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FLUOROQUINOLONES AT THE BACK FOOT : A STUDY ON FLUOROQUINOLONE RESISTANCE IN ENTEROCOCCUS SPECIES ISOLATED FROM URINARY SPECIMENS IN A TERTIARY CARE HOSPITAL IN KOLKATA, INDIA.

Anindita Rakshit M.D. , Demonstrator , Department of Microbiology, Calcutta School of Tropical Medicine, Kolkata.

Bishal Gupta MBBS , PGT, Department of Microbiology, Calcutta School of Tropical Medicine, Kolkata .

Banya Chakraborty* M.D. ,Professor, Department of Microbiology, Calcutta School of Tropical Medicine, Kolkata ,*Corresponding Author.

ABSTRACT

OBJECTIVE: The study aims to detect the resistance pattern of fluoroquinolones (ciprofloxacin & levofloxacin) in Urinary Tract Infection (UTI) caused by Enterococcus species.

MATERIALS AND METHOD: 77 isolates of Enterococcus species from the urine samples of clinically suspected cases of UTI were studied. Identification and antimicrobial susceptibility testing was performed by conventional as well as automated methods.

RESULT: *Enterococcus faecalis* (53.25%) was the commonest. Most of the isolates were resistant to both levofloxacin (83.12%) and ciprofloxacin (85.71%).

CONCLUSION: Resistance to fluoroquinolones is of concern as it serves as an excellent oral choice of drug. So, the inclusion of this group of drug in the treatment regime should be reconsidered and effective strategies developed to contain the same.

KEYWORDS : UTI, fluoroquinolones, *Enterococcus species.*

INTRODUCTION:-

UTI is one of the most common infection both in the community as well as in a nosocomial set up. The syndrome can be divided into complicated and uncomplicated category (1, 2). Uncomplicated UTI is acute cystitis or pyelonephritis in a young woman without an underlying urinary tract or systemic disease. Complicated UTI is one where cystitis or pyelonephritis occurs in male, children, chronically catheterized patients and women with recurrent infection or underlying diseases.

Emperic anti- microbial therapy is the commonly employed protocol as there is delay in the receipt of the culture and anti bacterial susceptibility test reports. Hence, it is very essential to have an overview of the resistant pattern that the clinicians might face. Commonly the Cephalosporines, fluoroquinolones and aminoglycosides are usually started before the culture results are available(3).

However, injudicious use of empiric antibiotics is the commonest reason behind the emergence and spread of antimicrobial resistance amongst microorganisms (3-7).It is high time that the entire medical fraternity work in unison to fight against the menace of overwhelming antimicrobial resistance.

Perhaps, the predominant clinical sample received in any microbiological laboratory is urine from a suspected case of UTI. Expenses on this head are thus quite high (8). The present study aims to detect the resistance pattern of *Enterococcus species* to fluoroquinolones which plays an important role in the therapy of UTI caused by both Gram positive and Gram negative bacteria with lesser side effects and convenient oral dosage. Resistance to the fluoroquinolones group is caused by mutations in the chromosomal genes coding for DNA gyrase and DNA topoisomerase IV, which are the target enzymes, resulting in changes in drug accumulation (9).
This retrospective study was conducted on randomly isolated *Enterococcus species* from urinary samples at the bacteriology laboratory of the Calcutta School of Tropical Medicine, between November 2017 to August 2018. Detection of resistance to the two most commonly used drugs, Ciprofloxacin and Levofloxacin was done, along with speciation and determination of Minimum Inhibitory Concentration(MIC) values.

MATERIALS AND METHODS:-

The Study was conducted in the bacteriology laboratory of the School of Tropical Medicine, Kolkata between November 2017 to August 2018.Clean catch midstream urine specimens were collected into sterile containers from clinically suspected adult cases of UTI. After proper labeling, the specimens were processed immediately. Semi-quantitative culture of uncentrifuged urine was done by streaking onto the surface of blood Agar and Mac Conkey Agar plates. The plates underwent routine aerobic incubation for 18-24 hours and the counts were expressed in colony forming units(CFU) per milliliter(ml).Significant bacteriuria was taken as 10^5 CFU/ml of urine(10). Seventy seven isolates were identified as *Enterococcus species* as they were Gram positive cocci in chains, Bile-esculin test positive, grew on 6.5% NaCl and L-pyrollidonyl beta naphthylamide (PYR) positive.

Conventional Antibiotic Susceptibility testing on Mueller Hinton Agar by Kirby Bauer's disc diffusion method (by using disc strength of 5mcg each of ciprofloxacin and levofloxacin) was performed following Clinical Laboratory and Standards Institute(CLSI) guidelines(11). Simultaneously, the isolates were tested by an automated (VITEK 2D Compact ID/AST, Bio Merieux) for speciation ,antibiotic susceptibility along with determination of Minimal Inhibitory Concentration (MIC) value of the antibiotic.

All the Antibiotic susceptibility tests (ABST) discs and Media were obtained from Hi media Laboratory Pvt. Limited, Mumbai, India. Quality Control (QC) checks were performed at all steps of the processing.

RESULTS:

A total of 77 isolates of *Enterococcus species* obtained from urine samples of Clinically suspected UTI adult patients were included in the study. All the specimens showed monomicrobial growth. *Enterococcus faecalis* was the most commonly detected species (53.25%), followed by *Enterococcus faecium(41.56%),Enterococcus gallinarum(3.90%) and Enterococcus durans(1.3%)*

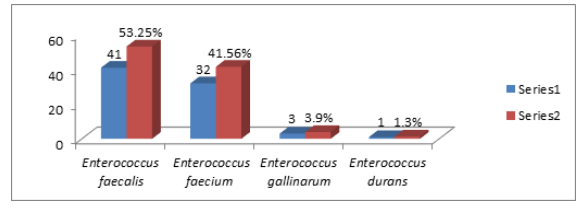

Fig1: Number and percentage of different species isolated.

The sex predilection was slightly more in males(42 out of 77) than females(35 out of 77).

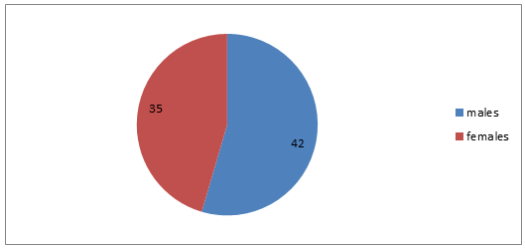

Fig2: Sex distribution of cases under study.

The highest number of isolates was obtained in the age group ranging between 21-40 years

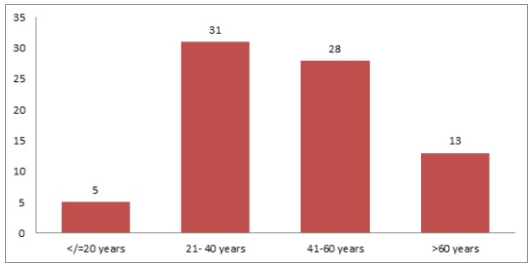

Fig3: age distribution of cases under study

Resistance to Ciprofloxacin was seen in 85.71% of isolates and to Levofloxacin was 83.12%. Sensitivity to Ciprofloxacin was 12.99% and that to Levofloxacin was 14.30%.The MIC value of all the isolates that were resistant to both Ciprofloxacin and Levofloxacin was greater than or equal to 8.

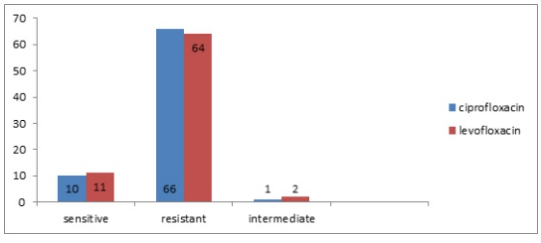

Fig4: antibiotic susceptibility pattern of the two fluoro quinolones tested under the study.

DISCUSSION AND CONCLUSION:

Urinary tract infection (UTI) is the most common bacterial infections caused by wide range of pathogens which is encountered affecting150 million people worldwide (12). It is perhaps, the commonest specimen received by any bacteriology laboratory in common clinical Microbiology parlance. The primary organisms that cause UTI are bacteria and the diseases ranging from asymptomatic to severe sepsis affecting millions of people every year. (13,14,15)

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 (MIC) against most organisms (16). However, our study showed a higher MIC value of >/=8 in all the resistant isolates. Only two isolates were sensitive to levofloxacin but resistant to ciprofloxacin.

However, over the years, the uropathogens show a variable fluoroquinolone susceptibility patterns that are based on factors such as changing patient profile and injudicious use of antimicrobial agents (17).

Studies across India also reported various degree of Fluoroq uinolone resistance up to 68.5% which is almost comparable to the present study (18) as this study also depicted a nearly similar resistance pattern(ciprofloxacin- 85.71%, Levofloxacin - 83.12%).

Although women, particularly those aged 16–64 years, are significantly more likely to experience UTIs than men (19), urinary infections frequently occur in both genders and across all age groups (19,20). In the present study, the incidence was also slightly more in male patients.

Resistance to fluoroquinolones is of concern as it serves as an excellent oral choice of drug. So, the inclusion of this group of drug in the treatment regime should be reconsidered and effective strategies developed to contain the development and subsequent spread of resistance.

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