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Antibiotic susceptibility pattern of bacterial uropathogens isolated from patients at a tertiary care hospital

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Abstract

Background: Urinary tract infection (UTI) is one of the most common infections in both outpatients and hospitalized patients. The increasing prevalence of antimicrobial resistance is a major health problem & is associated with high morbidity & mortality.
Objectives of the study: 1. To analyse the antimicrobial resistance pattern of uropathogen during a period of 6 month in patients of UTI. 2. To know the prevalence of uropathogens.
Materials and Method: A prospective study was conducted on urine specimens suspected to be having urinary tract infection between July 2016 and December 2016 received at Department of Microbiology, SIMS Shimoga. Fresh midstream urine samples were aseptically collected in sterile containers and plated on Blood agar & MacConkey agar plates using a standard loop technique & the growth was processed by standard bacteriological technique. Antimicrobial sensitivity testing was done using Kirby-Bauer methods on Mueller-Hinton agar. Results were interpreted as per the CLSI guidelines.
Result: Out of 510 samples 250 samples showed significant bacteriuria. Most common uropathogen isolated was *Escherichia coli* 61. 6%(154/250) followed by *Staphylococcus aureus* 19. 2%(48/250), *Enterococcus species* 10%(25/250), *Klebsiella species* 3. 2%(8/250), *Pseudomonas species* 1. 2%(3/250), *CONS* 0. 8%(2/250). Gram negative organisms were highly sensitive to Fosfomycin, Nitrofurantoin, Imipenam and highly resistant to Norfloxacin, Ciprofloxacin, Levofloxacin. Gram positive organisms were highly sensitive to Linezolid, Vancomycin, Fosfomycin, Nitrofurantoin and least sensitive to Norfloxacin, Ciprofloxacin, Amoxyclavulanic acid.
Conclusion: This study showed that high resistance was observed for commonly used antibiotics. Fosfomycin and Nitrofurantoin were the most sensitive drug for gram negative organisms mainly *E. coli* which is the most common uropathogen isolated.

Keywords: *Fosfomycin, Nitrofurantoin, Antibiotic susceptibility, UTI.*

Introduction

Urinary tract infections(UTI) is one of the most common infections in both outpatient and hospitalized patients. Increasing prevalence of antimicrobial resistance is a major health problem and is associated with high morbidity and mortality.(1) It involves all age groups and both genders. Clinical study suggest that overall prevalence of UTI is higher in women. An estimated 50% of women have atleast one episode of UTI at some point in their life time and between 20-40% have recurrent episodes. Symptoms of UTI are dysuria, frequency, urgency, suprapubic tenderness. Most UTI are caused by gram negative bacteria like *E. coli, Klebsiella spp, Pseudomonas spp, Acinetobacter spp, Proteus spp, Serratia*. Gram positive bacteria like *Enterococcus spp, Staphylococcus aureus, Coagulase negative Staphylococcus*.(1,2) Antibiotic treatment is usually started empirically before urine results are available. Extensive and inappropriate use of antibiotics has resulted in emergence of multidrug resistant bacteria which is a major problem worldwide. Therefore the criteria for the selection of antimicrobial agent should be determined on the basis of most likely pathogen and its expected resistance pattern in that geographical area.(3)

Hence the current prospective analysis of uropathogens and their antimicrobial susceptibility pattern for the period of 6 months in patients with UTI in a tertiary care hospitals has been undertaken.

Materials and Method

The study was conducted in the department of Microbiology of tertiary teaching hospital. A prospective analysis was made on urine culture and sensitivity between July 2016-December 2016. A total of 510 clean catch midstream urine samples collected in wide mouthed sterile container were received at Department of Microbiology, Shimoga institute of medical sciences, Shivamogga

Isolation and Identification: Urine specimen was examined by wet mount preparation for the presence of pus cells, red blood cells, urinary casts, epithelial cells. They were further processed by Standard loop technique(A semiquantitative method). A loopful(0. 001 ml) of well mixed uncentrifuged urine was inoculated onto the surface of blood agar and MacConkey agar. Plates were then incubated at 37 degree celcius aerobically for 24hrs. Positive urine culture was determined by significant bacteriuria. (count > 10^5 /ml in a carefully taken and promptly examined sample). The organisms isolated were identified by their colony morphology, Gram stain and relevant standard biochemical methods. Catalase and oxidase test was done.

Antimicrobial susceptibility testing: Antibiotic susceptibility testing was carried out by Kirby Bauer Disk Diffusion method. Following antibiotics were used for gram negative organisms Fosfomycin(200µg) Ampicillin(10 µg) Gentamicin(10 µg), Nitrofurantoin(300µg), Cotrimoxazole(1. 25/23. 75 µg)

Norfloxacin(10µg), Ofloxacin(5 µg), Aztreonam(30µg), Ceftazidime(30µg), Cefotaxim(30 µg), Amikacin(30 µg), Amoxiclavulanic acid(30µg), Ciprofloxacin(5 µg), Levofloxacin(5 µg), Imipenam(10 µg), Pipercillin Tazobactam (100:10 µg). Antibiotics used for gram positive organisms Fosfomycin(200 µg), Nitrofurantoin(300 µg), Linezolid(10 µg), Vancomycin(30 µg), Erythromycin(15 µg), Azithromycin(15 µg), Clindamycin(2 µg) Doxycycline(30 µg), Gentamycin(10 µg), Ciprofloxacin(5 µg), Norfloxacin(10 µg), Cotrimoxazole(1. 25/23. 75 µg), Cefoxitin(30 µg). Interpretation was as per Clinical laboratory standard institute(CLSI) guidelines.[4]

Result

A total of 510 samples were received at clinical laboratory from patients with suspected UTI during the period of July 2016 to December 2016. Among 510 samples 250 samples showed significant bacteriuria and 10 showed yeast cells. *Escherichia coli* was most predominant organism isolated accounting for 61.6%(154/250)followed by *Staphylococcus aureus* 19.2%(48/250), *Enterococcus species* 10%(25/250), *Klebsiella species* 3.2%(8/250), *Pseudomonas species* 1.2%(3/250), *CoNS* 0. 8%(2/250). [Table 1]. Sex wise distribution of UTI showed female predominance with 183(73. 20%) samples and in males 67(26. 80%)[Table 2]

Antibiotic susceptibility pattern: In our study *E. coli* showed high sensitivity to Fosfomycin(100%), Nitrofurantoin(100%), Imepenam(77. 27%), Aztreonam(52.59%) and least sensitive to Norfloxacin(20.12%), Ciprofloxacin(15.58%), Levofloxacin(11.68%). *Klebsiella species* was highly sensitive for Nitrofurantoin(100%), Gentamicin(62.5%) and least sensitive to Levofloxacin, Ciprofloxacin, Norfloxacin. *Pseudomonas species* is highly sensitive to Piperacillin Tazobactam(100%), Aztreonam(66.66%), Amikacin(66.66%) and highly resistant to Levofloxacin, Ciprofloxacin, Norfloxacin[Table 3]

Among gram positive organisms *Staphylococcus aureus* high sensitivity to Linezolid (100%), Vancomycin(100%), Nitrofurantoin(100%) and least sensitive to Ciprofloxacin(12.5%), Norfloxacin (18.75%), Levofloxacin (12.5%). Enterococcus species highly sensitive to Fosfomycin(100%), Nitrofurantoin(100%), Linezolid(100%), Vancomycin(100%). *Coagulase negative staphylococcus*(*CoNS*) was highly sensitive to Linezolid, Vancomycin, Nitrofurantoin, Cefoxitin and least sensitive to Ciprofloxacin, Norfloxacin, Levofloxacin. [Table 4]

Table 1: Distribution of organisms

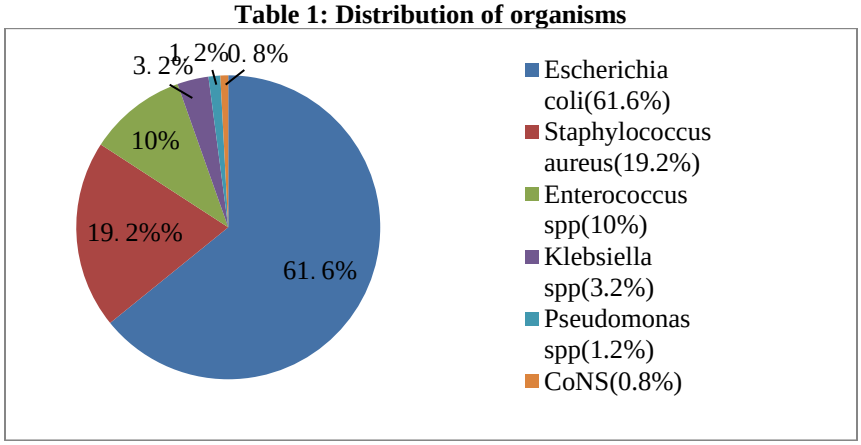

Table 2: Sexwise distribution of UTI

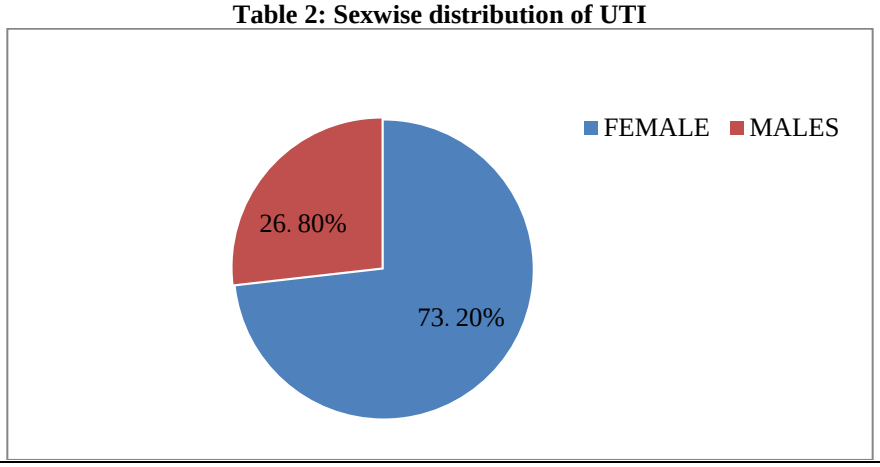

Table 3: Antibiotic Susceptibility pattern of gram negative organisms

Antibiotic	*E. Coli(%)*	*Klebsiella species(%)*	*Pseudomonas spp(%)*
Gentamicin	43.50	62.5	0
Ampicillin	12.98	-	0
Nitrofurantoin	100	100	-
Fosfomycin	100	-	-
Aztreonam	52.59	37.5	66.66
Norfloxacin	20.12	0	0
Ciprofloxacin	15.58	0	0
Levofloxacin	11.688	0	0
Piperacillin Tazobactam	40.90	50	100
Amikacin	47.40	25	66.66
Ceftazidime	28.57	50	0
Cefotaxim	24.67	50	0
Imipenam	77.27	-	100
Cotrimoxazole	61.03	75	100
Amoxiclavulanic acid	14.93	12.5	0

Table 4: Antibiotic Susceptibility pattern of gram positive organisms

	Staphylococcus aureus(%)	*Enterococcus spp(%)*	*CONS(%)*
Linezolid	100	100	100
Vancomycin	100	100	100
Nitrofurantoin	100	100	100
Fosfomycin	100	100	100
Erythromycin	33.33	-	0
Azithromycin	33.33	-	0
Clindamycin	27.083	-	0
Doxycyclin	72.9	72	100
Ciprofloxacin	12.5	32	0
Norfloxacin	18.75	24	0
Levofloxacin	12.5	36	0
Cefoxitin	35.41	-	100
Cotrimoxazole	66.66	-	100
Ampicillin	-	60	-
Gentamycin	47.9	60	100

Discussion

Urinary tract infection (UTI) is one of the most common infections in both outpatients and hospitalized patients which affects all age groups of people including men, women and children worldwide. This study was conducted to know the prevalence of UTI and antibiotic susceptibility pattern of most common uropathogens isolated from patients visiting Mcghan Hospital, SIMS, Shimoga.

In this study *Esherichia coli* was most common organism isolated accounting for 61.6% of cases. In India incidence of *E. coli* is about 50-80% as reported by various studies. *Staphylococcus aureus* was the second most common organism isolated accounting for 19.2% of cases. According to study done by Somshekhara et al and Hassan et al *Klebsiella* species was second most common organism isolated.[5,6]

In our study *E. coli* most common gram negative isolate which showed high sensitivity for Fosfomycin (100%), Nitrofurantoin (100%). According to study done by Ekadashi Rajni Sabharwal and Rajni Sharma 338 (94.4%) isolates were found to be susceptible to fosfomycin. *E. coli*(65.4%) isolates showed high sensitivity to Fosfomycin (97.2%), Nitrofurantoin (94.5%).[7] Similar study done by Sultan et al showed *Enterobacteriae* group with high sensitivity to Fosfomycin(100%), Nitrofurantoin(100%).[8]

Among gram positive isolate *Staphylococcus aureus* was most common which showed high sensitivity to Linezolid (100%), Vancomycin (100%), Nitrofurantoin (100%). Similarly study done by Sultan et al showed high sensitivity to Fosfomycin(100%), Linezolid (100%), Vancomycin (100%), Nitrofurantoin (50%) and study done by Ekadashi Rajni Sabharwal and Rajni Sharma showed high sensitivity to Vancomycin(100%), Fosfomycin(100%).[7,8]

Study done by Banerjee et al *E. coli* showed 98.14% susceptibility to fosfomycin and Klebsiella species showed 95.52% susceptibility to fosfomycin.[9] Similarly study by Gupta et al showed all the ESBL

producing strains of *E. coli* were 100% sensitive to fosfomycin.[10] Study by Sahni et al showed *E. coli* (83%) and *Enterococcus spp*(90%) susceptibility to fosfomycin.[11]

Fosfomycin is a bactericidal agent with low level of resistance has emerged as a promising treatment option particularly those caused by *E. coli* and *Enterococcus faecalis*.[8,11] Along with long half life and low molecular weight which helps in penetration into tissue with ease, it also has rare adverse reactions like diarrhea, nausea, vomiting, skin rash, heartburn, vaginitis, headache, chills and asthenia occurring in about 1-8%.[12]

Nitrofurantoin is used as an alternative treatment of uncomplicated UTIs. Resistance is developed by stepwise mutations and acts at multiple targets in cell wall so that the resistance acquired is not as fast as drugs. It is important treatment agent for asymptomatic bacteriuria in pregnancy as it leads to pyelonephritis in pregnancy.[12] In contrast to the other classes of antimicrobial agents, acquired resistance to nitrofurantoin is said to be quite rare. Nitrofurantoin is increasingly being used at present to treat Vancomycin resistant enterococcus(VRE) nosocomial UTIs (i.e., catheter-associated bacteria), and oral antibiotics are preferred for nosocomial vancomycin-sensitive Enterococcus (VSE) or VRE catheter-associated bacteriuria. Nitrofurantoin has also has high activity against MRSA and MR*CoNS*.[12,13,14]

In our study high resistance was seen with Norfloxacin, Ciprofloxacin and Levofloxacin. Study done by Gupta et al showed high resistance to ciprofloxacin (85.5%) and levofloxacin (53.8%) and study done by Somshekhara et al *E. coli* showed higher resistance to Ampicillin(85.6%) followed by Norfloxacin(78.6%), Levofloxacin(76.5%).[5,17]

There is increase resistance pattern to fluoroquinolones. Fluroquinolones have assumed important role in therapy of UTI because of less side effects and also broad spectrum activity but because of indiscriminate use of empirical treatment has led to widespread resistance.[15,16,17]

Conclusion

Escherichia coli is the most common uropathogen causing UTI in patients of tertiary care hospital, SIMS, Shimoga. Fosfomycin and Nitrofurantoin were the most sensitive drug for both gram positive and gram negative organisms. Routinely used antibiotic like Norfloxacin, Ciprofloxacin, ofloxacin, Levofloxacin were highly resistant.

Most organisms showed multidrug resistance. This multidrug resistance is mainly because of biofilm formation and ESBL production. There is need of continuous surveillance of frequency and antibiotic susceptibility pattern of microogranisms for effective empiric therapy. This study highlights Fosfomycin and Nitrofurantoin as an important treatment option for uncomplicated UTIs in the current era of increasing fluoroquinolone resistance among uropathogens. The employment of Fosfomycin and nitrofurantoin as the first-line therapy may definitely contribute to a reduction in overall fluoroquinolone use, thereby helping to reduce selection pressure for increased resistance to fluoroquinolones.

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