IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 11 Ver. 6 (November. 2018), PP 54-57
www.iosrjournals.org

Susceptibility Pattern of Escherichia coli to Fluoroquinolones as a Uropathogen: Study in a tertiary care hospital @ Mangadu between 2016 to 2018

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Abstract: *Urinary tract infection (UTI) second largest infection, causing antibiotic resistance strains among uropathogens, urging attention and concern in medical treatment. The common uropathogen reported is Escheriacoli (E.coli), often treated by fluroquinolones.* ***Aim :*** *To update our knowledge on common local uropathogens, study aimed at identifying the common uropathogen in uncomplicated UTI infection and evaluating the susceptibility pattern of Escherichia coli towards the frequently prescribed fluroquinolones for uncomplicated UTI in our tertiary care hospital at Mangadu South India, from August 2016 to August 2018.* ***Study Subjects & Results:*** *A total of 4217 urine samples analysed, common uropathogen was E.Coli (59.6%) from uncomplicated UTI patients. Antimicrobial susceptibility performed for E.Coli towards the five common fluroquinolones showed the pattern of susceptibility as 86.8% Levofloxacin, 73.5% Gatifloxacin, 82.9% Ofloxacin, 47.6% Norfloxacin, and 28.1%, Ciprofloxacin. Resistance was noticed higher towards Ciprofloxacin, Norfloxacin and Ofloxacin.* ***Conclusion:*** *Study was able to standardize the fluroquinolone pattern of antibiotic treatment within the uncomplicated UTI patient group, after the analysis of antibiogram sensitivity in our local population.*

Keywords: *urinary tract infection, elderly, Bacterial agents, Antimicrobial susceptibility*

Date of Submission: 13-11-2018 Date of acceptance: 28-11-2018

I. Introduction

Urinary tract infection accounts for 40% of cases.[1] Escherichia coli is of clinical importance due to its cosmopolitan nature, ability to initiate, establish and cause various kinds of infections. Escherichia coli being identified in 50 % of UTI studies most commonest uropathogen[2,3]**.** Worldwide studies on resistance to antibiotics is increasing especially in developing countries, Fuoroquinolones being the commonest drug for the uropathogens is showing the resistance as per the global surveillance studies. Resistance is related to the increasing usage of antimicrobial agents; growing numbers of patients with impaired immunity; increasing instrumentation, emphasis on cost control.**[2]** Fluoroquinolone resistance increased in Enterobacteriaceae causing community acquired or healthcare associated urinary tract infections and intra abdominal infections, exceeding 50% in some parts of the world, particularly in Asia. Two thirds of Enterobacteriacea producing extended spectrum β-lactamases were also resistant to Fuoroquinolones. Based on these data, study is designed to analyse the pattern of E.coli to the common fluroquinolones used in our population at Chennai South India. The fluoroquinolone drugs used in our study were Norfloxacin, Ciprofloxacin, Ofloxacin, Levofloxacin and Gatifloxacin.

II. Aim and Objective

The Study aimed at gaining knowledge about the common uropathogens in our population, with the susceptibility pattern of E.Coli towards the commonly used Fluroquinolones.

III. Materials:

A prospective study on a total of 4217 patients attending the out patients and inpatient units of Sri Muthukumaran Medical College Hospital and Research Institute near Mangadu , Chennai, South India formed the study subjects. Urine culture was analysed by mid-stream, urine specimen from patients during August 2016- August 2018. Clinical Details was noted, urine culture was done and analysed in the Department of Microbiology.

IV. Methods of Isolation and identification:

A measured amount of urine, using calibrated loop was inoculated onto Nutrient, Blood and MacConkey agar plates by streaking method. Inoculated plates were incubated aerobically at 37°C for 24 hours. Identification of pure isolates was done by observing morphological, cultural and biochemical characters. Antibiotic sensitivity testing was performed using the Kirby–Bauer disc diffusion method according to the Clinical and Laboratory Standards Institute Guidelines [4]. Reference strains from the American Type Culture Collection (ATCC), 25922 strains were used for E.coli control of the susceptibility determinations. "A culture with growth of potentially pathogenic bacteria was normally considered positive if the number of colony forming units per liter (CFU/mL) was10^5. E.Coli culture positives were selected, five fluroquilones were processed for the study purpose, antimicrobial drug susceptibility testing for Norfloxacin *NX*, (10 µg), Ciprofloxacin *CIP*, (5 µg), Levofloxacin (5 µg) and Gatifloxacin (5 µg). Interpretation of results was done based on the diameter of the zone. Dermographic data on the type of bacterial isolates from the urine specimens were tested.

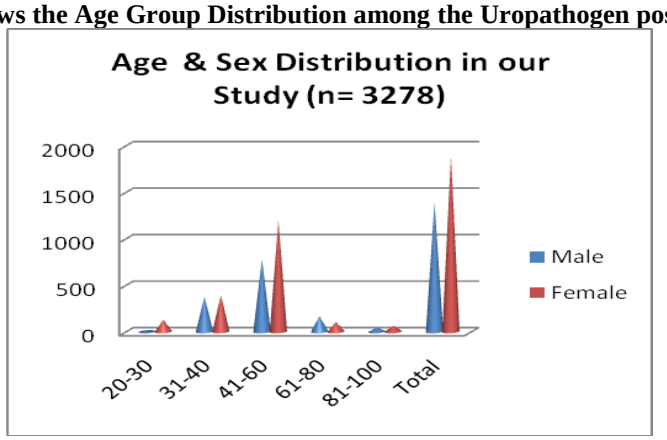
V. Results

Among the 4217 samples analysed 778 had no growth and 161 had mixed growth and non pathogenic contaminant. Uropathogens were seen in 3278 only. Among the 3278 samples analysed t*he study shows E. coli* is the most common uropathogen in acute uncomplicated UTI, which accounted for 59.6% in our hospital.

The Dermografic analysis shows the following:

Age group analysis among the uropathogen subjects showed highest growth among 41 to 60 years shown in Figure- I.

Figure- I: Shows the Age Group Distribution among the Uropathogen positive subjects



Among the 3278 the major uropathogen only 1955 (59.6%) was found to be E.Coli confirming the commonest uropathogen in our population, followed by Klebsiella species 864 (26.3%), other gram negative pathogens isolated from urine samples are Acinetobacter species(2.9%), Pseudomonas species(5.3%), Proteus species (1.7%), Citrobacter species(2.7%) and Enterobacter species(1.8%) as Shown in figure II

Figure –II Shows the Uropathogens among our Study Subjects

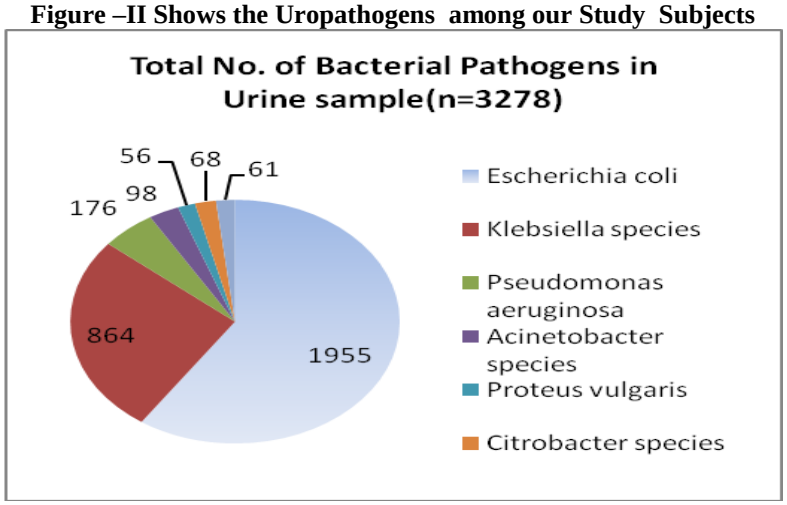


Table-I: Shows the Overall susceptibility pattern of fluroquinolones to E.Coli

The present study analysed 1955 culture positive Escherichia coli with a special reference to common fluoroquinolone used in our hospital for local population, the susceptibility for frequently used fluroquinolones were Norfloxacin , Ciprofloxacin, Levofloxacin , Ofloxacin and Gatifloxacin.

Table I: Overall Susceptibility pattern of Fuoroquinolones to Escherichia coli n=1955				
Drugs	**Susceptible**		**Resistance**	
	Total (n)	Percentage (%)	Total (n)	Percentage (%)
Norfloxacin	932	47.6	1023	52.3
Ciprofloxacin	550	28.1	1405	71.8
Ofloxacin	1621	82.9	334	17
Levofloxacin	1696	86.8	259	13.2
Gatifloxacin	1438	73.5	517	26.4

Escherichia coli showed the following resistance: Levofloxacin (13.2%) is followed by Ofloxacin (17%), Gatifloxacin (26.4%), Norfloxacin (52.3%) and Ciprofloxacin (71.8%). Study showed high resistance to ciprofloxacin and Norfoxacin. Overall fluroquinolones were showing around 12 to 70 % of resistance in our study, that needs immediate attention in future antibiotic policy evaluation.

VI. Discussion:

Fuoroquinolones are bactericidal, being the preferred drug to treat bacterial infections, recent studies on Escherichia coli shows a random increase in fluroquinolone resistance in the clinical fields. Both, the chromosomal mutations in the quinolones resistance-determining region (QRDR) of *gyrA* and *gyrB*, which encode DNA gyrase subunits, and *par C* and *par E*, which encode topoisomerase IV subunits and plasmid-mediated quinolone resistance (PMQR) genesplay a key role in Gram-negative bacteria including *E. coli*. WHO shows a serious threat by the happening in every region of the world with the potential to affect any one at any age in any country because of antibiotic resistance.[5] Antibiotic resistance genes is acquired by the bacteria by spontaneous mutation or genetic exchange with other bacteria, have the ability to resist one or more antibiotics due to multiple resistance traits, these traits over time become resistance to many different families of antibiotics, thus causing global public health problem. [5] India is largely affected by the resistant pathogenic strains because of faecal oral route, easy transmission within the large population. Further, environmental antibiotic resistant strain by pollution may encourage the transfer of resistance genes to human comensal and modify it as pathogenic bacteria. [6,7,8] Global surveillance shows, most UTI are often treated empirically, especially when caused by single bacterial pathogen especially E.Coli. Fuoroquinolones resistance by the bacterial uropathogens has increased, due to improper adherence of treatment with broad antibacterial spectrum and pharmacokinetic properties in UTI.. Fluoroquinolone resistance ranges from 2.2% to 69% for strains in uncomplicated, community acquired UTI (CAUTI) , 98% for strains from complicated CAUTIs. [9,10] Resistance especially to gram negative rods, due to various mechanisms, genes determining resistance to fuoroquinolones are located in the bacterial chromosome. Point mutations in gyrA and gyrB genes cause loss of the main target locus for fluoroquinolones. Resistance is low grade and develops when the concentration of the chemotherapeutic in the kidneys or urine is close to the MIC (minimal inhibitory concentration**.**[11,12] Research shows additional mutations, also in acr R and mar R genes produce a higher grade of resistance to fluoroquinolones, by an RND-type (resistance- nodulation-division family) pump, i.e. AcrAB-TolC, which is found in Escherichia coli. These mutations occur with a significantly lower incidence. The resistance of Gram-negative rods is also influenced by the availability of OMP (outer membrane protein) channels, through which the chemotherapeutic enters the cell. This type of resistance is exemplified by Omp F protein, which excessive expression reduces the ability of fluoroquinolones to penetrate the cell.[13,14,15,]

Antibiotic use is a major driver of antibiotic resistance, 2010 literature shows India is the worlds largest consumer of antibiotics for human health. [9,12] This may be due to the poor public health infrastructure, rising income, high burden of disease and unregulated sales of antibiotic leading to antibiotic resistance of infection in India

Current study shows the presence of fluroquinolone resistance in our hospital . Our study on shows E.Coli as the frequent uropathogen isolated among the enterobacteriaceae, and accounted for approximately 81% isolated from out patients. The suseptability to Ofloxacin was 82.9% whereas only 47.6% to Norfloxacin and 28.1%, Ciproflox. This study analysed increasing resistance between the most commonly used Ciproflox, Norflox and Ofloxacin getting into the resistane . Thus measures are required to urgently update for treatments in our local population. Our study reports was similar to NAUTICA (North American Urinary Tract Infection Collaborative Alliance) study revealed that ciprofloxacin resistance increased to 5.5% in 2004[17] shows the increase of resistance to fluroquinolones**.** Thus the resistance to fluroquinolones needs clear monitoring in

each hospital by analysing the antimicrobial susceptibility pattern on various bacteria for a large numbers. Whether all fluoroquinolones give equivalent results with short term therapy in acute uncomplicated UTI is a query. These data on the pattern on antimicrobial susceptibility will through light to determine and formulate the local antibiotic policies, to assist the microbiologist and clinicians to choose the antibiotic to prevent misuse or overuse of antibiotics.

VII. Summary & Conclusion

A drastic increase in Fuoroquinolones resistance and multidrug resistance among the recent years is increased, the prevalence of E.Coli being the common uropathogen that are responsible for urinary tract infections, along with in vitro resistance to fluroquinolones. Our study at a hospital located in a rural area shows the need to closely monitor the fluroquinolones developing resistance. Our data will surely help in determining the antimicrobial susceptibilities to fluroquinolone in our local population. Such studies will help in drug development. Paucity of new antimicrobial drugs for common infections like UTI which may continue to worsen in future.

Futurology:

Resistance traits are encoded genetically therefore specific genes can confirm the antibiotic resistance though it depends on mode and level of expressing gene. Our study will help us in future to isolate the specific gene responsible for the antibiotic resistance in our population.

Acknowledgment:

The author wishes to acknowledge the entire team the technicians, tutors, Assistant professor of Microbiology department of SMMCH & RI and MEDCT for the kind support and contributions for this project to be successful.

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