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Study of plasmid profile and susceptibility patterns of *Escherichia coli* isolated from patients with urinary tract infection in Basra

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Abstract

The present study was designed to investigate plasmid profiles and the prevalence of multidrug resistant *Escherichia coli*, which was done in Basra, Iraq, during the period between September 2012 and January 2013. A total of 306 urine sample were collected and cultured from patients with UTI , only 137 sample give positive growth.72 isolates diagnosed as *E.coli* isolates and tested for antibiotic susceptibility ,high antibiotic resistance toAmpcillin100%,Cefazolin93.05%,Augmentin83.33%,and Nitrofurantion70.83%, mid resistance to Piperacillin62.5%, Cefixime63.88%, Kanamycin48.61%, Cefepime43.05%, , ceftriaxone40.27%, , and Tobramycin36.11%,low resistance to Cotrimoxazole25%, Ciprofloxacin23.6%, Nalidixic Acid23.6% ,Aztreonam18.05%, Norfloxacin15.27%,Amikacin9.72%,Gentamicin8.33%, Chloramphenicol5.55%, cefoxitin1.38%, and Imipenen 0% .*E.coli* isolates showed multiple antibiotic resistance .The MAR index of the isolated ranged between 0.2 and 0.8 . Most isolates harbor large molecular weight plasmids ranging from (1- >10) Kbp**.**

Key words: *Escherichia coli*, Plasmid profile, Urinary tract infection, antibiotic resistance

دراسة النسق البلازميدي وانماط الحساسية الدوائية لبكتريا الاشريكية القولونية المعزولة من مرضى مصابين بأخماج المسالك البولية في البصرة

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الخلاصة

صممت هذة الدراسة لكشف عن النسق البلازميدي وكذلك المقاومة المتعددة لبكتريا الاشريكية القولونية. اجريت الدراسة في محافظة البصرة لفترة ما بين ايلول 2012وكانون الثاني2013 . جمعت 306 عينة ادرار من مرضى يعانون من اخماج المسالك البولية،اعطت 137عينة نمواً موجباً. 72 عزلة فقط شخصت على انها بكتريا الاشريكية القولونية اجريت لها اختبار الحساسية الدوائية بطريقة الانتشار بالقرص اظهرت العزلات مقاومة عالية للمضاد الحيوي Ampicillin 100% و Cefazolin 93.05% و Augmentin 83.33% و Nitrofurantion 70.83% ومقاومة متوسطة للمضاد الحيوي Tobramycin36.11%,Piperacillin62.5%, Cefepime43.05%, Cefixime63.88%, ومقاومة منخفضة للمضاد الحيوي Kanamycin48.61%, ceftriaxone40.27%, Cotrimoxazole25%, Ciprofloxacin23.6%, Nalidixic Acid23.6 %, Aztreonam18.05%, Norfloxacin15.27%,Amikacin9.72%,

8.33%Gentamicin, 5.55%Chloramphenicol, 1.38%cefoxitin و 0%Imipenen واظهرت العزلات مقاومة متعددة ومختلفة للمضادات الحيوية وموشر مقاومة متعدد يتراوح مابين 0.2– 0.8 وكذلك بينت الدراسة ان غالبية العزلات تحمل بلازميدات ذو اوزن جزيئة تتراوح مابين 1 كليو قاعدة واكثرمن 10 كليوقاعدة

الكلمات المفتاحية :الاشريكية القولونية،النسق البلازميدي،اخماج المسالك البولية،المقاومة للمضادات الحيوية.

Introduction

Urinary tract infection(UTI) are the most common of all infection and can occur at any time in the life of individual[1].It is an infection caused by the presence and growth of microorganisms anywhere in urinary tract ,it is usually due to bacteria from the digestive tract which climb the opening of the urethra and begin to multiply to cause infection[2-3].In contrast to men ,women are more susceptible to UTI,and this is mainly due to short urethra ,absence of prostatic secretion,pregnany and easy contamination of the urinary tract with fecal flora[4].Urinary tract infection is a common bacterial disease, often contributes to frequent cause of morbidity in out-patients as well as hospitalized patients[5].The most important cause of UTI represented by gram negative bacteria belong to Enterobacteriacea family specially Escherichia coli [6].It is accounting for 65%-90% of urinary infection [7-8].*E.coli* can be classified into one of three groups: commensal (non pathogenic) *E.coli* strains that coexist with the host without causing overt disease ,intestinal pathogenic(diarrh-eagenic)*E.coli* ,and extra intestinal pathogenic *E.coli* (ExPEC).The latter category ,ExPEC, was proposed in 2000 to classify *E.coli* isolated capable of causing disease outside of the intestinal tract ,including uropathogenic *E.coli* (UPEC),sepsis-associated *E.coli* and neonatal meningitis-associated *E.coli* [9]. Treatment of UTIs cases is often started empirically and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens [10].

However, a large proportion of uncontrolled antibiotic usage has contributed to the emergence of resistant bacterial infection [11-12].As a result, the prevalence of antimicrobial resistance among urinary pathogens has been increasing worldwide. Associated resistance, i.e. the fact that a bacterium resistance to one antibiotic is often much more likely to be resistant to other antibiotics drastically decreases our chances of getting a second empirical attempt right [13]. The development of E.coli resistance to older agents such as ampicillin and trimethoprim-sulfamethoxazol as well as the emerging problem of fluoroquinolone resistance, may substantially limit our antibiotic choices [14] . E.coli had a wide range to resist antibiotic due to it has some of genetic factors that able it to resust these antibiotic ,such as plasmids [15].Which can transfer between genera and species of bacteria lead to prevalence the resistance by conjugation and transformation [16]

Materials And Methods

Isolation of Bacteria

A total 72 E.coli strains were isolated from urine samples .The samples were collected between September 2012 to January 2013 from inpatients as well as the outpatient department of Al-Medina General hospital, Basra General hospital and Al-Shefia General hospital. The midstream urine sample collected from all patients .A stander loop technique was used to place 0.01 ml of urine on McCaskey's agar(Lab M,UK)and blood agar (Himedia,India).Bacteria were cultured on these media in aerobic conditions at 37C for 24 h and colony count was performed, More than 10 colonies per ml of urine were considered significant[17]. While count less then that were taken as not significant. The colonies were identified by stander biochemical test according to [18] and by the API20E system (BioMerieux, France).

Antibiotic susceptibility testing

Antimicrobial susceptibility testing of the isolates was performed via the Kirby –Bauer disc diffusion technique on Mueller-Hinton agar to determined the antibacterial activity of 20 antibiotics [19] Ampicillin (10mg), Aztreonam (30mg), Norfloxacin](10mg) Augmentin (30mg) , Ceftriaxone (30mg) Amikacin (10mg), Kanamycin (30mg) Cefazolin (30mg) NalidixicAcid (30mg) Chloramphenicol (30mg)Imipenen (10mg) Ciprofloxacin (5mg) Nitrofurantin(300mg)Cotrimoxazol(25mg) Cefoxiti (30mg)Piperacilin(100mg)Tobramycin(10mg) Cefepime (30mg) Gentamicin (10mg) Cefixime(30mg)

Plasmid DNA extraction

A total of 67(93%) multidrug resistant isolated of E.coli are selected for plasmid extraction plasmid DNA was extracted by a stander method then estimated by spectrophotometric Plasmid extraction was carried out by using Kit Pure Yield plasmid Miniprep System (Promega USA)

Electrophoresis analysis of the plasmid DNA

Agarose gel electrophoresis for plasmid DNA of multidrug resistant isolated of E.coli was carried out on 1% agarose gel (promega, USA),in TAE buffer for 4 hr. Plasmid DNA bands were viewed by fluorescence of band ethidium bromide under a short wave ultraviolet light trans illuminator and the photograph were taken using a digital camera .The plasmid DNA bands were matched with those for DNA Ladder (Bioneer.korea) molecular weight marker in the range 500-10200 bp

Results

A total of 306 urine sample were collected and cultured, only 137 sample give positive growth, and only 72 sample identified as E.coli strain table (1). According to their growth morphology and biochemical reaction patterns such as Indol production, methyl red test ,voges-proskaure,citrate utilization test ,oxidase test, motility ,Urease test.

Table (1) Frequency of *E.coli* and other bacteria from urinary tract infection

No.of samples (%)	No.of positive growth (%)	No.of *E.coli* strain (%)	Others (%)
306	137(44.77%)	72(52.55%)	65(47.44%)

Antibiotic susceptibility test:

All the seventy two E.coli isolates were tested in vitro to determine their antibiotic susceptibility patterns by antibiotic disc diffusion ,the results show in table(2).All the isolates (100%) were resistant to Ampicillin, While ,cefazolin show resistance (93.05%), Augmentin (83.33%), Nitrofurantion (70.83%), Cefixime (63.88%),Piperacillin (62.5%), Kanamycin(48.61%) Cefepime (4305%), Ceftriaxone (40.27%),Tobramycin (36.11) ,Cotrimoxazole(25%), Nalidixic Acid(23.6%),Ciprofloxacin(23.6%), Aztreonam (18.05),Norfloxacin(15.27%), Amikacin(9.72%), Gentamicin (8.33%) ,Chloramphenicol (5.55%) ,Cefoxitin(1.38%), and there was no resistance found to Imipenen only .This antibiotic the most effective against E.coli isolated from urinary tract infection

Table (2): Susceptibility of clinical isolates of *E.coli* to different antibiotics

Antibiotic	Abbreviate	Resistans	%	Intermediate	%	Sensitive	%
Ampicillin	AM	72	100	0	0	0	0
Aztreonam	ATM	13	18.05	19	26.38	40	55.55
Norfloxacin	NOR	11	15.27	0	0	61	84.72
Augmentin	AMC	60	83.33	12	16.66	0	0
Ceftriaxone	CRO	29	40.27	5	6.94	38	52.77
Amikacin	AK	7	9.72	27	37.5	38	52.77
Kanamycin	K	35	48.61	14	19.44	23	31.92
Cefazolin	CZ	67	93.05	5	6.94	0	0
NalidixicAcid	NA	17	23.6	3	4.16	52	72.22
Chloramphenicol	C	4	5.55	0	0	68	94.44
Imipenen	IPM	0	0	3	4.16	69	95.83
Ciprofloxacin	CIP	17	23.6	1	1.38	54	75
Nitrofurantion	F	51	70.83	12	16.66	9	12.5
Cotrimoxazole	COT	18	25	17	23.61	37	51.38
Cefoxitin	FOX	1	1.38	5	6.94	66	91.66
Piperacilin	PRL	45	62.5	13	18.05	14	19.44
Tobramycin	TOB	26	36.11	11	15.27	35	48.61
Cefepime	FEP	31	43.05	8	11.11	33	45.83
Gentamicin	CN	6	8.33	4	5.55	62	86.11
Cefixime	CEF	46	63.88	2	2.77	24	33.33

Multiple antibiotic resistances

From 72 E.coli isolates ,67 isolates showed multiple antibiotic resistance ,Such that ,eight isolates resisted four types of antibiotics. Nine isolates resisted five types of antibiotics. Nine isolates resisted six types of antibiotics. Eight isolates resisted seven types of antibiotics. Seven isolates resisted eight types of antibiotics .Eight isolates isolated resisted ten types of antibiotics. Two isolates resisted eleven types of antibiotics. One isolates resisted twelve types of antibiotics .Three isolates resisted thirteen types of antibiotics. Three isolates resisted fourteen types of antibiotics .Three isolates resisted fifteen types of antibiotics. Only one isolates resisted sixteen types of antibiotic. (table 3) and (table 4)

Table (3): Antibiogram patterns to multiple antibiotic resistance isolates

Multiplicity	No.of isolates	Patterns of multiple antibiotic resistance
4	1	AM ,AMC ,CZ ,F
4	3	AM ,AMC ,CZ ,K
4	4	AM ,AMC ,K ,F
5	2	AM , AMC ,CZ ,K ,F
5	1	AM ,AMC ,CZ ,F,CEF
5	1	AM ,AMC ,CZ ,K,PRL
5	2	AM ,AMC ,CZ ,F,TOB
5	2	AM ,AMC ,CZ ,F ,PRL
5	1	AM ,AMC ,C ,FEP,CN
6	1	AM ,AMC , CZ ,K ,F ,TOB
6	2	AM ,AMC ,CZ,F,PRL,TOB
6	1	AM ,AMC ,CZ,F,PRL,CEF
6	3	AM,CZ,CRO,PRL,FEP,CEF
6	2	AM , CZ , AK , K , F ,CEF
7	1	AM,CZ,CRO,NA,PRL,FEP,CEF
7	1	AM ,CZ , K ,CIP , F , PRL ,CEF
7	2	AM ,AMC,CZ,CRO,F,PRL,FEP
7	2	AM , CZ , K ,F ,CIP , PRL ,CEF
7	1	AM , AMC , CZ ,F,PRL,CN,CEF
7	1	AM , AMC ,CZ ,F,PRL,TOB,CEF
8	1	AM,AMC,CZ,CRO,NA,FOX,FEP,CEF
8	1	AM , AMC , CZ , C , K , F , COT ,CEF
8	1	AM , AMC ,CZ ,F ,PRL,FEP,CEF,COT
8	4	AM,AMC,CZ,CRO,PRL,TOB,FEP,CEF
9	3	AM , AMC , CZ ,K ,F ,CIP ,PRL ,TOB ,CEF
9	3	AM , CZ , K ,F ,NA ,PRL , TOB ,FEP ,CEF
9	2	AM,AMC ,CZ ,CRO ,AK , F, PRL,FEP,CEF
10	2	AM, AMC ,CZ ,CRO, K ,F,PRL,FEP,CEF,ATM
10	3	AM ,AMC ,CZ ,CRO,K ,F ,COT, PRL,TOB,CEF
11	2	AM,AMC,CZ,CRO,F ,NOR,NA,CIP,COT,CEF,ATM
12	1	AM,AMC,CZ,CRO,F ,NOR,PRL ,CIP,COT,CEF, FEP,ATM
13	3	AM,AMC,CZ,CRO,F ,NOR,NA,CIP,COT,CEF,PRL, FEP,ATM
14	1	AM,AMC,CZ,CRO,K,F,NOR,NA,CIP,COT,CEF,TOB, FEP,ATM
14	2	AM ,AMC ,CZ ,K ,F, NA ,AK ,COT ,PRL,TOB,FEP,CN,CEF,ATM
15	1	AM,AMC,CZ,CRO,K, ,NOR,NA,CIP ,CN ,COT,CEF,TOB, FEP,PRL,ATM
15	2	AM ,AMC ,CZ ,CRO ,K ,F ,NOR ,NA ,CIP ,C ,COT,CEF,TOB, FEP,PRL
16	1	AM ,AMC ,CZ ,CRO ,K , ,NOR,NA,AK,CN ,COT,CEF,CIP,TOB , FEP,PRL,ATM

Table (4) Multiple antibiotic resistance index.(MAR Index)

No.of isolates	8	9	9	8	7	8	5	2	1	3	3	3	1
%	11.9	13.4	13.4	11.9	10.4	11.9	7.4	2.9	1.4	4.4	4.4	4.4	1.4
No.of antibiotic	4	5	6	7	8	9	10	11	12	13	14	15	16
MAR Index	0.2	o.25	0.3	o.35	0.4	0.45	0.5	0.55	0.6	o.65	0.7	0.75	o.8

Electrophoretic analysis of the plasmid DNA and Plasmid profile

Electrophoretic analysis of the plasmid DNA prepared was carried out by agarose gel electrophoresis on 1% agarose ,60V .4 hr. Plasmid profiling demonstrated that 54 of 67 isolates have 1 to 7 plasmid bands with sizes ranging from 1 kbp to >10 kbp .The most common plasmid of >10 kbp was detected in almost all isolated strain (Figure 1).

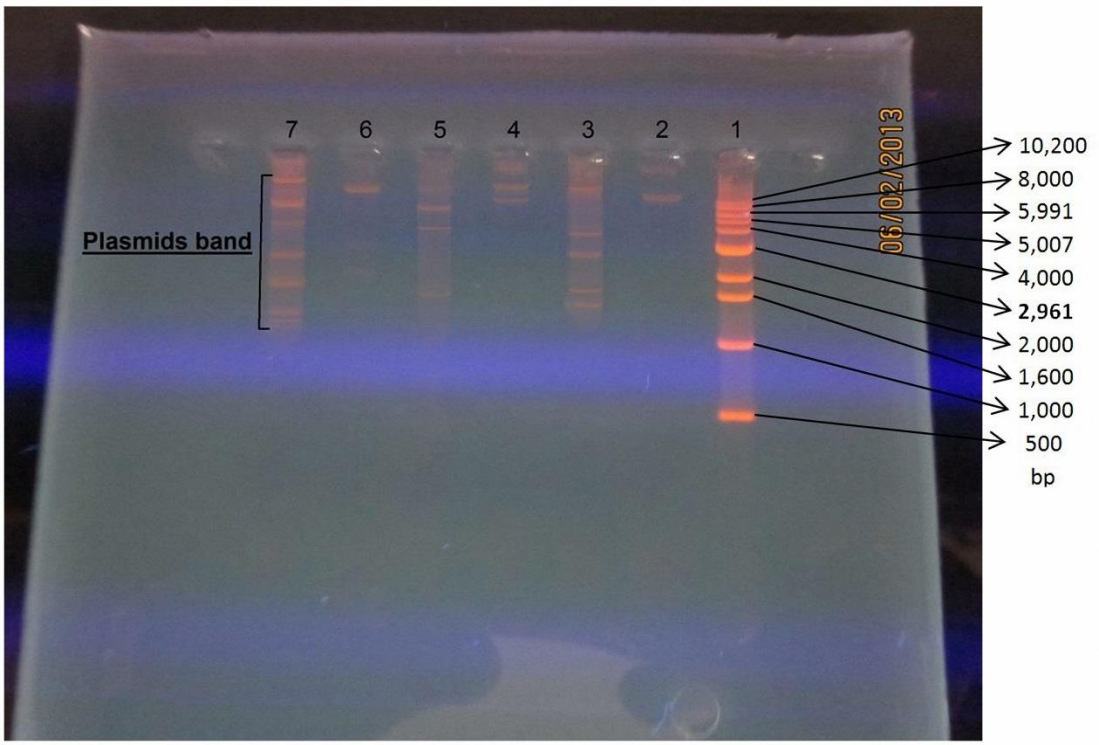

Figure (1) plasmid patterns of some clinical isolated *E.coli*

Disscusion

All urine sample were cultured on Blood agar and McConkeys agar ,the rustles of isolation of E.coli from patients with urinary tract infection in this study was 72 isolates(52.5%).The results agreed with the study done by[20,21,22,23] .E.coli was common agent in patients with urinary tract infection ,the results study agreed with study done by [24,25] In this study we observed a high incidence of antibiotic resistance among the isolation of E .coli .Although resistance to ampicillin was high (100%) ,cefazolin (93.%) was the most resistant followed by augmentin (83.3%) the results study agreed with study done by.[21,24,26]No resistance to imipenem was observed in the studied isolates .A high sensitivity of E.coli strain to imipenem has been previously reported [27,28,29]It seems this antibiotic can serve a medication of choice for the treatment of UTI caused by E.coli. However, it should be noted that unlimited use of a medicine can gradually lead to rising antibiotic resistance. Resistance to nalidixic acid and chloramphenicol in our isolates was lower than that observed in studies performed in other parts of the world[21,30] A high incidence of multidrug resistant (MDR) strains was also detected among the present isolates .A bout 93% were resistant to 4 or more tested antibiotic. The level of MDR among UTI isolates varies from country to country and resistance patterns of causative uropathogens are vary between regions and countries[31]. For example,it was reported to be 7.1 % in the USA [32],while 42% of the UPEC isolates in Slovenia in 2006 were MDR[33].The WHO guidelines recommend trimethoprim-sulfamethoxazole and ampicillin as the first choice

for UTI treatment [34] . In contrast, as revealed in the present study ,these two antibiotic cannot serve as treatment of choice in our region. The results showed that 55 (82.08%) of the isolates harbored plasmids ,other reported results agreed with our study woo-Joo et al.have reported that 87.5% and 72% of UPEC strains carried plasmids [35] In another study undertaken by Fluit , the prevalence of plasmid in the isolates was 81% which was also similar to our results [36] In the present stud, the range of plasmids was 1-7 while Malkawi has reported the numbers of plasmids to be approximately 1-6 in E.coli strains[37] Molecular weights of the plasmids were between 1 - >10 kp . This result was similar to those found in anther study In Turkey Celebi et al. were found molecular weigh of the plasmid between 1-19 kp[38]. On the other hand, 12 (17.9 %) of our isolates have no plasmid ,yet they were resistant to a large number of antibiotic .possibly ,some antibiotic resistance genes may not be located in the plasmid may be on the bacterial chromosome .In order to prove the relationship between the plasmid and its resistance ,additional studies such as plasmid curing and transferring of the plasmid to other known bacteria should be performed.

Conclusions

This study revealed that urinary tract infection in patients is highly prevalent caused by E.coli ,and there is the prevalence of antibiotic resistant strain which make a problem in treatment urinary tract infection Since urinary tract infection is a nosocomial and community acquired infection , it is recommended that over crowding in the health institution should be avoided to reduce the spread of the infection within the hospital .E.coli isolates are sensitive to imipenem by disc diffusion method ,High percent of isolated E.coli found to be resistant to Ampicillin and cefazolin and Augment that may be due to the irrational use of this antibiotic. The results obtained from electrophoresis analysis and fluorescence of bands under short wave ultraviolet light trans illuminator showed that multidrug resistance mediated by plasmids.

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