Antibiotic Resistance Pattern of Uropathogens in Community and Hospitatl Acquired Urinary Tract Infections

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Abstract: The aim of the study was to identify the most frequent etiological agents and the profile of antimicrobial agents of the bacteria isolated from urine cultures among community and hospital acquired urinary tract infections, to provide guidelines for choosing an effective antibiotic therapy. A retrospective study conducted at King AbdulAziz University Hospital, a tertiary care teaching hospital. Total of 880 positive urine cultures were reviewed during a period of May 2007 to May 2008. Charts were reviewed for age, sex, presence or absence diabetes mellitus pregnancy, department from where the specimen was sent, duration of culture (hospital or community), bacterial isolates with their sensitivity and resistance to different antibiotics was recorded. The study revealed that, *E. Coli* was the commonest pathogen followed by Klebsiella and Pseudomonas in both hospital and community infections. It also dominstrated that Ampicillin, Sulphamethoxazole/Trimethoprim (SMXTMP), Amoxycillin/Clavunic acid cannot be used as empirical therapy for *E. Coli* infections in both the groups. For Klebsiella and Pseudomonas infection in community and hospital acquired infections and during pregnancy Nitrofurantoins showed high resistance, Quinolines and Cepahlosporins can be used in this group empirically. This study is useful for clinician in order to improve the empiric treatment.

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1. Introduction:

Urinary tract infections (UTIs) are among the most common bacterial infections and frequently recurring problems encountered by clinicians in community practice. The approach to these infections remains a difficult and sometimes controversial issue, especially in asymptomatic and symptomatic bacteruria. Worldwide, about 150 million people (**Stamm and Norrby, 2001**) are diagnosed with UTI each year, costing in excess of 6 billion dollars (**Gonzalez and Schaeffer, 1999**). Among both outpatients and inpatients, *Escherichia coli* is the primary clinically relevant organism, accounting for 75% to 90% of uncomplicated UTI isolates (**Gupta, et al., 2001 and Nicolle, 2001**). Staphylococcus saprophyticus, Klebsiella spp., Proteus spp., Enterococcus spp., and Enterobacter spp. are organisms less commonly isolated from outpatients.

Urinary tract infections are common in the paediatric age group and may be associated with a risk of renal scarring which may lead to hypertension and/or renal damage (**Vernon, 1997**). To minimize this risk, prompt and appropriate antibiotic therapy is imperative, and is usually initially started empirically before the results of urine culture and bacterial susceptibility are available. Many guidelines exist to recommend the choice of empirical antibiotic treatment, usually based on the knowledge of which organisms are commonly involved and on their antibiotic susceptibility. However, as the latter is known to change over time with the development of antimicrobial resistance, a regular evaluation of the pattern of antibiotic sensitivities is imperative to facilitate the choice of treatment (**Hannan et al., 1993; Dyer,1998 and Shigemura, et al. 2005**).

In most Western countries, microbiological testing may be unnecessary in acute uncomplicated UTI, except for surveillance purposes (**McNulty, et al. 2006**), because in most cases urine culture and susceptibility testing cost more than the antibiotic treatment itself. The Infectious Diseases Society of America (IDSA) guidelines currently recommend empirically treating acute, uncomplicated bacterial cystitis in healthy adult, non-pregnant females with a 3-day course of double-strength trimethoprim-sulfamethoxazole (SXT) in settings where the prevalence of SXT resistance is <10-20% (**Echols et al., 1999 and Warren, et al., 1999**). Alternative therapy for uncomplicated UTI include a fluoroquinolone, nitrofurantoin or fosfomycin, wherever SXT resistance is >10-20% (**Warren, et al., 1999**). However, these guidelines may not be applicable in other countries. The resistance pattern of community acquired uropathogens has not been extensively studied in the Indian subcontinent (**Akram, et al., 2007**).

The aim of the study was to identify the most frequent etiological agents and the profile of

antimicrobial agents of the bacteria isolated from urine cultures among community and hospital acquired urinary tract infections in KSA, to provide guidelines for choosing an effective antibiotic therapy.

2. Method:

Culture proven urine isolates were retrospectively studied.The samples were collected between May 2007 to May 2008 from both the inpatients and outpatients department of King Abdul Aziz university hospital, a tertiary care teaching hospital. Majority of samples were midstream urine specimen, others included catherterized urine samples. Culture was done by the caliberated loop technique delivering 0.001ml of urine and plated on Cystine –Lactose-Electrolyte-Defecient (CLED) agar plates. Each plate inoculated with 6 tests, each in dublicate, after overnight incubation at 37 degree. The number of colonies in the impression area were counted and if over 25 colonies were present the original urine sample was known to have contained greater than 105 organisms per milliliter, indicating significant bacteriuria. The isolates were identified using the standard method (**Cowan, et al., 1981**). Gram negative bacilli are identified using API 20 (Analylab Inc). The antibiotics tested on each disc were ampicillin 10 mcgm per disc, Norfloxacin 10 mcgm, Amoxicillin/Clavunic 30 mcgm, Pipracillin 100 mcgm, Trimethoprim 5mcgm, Ciprofloxacin 10 mcgm, Cefuroxime 30 mcgm, ceftazidime 30 mcgm, Ceftriaxone 30mcgm, Cefepime 30 mcgm, Amikacin 30 mcgm, Gentamycin 30 mcgm, Aztreonam 30 mcgm, Meropenam 10 mcgm and Imipenam 10 mcgm, Nitrofurantoin 300 mcgm, Levofloxacin 5 mcgm, Oxacillin 1 mcgm, Cefatoxime 30 mcgm, Tetracycline 30 mcgm, Pipracillin/Tazobactam 75 mcgm.

Charts of patients were reviewed for age, sex, department from where the specimen was sent, presence or absence of diabetes mellitus, pregnancy, duration of culture, whether hospital acquired or community acquired. (cultures within the 72 hours of admission were considered community acquired and those after as hospital acquired), the organism isolated and its sensitivity and resistance were recorded.

3. Results:

Out of 16200 urine samples received for culture during the period of May 2007 to May 2008, 880 were positivly significant bacteria with a prevalence of 5.4%. 372 urine samples (42.3%) of clinical isolates were from the department of Ob/Gyne, 324 urine samples (36.8%) were pregnant. Male to female ratio of 1:3.6. Diabetics were 138 (15.7%) whereas non diabetics 742 (84.3%). Urinary catheter was the cause of infection in 195 of patients (22%). Infection was community acquired in 589 (66.9%) whereas 291 (33.1%) were hospital acquired. *E. Coli* was the commonest pathogen both in hospital and community acquired infection, 186/589 (31.6%) and 86/291 (29.6%), (table 1).

Table (1) Community and hospital acquired urinary Isolates

Organism	**Community acquired**	**Hospital acquired**
E. Coli	186 (31.6%)	86 (29.6%)
Srep. Agalactaei	182 (30.9%)	56 (19.2%)
Klebsiella	59 (10.0%)	30 (10.1%)
E. Feacalis	55 (9.3)	26 (8.9%)
A. Baumannii	29 (4.9%)	16 (5.5%)
Pseudomonas	22 (3.7%)	21 (7.2%)
Candida Albicans	18 (3.0%)	17 (5.8%)
A. Cloacae	12 (2.0%)	8 (2.7%)
Staph.Epidermidis	7 (1.2%)	2 (0.7%)
Staph.Aureus	7 (1.2%)	9 (3.0%)
Proteus	6 (1.0%)	13 (4.5%)
Diptheroids	5 (0.84%)	3 (1.0%)
Morganella Morgani	1 (0.16%)	4 (1.3%)

Community acquired *E. Coli* was greater than 40% resistant to Sulphamethoxazole/Trimethoprim (SMX/TMP), Pipracilline and more than 70 % to Ampicillin, Amoxycillin/clavunic, where as hospital acquired *E. Coli* was 75% resistant to Ampicillin, 52.8% to SMX/TMP, 57.1% to Pipracillin and more than 40% resistant to Oxacillin, Ciprofloxacin and Norfloxacin and 100% to Ceftriaxone. Hospital and community acquired Klebsiella was more than 70% resistant to Nitrofurantoin, Pipracillin and Ampicillin. On the other hand Pseudomonas was sensitive to most antibiotics in both groups except Nitrofurantoin and Amoxucillin/Clavunic acid 66.7%, and 100 % to Ampicillin as illustrated in table, 2.

Table 2 - Resistance pattern of antibiotics in Hospital and Community acquired urinary pathogens

Antibiotic	C.A *E. Coli* %	H.A – *E. Coli* %	CA Klebsiella %	H.A Klebsiella %	C.A Pseudo. %	H.A Pseudo. %
Nitrofurant	16	9.6	70.6	76	NT	66.7
Ciproflox	25.4	45.5	11.5	18.5	10	23.5
Levoflox	36.4	33.3	0.0	NT	NT	NT
Oxacillin	17.3	46.2	10.8	NT	11.8	33.3
Norflox	19.7	40	11.4	15.4	10	26.7
Pipracillin	43.3	57.1	88.7	93.1	0.0	22.2
Ampicillin	70.9	75	0.0	96.4	100	100
Amox/clav	70.1	37.7	11.5	18.5	0.0	66.7
Genta	6.1	23.5	7.1	17.2	5	29.4
Amikacin	32.4	1.3	0.0	3.4	10	5.6
Cefurox	21.4	NT	10.9	12	0.0	0.0
Ceftaz	9.8	23.9	7.8	15.4	15.8	29.4
Ceftriax	8.3	100	0.0	NT	NT	NT
Cefatox	7.9	21	6.3	12.5	NT	0.0
Cefepime	8.6	22.4	7.3	17.9	5.3	16.7
Tetracyc	50	66.7	33.3	100	NT	NT
Pip/Tazob	4.8	6.3	11.1	15.4	0.0	5.0
meropenam	0.6	0.0	13.6	3.4	5.0	12.5
Tmp/smx	43.9	52.8	29.6	3.4	NT	0.0

NT = Not Tested, CA=community acquired, HA=hospital acquired

E. Coli in pregnant women was 62.2% resistant to Ampicillin, 36.6% to Pipracillin, whereas Klebsiella and Pseudomonas were more than 75 % resistant to Nitrofurantoin, Pipracillin and Ampicillin. For *E. Coli* infection in pregnancy Nitrofurantoin can be used empirically and Cefuroxime, Amoxycillin/Clavunic can be used as an oral agent for Klebsiella and Pseudomonas during pregnancy (table 3).

Table 3 - Antibiotic resistance pattern in pregnant and non Pregnant women to commonly grown pathogens

Antibiotics	Pregnant *E. Coli* %	Non preg *E. Coli* %	Pregnant Klebsiella %	Non preg Klebsiella %	Pregnant Pseudomo %	Non preg Pseudomo %
Nitrofurant	7.4	11.7	75.0	72.5	100	50
Ciprflox	11.1	41.7	12.0	14.8	0.0	17.1
Levoflox	16.7	45.5	0.0	0.0	NT	NT
Oxacillin	5.7	34.5	0.0	16.7	0.0	23.7
Norflox	5.6	35.9	4.8	14.6	0.0	18.2
Pipracillin	36.6	54.1	88.5	90.9	50	8.6
Ampicillin	62.2	76.9	96.2	100	100	100
Amox/clav	22.4	37.0	8.0	17.0	0.0	66.7
Genta	4.1	15.3	3.8	13.8	0.0	17.1
Amikacin	0.0	0.6	0.0	1.8	0.0	8.3
Cefurox	12.5	32.8	0.0	0.0	0.0	0.0
Cetazid	4.5	18.6	4.5	13.0	0.0	23.5
Ceftriax	0.0	25	0.0	0.0	NT	0.0
Cefatox	7.4	14.3	4.8	10.0	0.0	0.0
Cefepime	5.5	16.4	4.2	13.8	0.0	11.4
Tetracyc	50	57.1	50.0	50.0	NT	NT
Pip/tazob	1.9	7.5	9.5	14.3	0.0	2.8
meropenam	NT	NT	0.0	5.3	0.0	8.8
TMP/SMX	38.2	50.3	26.9	30.2	0.0	NT

NT= Not Tested

4. Discussion:

Urinary tract infection (UTI) is the most common of all bacterial infections to affect persons throughout their life span, females are more likely to be affected than males except in neonates where the trend is reversed (**Kalpana and Walters, 2003; Gupta, et al., 1999 and Karlowsk, et al., 2002**). The bacteriological profile varies from country to country and from city to city, in recent years, bacterial resistance to different antibiotics has risen

dramatically leaving physicians with few therapeutic options.

The prevalence of bacturia at King Abdul Aziz University hospital has fluctuated over the years from 6 % in 1986 (**El Tahawy and Khalaf, 1988**) to 11% in 2000 and 5.4% in the current study. The pathogens causing urinary tract infections (UTI) are well known and *E. Coli* is the main etiologic agent in both community as well as hospital acquired infections (**Gupta, et al., 1999; AM Bashier, 2011; Hooton and Stamm, 1997, and Akbar, 2000**). In the present study *E. Coli* was also the predominant pathogen in both groups. Klebsiella was the 2nd common organism in hospital acquired infection followed by Pseudomonas. It is recommended that in a community where the rate of resistance to Sulphamehoxazole/Trimethoprim (SMX/TMP) is greater than 20% among urinary tract isolates, alternate antimicrobial agents should be considered as the first line of treatment (**Sahm, et al., 2000**; **Farell, et al., 2000; Zhanel et al., 2000 and Mathai et al., 2001).** Our study showed resistance of 43.9% in community acquired versus 52.5% in hospital acquired infections, whereas Nitrofurantoin and Flouroquinolones, Aminoglycoside and Cepahlosporins showed sensitivity of 70-90% in both groups of UT I. A study done by Al Ghamdi from the eastern province of Saudi Arabia showed that the most frequent antibiotic dispensed by the pharmacist over the counter without the prescription from the physician was Flouroquinolones 69% followed by Co-trimaxazole and oral Cephalosporins, (**Al Ghamdi, 2001**) unless this practice is stopped,there will be emerging resistance to these antibiotics very soon.In USA the empiric regime for acute uncomplicated cystitis is a 3 day course of double strength of SMX/TMP, this current empirical regimen is likely to be replaced by alternative therapy such as the Fluoroquinolones or Nitrofurantoin (**Zhanel et al., 2000; Karlowsky, et al., 2003; Blondean, 2004**, **and Zhanel, et al., 2000**).The antibiotic resistance against SMX/TMP could be attributed to their wide usage for a variety of Indications, Aminoglycosides and Cephalosporins, being injectable, are used restrictively in the hospital care setting and hence have shown better sensitivity rate.

Bacteuria occurs in 2-7% of pregnant women, similar prevalence as in non pregnant women. The organisms are also similar in virulence in pregnant and non pregnant women (**Stenqvist, et al., 1987**), this was in accordance with our study where streptococcus agalactaie was the commonest organism followed by *E. Coli*,Klebsiella and Pseudomonas.

Early screening for and treatment of any potential bacteuria has maternal and fetal benefit (**Rouse, et al., 1995; Gratacos, et al., 1999, and Smaill, et al., 2001**),this was the reason for the majority of positive urine cultures where from the Ob/Gyne ward (372/880: 42.3%). There is little information about the safety of many newer antibiotics in pregnancy. It is generally accepted that Cepahlosporins and Nitrofurantoin are safe in pregnancy (**Warren, et al., 1999 and Gupta et al., 2001**).Our study showed Nitrofurantoin,can be used for *E. Coli*, whereas Cepahlosporins, Flouroquinolones can be used for Klebsiella and Pseudomonas.

Conclusion:

The changing spectrum of micro organism involved in UTI and the emerging resistance requires a continous monitoring to guide empirical therapy. *E. coli*, Klebsiella and Pseudomonos remain the common pathogens causing UTI both in hospital and community acquired infections. Ampicillin, SMX/TMP, Pipracillin, Amoxycillin /Clavunic cannot be used as first line treatment in *E. coli* in both hospital and community infections.

Cephalosporins except Ceftrixone and Nitrofurantoin can be used as empirical therapy in these patients. Nitrofurantoin cannot be used for Klebsiella or Pseudomonas infections during pregnancy or for hospital and community acquired infections, Quinolones and Cephalosporins are the antibiotics of choice. Treatment should as far as possible be on local data and since that may also vary from time to time in the same hospital, periodic surveillance is recommended.

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