FLUOROQUINOLONE RESISTANCE PATTERN AMONG THE PATHOGENS CAUSING URINARY TRACT INFECTION IN A TERTIARY CARE HOSPITAL IN KANCHIPURAM DISTRICT, TAMIL NADU, INDIA

SHANTHI BANUKUMAR*, KANNAN I, SUKUMAR RG
Department of Microbiology, Tagore Medical College and Hospital, Tamil Nadu Dr MGR Medical University, Rathinamangalam, Chennai - 600127, Tamil Nadu, India. Email: shanthibanukumar@gmail.com

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INTRODUCTION
Urinary tract infection (UTI) is the most common bacterial infections caused by wide range of pathogens which is encountered affecting 150 million people worldwide. It is a severe public health problem affecting the economic burden of the country. UTI is of two types. First is uncomplicated one typically affecting otherwise healthy individual involving women, children, and elderly patients. The second is complicated UTI occurring in patients with indwelling catheters, UTI abnormalities, and immunosuppression either drug-induced or physiological or exposure to antibiotics.

The UTI plays a major role in causing morbidity in infant boys, older men, and women of all ages. It leads to serious complications such as recurrences, pyelonephritis with sepsis, renal damage in young children, preterm birth, and complications caused by frequent antinflammatory use, such as high-level antibiotic resistance and Clostridium difficile colitis. The indiscriminate use of antibiotics against these uropathogens is the main reason for the emergence and spread of resistance against the antibiotics used. Now, it has become a worldwide problem affecting all the people around the globe and initiating them to fight against this menace.

Fluoroquinolones were used by clinicians to treat the UTI because of very less chances of emergence of drug resistance due to the low minimum inhibitory concentrations against most organisms. They have assumed an important role in treating UTI since they have lesser side effects and also can be given orally. These drugs have a broad spectrum of activity to Gram-positive and in particular to Gram-negative infections. Fluoroquinolones are bactericidal and rapidly acting against Gram-negative bacilli in vitro. Nalidixic acid, the first quinolones used has a narrow influence spectrum with high resistance rates. Even though resistance to nalidixic acid has less clinical importance given to its infrequent use in the treatment of infections, it serves as a marker of the future increase in resistance to fluoroquinolones which has happened with Escherichia coli.

Mechanism of fluoroquinolone resistance is decrease in binding target enzymes because of change in DNA gyrase enzyme and/or the topoisomerase enzyme (s). Mutations can occur in gyrA and parC genes. Second mechanism is decrease in the amount of quinolones entering the cells because of defective function of porin channels. The third mechanism is the various efflux system localized in the membranes of many bacteria which pump the drug out of the bacteria.

Higher rates of resistance to quinolones have been reported from other parts of the world. About 60% of E. coli strains isolated from hospital-acquired infections in Beijing were resistant to ciprofloxacin. Resistance has become a problem when the usage of quinolones was needed to treat other infections caused by organisms such as gonococcus, salmonella, shigella, or campylobacter. The initiation of antimicrobial therapy in UTI is empirical, and the knowledge about the antimicrobial resistance pattern among common uropathogens is essential to the clinicians. This can facilitate appropriate and cost-effective therapy to be instituted in a hospital environment. By this, we can achieve both a favorable clinical outcome and a reduction in microbial resistance in health-care institutions.

METHODS
The present study is a cross-sectional study and was conducted in Tagore Medical College and Hospital, a tertiary care hospital at...
Kanchipuram district for 7 months from January 2016 to July 2016. A total of 2695 urine samples were collected from patients suspected to have UTI from both inpatient and outpatient departments.

Ethical committee clearance
Before the study, it was presented to the Institutional Ethical committee of Tagore Medical College, Chennai, and clearance obtained.

Sample collection and diagnostic procedure
The mid-stream urine samples collected in a sterile container from the outpatient and inpatient departments of hospital were sent to microbiology diagnostic laboratory. The samples were subjected to gram stain, and the relevant samples were taken for culture and sensitivity. Under strict aseptic precautions, each sample was streaked in respective culture plates such as MacConkey agar, blood agar, and nutrient agar. They were subjected to incubation aerobically for 24 hrs at 37°C. A total of 718 isolates were culture positive. Culture was positive for various pathogens such as E. coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Proteus mirabilis, Enterococcus, and Staphylococcus saprophyticus. All these organisms were identified after performing relevant biochemical tests and other confirmatory tests [17]. Their sensitivity was determined using Kirby-Bauer’s standard disc diffusion method with Mueller-Hinton agar. Zones were determined by the Clinical and Laboratory Standards Institute guidelines. For quality control, each pathogen’s ATCC strains were used as standard, and susceptibility was analyzed for each drug.

Those samples which showed different resistant patterns were selected, and fluoroquinolone-resistant strains were alone taken for the study.

RESULTS
Among 2695 urine samples, 718 patients showed culture positive. A total of 366 (50.9%) bacteria were fluoroquinolone resistant.

Table 1: Fluoroquinolone-resistant bacteria isolated from UTI patients

| S. No. | Bacteria isolated | Total number of isolates (n=366) (%) |
|-------|-------------------|-------------------------------------|
| 1.    | Escherichia coli  | 222 (61)                            |
| 2.    | Klebsiella pneumonia | 60 (16)                         |
| 3.    | Pseudomonas aeruginosa | 21 (6)                        |
| 4.    | Proteus mirabilis   | 12 (3)                             |
| 5.    | Enterococcus        | 27 (7.4)                           |
| 6.    | Staphylococcus saprophyticus | 24 (6.6)            |

UTI: Urinary tract infection

A total of six fluoroquinolone-resistant bacteria species were isolated (Table 1). E. coli is the predominant bacterium (61%) followed by K. pneumonia. 86% of the bacteria were Gram-negative bacilli and 14% of them were Gram-positive cocci.

Table 2 shows the number of different fluoroquinolone-resistant isolates collected from January to July and their distribution pattern.

Table 3 shows the resistance pattern of the bacteria isolated. The present study revealed that ofloxacin resistance in K. pneumoniae (10%) is more when compared to E. coli and other Gram-negative bacilli. Among the Gram-positive organisms, S. saprophyticus showed more percentage of resistance (62.5%) followed by enterococcus (11.1%) [18]. When compared to the Gram-negative bacilli, Gram-positive bacteria showed more resistance to ofloxacin drug among the uropathogens isolated here.

Naldixic acid resistance is more in P. aeruginosa (71.4%). The resistance pattern of ciprofloxacin is more in P. mirabilis 25% when compared to other Gram-negative bacilli. Among Gram-positive bacteria, S. saprophyticus showed 25% resistant which is higher compared to other Gram-positive bacteria. Norfloxacin resistance is more in E. coli (51.4%), and no resistance pattern was observed in P. aeruginosa.

Highest percentage of resistance is noted in S. saprophyticus to ofloxacin (62.5%), P. aeruginos to nalidixic acid (71.4%), P. mirabilis to ciprofloxacin (25%), and S. saprophyticus to norfloxacin (51%).

DISCUSSION
The usage of norfloxacin and nalidixic acid should be brought under control to prevent development of resistant pattern among the uropathogens in a health-care institution.

Over the years, the uropathogens show a variable fluoroquinolones susceptibility patterns that are based on factors such as changing patient population and extensive use and misuse of antimicrobial agents [19]. This indirectly relates to local practices of antimicrobial prescriptions. According to surveillance, the resistance to fluoroquinolones ranked as one of the four of the highest priority. Among the critically important drugs used against the microbes [20], they have a very important role in the treatment of more severe life-threatening infections such as septicemia. National data from the five World Health Organization [20] regions showed at least 50% resistance to fluoroquinolones in E. coli. In the present study, the resistance rate of E. coli to fluoroquinolones is higher (51.4%) among the uropathogens isolated.
CONCLUSIONS

The study reports indicate that the resistance to fluoroquinolones by the uropathogens differs in different organisms. Henceforth, restriction of their usage in appropriate bacterial infections and reservation of their prescription for important life-threatening infections will reduce emergence and spread of resistance strains within a health-care setup. This helps in maintaining an antimicrobial policy according to the resistant pattern observed in the laboratory-based surveillance studies. A periodically revised antibiotic stewardship in a health-care hospital is mandatory to maintain a good health-care system.

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