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Alterations in antibiotic susceptibility of urinary tract infection pathogens

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ABSTRACT

Background: Urinary tract infection (UTI) is the third most common infection in human. New resisted strains of uropathogens have been developed due to different factors such as widespread use of antibiotics.

Objectives: We conducted this study to assess the recent pattern and susceptibility of uropathogens.

Materials and Methods: This descriptive cross-sectional study was carried on 32600 ambulatory patients' urine samples from six laboratories from 2008 to 2010 in Ahvaz, Khuzestan. Of those, 3000 positive culture were found. Data including underlying disease, pregnancy, catheterization and drug history were gathered by questionnaire. Susceptibility of pathogens to eight antimicrobial agents was determined. **Results:** Mean age of patients was 33.87 ± 3.80 years and 84.9% of them were female. The results showed that, E. coli, Kelebsiella and Enterobacter were the most common pathogens (73.5%, 13.8% and 6.6%, respectively). E. coli was susceptible to Ciprofloxacin, Amikacin, and Nitrofurantoin in 76.9%, 76.4% and 76.1% of cases, respectively. Klebsiella was more susceptible to Ciprofloxacin, Ceftizoxim and Amikacin in 81.1%, 79.9% and 87.7% of positive cultures. Enterobacter was most susceptible to Ciprofloxacin (71.7%), but completely resistant to Ampicillin unexpectedly.

Conclusions: E. coli and other isolates were more sensitive to Gentamicin, Amikacin and Ciprofloxacin compared to the other antibiotics tested and therefore these may be the drugs of choice for the empiric treatment of community-acquired UTI in our region.

Implication for health policy/practice/research/medical education:

Urinary tract infection (UTI) is the third most common infection in human. In a study on 32600 ambulatory patients' urine samples from six laboratories, E. coli, Kelebsiella and Enterobacter were the most common pathogens. E. coli and other isolates were more sensitive to Gentamicin, Amikacin and Ciprofloxacin compared to the other antibiotics tested and therefore these may be the drugs of choice for the empiric treatment of community-acquired UTI in our region.

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1. Background

Urinary tract infection (UTI) is the third most common infection experienced by human and the most common cause of both nosocomial and community acquired infections for patients admitted to hospitals in the United States (1).

2. Objectives

Women (especially in pregnancy period), renal transplant recipients, patients with a chronic indwelling bladder catheter, stone formers and patients with anatomical or functional abnormalities of genitourinary tracts, are more prone (1-6). Although a broad range of pathogens can cause UTI, gram-negative bacteria, particularly *Escherichia coli* is remained the most common (7-9). Due to the spread of strains producing extended-spectrum β -lactamases, resistant to the normally prescribed agents, has been increasing (7). Hence, it seems that determination of the etiology and susceptibility of uropathogens identified in patients with UTI is essential to make a better option for empiric therapies to avoid of treatment failure and particularly the development of antimicrobial resistance.

3. Materials and Methods

3.1. Study population

Thirty-two thousands and sixty hundred (32600) urine cultures from 6 participating laboratories in Ahvaz, Iran, during 2008 to 2010 were studied in this prospective cross-sectional trial. The only criterion to enroll the patients in the study was presence of positive urine culture, which was considered as 105 or more bacteria in each millilitre of midstream urine sample. Regarding the criterion for inclusion of patients into the study, a questionnaire including questions about the underlying disease (stones, urinary tract neoplasm, renal transplantation, chronic kidney disease, diabetes mellitus and/or anatomi-

cal malformations of urinary tracts), pregnancy, catheterization and drug history was designed and completed for each patient who had positive urine culture.

As the organisms isolated from culture, each laboratory determined the susceptibility of pathogens to at least 8 antimicrobials, including Ampicillin, Amikacin, Cephalothin, Ciprofloxacin, Ceftizoxime, Nitrofurantoin, Gentamicin, Nalidixic acid, and/or Trimethoprim – Sulfamethoxazole.

3.2. Data analysis

Descriptive statistics including Mean, Standard deviation and percent were considered for analysing using SPSS, version 16 (SPSS, Chicago, IL, USA).

4. Results

Three thousands positive urine culture were found between the total number of 32600 samples which were enrolled in to the study. Of those, 2546 samples (84.9%) were female. Mean age of patients was 33.87 ± 3.8 years and 85% of them were older than 12 years. Diabetes mellitus was found in 282 (9.4%) of the cases. One hundred patients (3.33%) were stone formers. Chronic kidney disease and renal transplantation were found in 128 (4.26%) and 80 (2.66%) of the patients, respectively. Twenty one cases (7%) were suffered of urinary tract neoplasm. Anatomical malformations were found in 91 patients (3.03%). Probable leading causes for urinary tract infection were summarized in table 1. Internal and external catheterization were performed for 33 (1.1%) and 47 (1.56%) patients, respectively. Two weeks before sampling, Nelaton catheter was inserted for 48 (1.6%) patients and 775 (28.53%) patients received antibiotics therapy.

Escherichia coli were the commonest pathogen in both gender and all ages accounting for 73.5% of isolates was followed by *Klebsiella* (13.8%) and

Enterobacter (6.6%) except in infants and teenagers. In infants, after Escherichia coli, Enterobacter and pseudomonas were more frequent. In young adults after Escherichia coli, Klebsiella and Staphylococcus aureus were more frequent. In patients whom had urinary tract neoplasm, or whom underwent renal transplantation, Klebsiella was more common than Escherichia coli. Prevalence of pathogens based on age, gender and probable leading cause are shown in table 1.

Escherichia coli showed a high rate of sus-

ceptibility to Ciprofloxacin (76.9%), Amikacin (76.4%), Nitrofurantoin (76.1%) and somewhat Ceftrizoxime (69%). Approximately, 84% of the Escherichia coli strains were resistant to Ampicillin. Klebsiella was highly susceptible to Ciprofloxacin (81.1%), Ceftrizoxime (79.2%), and Amikacin (78.7%) but highly resistant to Ampicillin (93.5%). Likewise, Enterobacter was demonstrated a high rate of susceptibility to Ciprofloxacin (71.7%), Ceftrizoxime (66.7%), and Amikacin (66.7%). All of the Enterobacter strains

Table 1. Prevalence of pathogens based on age, gender and probable leading cause. Numbers show the percentage in each row.

	Escherichia coli	Klebsiella	Enterobacter	Strep viridans	Pseudomonas	Serratia marcescens	Proteus	Staph aureus	Staph saprophyticus	Staph epidermidis	Citrobacter
Age											
Infants	86.1	0.7	7.9	0	5.3	0	0	0	0	0	0
Children	71.0	6.1	5.2	5.2	3.5	0	0	0	0	0	0
Teen ages	51.3	28.3	7.9	0	0	0	0	12.5	0	0	0
Adults	75.8	13.4	6.8	0.2	1.1	0.6	0.6	0	1.1	0.2	0.2
Olds	69.9	18.0	5.3	2.7	4.4	0	0	0	0	0	0
Gender											
Males	56.5	20.0	8.6	5.3	5.1	2.7	1.8	0	0	0	0
Females	76.5	12.8	6.3	0.1	1.3	0.0	1.0	0.9	0.8	0.2	0.1
Probable leading cause											
Diabetes Mellitus	57.1	23.4	9.6	5.3	4.6	0	0	0	0	0	0
Stone	38.0	19.0	3.0	12.0	1.0	12.0	12.0	0	0	3.0	0
Renal transplantation	42.5	56.3	1.2	0	0	0	0	0	0	0	0
Chronic kidney disease	59.4	28.9	11.7	0	0	0	0	0	0	0	0
Pregnancy	63.9	25.7	5.7	0	2.0	0	1.9	0	0.3	0.5	0
Urinary tract neoplasm	28.6	71.4	0	0	0	0	0	0	0	0	0
Anatomical malformations	53.8	29.7	3.3	0	9.9	0	0	0	0	0	3.3
Internal catheterization	57.8	24.2	0	0	0	0	0	0	0	0	0
External catheterization	48.9	17.0	27.7	0	6.4	0	0	0	0	0	0
Nelaton insertion in past 2 week	50.0	0	0	25.0	0	25.0	0	0	0	0	0
Antibiotics therapy in past 2 week	74.5	9.7	8.3	1.5	2.6	1.5	0	1.5	0	0	0.4

were completely resistant to Ampicillin (100%). Generally, other pathogens were susceptible to aminoglycosides and Fluoroquinolone (figure1). Citrobacter was completely (100%) eliminated by each one of the studied antimicrobials.

There was a variation in either percent resistance or susceptibility against different antibiotics based on age and gender of the patients. Age wise distribution of antibiotic susceptibility and resistance pattern revealed that uropathogens isolated from the infant patients were mostly resistant to Cephalotin (85.4%), whereas 84.8% of them were susceptible to Cephalotin in young adults.

5. Discussion

Since investigations is established that the resistance of bacteria causing UTI has been in progress, it seems that intermittent evaluation of the resistance to antimicrobial agents has to be performed in each geographic region (9). Resistance rates may vary from region to region but in general, isolates from Latin American countries show the lowest susceptibility rates to all antimicrobial agents followed by Asian-Pacific isolates and European strains (10). Unfortunately in Iran, self-medication and self-prescription practices are widespread. In a study by Zargarzade et al. in Isfahan, about 30% of drugs were dispensed

without prescription (10). Sahebi and Vahidi, demonstrated that the highest demand for non-prescription drugs in Tabriz was for analgesics and antibiotics (11). The consequence has been several treatment failures in patients who received inappropriate antibiotics and outbreaks of resistant pathogens (12). On the other hand, extended-spectrum β -lactamases *Escherichia coli* can occur in the community and may resistant to trimethoprim, quinolones and aminoglycosides. Therefore, the choice of agents to eliminate the bacteria is losing ground (7,12,13).

In this study preponderance of pathogens were isolated from adult patients and predominantly women. It has been extensively reported that adult women have a higher prevalence of UTI than men, principally owing to anatomic and physical factors (14). As many other authors noted in previous studies, in our study the most common causative pathogens in urinary tract infection were Enterobacteriaceae, especially *Escherichia coli* (73.5%), followed by *Klebsiella* (13.8%) and *Enterobacter* (6.6%), mostly susceptible to Ciprofloxacin and Amikacin, but resistant to Ampicillin. Although some investigators reported that *Klebsiella* is not a common pathogen in urinary tract infections (14-16), but there are some studies in which *Klebsiella* was

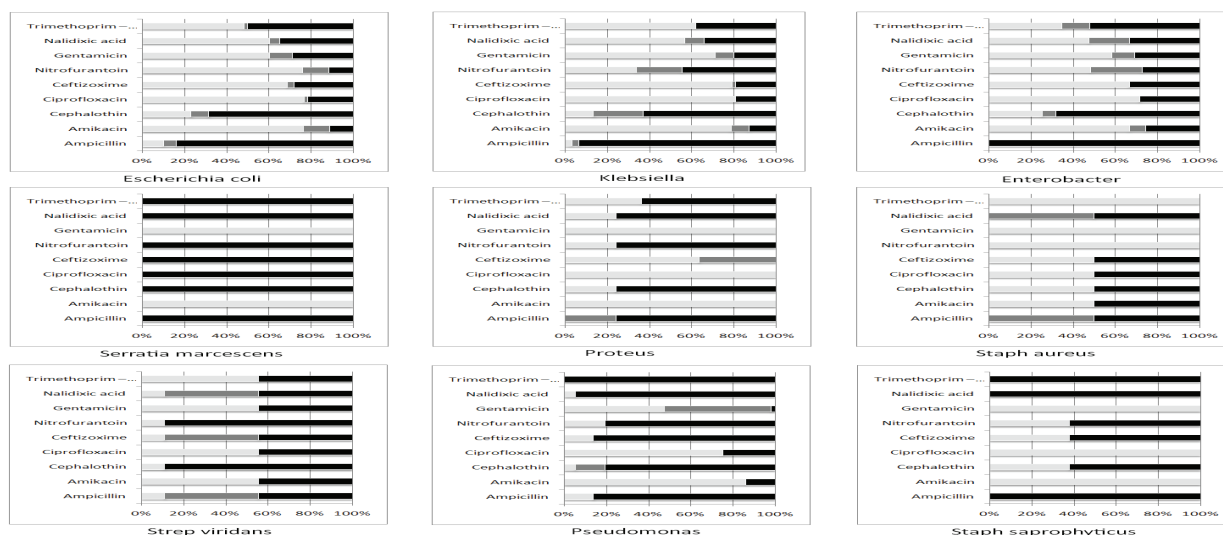


Figure 1. Susceptibility of microorganism to each one of the antimicrobials

the second common uropathogen, especially in children (10,16).

Our previous study in Ahvaz between 2002 and 2003, demonstrated a different outline of prevalence and susceptibility of pathogens. *Escherichia coli* were isolated from the 46% of samples, followed by *Staphylococcus aureus* (26%) and *Klebsiella* (17%) (16). This could be a result of extensive antibiotic usage. In our previous study, the most susceptible antibiotics for the most prevalent pathogens were Nalidixic acid, Vancomycin and Nitrofurantoin, respectively. Although in our recent study, *Escherichia coli* were best eliminated by Ciprofloxacin, but still have an acceptable susceptibility to Nalidixic acid and Nitrofurantoin. In another study in Ahvaz, contemporary to our previous study, Ahmadzadeh et al. demonstrated that the most prevalent uropathogens in children are *Escherichia coli*, *Klebsiella* and *Proteus* (17). Despite of rare *Klebsiella* urinary infection in infants in our recent study, it is the second most common uropathogens in children. Moreover in our study, *Proteus* was isolated from 9% of children's samples.

There is a general agreement that for the best management of patients with UTI, distinguishing between complicated and uncomplicated infections is very important (1). Previously, in the case of pregnancy or elderly, it was well known that functional or anatomic abnormalities of the genitourinary tract, and recent instrumentation or antimicrobial treatment, acute UTIs in the adult patient should be considered as complicated (8). In general, the pathogens in complicated UTI in our study, as uncomplicated infections were susceptible to Ciprofloxacin, Amikacin and Gentamicin. However, our results showed that in case of internal catheterization, pathogens were completely resistant to Ciprofloxacin, Gentamicin, Ampicillin and somewhat Amikacin, Trimethoprim-Sulfamethoxazole, and also Cefti-

zoxime. They were mostly susceptible to Nitrofurantoin (100%). Uropathogens in patients used Nelaton in past 2 weeks, were almost susceptible to all kind of antibiotics used in this study, except Gentamicin, Trimethoprim-Sulfamethoxazole, and Nitrofurantoin.

6. Conclusions

At this study it was shown that, *E. coli* and other isolates were more sensitive to Gentamicin, Amikacin and Ciprofloxacin compared to the other tested antibiotics and therefore these may be the drugs of choice for the empiric treatment of community-acquired UTI in our region.

Author's contributions

AG, AE, NR and BO designed and performed the research. AG analyzed data and wrote the draft. AE, BO and NR provided extensive intellectual contribution and reviewed the manuscript. AG prepared the final manuscript.

Conflict of interest

The authors declared no competing interests.

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