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Research Paper

Urinary Bacterial Profile and Antibiotic Susceptibility Pattern among Patients with Urinary Tract Infection in Duhok City, Kurdistan Region, Iraq

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Abstract: *The study of the UTI causative pathogens in a region and their susceptibility to antimicrobial agents is mandatory to determine the empirical therapy. This study aimed to determine the prevalence of microorganisms causing UTI and to study their antimicrobial susceptibility in Duhok. 141 urine samples were collected from UTI patients from January to December 2014. Bacterial isolates were identified and their susceptibility to different antibiotics was determined by the Vitek-2 system. The gender distribution of UTI was 68.79 %(97/141) in women and 31.2%(44/141) in men. The prevalence of Gram-negative bacteria and Gram-positive bacteria were 52.48% (74/141), 47.51% (67/141) respectively. The highest infection was by Escheria. coli 74.32% (55/74), Staphylococcus haemolyticus 23.88%(16/67), and Enterococcus faecalis 23.38%(15/67). Gram-negative isolates were susceptible to Aminoglycosides and Carbapenems. While Gram-positive bacterial isolates showed sensitivity to vancomycin, linezolid, tigecycline and nitrofurans. Most isolates were resistant to penicillin group. Gram-negative isolates showed a heavy resistance to cefuroxime, while Gram-positive isolates were resistant to erythromycin and tetracycline.Therefore, we conclude thatE. coli and*

Staphylococcus haemolyticus were the most prevalent isolated uropathogens in Duhok. Susceptibility test showed resistance to penicillins, cefuroxime, erythromycin and tetracycline. Such results should be considered before deciding the empirical treatment of bacterial UTI.

Keywords: Urinary Tract Infections, Antimicrobial Agents, Iraq.

1. Introduction

UTI is a common acquired bacterial infection that affects about (150) million people all over the world (Foxman, 2014; Stamm and Norrby, 2001). Despite the knowledge about its microbial etiology (Wagenlehner et al., 2011), increasing rates of complicated UTI were recorded worldwide especially in developing countries (Beyene and Tsegaye, 2011). It has been demonstrated that the increasing resistance pattern to the commonly used antimicrobial agents, as a result of their use in UTI treatment without performing a susceptibility test, might be one of the main causes behind the occurrence of complicated UTI (Abat et al., 2015). Moreover, studies have shown variable antimicrobial resistance rates in different geographical and regional locations (Mathai et al., 2001). Therefore, Karlowsky and colleagues stated that the accurate and rapid bacterial identification and antimicrobial susceptibility investigations for patients with suspected UTI was the primary step for both correct treatment and antimicrobial resistance prevention (Karlowsky et al., 2001). In the last few years, area-specific monitoring studies were conducted to allocateUTI empirical treatment guidelines for different regions all over the world (Beyene and Tsegaye, 2011;Gupta et al., 2011; Koningstein et al., 2014). These studies showed causative pathogens and their resistance patterns in specific regions to help clinicians to choose the most appropriate treatment for their UTI patients (Beyene and Tsegaye, 2011). In Duhok city (Kurdistan region, Iraq), no information was available about the resistance rates in UTI due to the lack of surveillance data in general practice. Thus, this study was conducted to provide an insight about the empirical therapy for UTI through determining the prevalence of the common bacterial microorganisms that causing UTI and studying their resistance patternto antibiotics.

2. Materials and Methods

2.1 Methodology

This study was conducted in Duhok city, Kurdistan region, Iraq over 12 months duration (January to December 2014). Urine samples were collected from 141 patients suspected of having a UTI by clean catch midstream sampling method to avoid contamination. Patients were asked to give data on their age, sex, history of bladder catheterization and previous antibiotic therapy. All samples were inoculated on blood agar as well as MacConkey agar, incubated at 37 ^{o}C for 24 hours and then inspected for bacterial growth. Strict definition of UTI was used for the purpose of this paper. Subjects were regarded having UTI, if there was microbiological evidence of UTI, pyuria and two of symptom of dysuria, lower abdominal pain, fever or back pain. The presence of $\geq 10^5$ identical colonial morphotypes (10^5 CFU /ml) was regarded as microbiological evidence of a UTI. Bacterial colonies were initially classified by Gram-stain morphology and then definitively identified depending on standard culture and biochemical characteristics of isolates by using Vitek-2 system (bioMerieux) according to the manufacturer's instructions. The antibiotic susceptibility of isolates was determined to different antimicrobial groups (Table 1).

2.2 Ethics Statement

Consent was obtained from subjects involved in the study. This study and method of attaining consent were approved by the ethics committeeat the University of Duhok, School of Medicine, University of Duhok, Kurdistan Region, Iraq.

Table 1: Antimicrobial agents used in this study

Antimicrobial group	Antimicrobials (Abbreviation)
Beta-Lactams	**Penicillins**
	Benzyl penicillin (Bpc)
	Oxacillin (Oxa)
	Ampicillin (Amp)
	Amoxicillin (Amx)
	Piperacillin (Pip)
	Cephalosporins
	Cefuroxime (Cxm)
	Cefoxitin (Fox)
	Ceftriaxone (Cro)
	Ceftazidime (Caz)
Macrolides	Erythromycin (Ery)
Quinolones	Ciprofloxacin (Mathai et al.)
	Levofloxacin (Lvx)
	Moxifloxacin(Mxf)
Aminoglycosides	Amikacin (Amk)
	Gentamicin (Wagenlehner et al.)
Carbapenems	Imipenem (Imp)
	Meropnem (Mem)
Glycopeptides	Vancomycin (Van)
Lincosamides	Clindamycin (Cli)
Others	Cotrimoxazole (Cot)
	Rifampin (Rif)
	Linezolid (Lzd)
	Tetracyclines (Tet)
	Nitrofurans (Schaeffer et al.)
	Tigecycline (Tgc)

3. Results and Discussion

3.1 Results

This study was conducted from January 2014 to December 2014 in Duhok city, Kurdistan region, Iraq. A total of 141 isolates of different strains of urinary tract infection from adults were investigated. 68.79% (97/141) of the patients were female, whereas 31.2% (44/141) of the patients were male. The total percentage of Gram-negative and Gram-positive bacteria isolates were 52.48% (74/141) and 47.51% (67/141), respectively. The highest infection by Gram-negative bacteria was by Escherichia coli 74.32% (55/74) (Table 2) and the highest infection by gram-positive bacteria was by Staphylococcus haemolyticus 23.88% (16/67) (Table 3).

Table 2: The types and percentages of gram negative isolates

Strain spp	**Number (%) of isolates**
Escherichia coli	55 (74.32)
Klebsiella pneumonia	8 (10.81)
Pseudomonas aeruginosa	5 (6.75)
Proteus mirabilis	2 (2.7)
Aeromonas cavia	1 (1.35)
Raoultella ornithinolytica	1 (1.35)
Acinetobacter baumannii	1 (1.35)
Moranella morganii	1 (1.35)
Total	74

Table 3: The types and percentages of Gram positive isolates

Strain spp	**Number (%) of isolates**
Staphylococcus haemolyticus	16 (23.88)
Enterococcus faecalis	15 (23.38)
Streptococcus agalactiae	5 (7.46)
Staphylococcus lentus	5 (7.46)
Staphylococcus hominis	4 (5.97)
Staphylococcus epidermids	3 (4.47)
Staphylococcus warneri	3 (4.47)
Enterococcus gallinarum	2 (2.98%)
Staphylococcus aureus	2 (2.98%)

Streptococcus salivarius	2 (2.98%)
Streptococcus sanguinis	2 (2.98%)
Kocuria rosea	2 (2.98%)
Pedicoccus pentosaceus	2 (2.98%)
Staphylococcus saprophyticus	2 (3.98)
Streptococcus thoraltensis	1 (1.49)
Helcococcus kunzii	1 (1.49)
Total	67

The bacterial isolates showed variable patterns in their susceptibility to antibiotics as it is shown in Table 4 and Table 5.

3.2 Discussion

UTI is one of the most common infections that affects people in the community and in the hospital. Hospital acquired UTI increasestreatment cost and it increasesboth morbidity and mortalityrates. In the last few years, constantly increasing antibiotic resistance rates for commonly prescribed antimicrobial agents, due to their inappropriate use, has emerged as a serious public health issue.Therefore, many local-specific studies, like our study, have been conducted to allocate UTI empirical treatment to decrease the inaccurate use of antibiotics.

Table 4: Averaged antimicrobial resistance rate (%) of the Gram-negative uropathogenes

Antimicrobial group	**Antimicrobial**	**Strain (Number of isolates)**							
		E. coli (55)	**K. peumoniae** (8)	**P. aeruginosa** (5)	**P. mirabilis** (2)	**A. caviae** (1)	**R. ornithinolytica** (1)	**A baumannii** (1)	**M. morganii** (1)
Penicillins	**Ampicillin**	85	100	100	0	100	100	100	100
	Amoxicillin	33	0	100	0	0	0	100	00
	Piperacillin	7	0	100	0	0	100	0	0
Cephalosporins	**Cefuroxime**	59	37.5	100	0	100	100	100	100
	Cefoxitin	18	0	100	0	0	0	100	0
	Ceftriaxone	65	50	100	0	0	0	0	0
	Ceftazidime	70	37.5	25	0	0	100	0	0
Aminoglycosides	**Gentamycin**	38	37.5	20	0	0	0	0	100
	Amikacin	0	0	0	0	0	0	0	0

Carbapenems	**Impenem**	0	0	0	0	0	0	0	0
	Meropnem	0	0	0	0	0	0	0	0
Quinolones	**Ciprofloxacin**	48	0	40	0	0	100	0	0
Other	**Nitrofurans**	9	0	0	50	0	0	100	0
	Cotrimoxazol	65	37.5	0	0	100	0	0	100

Table 5: Averaged antimicrobial resistance percent (%) of the Gram positive uropathogens

Antimicrobial group	**Antimicrobials**	**Strain (Number of Isolation)**											
		S.Haemolyticus (16)	**S. lentus (5)**	**S.hominis (4)**	**S.epidermids (3)**	**S. warneri (3)**	**S. aureus (2)**	**S. Saprophyticus (2)**	**E. faecalis (15)**	**E. gallinarum (2)**	**Strep.agalactiae (5)**	**Strep. sanguinis (2)**	**Strep. salivarius (2)**
Cephalosporins	**Fox**	20	75	0	0	33	100	50	0	0	20	0	50
Penicillins	**Bpc**	94	100	100	100	100	50	100	67	50	100	100	100
	Ox	75	80	75	100	33	0	100	0	0	80	50	0
Aminoglycosides	**Gen**	27	0	33	0	33	0	0	60	0	40	50	0
Quinolones	**Cip**	50	0	33	33	0	0	50	33	50	20	0	50
	Lvx	25	0	25	0	0	0	50	64	0	0	100	100
	Mxf	7	0	33	0	0	0	50	29	50	60	0	50
Macrolides	**Ery**	81	20	100	33	100	0	100	92	0	80	100	0
Lincosamide	**Cli**	44	25	50	33	0	0	0	71	100	100	100	100
Glycopeptid	**Va**	6	0	0	0	0	0	0	0	0	0	0	0
Others	**Lzd**	0	0	0	0	0	0	0	0	0	0	0	0
	Tet	62.5	60	75	0	100	0	100	100	100	80	100	100
	Tgc	0	0	0	0	0	0	0	0	0	0	0	0
	Nit	0	0	0	0	0	0	0	0	0	0	0	0
	Rif	25	0	67	0	0	0	100	0	50	0	50	0
	Cot	25	0	0	33	0	0	100	100	100	0	0	0

In our study, UTI was significantly more in female than male with percentages of 68.79% and 31.2%, respectively.This is in agreement with previous studies which showed that the UTI was more commonly occurred in women than men (Dason et al., 2011; Foxman et al., 2000; Linhares et al.,

2013). Moreover, Linhares and colleagues estimated that one-third of women would have at least a physician-diagnosed UTI during their lives (Linhares et al., 2013). It is believed that females are at greater risk for UTI than the male due to their anatomical and physiological characteristics (Schaeffer et al., 2001).

In this study, the prevalence of Gram-negative bacteria was higher than that of Gram-positive bacteria. In the total 141 isolates, the most commonly isolated bacteria was Escherichia coli, followedby Staphylococcus haemolyticus. Among the gram-negative bacteria, the most common isolates were E. coli, Klebsiella Pneumonia (K. Pneumonia), Pseudomonas aeruginosa (P. Aeruginosa), and Proteus Mirabilis (P. Mirabilis). Similar results were reported by previous studies that showed a high frequency of UTI caused by these bacterial strains (Farrell et al., 2003; Rizvi et al., 2011; White, 2011). Pathogenic E. coli is responsible for about 90% of all community-acquired UTIs (Foxman, 2002; Marrs et al., 2005)while Klebsiella, Pseudomonas, Proteus, and other organisms are more common in hospital acquired complicated UTI (Kodner and Thomas Gupton, 2010).

The most common Gram-positive uropathogens were Staphylococcus haemolyticus followed by Enterococcus faecalis, Streptococcus agalactiae, Staphylococcus lentus and Staphylococcus hominis. Many studies have identified these pathogens as causative agents for UTI (Gunn and Davis, 1988; Orrett and Shurland, 1998; Schmiemann et al., 2012). Campbell et al. showed that most of these pathogens werecommensal within the genital tract flora of healthy adult (Campbell et al., 2000).
Antibiotic resistance is a major threat to public health worldwide (De Kraker et al., 2011). In the last few years, the frequency of UTI caused by antimicrobial resistant bacteria has increased in both hospital and community (Lau et al., 2008; Moreno et al., 2009). The rapid identification and knowledge of antimicrobial susceptibility patterns is critically important for the correct treatment and to eliminate uropathogenic bacterial strains from patients with bacterial UTI (Moreno et al., 2009).
This study was carried out to provide an insight into resistance patterns to different type of antibiotics in Duhok city, Iraq. The antibiogram pattern of the 141 UTI isolates was checked to different antibiotics belonging to different groups. Our study showed that almost all Gram-negative isolates were susceptible to imipenem and meropnem (carbapenems), and gentamicin and amikacin (aminoglycosides). Almost all Gram positive UTI bacterial isolates showed a high pattern of sensitivity towards vancomycin, linezolid, tigecycline and nitrofurans. This results were similar to other studies that found the same pattern of antibiotic sensitivity pattern (Arias et al., 2010; Farajnia et al., 2009; Nathwani et al., 2008).

Our study showed that the highest resistance was against penicillins (ampicillin, amoxicillin, benzyl penicillin). It is known that ampicillin and amoxicillin are no longer recommended as reliable antibiotics for community acquired UTI because E. coli, which cause 90% of community acquired UTI, is resistant to these agents (den Heijer et al., 2012; Habeeb et al., 2014; Jancel and Dudas, 2002). The data analysis revealed that almost all Gram-negative isolates were resistant to cefuroxime (cephalosporins), while Gram-positive isolates exhibited an increased resistance pattern toward erythromycin and tetracycline. The isolated uropathogens from various studies showed resistance pattern toward macrolides, cephalosporins, tetracycline, quinolones, aminoglycosides, carbapenems, and nitrofurans (Ahmed et al., 2014; Akram et al., 2007; Al Sweih et al., 2005; Kanj and Kanafani, 2011; Shigemura et al., 2009). Many factors may contribute to the development and spread of antibiotic resistance. However, a significant reason for antimicrobial resistance is the inappropriate antibiotic use (Larsson et al., 2000). This high resistance rate to commonly used antibiotics is alarming and immediate and urgent measures should be taken to combat such resistance patterns.

4. Conclusion

In Duhok, the incidence and causative uropathogens in both females and males were similar to that reported elsewhere. Imipenem, meropnem, gentamicin, amikacin, vancomycin, linezolid, tigecycline and nitrofurans exhibited adequate antibiotic activity against uropathogens. On the other hand, penicillins, cefuroxime, erythromycin and tetracycline were inactive antimicrobial agents against

uropathogenes. For this reason, empirical antibiotic selection by physicians should be based on the awareness of the local prevalence of bacterial profile and antibiotic sensitivities rather than on universal or even national guidelines.

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