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Clinical, Etiology and Antibiotic Susceptibility Profiles of Community-Acquired Urinary Tract Infection in a Baghdad Hospital

Hussein NS*

Department of Urology, Al-Karamh teaching hospital, Baghdad, Iraq

Abstract

Objective of the study: To analyze clinical presentation, etiology and antibiotic sensitivity of bacteria causing Community Acquired Urinary Tract Infection (CA-UTI) among our patients to provide data that could guide empiric treatment.

Material and Methods: Outpatients urine cultures and clinical presentations were collected from April 2012 to October 2012. A positive urine culture was defined as growth of a single bacterium with colony count of more than 100,000 CFU/ml and disk diffusion technique according to Clinical and laboratory standards institute (CLSI) was performed to determine antibiotics susceptibility of isolated bacteria species. Clinical symptoms, causative uropathogens and their antibiotic sensitivity were recorded.

Results: Of 299 urine cultures processed, a positive urine culture was detected in 100 subjects. Dysuria and bladder irritability (frequency and urgency) were the most common clinical presentation, but were no specific in predicted CA-UTI. Escherichia coli (39%) and Staphylococcus strains (30%) were the most organisms causing CA-UTI s. The isolated organisms showed a substantial sensitivity reduction to most of test antibiotics.

Conclusion: Clinical presentation had a minor in diagnosis of CA-UTI and this study revealed that *E.coli* and Staphylococcus strains were the most prevalent isolated uropathogens among our population. Susceptibility test showed there was a high sensitivity to nitrofurantoin, amikacin and imipenem with reduction sensitivity to other commonly used antibiotics brings a concern for future studies to guidance empirical treatment.

Keywords: Antibiotic susceptibility; Baghdad; Clinical symptoms; Community–acquired urinary tract infection; Etiology

Introduction

Community acquired urinary tract infection (CAUTI) is one of the most common medical problem facing the urologist and family physicians in medical practice. Worldwide, about 150 million people are diagnosed with Urinary Tract Infection (UTI) each year costing the global economy in excess of 6 billion dollars [1]. However, its impact and frequency varies among different populations, the incidence of UTI among young sexually active women has been reported to exceed 0.5 episodes per year, with 20 to 30% of women experiencing recurring infections [2]. During reproductive life, the UTI is one of most important causes of work disabilities and morbidity in general population and is the second most common cause of hospital visits, hence, the need for prophylaxis and prompt treatment [3]. Most of UTI are uncomplicated (occurring in healthy individuals without metabolic, functional or anatomical abnormalities of urinary tract) with female predominant However, with advancing age, the prevalence and incidence of UTI increase progressively in men with a concomitant and progressive decrease in male: female ratio [4].

Theoretically, the result of urine culture and sensitivity test can be achieved 48 hours following sampling. However in resource poor settings may be take longer and as in most of cases, the urine culture and susceptibility testing costs more than antibiotic treatment itself. Furthermore, the contemporary studies demonstrate that etiology of CAUTI and their antibiotic sensitivity have been shown geographical variation; In majority of community acquired urinary tract infection, treatment decision is empiric, based on available guidelines and published studies [5,6].

To be successful and complained from subjects, the empirical treatment provided must be guided by clinical evidences as well as the safety profile and cost – effectiveness of the drug, and adhere to " antimicrobial stewardship" (using antibiotic in a way that helps to limit the development of resistance) [7].

With growing problem of drug resistance worldwide as documented by published studies as well as data on clinical, etiology of UTI and antimicrobial susceptibility of uropathogens in Iraq are scarce [8,9]. We conducted this study to record the common clinical presentation of CA-UTI and to identify the distribution of bacterial species association with Community- Acquired Urinary Tract Infection (CAUTI) in Baghdad and to determine their susceptibility to commonly prescribe antibiotics.

Material and Methods

This study was conducted at a teaching hospital, Iraq from April 2012 to October 2012.

Our hospital provided medical services to western half of Baghdad province with average of 75 patients treated daily on outpatient urology clinic for six days per week.

The work up for our patients seeking medical treatment for their urology symptoms (dysuria, bladder irritability, abdominal pain and fever) included full medical history, physical examination and urine analysis and urine culture.

The inclusion criteria were all subjects presenting with urology symptoms during study period, their urine examination showed WBC and had UTI confirmed by positive urine culture reports.

***Corresponding author:** Hussein NS, FEBU Senior Urologist, Al-Karamh teaching hospital, Post Office: 7 Abkar Box No.26047, Baghdad, Iraq, Tel: 964 77098 39 409; E-mail: dr_nasser73@yahoo.com

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Patients with pregnancy, those who underwent antibiotic treatment within 24-72 hours, those with more than three episodes of UTI in previous 12 months, those patients with complicated factors such as vesicoureteral reflux, ileal conduit, ureteropelvic junction obstruction, urinary stone disease, neurogenic bladder or patient on indwelling urethral catheter, patients with history of instrumentation within 48 h and those with clinical symptoms of UTI but their urine culture showed no growth were all excluded from this study.

After obtaining approval from ethical committee in our hospital, one clean–catch midstream specimen or suprapubic aspirate in subjects who were unable to void was collected in a sterile wide-mouth leak-proof container to hold about 50 ml of urine.

The urine sample divided into two parts, first part was centrifuged at 2000 rpm for 5 minute and sediment used for direct microscopical examination.

The second part was employed for urine culture and sensitivity by using a calibrated loop method, 10 µl of un-centrifuged specimen was transferred onto Blood agar and MacConkey agar.

Culture plates were incubated at 35-37 degrees Celsius for 18-24 h. A specimen was considered positive for UTI if a single organism was isolated at a concentration greater than 105 colony-forming units/ ml. Confirmation tests were done for identifying the organism.

Antibiotic sensitivity testing was performed using disk diffusion method on Mueller-Hinton Agar according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [10].

The antibiotics tested were amikacin, ampicillin, amocill-clav, cefotaxime, cefoxitin, ceftazidene, ceftriaxone, ciprofloxacin, nitofurantoin, co-trimoxazole, gentamycin, imipenem, nitrofurantoin, pipracillin, and tobramycin.

All antibiotic discs used for the study were obtained from commercial markets which monitoring through Central Public Lab, Ministry of Health –Iraq. These antibiotic discs were selected based on Clinical and Laboratory Standards Institute (CLSI) and also by considering the availability of these drugs in study area.

Statistical Analysis

Data were translated into a computerized database structure. The database was examined for errors using range and logical data cleaning methods, and inconsistencies were remedied.

An expert statistical advice was sought for. Statistical analyses were done using SPSS version 20 computer software (Statistical Package for Social Sciences) in association with Microsoft Excel 2010.

Frequency distribution for selected variables was done first. 95% CI: the 95% confidence interval is a statistical procedure to anticipate or predict the expected range of possible values of the calculated sample estimate of any statistic in the reference population with 95% confidence.

Associations between 2 categorical variables were explored by cross-tabulation. The statistical significance of such associations was assessed by Chi-square (c2) test. An estimate was considered statistically significant if its P value was less than a level of significance of 0.05.

Results

A total of 298 subjects presented with dysuria, bladder irritability (frequency, urgency), lower abdominal pain, and fever, suspected to have CA- UTI were investigated by urine analysis and urine culture.

Table 1 shows the relative frequency of fore mentioned UTI symptoms in the study sample, where dysuria and bladder irritability were the most common complained.

Table 2 shows that one third (33.6%) of study sample with UTI symptoms had an established diagnosis of UTI based on positive urine culture. The expected prevalence rate of UTI in the reference population ranges between 28.2%-39% with 95% confidence.

The mean patient age was 34.91 ± 18.3 (range 1-69 years). More of cases were recorded among females (61%) and all bacteria species isolated from males also isolated from females.

Gram–negative bacteria were isolated in 62 (62%) cultures followed by Gram- positive cocci with 38 (38%). *E.coli* presented the highest prevalence (39%), followed by Staph species (30%), Klebsiella spp. (17%), Enterococcus faecalis (7%) and 7% other species (Proteus mirabilis, Al caligenes, Pseudomonas aeruginosa and acinetobacter) Table 3. The antibiotics sensitivity of 14 classes of antimicrobial against uropathogens is summarized in Table 4. The uropathogens showed high sensitivity to amikacin (94%), followed by impenin (91%), nitrofurantoin (82%), gentamycin (56%), 40% to ciprofloxacin and least was to pipracillin 29%.

Chi-square test with P values for comparisons of antibiotics susceptibility among gender and Gram stain bacteria.

Table 5 shows there is no difference in antibiotic sensitivity between male and female.

Table 6 shows that Gram stain bacteria exhibited significantly

Symptoms (n=298)	N	%
Dysuria	165	55.4
Irritability	142	47.7
Abdominal pain	81	27.2
Fever	58	19.5

Table 1: The relative frequency of selected UTI symptoms in the study sample.

Symptoms	Total N	Final diagnosis of UTI based on urine culture		95% confidence interval (%)
		N	%	
Abdominal pain	81	27	33.3	
Fever	58	20	34.5	
Dysuria	165	65	39.4	
Irritability	142	39	27.5	
Total	298	100	33.6	(28.2 - 39)

Table 2: The rate of final diagnosis of UTI by symptoms.

Isolated bacteria in urine	N	%
Step spp.	30	30.0
E. coli	39	39.0
Enteroc faecalis	7	7.0
Klebsiella	17	17.0
Proteus	1	1.0
Strep spp.	1	1.0
Pseudomonas aeruginosa	2	2.0
A1 Caligenes faecalis	1	1.0
Acienatobacter	1	1.0
Aremonas salmonicida	1	1.0
Total	100	100.0

Table 3: Distribution of isolated bacteria

Antibiotic sensitivity (n=100)	N	%
Amikacin	94	94.0
Impenin	91	91.0
Nitrofurantoin	82	82.0
Gentamycin	56	56.0
Tobramycin	55	55.0
Cefotaxime	47	47.0
Ciprofloxacin	46	46.0
Cotrimoxazole	40	40.0
Ceftrioxone	33	33.0
Amoxiclave	33	33.0
Ampicillin	32	32.0
Ceftazidime	30	30.0
Pipracillin	29	29.0

Table 4: Antibiotic sensitivity of uropathogens in general.

	Gender				
	Female (n=61)		Male (n=39)		
Antibiotic sensitivity	N	%	N	%	P
impenin	55	90.2	36	92.3	0.71[NS]
Tobramycin	35	57.4	20	51.3	0.55[NS]
Pipracillin	20	32.8	9	23.1	0.3[NS]
Nitrofurantoin	49	80.3	33	84.6	0.59[NS]
Gentamycin	38	62.3	18	46.2	0.11[NS]
Cotrimoxazole	21	34.4	12	30.8	0.7[NS]
Ciprofloxacin	25	41	15	38.5	0.8[NS]
Ceftrioxone	21	34.4	16	41	0.5[NS]
Ceftazidime	21	34.4	9	23.1	0.23[NS]
Cefoxitin	26	42.6	21	53.8	0.27[NS]
Cefotaxime	30	49.2	16	41	0.42[NS]
Amoxiclave	19	31.1	14	35.9	0.62[NS]
Ampicillin	21	34.4	11	28.2	0.52[NS]
Amikacin	58	95.1	36	92.3	0.57[NS]

P<0.05 = statistically significant; NS = non-significant

Table 5: Antibiotic sensitivity with respect to genders.

higher sensitivity rate to cefotaxime (P value <0.05) compared to Gram stain bacteria.

Susceptibility pattern of isolated microorganisms was described in Table 7. *E.coli* presented sensitivity rate to amikacin of 97.4%, followed by 89.7% to imipenem, 84.6% to nitrofurantoin, 35.9% to ciprofloxacin and 17.9% to pipracillin. For ampicillin, amoxiclave, co-trimoxazole and cephalosporin groups, *E.coli* showed sensitivity rate ranged from 25.6% to 35.9%.

The susceptibility rates for Staph species, the second highest prevalent pathogen, were: amikacin (90%), imipenem (86.7%), nitrofurantoin (83.3%), cefotaxime (70%), tobramycin (60%), gentamycin (66.7%), cefoxitin (53.3%), ciprofloxacin (40%), ampicillin (36.7%), ceftrioxone (33.3%), co-trimoxazole (23.3%) and 26.7% for pipracillin, ceftazidime, amoxiclave.

The isolated Klebsiella from our cohort showed low sensitivity to conventional antibiotics used in treatment of CAUTI (ampicillin 11.8 %, amoxiclave 17.6% and ceftrioxone 17.6%) in comparison to 100%, 94.1%, 82.4%, 58.8%, 47.1%, 41.2% and 35.5% (imipenem, amikacin, nitrofurantoin, cefoxitin, tobramycin, pipracillin, gentamycin, ciprofloxacin, cotrimoxazole and cefotaxime). For Enterococcus faecalis group, an intrinsic sensitivity rates were observed to amikacin and imipenem (100%), with 85.7% sensitivity rate to nitrofurantoin, ceftrioxone and amoxiclave, followed by 42.9% to gentamycin, tobramycin, ceftazidime and cefotaxime. Also enterococcus faecalis showed susceptibility rates of 57.1% to cotrimoxazole, ciprofloxacin, cefoxitin and ampicillin, with low sensitivity rate observed against pipracillin (14.3%).

Other species showed 85.7% sensitivity rate to amikacin and imipenem, followed by 71.4% to pipracillin and gentamycin, 57.1 % to nitrofurantoin, ceftrioxone, cefoxitin, cefotaxime and amoxiclave and a considerable sensitivity rate (42.9%) to tobramycin, cotrimoxazole, ciprofloxacin, ceftazidime and ampicillin.

Discussion

Urinary tract infection ranks one of most common medical disease encountered in medical practice with significant morbidity and health costs, occurring from neonate to elderly [11,12].

Published studies showed there was a geographical variation in etiology of CAUTI. Moreover, the international resistance surveillance studies have demonstrated an increasing resistance pattern against commonly used community antibiotics [8,13,14]. Therefore regional studies analyzing etiology of CAUTI and their antimicrobial susceptibility are currently of great value to guide clinician in empiric treatment of CAUTI.

Although UTI is considered one of more common infection worldwide, in the present study the prevalence range of CAUTI was 28.2-39% proved by urine culture. this finding in accordance with other regional studies, as the percentage of UTI proved by urine culture 11.4% in Kuwait at Infection disease hospital, 9.17% in south India and 24.6% in Singapore. This indicates that urine culture is essential for a definitive diagnosis [7,15,16].

Increased frequency and dysuria were the most clinical symptoms among UTI in a study done by Little et al and Sepahi et al. Similar clinical symptomatology were seen in this study. But the predictability of UTI by these symptoms is to be questioned, as only one third (33.65%) of our study sample with clinical symptoms of UTI had established diagnosis of UTI proved by urine culture, This findings in agreement with Eshwarappa et al., where the clinical presentation have a minor role in diagnosing UTI, reconfirming the fact that urine culture is essential to diagnosis UTI [16-18].

The uropathogens profile in our study is similar to other studies, in

	Gram strain of bacteria				
	G-ve (n=62)		G+ve (n=38)		
Antibiotic sensitivity	N	%	N	%	P
impenin	57	91.9	34	89.5	0.68[NS]
Tobramycin	34	54.8	21	55.3	0.97[NS]
Pipracillin	19	30.6	10	26.3	0.64[NS]
Nitrofurantoin	50	80.6	32	84.2	0.65[NS]
Gentamycin	32	51.6	24	63.2	0.26[NS]
Cotrimoxazole	22	35.5	11	28.9	0.5[NS]
Ciprofloxacin	24	38.7	16	42.1	0.74[NS]
Ceftrioxone	20	32.3	17	44.7	0.21[NS]
Ceftazidime	19	30.6	11	28.9	0.86[NS]
Cefoxitin	26	41.9	21	55.3	0.19[NS]
Cefotaxime	21	33.9	25	65.8	**0.002**
Amoxiclave	18	29	15	39.5	0.28[NS]
Ampicillin	16	25.8	16	42.1	0.09[NS]
Amikacin	59	95.2	35	92.1	0.53[NS]

P<0.05 = statistically significant

Table 6: Antibiotic sensitivity with respect to Gram stain.

Bacteria isolate	AMK	AMP	AMO	CEF	CEX	CET	CER	CIP	COT	GEN	IMP	NIT	PIP	TOB
E.coli (n=39)	97.4	30.8	30.8	30.8	33.3	25.6	35.9	35.9	30.8	53.8	89.7	84.6	17.9	59
Staph spp. (n=30)	90	36.7	26.7	70	53.3	26.7	33.3	40	23.3	66.7	86.7	83.3	26.7	60
Klebsiella (n=17)	94.1	11.8	17.6	35.3	58.8	35.3	17.6	41.2	41.2	41.2	100	82.4	47.1	47.1
Enteric faecalis (n=7)	100	57.1	85.7	42.9	57.1	42.9	85.7	57.1	57.1	42.9	100	85.7	14.3	42.9
Others (n=7)	85.7	42.9	57.1	57.1	57.1	42.9	57.1	42.9	42.9	71.4	85.7	57.1	71.4	42.9

AMKk= Amikacin; AMP= Ampicillin; AMO= Amoxiclave; CEF= Cefotaxime; CEX= Cefoxitin; CET= Ceftazidime; CER= Ceftriaxone; CIP= Ciprofloxacin; COT = Cotrimoxazole; GEN= Gentamicin; IMP= Imipenem; NIT= nitrofurantoin; PIP= pipracillin; TOB= tobramycin; Staph spp. = Staphylococcal species; others = Proteus, streptococcal strain, Pseudomonas aeruginosa, Al Caligenes faecalis, Acienatobacter, Aeromonas salmonicida.

Table 7: Antibiotic sensitivity of uropathogens detected by urine culture (%).

that the frequency of UTI- causing gram-negative is more than gram-positive bacteria, where *E.coli* microorganism is the first predominant isolated from urine samples, An exception was the linkage of CA-UTI with the existence of staphylococcus species in isolated samples, this finding of staphylococcus predominance is in agreement with Khleifat et al, and observation experience. As it is known that local drinking water used for domestic consumption, particularly in summer time, contains high amounts of salt. Therefore, it is possible that salt resistant bacteria like Staphylococcus might the second commonest bacteria in our study group [19-21].

The Infectious Disease Society of America (IDSA) guideline suggested that a 10%-20% resistance should warrant a change in the recommendation of the antibiotic to be used as first –line but acknowledged that no specific data supports this recommendation [22].

Generally, the isolated bacteria showed highest sensitivity to amikacin and imipenem (range 85.5-100%), although 10% of isolated uropathogens showed resistance against imipenem, raise a concern over the available options to treat complicated and drug–resistant cases, As until recently carbapenems were almost uniformly active against resistant Gram-negative organism but some strains have now developed effective ways to deal with carbapenems [16].

Our data demonstrated that sensitivity rate to nitrofurantoin was 82% in contradiction to others where sensitivity rate to nitrofurantoin less than 50% [23].

Over decades the sensitivity pattern of uropathogens to commonly used antibiotics have been changed, as our findings showed that cephalosporin group (cefoxitin, cefotaxime, ceftriaxone and ceftazidime),co-trimoxazole, amoxiclave, ampicillin, quinolones and pipracillin were most inactive drugs as they exhibited susceptibility rate less than 50%, with marginal sensitivity rate to gentamicin and tobramycin (56 and 55% respectively),in agreement with other studies, these low susceptibility limited there useful in treatment of CAUTI in our population [23-25].

Our result also showed that *E.coli* isolates demonstrated a substantial reduction in drugs susceptibility frequently used in community such as cotrimoxazole, ciprofloxacin, ceftriaxone, ceftazidime, cefoxitin, cefotaxime, amoxiclave, ampicillin, gentamicin and pipracillin, in agreement with other studies, where *E.coli* resistance to cotrimoxazole and ciprofloxacin 37.8% and 24.4, and 70% and 83.2% in Singapore and Iran respectively, however in a study conducted for United States as a whole in 2001, *E.coli* resistance to cotrimoxazole was 16.1% and 2.5% to ciprofloxacin. In another Canadian study done in 2001 to evaluate antimicrobial resistance in UTI, *E.coli* resistance to cotrimoxazole was found to be 8.4%-19.2% and 0%-1.8% for ciprofloxacin. This geographical variation in *E.coli* strains sensitivity is worrying because these antibiotics used for treatment of UTI in both outpatients and hospitalized patients for long time [7,26-28].

Staph.spp represented 30% of patients suffering from CAUTI and exhibited good susceptibility to amikacin (90%), imipenem (86.7%), nitrofurantoin (83.3%), cefotaxime (70.0%) and 66.7% to gentamicin in comparison to less than 50% to other antibiotics (pipracillin, cotrimoxazole, ciprofloxacin, ceftriaxone, ceftazidime, cefoxitin, amoxiclave and ampicillin).

The prevalence and antibiotic sensitivity of Klebsiella strains was varied among published literatures, as study from Kuwait University, Kuwait, showed that Klebsiella was accounting for 12.2% of the organism isolated. In a study done in Aligarh, India, Klebsiella was isolated in 22% of cultures of 920 patients with CAUTI. In our study the Klebsiella was third common isolated bacteria (17%) and showed a low degree of sensitivity to most antibiotics tested except an 100% sensitivity to imipenem, 94.1% to amikacin, 82.4% to nitrofurantoin and 58.8% to cefoxitin [15,24].

Enterococcus faecalis can produce UTIs in certain patient populations such as patient with indwelling urethral catheter, complicated UTI or patient received broad- spectrum antibiotics for another infection. The low prevalence of enterococcus (7%) in this study is in agreement with other studies and is consistent with the fact that the patients in this study were outpatients with no indwelling catheters. However in this work enterococcus showed a high degree of sensitivity to most antibiotics testes with 100% susceptibility to amikacin and imipenem except pipracillin, tobramycin, gentamicin, ceftazidime and cefotaxime [15].

Although the other species (Proteus 1%, Strep spp. 1%, Pseudomeras areogenosa 2%, Al Caligenes faecalis 1%, Acienato bacter 1% and Aremonas salmonicida1%) represented a low percentage of isolated bacteria, with good antibiotics susceptibility to most of tested antibiotics, except ciprofloxacin and tobramycin. Even though the prevalence of these isolates was low, but these data suggests evolution in uropathogen etiology and emphasizes the need for periodic assessment of uropathogens and their antibiotics susceptibility pattern at local and national level to guarantee successful empiric treatment in agreement with other studies [23].

Management of CAUTI is worsening by the day. The most active drugs in our study were amikacin, imipenem, nitrofurantoin, gentamicin and tobramycin, with less than 50% sensitivity to drugs recommended by European urology association guidelines, such as ampicillin, amoxiclave, co-trimoxazole, ciprofloxacin and cephalosporin groups. In developing countries, the low sensitivity for commonly used antibiotics due to fact that these antibiotics have been extensively used in treatment of CAUTI and other infections in the past years, in addition it is well known that majority of persons in study regions self-medicate suggesting uncontrolled of consumption of these antimicrobial agents particularly as they are cheap, furthermore the implementation policy on sale of antibiotics in study region is weak : many unauthorized persons sell drugs out of pharmacy and in pharmacies sale is not restricted exclusively to those with prescription. These factors could contribute to emergency of resistance [23,29].

Our findings demonstrate that urine culture and sensitivity is essential for diagnosis of UTI as the clinical presentation plays a minor role in confirming diagnosis in UTI. *E.coli* is still the most widely prevalent organism causing UTI in the community, followed by Staph spp. Susceptibility profile showed that nitrofurantoin is most active oral antibiotic for treatment CAUTI. in addition the sensitivity pattern to other testing antibiotics have been reduced due to uncontrolled abuse of the available antibiotics, calling for issuing a strong policy to avoid over counter sale of drugs and encouraging for multi centers periodical studies at local and regional levels to win the battle against uropathogens.

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