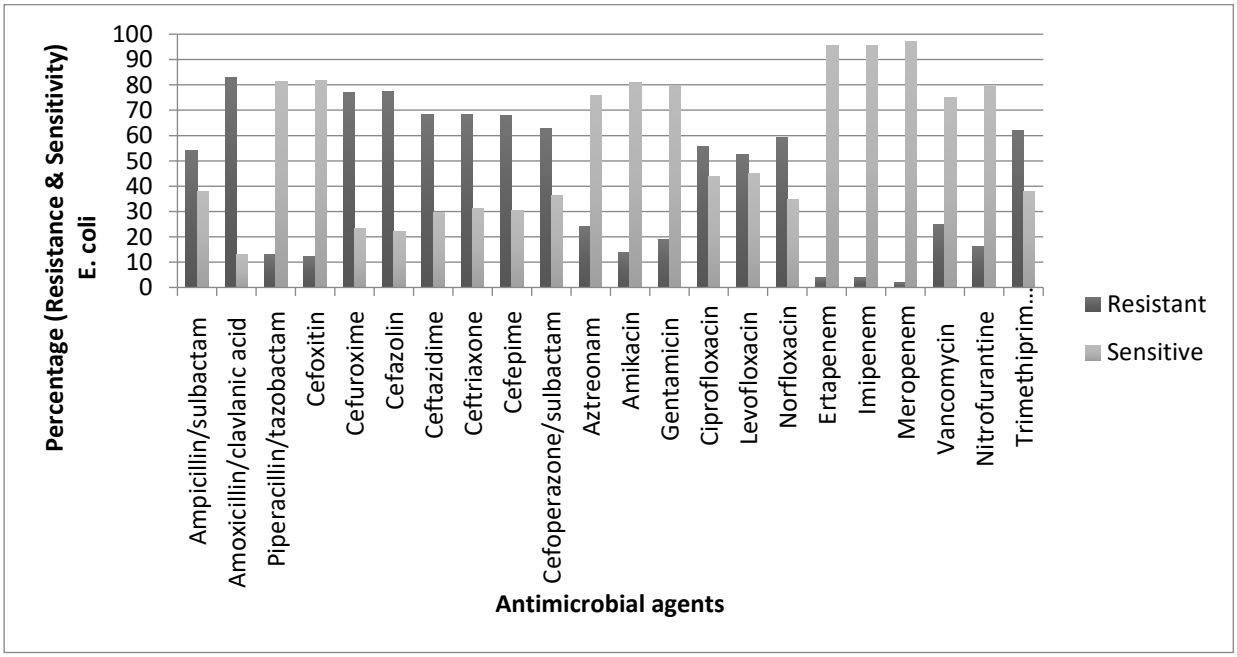

Figure 3. Antimicrobial resistance and sensitivity pattern of *E. coli*

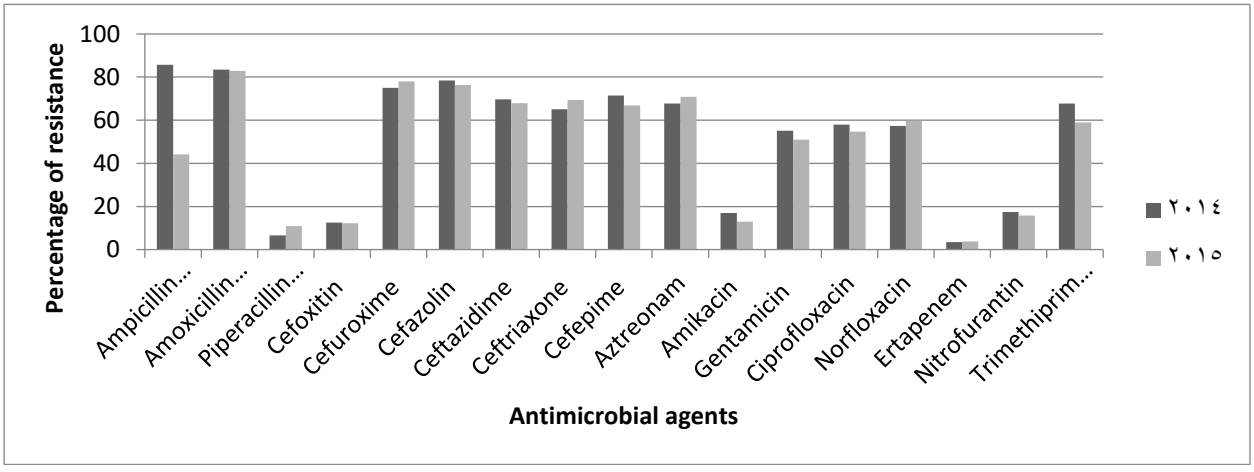

Figure 4. Resistance pattern of *E. coli* to antibiotic in 2014 and 2015.

4. DISCUSSION

This study showed the distribution of microbial species causing UTIs in the Duhok city for 2014 and 2015 and their patterns of susceptibility to antimicrobial agents. The most common uropathogens in this study were *E. coli* (52%) followed by *S. aureus* (11%). The same results were obtained in a study conducted in Teaching Hospital in Erbil and Sulaimania cities (Al-Barzinji *et al.*, 2010). While another study in Duhok showed *Enterococcus faecalis*as is the second most common uropathogen (Yassin, 2012). This variation in the bacterial species could be due to variation in the study methodology, host and environmental factors that exist.The fact that *Staphylococcus spp.* is a normal flora of peri-anal and vaginal region this may account for the high prevalence of *Staphylococcus spp.* in the study. Whereas, a studies showed that the second most common uropathogen in Baghdad and Tikrit were *Enterobacter spp* and *Proteus mirabilis* respectively (Mahmood, 2011; Al-Jebouri and Mdish, 2013).

In this study, the predominance incidence of infection was in females (73.3%). This gender distribution of patients is comparable with other reported studies. This is could be related to the differences between male and female genitourinary systems in anatomy and host factors (Foxman, 2010). Generally, this study showed that the majority of isolates were sensitive tocarbapenems (meropenem, imipenem, ertapenem) (94.9%, 89.7%, 88.7% respectively). Thus, the use of these antibiotics as an empirical treatment for a suspected UTI would be the drugs of choice against most common isolated uropathogens. Similar results were observed by other researcher who found the sensitivity of uropathogen to meropenem and imipenem (Assafi *et al.*, 2015; Polse *et al.*, 2016a). However it is recommended that carbapenems should be used as a last line antibiotic to prevent the occurrence of carbapenem resistance (Kiffer *et al.*, 2006). A lowest percentage of sensitivity was found to cefazolin (20 %), amoxiclav (19.9%), cefuroxime (27.7%), ceftriaxone (35.1%), aztreonam (37.3%) and ceftazidime (36.8%). The same results were found in Baghdad showing low sensitivity against amoxiclav, ceftriaxone and ceftazidime (33%, 33% and 30% respectively)(Hussein, 2014).

There are an increasing number of antibiotic resistance pathogens locally and worldwide (Assafi *et al.*, 2015; Jasovsky *et al.*, 2016; Assafi *et al.*, 2017). Extended spectrum beta-Lactamases-producing uropathogenic *E. coli* is a leading cause of UTI in Iraq (Polse *et al.*, 2016b).*E. coli* as the commonest uropathogen isolated showed high resistance to amoxicillin/clavlanicacid (83.1%). Similar results were found in a study in Hawler city showing percentage of *E. coli* resistance to amoxiclav (85.4%) (Saeed *et al.*, 2015).An increased resistance of *E. coli*reported against Fluoroquinolones as one of commonly used antibiotics, ciprofloxacin (55.7%), Levofloxacin (52.4%) and norfloxacin (59.1%). A higher rate of resistance compared to other studies such as that conducted in Turkey (Kayaş *et al.*, 2011). This increased rate of resistance due to overuse of fluoroquinolones for such common infections increase the possibility for the development of resistance. While comparing the data obtained from 2014 and 2015, the resistance of *E. coli* to ceftriaxone, cefuroxime, aztreonam and norfloxacin were more in 2015 than 2014. On the other hand the resistance to Ampicillin and TMP-SMX is lower in 2015 than 2014, this may be due to the fact that these drug now is not always prescribed to patients by health care giver and physicians as they considered them not working due to high level of resistance.

5. CONCLUSION

Based on the findings of this study, it is concluded that UTI is in females more than males. The main uropathogen causing UTI is *E. coli* followed by *S. aureus*. Many isolates were resistant to commonly prescribed antibiotics. Many of these showing resistance to more than 2 antibiotics, this is an alarming situation. The maximum sensitivity of uropathogens in general was seen for meropenem (94.9%), followed by imipenem (89.7%), ertapenem (88.7%), vancomycin (87.7%), piperacillin/tazobactam (79.9%) and amikacin (74.3%). Thus, an urgent plan to control this threatening development is required. Few new antibiotics are expected to be produced in the coming years. Therefore, the urological community has a responsibility in careful use of available antibiotics in order to reduce the development of resistance.

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