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Evaluate Antimicrobial Agents to Treatment of Urine Tract Infection Caused by *E. coli* and ESBL-Producing *E. coli.*

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تأثير المضادات الميكروبية في علاج التهاب المسالك البولية الناتج عن بكتيريا *E. coli.* وبكتيريا *E. coli.* المنتجة للجين ESBL

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Abstract

Escherichia coli is the most common pathogen of bacterial infections worldwide. As many as 80% of urinary tract infections are caused by *E. coli*. Infections caused by *extended-spectrum β-lactamase* (ESBL)–producing gram-negative bacteria are occurring more frequently in hospitalized patients. These organisms can cause a variety of infections including, but not limited to, pneumonia, urinary tract infections, and bacteremia. Carbapenems are considered the drugs of choice for ESBL-producing bacteria.

Retrospective study of patients with ESBL-producing *E. coli*. were taken retrospectively from Phoenix 100. The result shows that the percentage of ESBL-produced *E. coli* was 27.5% from total *E. coli* isolation. None of the 59 isolates (*E. coli* with no resistant marker and ESBL-producing *E. coli*) show resistance to ertapenem, meropenem, or promising made them promising as a therapy for ESBL-producing *E. coli.* The result shows also a high rate of resistance to quinolons (Ciprofloxacine, Cephalothin, Cefrazidime, Levofoxacin) in ESBL-producing *E. coli with* a resistance rate of >60% (Table1), must be ruled out as a therapy option for the treatment of UTIs caused by ESBL- producing organisms.

Keywords: *UTI, ESBL-producing, E. coli.*

الملخص

بكتيريا *E. coli* هي البكتيريا المسببة للأمراض البكتيرية المعدية الأكثر شيوعا في جميع أنحاء العالم. وهي سبب ما لا يقل عن 80٪ من التهابات المسالك البولية. الالتهابات تحدث بواسطة البكتيريا السالبة لجرام الحاملة للجين المقاوم *Extended-Spectrum β-Lactamase* (ESBL) وهي تنتشر أكثر في مرضى المستشفيات، ويمكن لهذه الكائنات أن تسبب مجموعة متنوعة من الأمراض بما في ذلك، على سبيل المثال لا الحصر، الالتهاب الرئوي، والتهابات المسالك البولية وتسمم الدم.

في هذه الدراسة للمرضى الذين يعانون من التهاب المسالك البولية الناجمة عن الإصابة *E. coli* التي لا تحمل العوامل المقاومة والبكتيريا التي تحمل عوامل المقاومة (ESBL). أخذت من مستشفى زليتن التعليمي لسنة 2013 من جهاز Phoenix-100. أظهرت النتائج أن نسبة البكتيريا E. *coli* الحاملة للجين المقاوم من النوع (ESBL) تمثل 27.5٪ من إجمالي العزلات.

لم تظهر اي واحدة من 59 من العينات المعزولة (*E. coli*) التي لا تحمل العوامل المقاومة والبكتيريا التي تحمل عوامل المقاومة (ESBL) مقاومة

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للمضادات الحيوية من مجموعة Carbapenems (Ertapenem, Meropenem and Imipenem) مما جعل منها علاج واعداً لالتهابات المسالك البولية الناتجة عن الاصابة بالبكتيريا *E. coli* الحاملة للجين (ESBL). وعلى العكس فقد اظهرت النتائج نسبة عالية من المقاومة للمضادات الحيوية من مجموعة Quinolons (Ciprofloxacine, Cephalothin, Cefrazidime, Levofoxacin) ، في حالات الاصابة ببكتيريا *E. coli* الحاملة للجين المقاوم (ESBL) بمعدل مقاومة > 60٪، ولذا ينصح باستبعادها كخيار لمعالجة حالات الاصابة التي تسببها البكتيريا التي تحمل عوامل المقاومة (ESBL).

الكلمات الدلالية: بكتيريا، *E. coli*، عوامل المقاومة، مضادات حيوية.

1. Introduction

Escherichia coli is the most common pathogen of bacterial infections worldwide. As many as 80% of urinary tract infections are caused by *E. coli.* In 1980, resistance to third class cephalosporines was found for the first time in *Enterobacteriaceae* showing no chromosomal-coded AmpC overexpression. This newly detected plasmid-encoded resistance was selected by the frequent use of cephalosporines. These bacterial enzymes have been named *Extended-Spectrum-Beta-Lactamases* (ESBL) due to their capacity to inactivate practically all cephalosporines (Alhambra et al., 2004). ESBL-producing phenotypes of the family of *Enterobacteriaceae* were primarily considered as multiresistant organisms originating in hospitals. In the recent years, an increase of such ESBL- producers has been observed in outpatient settings, especially related to urinary tract infections (UTI), reducing the treatment options to a limited number of antibiotics (Bradford, 2001; Chaudhary & Aggarwal, 2004; Livermore et al., 2007; Paterson, 2006; and Turner, 2005). Of special concern are associated coresistances to other classes of antimicrobials which aid the spreading of multiresistant isolates (Morosini, 2006). *ß- lactamases* producing *Enterobacteriaceae*, which are commonly found in outpatients and isolated from UTIs, are typically also resistant to quinolones, aminoglycosides and sulfonamides such as ciprofloxacine, gentamicin and trimethoprim/sulfamethoxazole, respectively (Machado *et al*., 2006; and Perez *et al*., 2007).

2. Materials and Methods

Susceptibility results for Amikacin, Cefepime, cefuroxime, Gentamicin, Nitrofurantion, Ceftrazidime, Imipenem, Ampicillin, Ceftriaxone, Ciprofloxacin, Levofloxacin, Septrin, Amoxicillin-cavulanate, Cephalothin, Ertapenem, meropenem were taken retrospectively from phoenix 100 ID/AST system (Becton Dickinson Co., Sparks, MD) that employed software version 3.22G.

3. Statistic Method

Data were analyzed using SPSS software, version 20. Fisher exact test was used. Significance was set at $P<0.05$ using two-sided comparisons.

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4. Results and Discussion

E. coli isolates were collected consecutively (2013) from Zliten teaching hospital. Many specimens were submitted by inpatient Zliten teaching hospitals 192 patients recorded as UTI. In our study we focused just for *E. coli* with no resistant marker and ESBL-producing *E. coli*. The result shows that percentage of ESBL produsedd *E. coli* was 27.5% from total *E.coli* isolation. Limited information was available concerning patients' previous treatment with antibiotics, Patients' ages ranged from 2 months to 90 years, 75% UTI infection from female and 25% from male patients.

None of the 59 isolates of (*E. coli* with no resistant marker and ESBL-producing *E. coli*) tested against ertapenem, meropenem and Imipenem exhibited resistance to these antimicrobial agents with no different between the two *E. coli* strains (Figure 1-2) with *p* value more than 1. The data of Table (1) are congruent with data from (Mody *et al*., 2007; Tamayo *et al*., 2007; and Alhambra *et al*., 2004). They reported no resistance of ESBL-producing *E. coli* to ertapenem (Alhambra et al., 2004; Mody et al., 2007; and Tamayo et al, 2007). The option of using ertapenem once- a-day makes it a useful parenteral antimicrobial agent for the treatment of serious infections of the urinary tract in nursing homes and outpatient healthcare settings (Paterson & Bonomo, 2005). Carbapenems (imipenem and meropenem) are currently considered to be the treatment of choice for serious infections caused by ESBL-producing bacteria (Shah *et al*., 2008).

Results of Levofoxacin susceptibility rate was 87.5% and 12.5% resistant in *E. coli* with no resistant marker with reduced susceptibility in ESBL-producing *E. coli* susceptibility rate 25% and 75% resistant (Table 1), make it not good choice to treat UTI.

Nitrofurantoin is a bactericidal drug. It is reduced by bacterial flavoproteins to reactive intermediates which inactivate or alter bacterial ribosomal proteins and other macromolecules. A 7-day twice-daily administration of 100 *mg* is recommended (FDA, 2015).

Nitrofurantoin exhibited in *E. coli* with no resistant marker 93.8% susceptibility and 6.2% were resistant in front of 75% susceptibillity and 25% resistant in case of ESBL-producing *E. coli* (Figure 1 and 2).

Table 1. Sensitivity and resistant rate of *E.coli* with no resistant marker

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and *E.coli* strain with ESBL resistant marker

No.	Antibiotic type	E.coli -ESBL producing		E.coli- with no ESBL		P. Value
		Resistant	Sensitive	Resistant	Sensitive	
1	Amikacin	12.5	87.5	6.2	93.8	0.5
2	Cefepime	43.8	56.2	25	75	0.229
3	cefuroxime	62.5	37.5	31.2	68.8	0.078
4	Gentamicin	50	50	12.5	87.5	0.027
5	Nitrofurantion	25	75	6.2	93.8	0.166
6	Ceftrazidime	100	0.0	25	75	0.00
7	Imipenem	0	100	0	100	> 1
8	Ampicillin	100	0	87.5	12.5	0.242
9	Ceftriaxone	100	0	18.8	81.2	0.00
10	Ciprofloxacin	62	37	25	75	0.037
11	Levofloxacin	75	25	12.5	87.5	0.00
12	Septrin	43.8	56.2	37.5	62.5	0.5
13	Amoxicillin-cavulanate	100	0	31.2	68.8	0.00
14	Cephalothin	100	0	25	75	0.00
15	Ertapenem	0	100	0	100	> 1
16	meropenem	0	100	0	100	> 1

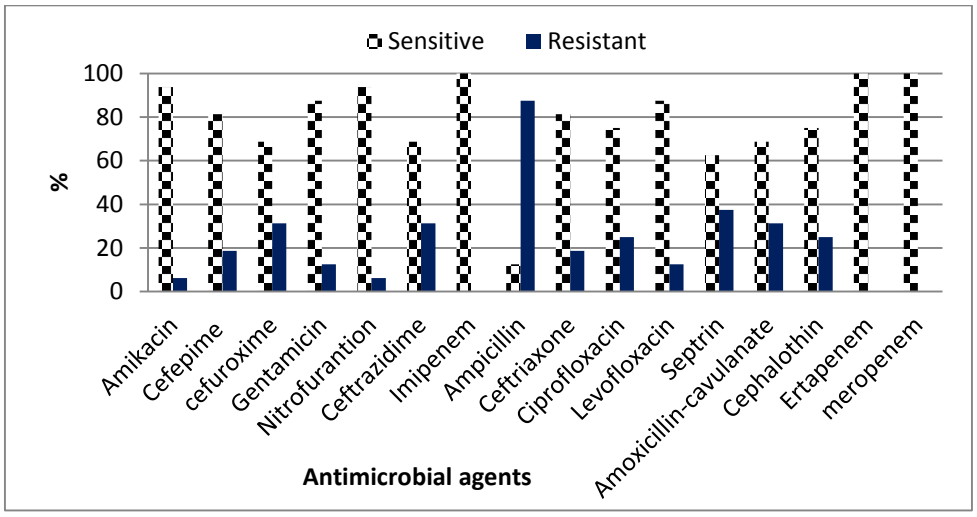

Figure 1. Sensitive and resistant of *E.coli* strains with no ESBL resistant marker against antimicrobial agents.

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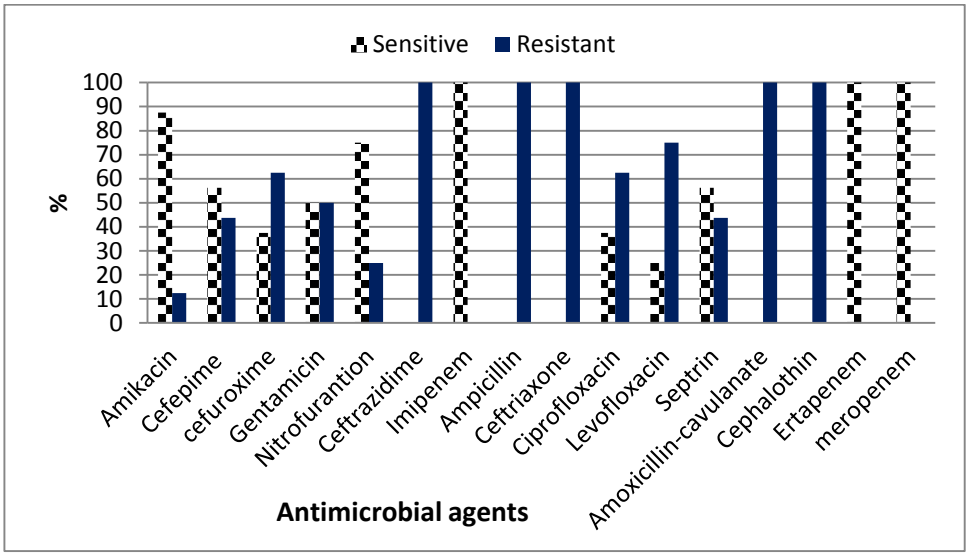

Figure 2. Sensitive and resistant of *E.coli* strains with ESBL resistant marker against antimicrobial agents.

Nitrofurantoin comparable to the 94,9% susceptible *E. coli* isolated from 240 recurrent UTIs in the ARESC study 2009 (Schito *et al*., 2009).

The study of further resistances by means of the evaluation of antibiograms revealed a susceptibility rate of 50% for gentamycine in both *two E. coli* strains as presented in Table (1). The results show a high rate of resistance to quinolons (Ciprofloxacine, Cephalothin, Cefrazidime, Levofoxacin) in ESBL-producing *E. coli.*, a resistance rate >60% (Figure 1 and 2), must be ruled out as a therapy option for the treatment of UTIs caused by ESBL-producing organisms. Schwaber *et al*. (2005), examined 70 ESBL-expressing *E. coli* and detected >80% resistance to the agents mentioned above. Also the administration of Ampiniilin and Amoxicilin-cavulante with a resistance rate of 100 % is not indicated for the treatment of ESBL-associated UTIs.

5. Conclusion

27.5% of *E. coli* isolated was ESBL-producing *E. coli*. None of *E. coli* with no resistant marker and ESBL-producing *E. coli* shows resistant to ertapenem, meropenem or promising made them promising as a therapy of ESBL-producing *E. coli*. The result show also a high rate of resistance to Quinolons (Ciprofloxacine, Cephalothin, Cefrazidime, Levofoxacin) in ESBL-producing *E. coli with* resistance rate of >60%, must be ruled out as a therapy option for the treatment of UTIs caused by ESBL- producing organisms.

So, according to this conclusion Patients should not take any antibiotic with no culture and sensitivity test to avoid ineffective antibiotic especially in UTI caused by ESBL-producing *E. coli*

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