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ANTIBIOGRAMS OF COMMUNITY-ACQUIRED UROPATHOGENS FROM A SECONDARY CARE RURAL HOSPITAL IN SOUTHERN INDIA

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ABSTRACT

Introduction: Antimicrobial resistance to uropathogens is a growing problem and a cause of major concern in many countries including India. The current study was done with the objective to study the antibiotic sensitivity pattern of pathogens causing Urinary Tract Infections (UTIs) in a secondary care hospital in Tamilnadu.

Methodology: This was a retrospective study of antimicrobial susceptibility data for urine samples collected at a 300 bedded secondary care rural hospital in Dindigul district, Tamilnadu, southern India. Results of urine culture of patients attending the Outpatient and inpatient departments of the hospital over a period of six months from Feb 2011were collected. The data collected from the laboratory were entered into the WHONET 5.6 program and frequencies and percentages were calculated.

Results: Of the 1414 samples processed for culture during the study period, 384 (27.15%) samples showed significant growth of micro organisms. E.coli (80.9%), Klebsiella spp. (9.6%) and Enterobacter spp. (4.9%) were the three most common pathogens isolated. Seventy two percent of all E.coli isolates were resistant to sulphamethoxazole/trimethoprim, 70.7% to ciprofloxacin and 30.8% to nitrofurantoin. E.coli showed a resistance of less than 25% to Imepenem, amikacin and chloramphenicol.

Conclusion: The antibiotic resistance pattern of common organisms causing UTIs to commonly used antibiotics, in the current hospital based setting in alarming. Guidelines based on local susceptibility patterns of uropathogens need to be formulated.

Key words: Antibiotic susceptibility, Drug resistance, Escherichia coli, Urinary tract infections.

INTRODUCTION

Urinary tract infections (UTIs) are one of the most common infections encountered in clinical practice.[1] Globally, UTIs cause not only a significant amount of morbidity, but also a significant financial burden. [2]

The treatment of UTIs depends on various factors like the age, gender, underlying disease, infecting agent, level of risk of infection with resistant pathogens, use of catheter, pregnancy and whether there is involvement of lower or upper urinary tract. Infectious Diseases Society of America (IDSA) recommends Trimethoprim/sulphaethoxazole and Nitrofurantoin as the first line drugs for the treatment for acute uncomplicated UTIs.[3] The other agents recommended in the treatment of UTIs include fluoroquinolones, cephalosporins and other β-lactams.[3]

Reports of uropathogens resistant to previously effective antibiotics have emerged globally in recent years.[4-6] Antimicrobial resistance to uropathogens is a growing problem and a cause of major concern in many countries including India.[7,8] With the increasing trend of antibiotic-resistance, the management of urinary tract infections is likely to become complicated with limited therapeutic options.

The selection of antimicrobial drugs for empiric therapy is best based on the susceptibility pattern of the species isolated in a given area and, if determined, can update the prevailing efficiency of commonly prescribed antibiotics. The knowledge of the susceptible organism and the resistance patterns in the local area is imperative for optimizing

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treatment and minimizing the emergence of resistant strains. The current study was done with the objective to study the antibiotic sensitivity pattern of pathogens causing UTIs in a secondary care hospital in Tamilnadu.

MATERIALS AND METHODS

This was a retrospective study of antimicrobial susceptibility data for urine samples collected at a 250 bedded secondary care rural hospital serving a population of around 200,000 in Dindigul district, Tamilnadu. Results of urine culture of patients attending the Outpatient and inpatient departments of the hospital over a period of six months from Feb 2011were collected using a proforma. Urine culture was sent for all suspected UTI cases during the study period. Only the initial sample of an individual received was included to avoid duplication. All samples were collected as part of routine patient care. Samples were excluded from the dataset if there were duplicate samples with differing sensitivities, if there were duplicate samples listed over months, or if samples grew multiple pathogens.

Semi quantitative urine culture using a calibrated loop was used to inoculate blood agar and MacConkey plates. Cultures growing $>10^5$ cfu/ mL were considered positive. The bacteria were subsequently isolated as pure cultures.[9] Antibiotic susceptibility was done on Mueller-Hinton agar according to the Kirby-Bauer method.[10]All agar preparations were fully dissolved and autoclaved at 121°C for 15 minutes. After sterilization, 25 ml was gently poured onto each sterile petri dish (90 mm diameter) placed on a horizontal work top and allowed to cool to room temperature.

Three to five morphologically similar colonies of each organism (aged 18–24 h) were touched with a sterile loop and inoculated in 4 ml of peptone water prepared according to manufacturer's recommendations. The peptone water was incubated at 36°C for 2 to 5 hours until turbid, and standardized to 0.5 McFarland nephelometer prepared by dissolving 0.6ml of 1% solution of Barium chloride dehydrate into 100ml of 1% sulphuric acid. The entire surface of agar was inoculated by swabbing and allowed to dry for 3 to 5 minutes before aseptically placing 4 antibiotic disks per plate.

Commercially prepared antibiotic disks were used. Inhibition zone diameters were read at 18 h for all organisms except for Staphylococcus which was read at 24 h. Clear zone diameters were measured to the nearest millimeter using a millimeter ruler under natural light. Each measurement of the inhibition zone diameter was interpreted as 'sensitive', 'intermediate' or 'resistant' according to reference charts.

The data collected from the laboratory were entered into the WHONET 5.6 program and frequencies and percentages were calculated.[11] WHONET is freely downloadable Windows-based database software which was developed by the WHO for the management and analysis of microbiology data, with a special focus on the analysis of the antimicrobial susceptibility test results. It is also possible to retrieve, correct and print clinical records by using this program.

RESULTS

Of the 1414 samples processed for culture during the study period, 384 (27.15%) samples showed significant growth of micro organisms. Urinary tract infection was confirmed in 150/615 specimens from males and 234/799 specimens from females. The age and gender distribution of the study subjects were shown in Table 1. The mean age of the study subjects were 45.2 (SD 19.3). Women in the age group 20-60 years constituted 42% of the study subjects. Among men, UTIs were more among elderly men over 60 years (45.3%).

Table 1. Age and gender distribution of the study subjects (N=384)

Age group	Male (N=150)	Female (n=234)	Total (N=384)
< 20 years	17 (11.3%)	26 (11.1%)	43 (11.2%)
20-39 years	20 (13.3%)	89 (38.0%)	109 (28.4%)
40-59 years	45 (30%)	73 (31.2%)	118 (30.7%)
>60 years	68 (45.3%)	46 (19.6%)	114 (29.7%)

Among males, most common uropathogens identified were Escherichia coli (82.6%) followed by Klebsiella spp. (6.6%) and Proteus spp. (5.3%). E.coli (79.9%), Klebsiella spp. (11.5%) and Enterobacter spp. (6.8%) were the three most common pathogens

isolated from the urine of female patients. The details of micro organisms identified from urine samples were shown in Table 2.

Table 2. Causative micro organisms for Urinary Tract Infections (N=384)

	Male (n=150)	Female (N=234)	Total (N=384)
Escheria coli	124 (82.6%)	187 (79.9%)	311 (80.9%)
Klebsiella spp.	10 (6.6%)	27 (11.5%)	37 (9.6%)
Proteus mirablilis	08 (5.3%)	02 (0.85%)	10 (2.6%)
Enterobacter spp.	03 (2%)	16 (6.8%)	19 (4.9%)
Others	05 (3.3%)	02 (0.85%)	07 (1.8%)

Seventy two percent of all E.coli isolates were resistant to sulphamethoxazole/trimethoprim, while the figure was 70.7% to ciprofloxacin. E.coli showed a resistance of less than 25% to Imepenam, amikacin and chloramphenicol. Ciprofloxacin resistance was comparatively lesser among Klebsiella (24.3%). Nitrofurantoin resistance was shown by 30.8% of E.coli isolates and 70.9% of Klebsiella. The details of antibiotic susceptibility to the uropathogens are shown in Table 3.

Table 3. Antibiotic susceptibility pattern (% resistance) of the micro organisms causing Urinary Tract Infection

	E. coli N=311	Proteus spp. N=10	Klebsiella spp. N=37	Enterobacter spp. N=19
Amikacin	23.1%	10%	8.1%	21.05%
Amoxycillin	97.7%	80%	97.2%	94.7%
Cefotaxime	28.9%	20%	18.9%	10.5%
Chlorampenicol	23.4%	20%	21.6%	42.1%
Ciprofloxacin	70.7%	40%	24.3%	47.3%
Gentamicin	60.2%	20%	35.1%	57.8%
Imipenem	0.96%	0%	0%	0%
Nitrofurantoin	30.8%	60%	72.9%	42.1%
Trimethoprim-Sulfamethoxazole	72.0%	60%	29.7%	63.1%

DISCUSSION

Worldwide, the microbial spectrum of uncomplicated UTIs and pyelonephritis mainly consists Escherichia coli (75%–95%).[3,12] So, local antimicrobial susceptibility patterns of E. coli should be considered in empirical selection of antibiotics for uncomplicated UTIs. As the antibiotic susceptibility of E. coli strains causing uncomplicated UTIs vary considerably between regions, a specific treatment recommendation may not be universally acceptable for all regions. International guidelines may not be applicable for treating UTIs in India, and guidelines based on local susceptibility patterns need to be considered.

It has been extensively reported, as in this study, that adult women in the reproductive age group have a higher prevalence of UTIs than men, principally owing to anatomic and physiological factors.[13] Consistent with earlier studies, elderly (61 years or more) males had a higher incidence of UTI compared to the elderly females.[14-16]This could be because of the fact that with advanced age, prostate enlargement and neurogenic bladder might increase the chances of UTIs.

The most commonly isolated organism in UTIs in our study was E. coli. The proportion of bacterial species isolated was similar to those described in several previous studies.[17-19]The data collected from other places around the world, also showed that E. coli and Klebsiella spp. are still the commonest uropathogens isolated in community acquired UTI patients. The culture positive rate for UTIs was higher in our study (27.15%) in comparison with studies conducted in Jaipur (17.19%) and Aligarh (10.86%) but lower than that in Odissa (34%).[13,15,16]

The IDSA guidelines consider cotrimoxazole and nitrofurantoin as the current standard therapy for uncomplicated UTIs.[3] There is unacceptably high resistance to cotrimoxazole, amoxicillin, and ciprofloxacin among uropathogens isolated in our setting. Continued use of these drugs is likely to be associated with a high risk of treatment failure. This makes empiric management of outpatient UTIs

challenging. The findings from this study, when corroborated with other previous studies, reiterates that ciprofloxacin and cotrimoxazole cannot be used as antimicrobial agents for empirical treatment of UTIs in our setting.[8,15,16] Overall resistance to nitrofurantoin was low, suggesting that it could be used as empiric monotherapy for uncomplicated UTIs. Previous Indian studies have also shown lower resistance rates to nitrofurantoin. [8,15,16,21]

The increasing resistance to fluoroquinolones has been documented in the country by previous studies.[8,15,16,20,21] Ciprofloxacin is being recommended as the first line of treatment in acute pylonephritis.[3]But the high rate of resistance to the drug is alarming. An association between the increase in quinolone prescriptions and an increase in bacterial resistance has been documented.[22-24] Ciprofloxacin is widely prescribed to treat a number of diseases including UTIs, Reproductive tract infections, gastroenteritis, infections of bones and joints, lower respiratory tract infection and enteric fever. However the resistance rates for ciprofloxacin against uncomplicated UTI pathogens were reported low as 0-14.7 per cent in the ECO-SENS Project, 2.5 per cent in the USA and 1.2 per cent in outpatients in Canada.[5,24]

Antibiotic resistance is a major global public health concern, particularly in settings where few treatment options are available, either due to lack of availability or affordability of second line therapies. Antibiotic misuse augments the antibiotic resistance. Irrational prescription of antimicrobials which are available over-the-counter in India, has its own contribution to this alarming situation.[25,26] In addition, weak government regulation allows for the importation and sale of substandard drugs in the country.[26] The widespread use of antimicrobials in veterinary practice may be another possible factor for the emergence of resistant strains.[26,27] Unqualified practitioners, pharmacists and nurses all over the country use antimicrobials indiscriminately.[26,28] The current evidence of increasing antibiotic resistance trends in UTI patients in India indicate that it is imperative to rationalize the use of antimicrobials and to use these cautiously.

The predictive value of in-vitro resistance testing among pathogens causing UTIs have been questioned.[29]Many antibiotics achieve higher concentrations in urine than those tested in laboratory assays. The urine levels of trimethoprim and sulfamethoxazole may be 35 and 3 times, higher than the levels in serum.[30]In such cases, it is possible that even with apparent in-vitro resistance, successful cure may be realized. Detailed studies are warranted with this regard.

This study presents hospital based antibiograms of uropathogens isolated from consecutively selected participants presenting to hospital and there is always a possibility of selection bias towards complicated UTI and therefore, to over-estimate resistance prevalence in a particular community. Patients may visit hospitals only when symptomatic and sometimes after taking medications including antibiotics. Local resistance rates reported in hospital antibiograms might be skewed by cultures of samples obtained from inpatients or those with complicated infections. Prospective and unbiased resistance surveillance of uncomplicated uropathogens at the local practice and/or health care system levels is critical for informing empirical antimicrobial decisions.

To conclude, the antibiotic resistance pattern of common organisms causing UTIs to commonly used antibiotics, in the current hospital based setting in alarming. Guidelines based on local susceptibility patterns of uropathogens need to be formulated. Regional surveillance systems have to be strengthened for monitoring antibiotic susceptibility of common pathogens causing UTIs.

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