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Research Article

FOSFOMYCIN SUSCEPTIBILITY PATTERN AMONG EXTENDED SPECTRUM BETA LACTAMASE (ESBL) & NON EXTENDED SPECTRUM BETA LACTAMASE PRODUCING UROPATHOGENIC ESCHERICHIA COLI FROM TERTIARY CARE REFERRAL HOSPITAL

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A B S T R A C T

Introduction: Urinary tract Infections (UTIs) are the most common encountered infectious diseases in our community and hospital.
Aims: The current study was undertaken with a dual purpose, to provide the current scenario of the microorganisms causing UTI, their antimicrobial sensitivity Patterns and in vitro activity of fosfomycin against ESBL and non ESBL producing *E. coli*.
Materials and Methods: The study was conducted prospectively in the Department of Microbiology of a tertiary care hospital from July 2019 to Dec 2019. A total of 271 urinary isolates of the patients with a diagnosis of urinary tract infection were included. Antibiotic sensitivity testing (ABST) and extended spectrum beta lactamase (ESBL) Production testing was done as per CLSI guidelines.
Results: A total of 898 urine samples were processed, among which 271(30.2%) urine sample showed significant bacterial growth. Of total 216(79.7%) bacterial isolates were gram negative bacilli (GNB) and 55(20.3%) isolates were gram positive cocci. Among GNB, 77.6% were *E. coli* and it was 53.5% of total isolates. Among *E. coli*, 68.3% were non ESBL producer which showed 90.7% of susceptibility to fosfomycin.
Conclusion: Fosfomycin showed good in vitro antibiotic susceptibility against both ESBL and non ESBL Producing E. coli. Thus, Fosfomycin may be a valid option for oral treatment of UTIs caused by ESBL Producing pathogens for which very few antibiotic options remain.

INTRODUCTION

Urinary tract infection (UTIs) is a spectrum of disease in which microbial invasion of the urinary tract that extends from the renal cortex of the kidney to the external urethral meatus[1]. UTI encompasses a variety of clinical entities, including asymptomatic bacteriuria (ABU), cystitis, prostatitis and pyelonephritis [2]. It is more prevalent in women than men, which is likely the result of several clinical factors including anatomical differences, hormonal effects and behavior patterns [3]. About 150 million people are being diagnosed every year with urinary tract infection worldwide. Every woman has a lifetime risk of 60% for developing UTI, but men have only 13% [4]. Urinary tract infectioos are usually caused by gram-negative bacteria, but gram-positive pathogens may also be involved. The most common pathogen causing uncomplicated UTIs is E. coli (75-95%); followed by klebsiella pneumonia, Staphylococcus saprophyticus, Enterococcus faecalis, group D streptococci and Proteus mirabilis [5].

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Antibiotic resistance to E. coli has steadily been increasing; thus, incorporating the local antibiotic susceptibility patterns of E. coli into clinical decision process is critical to optimal antibiotic selection [6]. Worldwide spread of ESBL producing E. coli had emerged recently as a significant cause of community associated UTIs [7]. ESBL producing pathogens are often seen in combination with resistance e to multiple antimicrobial groups, leaving only few remaining antimicrobial treatment options [8].

Carbapenem is choice of antibiotics for the treatment fo these infections. More ever increase in carbapenem resistance and the need for parenteral administration [9] had led to growing interest in older antibiotics like forfomycin [10]. Fosfomycin acts by interfering with bacterial peptidoglycan synthesis, thereby disrupting cell wall [11]. Fosfomycin has good oral bioavailability. After a single three gram oral dose, Peak urinary concentrations occur within four hours. Urine fosfomycin levels 128 mg/L are maintained for at least 36 to 48 hours [12]. It is sufficient to inhibit most urinary pathogens. Hence, Aim of this study is Fosfomycin susceptibility pattern among extended spectrum Beta lactamase producing

uropathogenic E. coli so that to increase the functional capacity and reducing the economic burden in UTI patients.

MATERIAL AND METHODS

A cross-sectional study was carried out from July 2019 to December 2019 in Department of Microbiology, Narayan Medical College & Hospital (NMC&H); Jamuhar Bihar, (India) a tertiary care teaching hospital with 695 patient beds. Mostly covers the rural population. Written approval was taken from Institutional Ethical Committee (IEC), NMC&H, and Jamuhar.

A total number of 898 non-repetitive 'Clean Catch' Midstream and Catheter aspirated urine specimens were collected in a presterile leak proof universal plastic container. Samples were processed immediately within 30 minutes. Direct microscopy of uncentrifused urine was done. Pus cell and bacteria were noted. The specimens were processed semi-quantitatively by inoculating 0.001 ml capacity of a calibrated wire loop onto the cystine lactose electrolyte deficient (CLED) agar for the isolation and identification for uropathogens. The inoculated plates were incubated for 18-24 hours at 37°C in aerobic condition.

Pure culture growth of a single organism with a count of $\geq 10^5$ bacteria/ml was considered. The isolated were identified to the species level by using appropriate routine identification methods including colony morphology, Gram-stain and in-house set a of conventional biochemical tests like Catalase test, oxidase test, IMVIC, triple sugar iron (TSI) test, Urease test, Motility test, Bile esculin agar (BEA) media and coagulase test[13].

Antibiotics susceptibility of isolates against different antibiotics was tested by Kirby-Bauer disk diffusion method on Mueller Hinton agar (MHA, Hi-Media, India) by standard operative procedures recommended by the Clinical and Laboratory Standards Institute (CLSI), Wayne, USA [14].

In our study, Antibiotics tested were Amplicillin (AMP 25µg), Amoxycillin clavulanate (AMC 20/10 µg), Gentamycin (GEN 10µg), Amikacin (AK 30µg), Ciprofloxacin (CIP 5µg), Levofloxacin (LE 5µg), trimethoprim sulfamethoxazole (COT 30µg), Cefixime (CFM 5µg), Ceftriaxone (CTR 30µg), Ceftazidime (CAZ 30µg), Ceftazidime-clavulanic Acid(CAC 30/10µg), Piperacillin-tazobactam (PIT 100/10µg), Imipenem (IMP 10µg), Meropenem (MRP 10µg) & Fosfomycin(FO 300µg) (HIMedia Laboratories, India).

Interpretations of antibiotic susceptibility results were made according to the 'zone of inhibition' size interpretative standards of CLSI. E. coli ATCC 2522 was used as a control strain for antibiotic susceptibility testing. Detection of ESBL producing E. coli were done as per CLSI guide line where, Ceftazidime (30 µg) disc alone and in combination with clavulanic acid (Ceftazidine + clavulanic Acid 30/10 µg) discs were used. Isolates that showed increase of ≥5 mm in the 'zone of inhibition' of the combination an ESBL producer [15].

During the study period, patients presented to the outpatient department (OPD) and inpatient ward with a clinical diagnosis of UTI were included. The patients who had known history of antimicrobial therapy within 48 hours prior to attending the hospital and samples which grew more than two type of organism was considered as contaminated and excluded. Patient's profile, isolates, their antibiotics sensitivity and the results were entered into a computer program on excel sheet and presented in percentage base distribution.

RESULT

A total of 271 (30.2%) urine samples showed significant bacterial growth, of which 50.6% were male and 49.4% females. Out of 271(30.2%), 233 urine isolates were from OPD and 48 urine from IPD. 216(79.7%) bacterial isolates were gram negative bacilli (GNB) and 55(20.3%) were gram positive cocci. Among GNB, 77.6% were *E. coli.*

Out of 77.6% of E. coli, 45(31.7%) isolates were ESBL producer by Combination disk diffusion method using ceftazidime (CAZ) and ceftazidime/clavulanic (CAC) acid disc. The maximum number of ESBL *E. coli* were isolated from medicine department (46.7%) followed by urosurgery (35.6%), OBG(13.3%), neurosurgery (22.2%) and surgery (22.2%).

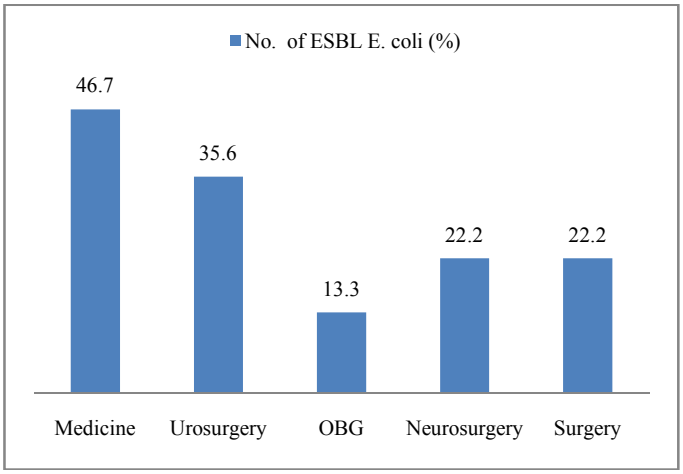

Fig 1 Distribution of ESBL producing *E. coli* according to Department

Fosfomycin Susceptibility Pattern among ESBL & non ESBL E. coli

Among 77.6% *E. coli*, 45(31.7%) were ESBL producer which showed 95.6% of susceptibility to fosfomycin and 97(68.3%) of non ESBL producing *E. coli* showed 90.7% susceptibility to fosfomycin. Not only in fosfomycin, we have also notice that PIT(66.7%) were more sensitive in ESBL *E. coli* compare to non ESBL E. coli. Other antibiotics were more sensitive in non ESBL *E. coli* in compare to ESBL *E. coli* while fosfomycin and PIT showed more sensitivity towards ESBL *E. coli.*

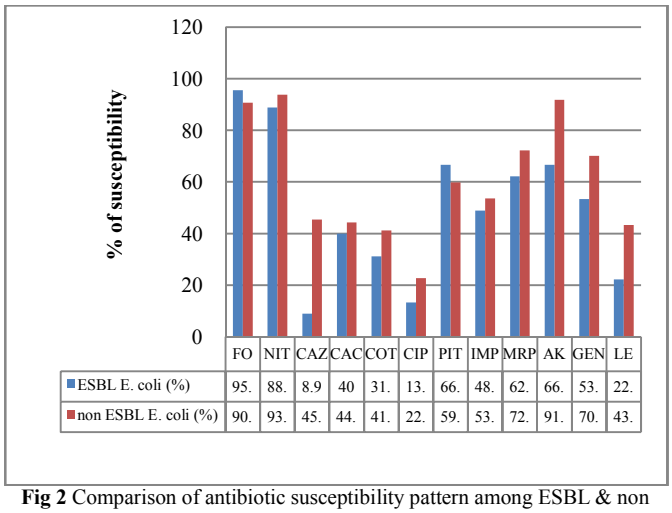

Fig 2 Comparison of antibiotic susceptibility pattern among ESBL & non ESBL *E. coli*

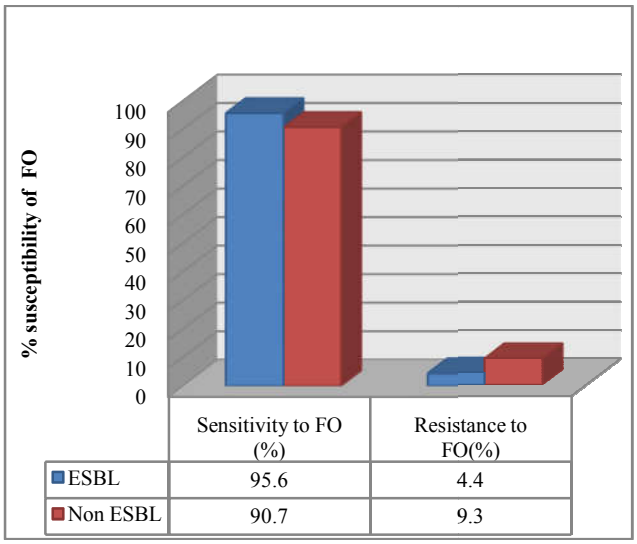

Fig 3 Fosfomycin Susceptibility Pattern among ESBL & non ESBL *E. coli*

DISCUSSION

E. coli is the commonest bacteria isolated from clinical specimens of which majority were from urology department. This may be due to the larger number of patient included from urology department in our study. ESBL producing *E. coli* were mostly from medicine department. In our study, *E. coli* (53.5%) was most frequently isolated gram negative bacteria. A similar isolation rate was also reported by Poudyal *et al*. [16].

In our study, ESBL producing *E. coli* was 31.7%. The prevalence of ESBL producing *E. coli* was found as low as 18.2% in a study conducted by Raut *et al*. [17], shettigar *et al*. (37.7%) from India [18], Pourakbari *et al*. (37%) and Rezai *et al*. (30.5%) from Iran [19,20]. Extremely higher rates of ESBL *E. coli* have also been reported by Chinnasami *et al*. (83%) from India [21] and Masud *et al*. (53.8%) from Bangladesh [22].

In our study, 95.6% of ESBL *E. coli* were sensitive for fosfomycin. This is similar to other study conducted by Poudyal S *et al*. [16], Muvunyi CM e al. [23], Maraki S *et al*. [24] & EIKady RAEH, 2017 [25].

The prevalence of antibiotic resistant bacteria may vary country wise and also from institutions to institutions. This can be explained by the difference in local antibiotic prescribing habits and difference in effectiveness of infection control program in different health institutes.

CONCLUSION

As drug resistance among bacterial pathogens is changing, updated information on most effective empirical treatment of UTI is very important. From this study we believe fosfomycin may be a valid option for oral treatment of UTIs caused by ESBL producing pathogens, for which very few antibiotic options remains. Even patient compliance is better with fosfomycin because of single dose regimen.

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