

MULTIPLE DRUGS RESISTANCE AMONG URINARY TRACT INFECTION PATIENTS IN DUHOK CITY –KURDISTAN REGION –IRAQ

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ABSTRACT

Background: Anti-microbial resistance could be a major public-health problem worldwide and universal endeavors are required to counteract its rise and the moment most common reason for observational antibiotic treatment. Optimal treatment seems diminish mortality and morbidity in surgical patients and play a crucial part in combating the continuous emergencies of expanding antibiotic resistance. The aim of this study is to study the pathogens and their antibiotic susceptibility in urinary cultures to Central laboratory in Duhok City and to study the rationality of antibiotic treatment urinary tract infection.

Patients and Methods: One hundred fifty-one UTI urine samples (culture positive) were collected from patient of central laboratory. Identified and isolated bacteria were determined by biochemical tests like Gram staining, Indole, oxidase, catalase, methyl red, Voges-Proskauer, citrate utilization, hemolysis, motility; and urea; fermentation and utilization tests of glucose, lactose and sucrose. Sensitivity pattern of isolates was determined against some traditional and conventional antibiotics.

Results: *Staphylococcus aureus* was the most common bacteria (40.4 %) followed by *E.coli* (31.8%). The overall levels of resistance to commonly used antibiotics were moderate in all pathogens. Amikacin and Nitrofurantoin were generally the antibiotics with lowest rates of resistance. Aminoglycosides and Fluoroquinolones were the most often used antibiotics. In first-line treatment, only 55 % of cases were given at least one antibiotic to which the bacteria were sensitive. A statistically significant higher resistant to both Amoxicillin and Erythromycin were found in cultures from UTI patients ($P = 0.02$ and $P = 0.002$).

Conclusions: Commonly encountered bacteria in this study which are *Staphylococcus*, *Escherichia coli* and *Klebsiella* were found to be highly sensitive to Nitrofurantoin, Amikacin and, to lesser extent, to ciprofloxacin, while low sensitivity pattern was recorded against Amoxicillin and Gentamicin, pointing to that antibacterial misuse is the leading cause for their resistance. The most commonly prescribed antibacterial Trimethoprim.

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Keywords: Urinary tract infection, Duhok city, Antibiotic, Infection.

Urinary tract infection (UTI) remains a worldwide therapeutic problem, not only as a nosocomial disease but also as a community-acquired infection¹. UTI can affect lower and sometime both lower and upper urinary tract the term cystitis has been used to define the lower UTI infection is characterized by symptoms such as dysuria, frequency, urgency, and suprapubic tenderness. The presence of the

lower UTI symptoms does not exclude the upper UTI, which is often present in most UTI cases². The types of UTI is classified into uncomplicated and complicated based on their choice of treatment³. The distribution of antimicrobial susceptibility data of UTI-causing microorganisms changes from time to time and from place to place⁴. The susceptibility data provided by regional microbiology laboratories help

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to choose the empirical choice of antimicrobials to treat UTI; however, these conditions are limited to complicate UTI as the samples of uncomplicated UTI were rarely sent to laboratories^{5,6}. Generally, the antimicrobial treatment is initiated before the laboratory results, which may lead to the frequent misuse of antibiotics⁷. Since most UTIs are treated empirically, the criteria for the selection of antimicrobial agents should be determined based on the most likely pathogen and its predictable resistance pattern in a geographic area. Therefore, there is a need for periodic monitoring of etiologic agents of UTI and the resistance pattern in the community⁸.

MATERIALS AND METHODS

Patients: This study was carried out on urinary tract infection recruited to Central laboratory-in Duhok City, (Kurdistan Region- Iraq). From November 2016 to April 2017. A total of 151 Patients had urinary tract infection were registered in this study.

Study Population: The urine samples of (151) culture positive, who attended the Central laboratory and had clinical evidence of urinary tract infection, determined by treating physicians, were included in this study. The age of patients included in the study ranged from (6-70) years and sex (31 males, 120 females). The patients on antibiotic therapy were excluded from the study.

Sample Collection: Clean catch midstream urine was collected from each patient into a 20mL calibrated sterile screw-capped universal container that was disseminated to the patients. All patients were well instructed on how to collect sample aseptically before sample

collection to avoid contaminations. Stated informed consent was obtained from all patients prior to specimen collection.

Sample Processing: A standardized loop method was used for the isolation of bacterial pathogens from urinary samples. A sterile 4.0mm platinum-wired calibrated loop was used which transported 0.001mL of urine. A loopful urine sample was plated, MacConkey agar, and blood agar medium. The inoculated plates were incubated at 37⁰C for 24 h and 48 h in negative cases. The number of isolated bacterial colonies was multiplied by 1000 for the estimation of bacterial load/mL of the urine sample. A specimen was measured positive for UTI if an organism was cultured at a concentration of $\geq 10^5$ CFU/mL or when an organism was cultured at a concentration of 10^4 CFU/mL and >5 pus cells per high-power field were detected on microscopic examination of the urine .

Identification and isolation of bacteria: Identification of bacterial isolates was done on the basis of their cultural and biochemical features. The standard biochemical tests identified gram-negative bacteria and Gram-positive microorganisms were identified with the corresponding laboratory tests: catalase, coagulase, and mannitol test for *Staphylococcus aureus*.

RESULTS

One hundred and fifty-one patients were included in this study (mean age 29.95, SD ± 11.81). All the studied individuals were (31 males, 120 females), **Table 1**.

A total of 151 bacterial isolate included of 71 (47%) Gram negative and 80 (53%) Gram positive were isolated from positive

urine samples. *Staphylococcus aureus* was found the dominant bacteria among all isolated bacteria with the prevalence rate of (40.4%). The second most prevalent isolate was *Escherichia coli* (31.8%) followed by *Klebsiella pneumonia* (10.6%), *Streptococcus* (9.9%), *Pseudomonas aeruginosa* (4%), *Micrococcus. spp* (1.3%) *Eterococcus. spp.* (1.3%), and *Hemophilus spp.* (0.7%).

Table 1: Distribution of Isolated Bacterial Cause UTI.

Bacterial pathogens	Number of Isolates	(%)
<i>Hemophilus</i>	1	0.7
<i>Enterococcus</i>	2	1.3
<i>Micrococcus</i>	2	1.3
<i>Pseudomonas aeruginosa</i>	6	4
<i>Streptococcus</i>	15	9.9
<i>Klebsiella Pneumonia</i>	16	10.6
<i>E.coli</i>	48	31.8
<i>Staphylococcus aureus</i>	61	40.4
Total	151	100

Antibiotic resistant

Antibiotic susceptibility results presented the resistant and susceptible antibiotics for the tested bacteria pathogen. Overall Amoxicillin was found the most resistant drug as 121 (80.1%) uropathogens were found resistant against Amoxicillin. The second most resistant drug was Erythromycin(70%) followed by Tobramycin(67.5%), Trimethoprim(64.2%), Ceftriaxon(60.9%), Tetracyclin(55.6%). However, the lowest drug resistant against all bacteria was Amikacin(24.5%) followed by Nitrofurantin (35.7%),

Norfloxacin(38.4%) and Gentamycin(39.07%).

Erythromycin was found the highest resistant drug against 77% *Staphylococcus* followed by Amoxicillin(75.4%) and Ceftriaxon(74.5%); however, both Amikacin and Gentamycin showed the highest sensitivity against 73.8% and 65.5% *Staphylococcus*. 83.3% of *E.coli* were resistant against Amoxicillin and Amikacin was found the most susceptible drug with the rate of 79.2%.

In circumstance of *Klebsiella spp* the highest resistant and susceptible antibiotics were Tobramycin(75%), and Ceftriaxon(62.5%). *Streptococcus spp.* were resistant against Norfloxacin and Ceftriaxon(40% and 66.6%) respectively while sensitive against both (Nitrofurantin and Amikacin). *Pseudomonas spp.* showed 85.7% resistance against both Gentamycin and Ceftriaxon, **Table 2.**

Table 2: Resistance of Isolated Bacteria against Tested Antibiotics

Antibiotics	Total resistance	%
Amoxicillin	121	80.1
Tobramycin	102	67.5
Trimethoprim	97	64.2
Ceftriaxon	92	60.9
Tetracyclin	84	55.6
Cephotaxime	71	44.6
Gentamycin	59	39.07
Norfloxacin	58	38.4
Erythromycin	56	37.1
Nitrofurantin	54	35.7
Amikacin	37	24.5

DISCUSSION

UTI Patients among Age and Gender

Antibiotic resistance is a major clinical problem in treating infections caused by bacteria. The resistance to the antimicrobials has increased over the years and normal intestinal microbial flora became a reservoir for resistant genes⁹. This may be due to an inevitable genetic response to the strong selective pressure imposed by antibacterial chemotherapy, which plays a vital role in the evolution of antibiotic resistance among bacteria. These bacteria then pass the plasmid containing resistant gene among other bacterial cells and species¹⁰. In this study, one hundred fifty-one samples were collected from Central lab in Duhok City, samples done by Gram staining and biochemical tests. Throughout the study, regarding the distribution of the patients according to gender, shows the gender group of most the patients with UTI was 79.47% females while for the 20.53% male patients which correlate with other findings which show that the rate of UTI is more in females as compared to males^{11,12,13}. The reason behind this high occurrence of urinary tract infection in females is due to the proximity of the urethra to the anus, shorter urethra, sexual intercourse, incontinence, and bad toilet^{14,15}. These results are associated with other studies showing that females are more likely to have UTIs than males during adolescence and puberty^{16,17,18}.

Bacteria of UTI

In this study, the Gram-positive cocci constituted 53% of the total bacterial isolates while Gram-negative bacilli constituted (47%), *Staphylococcus aureus*(40.4%) was found the most prevalent gram-positive bacteria in the

positive urine samples of UTI. These results agreed with some reports in developing countries¹⁹, while disagreed with others²⁰ who found *E. coli* to be the leading causative microorganism in community acquired urinary tract infection. This result is differs with reports from other studies⁶⁻²¹. Other isolated bacteria from UTI cases in this study were *E. coli* second most frequently isolated organism in UTI then *K. pneumonia* (10.6%), *Streptococcus* spp. (9.9%), *P. aeruginosa*(4%), *Micrococcus* spp.(1.3%), *Enterobacter* spp. (1.3%) and *Hemophilus*spp(0.7%). These findings were correlated with other reports local area find that *Staphylococci* and *Escherichia coli* were the leading cause of UTI proportion for 75% of all isolates. The rates and roles of other pathogens, including *Klebsiella* species (11%), *Enterobacter*, *Proteus*, and *Streptococci* were responsible for the remaining 6%⁶.

Multi Drugs Resistance

Both (Amikacin and Nitrofurantoin) used in this study were found to be the most sensitive drugs against all isolated uropathogens. The sensitivity rate of (Amikacin and Nitrofurantoin) among uropathogens was as follows: *Staphylococcus aureus* (Amikacin 75% and Nitrofurantoin 64.2%), *E. coli* (Amikacin; 80.5% and Nitrofurantoin; 82.9%), *Streptococcus* spp. (Amikacin; 66.6% and Nitrofurantoin; 73.33%) and *Klebsiella* spp. (Amikacin; 75% and Nitrofurantoin; 75%), however, *Pseudomonas* spp. did not show a high susceptibility to Nitrofurantoin; 42.8% but it was susceptible to Amikacin; 85.7%, the *micrococcus* did not show any susceptibility to (Amikacin and

Nitrofurantoin). These antibiotic susceptibility results correlate with another study conducted in Iraq showed that the tested antibacterial Amikacin and Nitrofurantoin were found to be the most effective against *staphylococcuspp*, *E.coli* and *Klebsiellaspp* which are responsible for 86% of all UTI in this study. This may be explained by low rate of prescription of these drugs⁶.

Tested fluoroquinolones in this study showed the moderate resistance among uropathogens as in *S. arueus*; Norfloxacin(58%), but have susceptibility to *P. aeruginosa*; (71.4%), ; however, III generation cephalosporin showed the highest resistance in *S. arueus*; Ceftriaxon(70.5%) and *S. arueus*; Cephotaxime(60%). This rise rate of resistance against fluoroquinolones was also proposed by other studies done in Spain and Iran²³⁻²⁷ and also by other studies done in India¹⁸.

Another study in Spain also showed a reduced susceptibility of *E. coli* isolates from UTI patients to fluoroquinolones (16%)²³. This low susceptibility due to the use of antibiotics may be unrestricted. In many studies, it has been shown that the guiding habits of physicians are of antibiotic resistance to this group of antibiotics²⁴⁻²⁵. For these organisms, drugs with inhibitors like Augmentin may be tried but such drugs should be reserved for the last line of treatment. The alarming result in this study is the resistance to third-generation cephalosporin; the highest resistance was seen against Ceftriaxon(71.61%) followed by Cephotaxime(67.74%) among all bacteria's. The possible explanation behind this situation is that the third-

generation cephalosporin has been in use for a long period and must have been abused and over time, organisms have developed resistant mechanisms due to changing their mode of action²⁶.

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ثوخته

گه لهک ده‌رمانین ب به‌رخودانی دناف نه‌خوشین توشی هه وه کردنی کوئه‌ندامین میزه رو ل باژی‌ری دهوکی ل کوردستانی عیراق

نیشه‌کی و نارمانج: هه‌وه‌کردنی کوئه‌ندمین میزه‌رو ئیک ل زورترین نیشین هه‌وه‌کردنی یه و پلا دووی دهیت ل نه‌گه‌رین بکارئینانا نه‌نتیبا‌یوتیک. باشت‌ترین چاره‌سه‌رو دی نساغی و مرنی دی کیم کات و روله‌کی سه‌رکی دی هه‌بیت دژی دروستیونی به‌رخودانی به‌کت‌ریا دژی نه‌نتیبا‌یوتیکا. نارمانجا فی فه‌کولینی بو ده‌ست‌نیشان‌کرنا جورین به‌کت‌ریا و جورین نه‌نتیبا‌یوتیکا ل نمونین میزی .

ریکین‌ظه‌کولینی: 150 نمونین میزی هاتینه کومکرن ل نه‌خوشین سه‌ردانا نا‌قیگه‌ها مه‌لبه‌ندی ل باژی‌ری دهوکی کرینه. هه‌می نموونه هاتینه پشکین ب ریکا بکارئینانا بویاغین گرام و اندول، اوکسیدوز، کته‌لیز، میتایل رید، بکارئینانا ست‌ریت، یوریا . پشکین هاتینه کرن بو جورین نه‌نتیبا‌یوتکا کارده‌کهن له‌سه‌ر به‌کت‌رین هاتینه دیتین.

نه‌نجام: به‌کت‌ریا ستا‌فیلوکوکاس اوریس ل 40.4% و ئی کولای ل 31.8% نمونین میزی نه‌خوشا هاتیه دیتین. به‌رخودان دژی نه‌میکاسین و نای‌تروفیورانتوین ل کیمترین ری‌زا بو. زورترین نه‌نتیبا‌یوتیک هاتیه بکارئینان ل جورین امینو‌گلا‌یکوساید و فلوروکوبینولون. به‌ردخودان دژی اموکسیسلین و اترومایسین ب ری‌زا زوور هاتیه ده‌ست نیشان کرن. **ده‌رته‌نه‌نجام:** زورترین به‌کت‌ریا هاتیه ده‌ست نیشان کرن ستا‌فیلوکوکاس، ئی کولای، کلیرزا و نه‌نتیبا‌یوتیکین کارده‌کات ب پلا ئیکی نای‌تروفیورانتوین و نه‌میکاسین و پلا دووی سپروفلوکساسین، ل پلا دیماهی نه‌نتیبا‌یوتیکا کو‌گه‌له‌گ ده‌ینه بکارئینان بو چاره‌سه‌ریا هه‌وه‌کردنی وه‌کو نالیدیسیک اسید، اموکسیسلین، بک‌تریم و جنتاماسین. بکارئینانا نه‌نتیبا‌یوتیک ب شیوه‌کی هه‌له نه‌گه‌رین سه‌ره‌کی یا دروستیونا به‌رخودانی یه.

الخلاصة

المضادات الحيوية المتعددة مقاومة لدى بين مرضى التهاب مسالك البولية في مدينة دهوك / كردستان - العراق.

الخلفية والأهداف: يمكن أن تكون مقاومة المضادات البكتيرية مشكلة رئيسية في مجال الصحة العامة في جميع أنحاء العالم ، كما أن هناك حاجة إلى مساعٍ عالمية للتصدي لظهورها وسبب ظهور الأكثر شيوعًا المضادات الحيوية. أفضل علاج يمكن أن يقلل من الوفيات والمرضاة يلعب دورا حيويًا في مكافحة الزيادة المستمرة لمقاومة المضادات الحيوية.

المواضيع و طرق البحث: دراسة مسببات التهاب مسالك البولية وحساسيتها لمضادات الحيوية لمرضى في مختبر الصحة المركزي في مدينة دهوك ودراسة العلاج بالمضادات الحيوية. تم جمع 151 عينة البول من المختبر المركزي. تم تحديد البكتيريا والمعزولها عن طريق الاختبارات الكيميائية الحيوية مثل صبغة غرام ، الإندول ، أوكسيديز ، الكاتالاز ، الأحمر الميثيل ، فوجس-بروسكاور ، استخدام سترات ، انحلال الدم ، الحركة. واليوريا اختبارات التخمر والاستفادة من الجلوكوز واللاكتوز والسكرورز. تم تحديد نمط حساسية من العزلات ضد بعض المضادات الحيوية التقليدية والتجارية .

النتائج: كانت *Staphylococcus aureus* الأكثر شيوعًا (40.4%) تليها *E.coli* (31.8%). كانت معدلات المقاومة لمضادات الحيوية شائعة متوسطة في جميع مسببات الأمراض. كان المضادات الحيوية Amikacin و Nitrofurantoin أقل معدلات المقاومة. كانت Aminoglycosides و Fluoroquinolones أكثر المضادات الحيوية المستخدمة. في علاج الخط الأول ، تم إعطاء 55% فقط من الحالات فيه حساسة من مضادات الحيوية لبكتيريا. ووجدت عن طريق علاقة إحصائية بأنه Amoxicillin و Erythromycin لها أعلى مستويات المقاومة من قبل البكتيريا المسببة التهابات المسالك البولية ($P = 0.02$ و $P = 0.002$).

الاستنتاجات: وجد أن البكتيريا الشائعة في هذه الدراسة هي *Escherichia coli*، *Staphylococcus* و *Klebsiella* شديدة الحساسية Amikacin ، Nitrofurantoin ، وإلى حد أقل ل Ciprofloxacin ، في حين تم كانت نسبة الحساسية ل Amoxicillin و Gentamicin ، مما يشير إلى هذه مضادات البكتيرية لها سوء الاستخدام هو السبب الرئيسي ظهور مقاومة . الأكثر شيوعًا وصفه مضاد للجراثيم Trimethoprim.