

## **Antibiotic sensitivity patterns of uropathogens isolated from females with urinary symptoms in Karbala**

انماط مقاومة المضادات الحيوية من قبل الجراثيم البولية المعزولة من مريضات الجهاز البولي في كربلاء

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### **Abstract**

Urinary tract infection is a common community-acquired bacterial disease which frequently affects female outpatients. *Escherichia coli* is the most common member of the family Enterobacteriaceae accounts for majority of all urinary tract infections in both inpatients and outpatients. Increasing rates of resistance among bacterial uropathogens has caused growing concern in both developed and developing countries, so that the objectives of this study are identifying the most frequent etiological agents of (U.T.I) in females and to determine their antibiotics sensitivity patterns. A total of (470) adult females were enrolled in this study. Middle stream urine samples were collected and cultured according to standard methods. The positive cultures (140) were tested for antibiotics sensitivity by using Kirby-Bauer's disk diffusion method. The predominant uropathogen was *Escherichia coli* 62 (44.4%), followed by *Pseudomonas aeruginosa* 28 (20%), *Salmonella* species 18 (12.8%), *Klebsiella pneumonia* 16 (11.4 %), *Shigella* species 12 (8.6%), and *Serratia* species 4 (2.8%). We found that 76% of *Escherichia coli* isolates were sensitive to Ciprofloxacin, (41%) for Trimethoprim, 41% for Nalidixic acid, 8% for Carbencillin, 57% for Nitrofurantoin, 27% for Cefotaxime, 0% for Ampicillin, 3% for Oxacillin, 42% for Trimethoprim- sulfamethoxazole, 54% for Gentamicin. While 59% of *Pseudomonas aeruginosa* isolates were sensitive to Ciprofloxacin, 30% for Trimethoprim, 46% for Nalidixic acid, 16% for Carbencillin, 47% for Nitrofurantoin, 15% for Cefotaxime, 8% for Ampicillin, 33% for Trimethoprim- sulfamethoxazole, 57% for Gentamicin. All *pseudomonas* isolates were resistance for Oxacillin. In addition, 88% of *Salmonella* species were sensitive to Ciprofloxacin, 22% for Trimethoprim, 66% for Nalidixic acid, 11% for Nitrofurantoin, 22% for Oxacillin, 44% for Trimethoprim- sulfamethoxazole, 88% for Gentamicin. All *salmonella* isolates were resistant to Carbencillin, Cefotaxime and Ampicillin. Also, 100% of *Klebsiella pneumonia* were sensitive to Ciprofloxacin, 42% for Trimethoprim, 71% for Nalidixic acid, 20% for Carbencillin, 37% for Nitrofurantoin, 30% for Cefotaxime, 25% for Ampicillin, 13% for Oxacillin, 75% for Trimethoprim- sulfamethoxazole, 100% for Gentamicin. As well as 20% of *Shigella* species were sensitive to Ciprofloxacin, as well as (20%, 16%, 23%, 50%) were sensitive for Trimethoprim- sulfamethoxazole, Nalidixic acid, Carbenicillin, Nitrofurantoin, but they were completely resistance for Cefotaxime, Ampicillin, Oxacillin, Gentamicin and Trimethoprim. And 100% were sensitive for Nitrofurantoin. In addition 50% of *Serratia* species isolates were sensitive to Ciprofloxacin, Trimethoprim, Trimethoprim- sulfamethoxazole, Gentamicin, Cefotaxime and Nalidixic acid, while 100% were resistant to Carbenicillin, Ampicillin, and Oxacillin.

### **المستخلص**

التهاب المسالك البولية هو من الامراض البكتيرية الشائعة في المجتمع و الذي غالبا ما يصيب النساء. و تعد الاشيريشيا القولونية اكثر مسببات عائلة الجراثيم المعوية شيوعا لاصابات القناة البولية في كل من المريضات الراقدا و كذلك المراجعات للمستشفيات. و ان ارتفاع معدلات المقاومة للمضادات الحيوية من قبل المسببات الجرثومية لاصابات الجهاز البولي لها اهمية متنامية في كل من البلدان المتطورة و بلدان العالم الثالث, لذا تهدف الدراسة الحالية الى تمييز اكثر مسببات التهاب الجهاز البولي عند النساء و تعيين انماط حساسية هذه المسببات للمضادات الحيوية. تضمنت الدراسة (474) مريضة حيث جمعت نماذج الادراج من منتصف الجريان للبول و زرعت العينات هوائيا حسب الطرق النموذجية, حيث كان هناك (140) عينة موجبة بالزرع الجرثومي والتي تم اختبار مدى حساسيتها للمضادات الحيوية حسب طريقة (كيريبي) – باور للانتشار حول

القرص). و اظهرت الدراسة ان اكثر المسببات الجرثومية لاصابات الجهاز البولي هي الاشريشيا القولونية بمقدار 62 عزلة اي بنسبة (44.4%) تلتها جرثومة الزوائف الزنجارية بمقدار 28 عزلة بنسبة (20%) ثم جرثومة السالمونلا 18 عزلة بنسبة (12.8%) ثم جرثومة الكلبسيلا 16 عزلة بنسبة (11.4%) ثم جرثومة الشيكلا 12 عزلة بنسبة (8.6%) وجرثومة سيرريشيا 4 عزلات بنسبة (2.8%). كما وجد ان (76%) من عزلات الاشريشيا القولونية حساسة للمضاد الحيوي السبروفلوكساسين و (41%) منها حساسة للتراي ميثوبريم و (41%) حساسة للنالديكسك اسيد و (8%) حساسة للكاربنيسيلين و (57%) حساسة للنايتروفيورانتوين و (27%) حساسة للسيفوتاكزيم و (3%) حساسة للاوكساسيلين و (42%) حساسة للتراي ميثوبريم-سلفاميثوكسازول و (54%) حساسة للجنتاميسين في حين ان جميع عزلات الاشريشيا القولونية مقاومة للمضاد الحيوي الامبيسيلين . كما وجد ان (59%) من عزلات الزوائف الزنجارية حساسة للمضاد الحيوي السبروفلوكساسين وان (30%) منها حساسة للمضاد الحيوي تري اميثوبريم و (46%) حساسة للنالديكسك اسيد و (16%) حساسة للكاربنيسيلين و (47%) حساسة للنايتروفيورانتوين و (15%) حساسة للسيفوتاكزيم و (8%) حساسة للامبيسيلين و (33%) حساسة للمضاد الحيوي تري اميثوبريم-سلفاميثوكسازول و (57%) حساسة للمضاد الحيوي الجنتاميسين وجميع عزلاتها كانت مقاومة للمضاد الحيوي الاوكساسيلين . كما لوحظ ان (88%) من عزلات المسبب المرضي السالمونلا هي حساسة للسبروفلوكساسين و ان (22%) منها حساس للتراي ميثوبريم وان (66%) حساسة للنالديكسك اسيد و (11%) حساسة للنايتروفيورانتوين و (22%) حساسة للاوكساسيلين و (44%) حساسة للتراي ميثوبريم-سلفاميثوكسازول و (88%) حساسة للجنتاميسين . وكانت جميع عزلات السالمونلا مقاومة بشكل مطلق لكل من المضادات الحيوية الكاربينيسيلين و السيفوتاكزيم و الامبيسيلين . و لوحظ ان جميع عزلات جرثومة الكلبسيلا هي حساسة للمضادات السبروفلوكساسين و الجنتاميسين و ان (42%) حساسة للتراي ميثوبريم و (71%) حساسة للنالديكسك اسيد و (20%) حساسة للكاربنيسيلين و (37%) حساسة للنايتروفيورانتوين و (30%) حساسة للسيفوتاكزيم و (25%) حساسة للامبيسيلين و (13%) حساسة للاوكساسيلين و (75%) حساسة للمضاد الحيوي تري اميثوبريم-سلفاميثوكسازول. كما لوحظ ان (20%) من عزلات جرثومة الشيكلا كانت حساسة للسبروفلوكساسين و (16%) حساسة للنالديكسك اسيد و (23%) حساسة للكاربنيسيلين و (50%) حساسة للنايتروفيورانتوين و (20%) حساسة للتراي ميثوبريم-سلفاميثوكسازول و كانت جميع عزلات جرثومة الشيكلا مقاومة لكل من التراي ميثوبريم و السيفوتاكزيم و الامبيسيلين و الاوكساسيلين و الجنتاميسين . وكانت جميع عزلات السيرريشيا حساسة للنايتروفيورانتوين و (50%) حساسة لكل من السبروفلوكساسين و التراي ميثوبريم و التراي ميثوبريم-سلفاميثوكسازول و الجنتاميسين و السيفوتاكزيم و النالديكسك اسيد بينما كانت جميع العزلات الباقية مقاومة لكل من الكاربينيسيلين و الامبيسيلين و الاوكساسيلين

## **Introduction**

Despite the widespread and availability of antibiotics, urinary tract infection (UTI) remains the most Common bacterial infection in the human populations. (1) Antibiotics are usually given empirically before the laboratory results of urine cultures are available. To ensure appropriate therapy, current knowledge of the organisms that cause UTI and their antibiotic susceptibility is mandatory.(2)

Incidence of UTI is higher in women, and ( 20.0-50.0% ) of whom usually suffer a clinical episode during their lifetime.(3) Bacteriuria occurs in ( 2.0-7.0% ) of pregnant women; of those who are not have bacteria in their urine at initial screening,(1.0-2.0%) will develop bacteriuria later in the pregnancy(5,6 )

Much of the data is available for community acquired infections. This may be different from that of hospital acquired infections. Since patterns of antibiotic resistance in a wide variety of pathogenic organisms may vary even over short periods and depend on site of isolation and on different environments, periodic evaluation of antibacterial activity is needed to update this information(7,8 )

For appropriate treatment of UTIs, it is essential to isolate the infectious agents from the patient and then determine the sensitivity or the resistance to antimicrobial agents used in therapy. The choice of antibiotics for treatment of UTIs should be, therefore, based on antibiotic susceptibility data. Hence, the present study was conducted to determine the antibiotic susceptibility patterns of the organisms isolated from female patients with UTIs attending Karbala hospital for Obstetrics and Gynecology.

## **Materials and methods**

This study was carried out in Karbala hospital of Obstetric and Gynecology to determine the antibiotic sensitivity patterns of the uropathogens isolated from inpatient and out patient suffering of urinary symptoms, with (18-50) years old.

### **Samples collection**

A total of (474) mid-stream urine samples (in a sterile wide mouth container) were collected during the period of (July - October) 2008. Urine samples were collected before the start of antibiotics therapy.

### **Diagnosis**

All the urine samples were tested within one hour or less after the collection for aerobic bacterial culture. A standard loop technique was used to place 0.03 ml of urine on Blood, MacConkey and E.M.B agar media (Himedia laboratories pvt. ltd.india). Plates were incubated at 37° C for 18 to 24 hours. The number of viable bacterial colonies were counted by semi-quantitative method.(9) Organisms were identified by doing standard biochemical tests(Api 20 E ,Biomerox, France ).(10)

### **Sensitivity testing**

Antibiotic susceptibility testing was done according to Kirby-Bauer's disc diffusion method for all the isolates.(9) The antibiotics used were ( Ciprofloxacin , Trimethoprim , Nalidixic acid , Carbenicillin , Nitrofurantoin , Cefotaxime, Ampicillin , Oxacillin, Trimethoprim – sulfamethoxazole and Gentamicin) ( Bioanalyse susceptibility discs, Turkey ) containing standard concentrations mentioned in table 1. (4 , 18 ) . Sensitivity, resistance and intermediacy were calculated and analyzed statistically and expressed with percentages (table 3).

Table (1): standard antibiotics concentrations and there inhibition zones diameter (mm).

<b>Antibiotic</b>	<b>symbol</b>	<b>Concentration</b>	<b>Resistant</b>	<b>Intermediate</b>	<b>Susceptible</b>
Ciprofloxacin	CIP	5 mcg	≤15	16-20	≥21
Gentamicin	CN	10 mcg	≤12	13-14	≥15
Nitrofurantoin	F	300 mcg	≤14	15-16	≥17
Nalidixic acid	NA	30mcg	≤13	14-18	≥19
Trimethoprim- Sulphamethoxazol	SXT	1.25 mcg/ 23.75mcg	≤10	11-15	≥16
Trimethoprim	TMP	5 mcg	≤10	11-15	≥16
Cephotoxim	CTX	30 mcg	≤14	15-22	≥23
Carbenicillin/ Enterobacteriaceae	PY	100 mcg	≤17	18-22	≥23
Carbenicillin/ Pseudomonas	PY	100 mcg	≤13	14-16	≥17
Oxacillin	OX	1 mcg	≤13	-	≥15
Ampicillin	AM	10 mcg	≤11	12-13	≥14

## **Results and discussion**

The current study describes the most common bacterial uropathogens of UTI in females in Karbala and the antibiotics susceptibility patterns. Enterobacteriaceae were isolated at the rate of (80%) and *E. coli* (44.4%) from total number of isolates (Table 2), and this corresponds with the data obtained by other countries (11, 12,13,14,16).followed by *Pseudomonas aeruginosa* (20%) and that corresponds (16).

The guidelines of the infectious disease society of America (IDSA) published in 1999 for treatment of UTI don't prescribe specific antibiotic for the empirical treatment when the local level of resistance among *E. coli* strains exceeds (20%).The (IDSA) also emphasizes that physicians should obtain information about local resistance rates(6).Also

in this study the overall prevalence of Trimethoprim –sulfamethoxazole sensitivity was (44%) while in other studies the sensitivity was (13.6%) and (8.8%) in (16, 17) respectively. and for *E. coli* isolates the rate was (42%), this results corresponds (15), the low sensitivity for Trimethoprim – sulfamethoxazole suggest that it would not provide adequate initial therapy and alternative therapies may be used as empirical choice in Karbala city population.

The current study demonstrated that Ciprofloxacin was more active than Trimethoprim - sulfamethoxazole against all uropathogens (65%) and *E.coli* with (76%) sensitivity respectively (Table 3).However resistance rates are relatively high compared to other countries (65% and 76%) ;data reported in non Asian countries indicted that Ciprofloxacin is effective in community UTIs and the rates of resistance is less than (5%) (11, 12, 13).

According to current study the most effective drug tested on the UTI isolates was Ciprofloxacin (65.5%) and this result corresponds (12,16); Although this rate is not considered a high rate of susceptibility in general, The *E.coli* sensitivity is lower than other studies in U.S. (65% - 83.2 %) respectively (12).

Ciprofloxacin have frequently been a reliable therapeutic intervention in UTIs because of it's broad spectrum activity as well as strong action on gram-negatives. However it is advocated that they should be used as a last line (not a first line Antibiotic) due to its serious side effects profile especially younger patients and it's cost (18).

According to the results of this study uropathogens sensitivity to Gentamicin was (58.1%) this result considered low to be used as empirical therapy, and corresponds results of (17) and differ from (16).

Nitrofurantoin sensitivity was (50.3%) this corresponds (16) and lower than the survey result of (16) were it was (75.2%).

Cefotaxime sensitivity was (20.3%) and this result is lower than in (16) were it was (54%).

Nalidixic acid sensitivity result was (48.3%) in contrast to (17) and (16) were their sensitivity are (34.2%) and (12%) respectively.

The activity of (Ampicillin, Oxacillin , Carbencillin) against uropathogen isolates from adult female outpatients attending Karbala hospital of Obstetric and Gynecology is so limited sensitivity (5.5% ,6.3%,11.1%) respectively .while the result of Ampicillin sensitivity in other study was (13%) (16), however both results are too low sensitivity pattern and indicates low activity of this antibiotic in treatment of UTIs in several countries recently.

In addition the high prevalent resistance to both Trimethoprim –sulfamethoxazole and Ampicillin suggest that they would not provide adequate initial therapy for UTI among female outpatients; therapies other than Trimethoprim- sulfamethoxazole may need to be considered in Karbala city.

Furthermore with the relatively high rate of resistance to Ciprofloxacin which represent (35.5%) in contrast to studies applied on areas of Canada, U.S., Poland (11,12,14).on going surveillance to identify changes among urinary tract isolates would be required.

Table 2: The number and percentage of uropathogens isolated from urine samples.

Uropathogen		Number	Percentage
Enterobacteriaceae	<i>Escherichia coli</i>	62	44.4%
	<i>Salmonella</i>	18	12.8%
	<i>Klebsiella pneumonia</i>	16	11.4%
	<i>Shigella species</i>	12	8.6%
	<i>Serratia species</i>	4	2.8%
Non Enterobacteriaceae	<i>Pseudomonas aeruginosa</i>	28	20%
Total		140	100%

Table 3: Antibiotics sensitivity patterns for uropathogen isolates From female patients

Uropathogen	Susceptibility %	CIP	CN	F	NA	SXT	TMP	CTX	PY	OX	AM
<i>Escherichia coli</i>	Sensitive	76	54	57	41	42	41	27	8	3	0
	Intermediate resistance	0	0	13	14	5	0	10	0	0	6
	Resistant	24	46	30	45	53	59	63	92	97	94
<i>Pseudomonas Aeruginosa</i>	Sensitive	59	57	47	46	33	30	15	16	0	8
	Intermediate resistance	0	0	15	8	17	10	15	0	0	0
	Resistant	41	43	38	46	50	60	70	84	100	92
<i>Salmonella species</i>	Sensitive	88	88	11	66	44	22	0	0	22	0
	Intermediate resistance	0	0	11	11	0	0	55	0	0	0
	Resistant	12	12	78	23	56	78	45	100	78	100
<i>Klebsiella pneumonia</i>	Sensitive	100	100	37	71	75	42	30	20	13	25
	Intermediate resistance	0	0	13	0	0	16	28	0	0	0
	Resistant	0	0	50	29	25	42	42	80	87	75
<i>Shigella species</i>	Sensitive	20	0	50	16	20	0	0	23	0	0
	Intermediate resistance	0	0	0	0	20	0	0	0	0	16
	Resistant	80	100	50	84	60	100	100	77	100	84
<i>Serratia species</i>	Sensitive	50	50	100	50	50	50	50	0	0	0
	Intermediate resistance	0	0	0	0	50	50	0	0	0	0
	Resistant	50	50	0	50	0	0	50	100	100	100
Sensitive Mean		65.5	58.1	50.3	48.3	44	30.8	20.3	11.1	6.3	5.5

CIP= Ciprofloxacin , CN = Gentamicin , F = Nitrofurantoin , NA = Nalidixic acid , SXT = trimethoprim – sulfamethoxazole , TMP= Trimethoprim , CTX = Cefotaxime , PY = Carbenicillin , AM = Ampicillin , OX = Oxacillin .

In conclusion the major uropathogens in adult female attending of Karbala Hospital of obstetrics and Gynecology were *Escherichia coli* followed by *Pseudomonas aeruginosa* the remaining were minors represents members of Enterobacteriaceae.

The most effective antibiotic against uropathogens in vitro were Ciprofloxacin followed by Gentamicin, Nitrofurantoin, Nalidixic acid, and co-trimoxazol.

Several members of the studied uropathogen isolates showed multi drug resistance while no isolate was found to be sensitive to all antibiotics under investigation. The high prevalence of resistance among uropathogens argues on going surveillance to ensure the provision of effective empirical therapy of urinary tract infection.

Due to high multi drug resistance rates for all antibiotics it is highly recommended to perform urinalysis and antibiotic susceptibility testing in all patients.

The present study data gives an idea about the common uropathogens and trend of increased antibiotics resistance for uropathogens in this region, which may be due to geographic environmental variation or indiscriminate or sub lethal use of antibiotic. The data will help the clinicians to give proper treatment and prescription of most sensitive antibiotic to the patients and avoid use of resistant antibiotics.

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