



A STUDY OF ORAL ANTIMICROBIAL THERAPY FOR PATIENTS INFECTED WITH ESBL PRODUCING URO-PATHOGENS IN A TERTIARY CARE HOSPITAL, NORTH KERALA.

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ABSTRACT

Introduction: Extended Beta Lactamase producing pathogens are one among the emerging pathogens which are usually resistant to most commonly used antibiotics. So, it is very important to find out alternative oral options to treat those pathogens. This study is conducted to find out the prevalence of ESBL producing uropathogens over a period of time and to find out effective oral antibiotics to treat such pathogens. **Methods:** All isolates with ESBL pattern of drug resistance detected by VITEK will be included in the study. Data on oral antibiotics like Nitrofurantoin, Norfloxacin, Nalidixic acid, Cotrimoxazole, and Fosfomycin will be taken and correlated. Patient demographic features will be taken from medical records. The study period was from April 2023 to April 2024. **Results:** About 3798 patients with suspected Urinary tract infections were screened for the study. Around 906 patients showed growth. 129 out of the 906 urine samples showed ESBL producing Enterobacteriaceae. Out of the 129 patients 91(70.5%) were females and 38(29%) were males. E. coli was the most common organism isolated (111, 86%) and Klebsiella is the next (17, 13%) and Proteus (1, 1%). The most common risk factor among them was Diabetes mellitus (41%). It was followed by prolonged ICU stay (31%) in the hospital. Comparing antibiotic susceptibility of the isolates it was clear that Nitrofurantoin (119, 92%), Fosfomycin (127, 98%) and Ertapenem (129, 100%) were having more susceptibility than others. A higher degree of resistance was noted in Ciprofloxacin (82, 63%), Norfloxacin (72, 55%), Cotrimoxazole (58, 45%) and Gentamicin (36, 28%). **Conclusion:** Due to the emergence of multi drug resistant organisms, there are limited treatment options available. ESBL producing urinary pathogens are resistant to most of the available antibiotics. Like beta lactam group of antibiotics and Ciprofloxacin. Nitrofurantoin and Fosfomycin are sensitive to these isolates and therefore these antibiotics can be used for treating uncomplicated urinary tract infections caused by ESBL producing uropathogens.

KEYWORDS : ESBL, Enterobacteriaceae, uropathogens, multi drug resistance

INTRODUCTION-

Urinary tract infections are the second common prevalent infection in the community after respiratory tract infections. In hospitals they are the most common cause of health care associated infections which accounts up to 40% of the hospital acquired infections and contributes to leading cause of morbidity in all ages (1). Frequent use of variety of antibiotics had resulted in development of antimicrobial resistance world-wide. The bacteria's coming under Enterobacteriaceae are the most common cause of urinary tract infections. The common antibiotics used for treating urinary tract infections are β -lactams, β -lactam/ β -lactamase inhibitory antibiotics, fluoroquinolones, and carbapenems. (2). But recently there is an increase in the resistance of Enterobacteriaceae to these antibiotics.

Most of the infections produced by ESBL producing organisms are associated with delayed clinical and microbiological response, increased stay in the hospital, higher treatment cost and higher mortality (3).

There are some comorbidities associated with this like diabetes, recurrent urinary tract infections, old age and staying in nursing home for longer duration. (3) Further risk factors are patients that have had intravenous treatments or with urinary abnormalities.

Extended spectrum β -lactamase (ESBL) is an enzyme produced by Enterobacteriaceae responsible for the increasing resistances worldwide (4). ESBL producing bacteria's which are more commonly found includes E. coli and Klebsiella (4). Enterobacteriaceae that are ESBL producers will be resistant to all penicillins, 1st, 2nd, 3rd and 4th generation cephalosporins and monobactams (1). ESBL enzyme is plasmid coded and they also bear genes that encode resistance to other frequently used oral antibiotics like aminoglycosides and quinolones (5). There has been a trend of increased resistance to antibiotics even to Carbapenems. So, aim of the study is to determine ESBL producing gram negative bacteria causing infection in urine samples of patients admitted in our hospital and their antibiotic profile in order to find out effective oral treatment options.

MATERIALS AND METHODS-

This study period is from April 2023 to April 2024. After receiving the urine samples in the laboratory, urine will be inoculated on MacConkey agar and Blood agar by semi quantitative technique. The next

step was incubating the plates at 37-degree Celsius for a duration of 24 hours. A count > 10⁵ organisms per mL of urine is considered as a positive culture. Then the colonies will be put in Vitek Machine or manual method for identification and sensitivity. ESBL resistance will be shown by the Vitek Machine. All isolates with ESBL pattern of drug resistance detected by VITEK will be included in the study. Data on oral antibiotics like Nitrofurantoin, Norfloxacin, Nalidixic acid, Cotrimoxazole, and Fosfomycin will be taken and correlated. Patient demographic features will be taken from medical records.

RESULTS-

This study was conducted among 3798 patients in our hospital with suspected urinary tract infections. 906 among them showed growth. 129 out of the 906 urine samples showed ESBL producing Enterobacteriaceae. Out of the 129 patients 91(70.5%) were females and 38(29%) were males.

Table-1 : Age and gender-based patient demographics

Age (in years)	Male	Percentage	Female	Percentage
0-20	2	5.26%	4	4.39%
21-40	6	15.7%	32	35.16%
41-60	4	10.52%	19	20.87%
61-80	9	23.68%	20	21.97%
81-100	17	44.7%	16	17.58%
Total	38		91	

In males UTI cases were more seen between the age group 81-100. And in females, majority of the UTI cases were found between the age group 21-40 as per table-1.

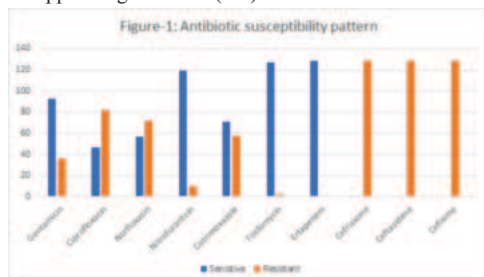
The organisms isolated from urine samples were Escherichia coli and Klebsiella pneumoniae and Proteus. E. coli was the most common organism isolated (111, 86%) and Klebsiella is the next (17, 13%) and Proteus (1, 1%).

The common risk factors for UTI with ESBL organisms are Diabetes mellitus, Prolonged ICU stay, recent history of catheterization, Immunosuppressing conditions, and recurrent urinary tract infections.

Table-2 : Frequency of risk factors in patients with urinary tract infections.

Risk factor	Frequency	Percentage
1.Diabetes mellitus	54	41%
2.Prolonged ICU stay	41	31%
3.Recent history of catheterization	18	13%
4. Immunosuppressing conditions	12	9%
5. Recurrent urinary tract infections	22	17%

The most common risk factor among them was Diabetes mellitus (41%). It was followed by prolonged ICU stay (31%) in the hospital. History of recurrent urinary tract infections (17%) was the next important risk factor. Recent history of catheterization is the significant risk factor in about 13% of the patients. Immunosuppressing condition (9%) is the other risk factor.



ANTIBIOTIC SUSCEPTIBILITY-

Comparing antibiotic susceptibility of the isolates it was clear that Nitrofurantoin (119,92%), Fosfomycin (127,98%) and Ertapenem (129,100%) were having more susceptibility than others. A higher degree of resistance was noted in Ciprofloxacin (82, 63%), Norfloxacin (72, 55%), Cotrimoxazole (58, 45%) and Gentamicin (36,28%).

DISCUSSION

The objectives of the study were to determine ESBL producing gram negative bacteria causing infection in urine samples of patients admitted in the hospital and their oral treatment options. In males most of the UTI occur after the age group of 80 and in females the infections are more in age group 21-40 yrs. The findings of Behera et al (6) and S. Gupta et al (7) were in agreement with these results. Shorter length of urethra in females is the reason why females are having more incidence of UTI compared to males. *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus* were the species isolated in the study. Among this *E. coli* was the most common organism isolated (111, 86%) and *Klebsiella* is the next (17,13%) and *Proteus* (1,1%). Fernando et al also obtained similar results in his study(8). A higher degree of resistance was noted in Ciprofloxacin (82, 63%), Norfloxacin (72, 55%), Cotrimoxazole (58, 45%) and Gentamicin (36,28%). Nitrofurantoin (119,92%), Fosfomycin (127,98%) and Ertapenem (129,100%) were having more susceptibility than others. Almost similar results were obtained by Chandrasekhar D. et al. (9) and Singh et al (10). Resistance to fluoroquinolones has been increasing among uro-pathogens because of excessive use of both oral and parenteral fluoroquinolones for treating UTI's. There has been least resistance in Ertapenem and Fosfomycin. The same results have been obtained by Simon Auer et al. (11). Nitrofurantoin also shows higher degree of sensitivity compared to others. So, Nitrofurantoin and Fosfomycin are suitable oral treatment options for treating uncomplicated UTI due to ESBL producing uropathogens.

CONCLUSION

Due to the emergence of multi drug resistant organisms there are limited treatment options available. ESBL producing urinary pathogens are resistant to most of the available antibiotics like beta lactam group of antibiotics and Ciprofloxacin. Nitrofurantoin and Fosfomycin are sensitive to these isolates and therefore these antibiotics can be used for treating uncomplicated urinary tract infections caused by ESBL producing uropathogens.

CONSENT FOR PUBLICATION

Not applicable

FUNDING

There was no funding involved in this study.

ETHICAL APPROVAL

This study was approved by the Institutional Ethics Committee of Malabar Medical College and Research Centre. (CDSCO Reg.No.ECR/1248/Inst/1248/Inst/KL/2019/RR-22, DHR Reg No:

EC/NEW/INST/2022/1471 and approval number -39).

CONFLICT OF INTEREST

No conflict of interest.

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