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Quinolone resistance among uropathogens in a tertiary care centre

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Abstract : Background objectives The resistance of bacteria causing urinary tract infections (UTI) to commonly prescribed antibiotics is increasing both in developing as well as in developed countries. Resistance has emerged even to more potent antimicrobial agents. The present study was undertaken to report the quinolone resistance among the uropathogens isolated in a tertiary care centre in south India.Methodology A total of 1431 consecutive urine samples were cultured in Department of Microbiology, from August to October 2014 and pathogens isolated were identified by standard methods. Antibiotic susceptibility was done by Kirby Bauer disc diffusion method to quionolones. The patients age, sex and admission status were also observed. Results Of the 1431 samples, 341 showed growth. Females were frequently infected and adults were mostly affected than children. Inpatients were commonly infected than outpatients. Escherichia coli (64.2) was the most common organism isolated followed by Klebsiella species (26.1). Overall resistance of organisms to Quinolones were Norfloxacin (67.5), Ofloxacin (42.8) and Ciprofloxacin(41.5) Conclusion This study indicates the emerging quinolone resistance among the bacterial pathogens of UTI which may be due to its frequent use. Hence our study indicates that it is imperative to rationalize the use of quinolones in the community and also to use them conservatively.

Keyword : Quinolone resistance, Uropathogens, UTI, Antibiotic overuse.

INTRODUCTION:

Urinary tract infections (UTIs) are the most common infections encountered in clinical practice[1] affecting people of all ages and both sexes. The primary treatment includes empirical antibiotic therapy even before the culture results are available. The treatment of UTIs varies according to the age of the patient, sex, underlying disease, infecting agent and whether there is lower or upper urinary tract involvement. As a result of their wide spectrum of activity, quinolones have been extensively used in the treatment of UTIs. Nalidixic acid was the first quinolone discovered and it was used for treating UTI. But nowadays it is not widely prescribed by the clinicians. Recently ciprofloxacin was pointed out as the most consumed antibacterial agent worldwide. This high level of use and to some degree of misuse or use of quinolones with poor activity in some developing countries has been blamed for the rapid development of bacterial resistance to these agents. The three main mechanisms of quinolone resistance are 1) Alteration in targets of quinolones by chromosomal mutations in DNA gyrase and Topoisomerase IV genes, 2) Decreased accumulation inside the bacteria due to impermeability of the membrane or an overexpression of efflux pump systems by chromosomal mutations and 3) Plasmid mediated qnr gene products protects DNA gyrase and Topoisomerase IV from quinolone inhibition. This is responsible for horizontal transfer of resistance genes. A precise UTI surveillance data is necessary because of the increasing antibiotic resistance. So the present study was undertaken to assess the quinolone resistance pattern in the common uropathogens isolated in a tertiary care hospital.

Material & Methods

The present study was conducted in and Hospital, for a period of three months from August 2014 to October 2014. Samples included in the study are clean catch mid stream urine, urine from Foley's catheter. All the urine samples were inoculated into MacConkey agar and Blood agar by a calibrated loop (volume 0.005 ml) within 30 minutes of collection and incubated for 18 - 24 hours at 37 ° C. Uropathogens which showed > 10 5 CFU/ml were identified and processed as per standard methods. The isolates were subjected for antibiotic susceptibility testing by using Kirby Bauer Disc Diffusion method according to CLSI guidelines. In the present study antibiotics to be tested are obtained commercially from Hi-media laboratories Limited, Mumbai - Ciprofloxacin (5μg), Norfloxacin (10μg) and Ofloxacin (5μg). The diameter of the zone was measured and interpreted as sensitive, intermediate, resistance according to the CLSI guidelines[2]. Escherichia coli 25922 was used as control.

RESULTS:

In the present study Escherichia coli (64.2%) was the most common organism isolated as in Chart I. Klebsiella (26.1%), P. aeruginosa (4.1%), Proteus (3.5%) and Acinetobacter (2.1%) were the other uropathogens isolated in our study.

Chart I:Organisms causing UTI
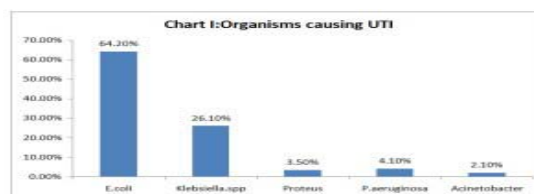
Among the E.coli isolates, females were more commonly affected than males and adults outnumber the children as seen in Table 1. These findings were same among Klebsiella and Acinetobacter isolates. Among P. aeruginosa and Proteus isolates males were affected more frequently than females but here also adults were more commonly affected than children.

Host characteristics	Organism causing UTI (n = 341)				
	E.coli n=219	Klebsiella.spp n=89	Proteus n=12	P.aeruginosa n=14	Acinetobacter n=7
Male	44.3%	43.8%	58.3%	57.1%	42.9%
Female	55.7%	56.2%	41.7%	42.9%	57.1%
Adults	78.5%	75.3%	75%	92.9%	100%
Children	21.5%	24.7%	25%	7.1%	-

Table 1:

The uropathogens were mostly isolated from the inpatients (71%) than the outpatients(29%) as from the Chart II. The following pattern of quinolone resistance among uropathogens were observed from the Table 2. All the uropathogens showed higher overall resistance to norfloxacin(67.5%) among the quionolones tested. The overall ciprofloxacin resistance in our study is 41.5% and the overall Ofloxacin resistance among uropathogens in our study is 42.8%. E.coli and Acinetobacter showed higher resistance (more than 50%) to ciprofloxacin and ofloxacin than the other isolates. E.coli showed 80% of resistance to Norfloxacin while Acinetobacter showed 71% of resistance to Norfloxacin. Proteus showed 25% resistance to ciprofloxacin and ofloxacin and 33% resistance to Norfloxacin. Klebsiella showed 20% resistance to ciprofloxacin and ofloxacin and 43% resistance to Norfloxacin. Pseudomonas showed 14% resistance to ciprofloxacin, 28% resistance to ofloxacin and 57% resistance to Norfloxacin.
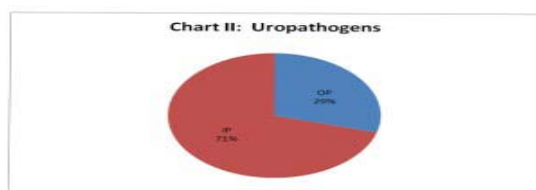

Chart II: Uropathogens

Table 2 Quinolone Resistance Among Uropathogens

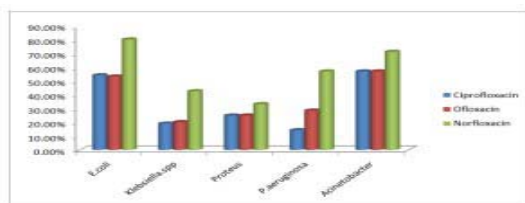|	Ciprofloxacin	Ofloxacin	Norfloxacin
E.coli	54.30%	53.40%	80.40%
Klebsiella.spp	19.10%	20.20%	42.70%
Proteus	25%	25%	33.33%
P.aeruginosa	14.30%	28.60%	57.10%
Acinetobacter	57.10%	57.10%	71.40%
Overall	41.5%	42.8%	67.5%

Chart III: Quinolone Resistance Among Uropathogens
DISCUSSION:
In our study the uropathogens were more commonly isolated from females than males because of their short urethra and its anatomical proximity to anus. This is similar to the study by Madumjer et al3 and Charles et al4.

Adults were predominantly affected than children. UTI in children is of great concern and should be well assessed and treated as it may lead to malfunctioning of urinary tract and systemic abnormalities later on in life. The inpatients (71%) were more frequently infected than outpatients in our study. This is also observed among children which correlates with the study by Kara et al5. Of the 341 culture positives, E.coli(64.2%) is the most frequent isolate followed by Klebsiella(26.1%). This is in accordance with the study by Kothari et al6, Quian et al7 and Ghosh et al 8. Because uropathogens largely originate from colonic flora, they are easy to predict and this is the rationale for empirical treatment in community acquired urinary tract infections. Ciprofloxacin, ofloxacin and norfloxacin are the most extensively used quinolones for the treatment of UTIs. E.coli showed more resistance to norfloxacin(80.4%) and ciprofloxacin(54.3%) which correlates with the study by Sharma et al9 which showed 66% resistance to norfloxacin and Jharna et al10 which showed 60% resistance to ciprofloxacin.. E.coli showed 53% resistance to Ofloxacin which correlates with the study by Quian et al7 which showed 45% resistance to Ofloxacin. To ciprofloxacin Klebsiella showed 19% resistance which is similar to the study by Astal et al11.To Ofloxacin, Klebsiella showed 20% resistance which is less than the study by Sharma et al9 . Acinetobacter showed 57% resistance to ciprofloxacin and ofloxacin which is in accordance with the study by Jharna et al10. Acinetobacter showed 74% resistance to Norfloxacin. Proteus showed 25% resistance to Ciprofloxacin which is higher than the study by Jharna et al10 which showed 55% resistance to Ciprofloxacin. Proteus showed 33.3% resistance to Norfloxacin which is higher than the study by Sharma et al9. To Ciprofloxacin, P.aeruginosa showed 14% resistance which is less than the study by Astal et al11 which showed 20% resistance to ciprofloxacin. P.aeruginosa showed 29% resistance to ciprofloxacin which is higher than the study by Sharma et al9. The overall ciprofloxacin resistance in our study is 41.5% which corresponds to the study by Otojevwo et al12, Sorlozona et al13 and Chatterjee et al14. Ciprofloxacin resistance could be augmented as it is used to treat a number of ailments including UTI, gastroenteritis, infections of bones and joints, endocarditis, lower respiratory tract infections, prostatitis and particularly enteric fever, inspite of its usage being associated with an increased risk of tendon rupture in all ages. It is not used in children except for cyctic fibrosis due to the risk of permanent injury to the musculoskeletal system. Among all uropathogens norfloxacin (67.5%) was most overall resistant quinolone which is similar to the study by Gaurav et al15. The overall Ofloxacin resistance among uropathogens in our study is 42.8% . In our hospital norfloxacin should be cautiously prescribed, as it is the most overall resistant antibiotic among quinolones.

CONCLUSION:
In the era of increasing antibiotic resistance, prudent use of antibiotics is critical to prolong the clinical effectiveness of existing agents. Excessive use of broadspectrum agents such as quinolones increases the evolutionary selective pressures that drive the increasing prevalence of resistance. In conclusion, the present results in increasing quinolone resistance among uropathogens in our study indicate that it is imperative to rationalize their use and to use them conservatively.

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