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Evaluating the Role of Fosfomycin Activity Against Extended-Spectrum-B-Lactamase- Producing Escherichia Coli and Klebsiella Pneumonia Isolated in Clinical Isolates

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ABSTRACT

Background: The management of infections in hospital settings has become considerably more difficult due to the emergence of Escherichia coli and Klebsiella pneumoniae that produce extended-spectrum beta-lactamases (ESBLs). Due to a lack of available treatments, interest in the efficacy of substitute antibiotics such as fosfomycin has grown. In a tertiary care hospital in India, this study sought to determine the in vitro susceptibility of K. pneumoniae and E. coli that produce ESBL to fosfomycin.

Aim and Objective: Evaluating the role of fosfomycin activity on ESBL producing Klebsiella Pneumoniae and E. Coli isolated in clinical isolates.

Methods: A total of 210 ESBL-producing isolates (E. coli n=126, K. pneumoniae n=84) were collected from various clinical specimens, including urine, pus, respiratory secretions, and wound swabs. ESBL production was confirmed using the combined disc method. Fosfomycin susceptibility was assessed using the disc diffusion method. Results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: In the present study a total of 210 ESBL-producing isolates, comprising Escherichia coli and Klebsiella pneumoniae, were included. In the current study 210 ESBL-producing isolates were found out of which 62.8% were from male patients and 37.1% from female patients.Among E. coli isolates, 65% were from males and 34.9% from females and in K.pneumoniae isolates, 59.5% were from males and 40.4% from females. This indicates a higher prevalence of ESBL-producing infections among male patients compared to females in this study. The majority of ESBL-producing isolates were found in patients aged 51–70 years (42.8%). Among E. coli isolates, 44.4% were from patients in the 51–70 age group. Fosfomycin demonstrated high in vitro activity against ESBL-producing Escherichia coli and Klebsiella pneumoniae, with 90.4% of E. coli and 78.5% of Klebsiella pneumoniae being susceptible by disc diffusion.

Conclusion: Particularly for urinary tract infections, fosfomycin showed strong in vitro action against K. pneumoniae and E. coli that produce ESBL. In situations where antibiotic resistance limits existing treatment options, this study supports the possible use of fosfomycin as an effective alternative. These findings indicate that fosfomycin is a viable treatment option for infections caused by ESBL-producing E. coli and K. pneumoniae in tertiary care hospitals.

Keywords: Fosfomycin, ESBL, AST, CLSI, Beta-lactamases

1. INTRODUCTION

Antimicrobial resistance has increased worldwide, thus leading to infections which are more difficult to treat, with higher mortality, morbidity, and costs. Beta-lactam resistance, particularly, is on the increase, and the production of antibiotic-inactivating enzymes in Gram-negative pathogens is one of the most common mechanisms of drug resistance. The increasing ubiquity of *Escherichia coli* positive for the production of antibiotic-inactivating enzymes in both community and hospital settings has been shown by several studies [1]. ESBL (extended spectrum beta-lactamase)-producing *E. coli* are emerging enterobacteria responsible for urinary tract infections (UTI) in patients , and urinary tract infections provoked by these pathogens have become a major public health problem today .

Infections caused by highly resistant Enterobacteriaceae continue to place a major burden on healthcare systems [2]. Carbapenem antibiotics are increasingly used for infections caused by these microorganisms. As the use of carbapenems acts as driver for carbapenem resistance by selective pressure, alternative treatment options are necessary. Fosfomycin is a relatively old, broad-spectrum antibiotic that was first marketed in the early 1970s. Recently, interest in the use of intravenous fosfomycin has increased as this drug appears to remain active against a broad range of otherwise highly resistant microorganisms

Bacteria are the major causative organisms and are responsible for more than 95% of UTI cases. *Escherichia coli* is the most prevalent causative organisms of UTI and is solely responsible for more than 80% of the infections [3].

With an increase in infections brought on by multidrug-resistant (MDR) organisms like *Klebsiella pneumoniae* and *Escherichia coli* that produce extended-spectrum beta-lactamases (ESBLs), the rise in antimicrobial resistance (AMR) represents a serious threat to global public health. Both community and healthcare-associated infections, especially in tertiary care facilities, are frequently caused by these organisms, which are well-known for their capacity to hydrolyse and provide resistance to third-generation cephalosporins [4]. Bloodstream infections (BSIs), hospital-acquired pneumonia, and urinary tract infections (UTIs) have all been linked to ESBL-producing strains, which has complicated treatment choices and frequently required the use of antibiotics like carbapenems as a last resort [5].

An uncomplicated UTI is a bacterial infection of the lower urinary tract that is not associated with structural abnormalities of the urinary tract or comorbidities such as diabetes, immunosuppression, or pregnancy, whereas a complicated UTI is associated with structural abnormalities of the urinary tract or comorbidities such as the above [6]. Indeed, the appearance of these bacteria in urinary tract infections is a medical emergency requiring long-term monitoring in order to implement appropriate probabilistic treatment [7].

Fosfomycin tromethamine is a stable salt of fosfomycin which is licensed for the single-dose treatment of acute uncomplicated urinary tract infections (UTIs) caused by susceptible organisms.

However, the increasing use of carbapenems has contributed to the emergence of carbapenem-resistant *Enterobacteriaceae* (CRE), further limiting treatment choices and urging the need for alternative therapies [5]. In this context, fosfomycin, a broad-spectrum antibiotic discovered in the 1960s, has re-emerged as a promising option due to its unique mechanism of action and retained efficacy against a variety of resistant pathogens, including ESBL-producing *E. coli* and *Klebsiella pneumoniae* [6]. By preventing the bacterial cell wall synthesis-dependent enzyme MurA from functioning, fosfomycin produces its bactericidal effect. It is not dependent on beta-lactam rings or other structures that are frequently the focus of resistance mechanisms, in contrast to many other antibiotics [6].

Fosfomycin is a promising treatment option for infections brought on by these resistant strains, particularly in situations where other antibiotics are ineffective, as recent research has shown that it maintains a high level of effectiveness against ESBL-producing organisms [7]. Specifically, its oral formulation has demonstrated encouraging outcomes in the management of simple UTIs, whilst its intravenous formulation is attracting attention for more serious infections such pneumonia and BSIs [8].

Fosfomycin acts as a phosphoenolypyruvate analog, preventing the initial stage of cell wall synthesis via the inhibition of MurA (UDP-N-acetylglucosamine enolpyruvyl-transferase enzyme), which catalyzes the initial step of N-acetylmuramic acid and peptidoglycan biosynthesis, leading to bacterial cell death . Fosfomycin is very well tolerated by the body, and adverse reactions vary from 1% to 5% of patients [9]. The ESBL-producing *Enterobacteriaceae* family has been detected worldwide, and the risk factors associated to it may be related to hospital care or antibiotic therapy. Fosfomycin has rekindled attention as a component of both monotherapy and combination regimens because to the increasing prevalence of ESBL-producing *E. coli* and *K. pneumoniae* in these environments. With an emphasis on dosage techniques, resistance development, and clinical outcomes, ongoing clinical studies are assessing the best way to utilise fosfomycin to treat these difficult infections [10]. Fosfomycin may be essential in maintaining the efficacy of currently available antibiotics and lowering dependency on carbapenems and other last-resort medications as AMR develops

It is imperative that the majority of these bacteria are tested for antibiotic resistance, so that strategies can be put in place to halt the continued spread of these pathogens . Therefore, the current study intended to assess the effectiveness of fosfomycin against ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from clinical samples.

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2. MATERIAL AND METHODS

Study Design
This was a cross-sectional study conducted over a period of 12 monthsi.e, from September 2023 to September 2024 at the Microbiology Department of a tertiary care hospital in India. The study aimed to evaluate the in vitro activity of fosfomycin against ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from clinical samples.

Sample Collection:
Patients admitted to the intensive care unit (ICU), general medicine, surgery, urology, and obstetrics and gynaecology were the subjects of clinical sample collection. The microbiology lab processed the samples, which included wound swabs, respiratory secretions, urine, and pus. Within two hours of being collected, all samples were taken using normal aseptic procedures and brought to the lab for sensitivity and culture testing.

Inclusion Criteria:
1. Samples from patients exhibiting infection-related symptoms, such as fever, elevated white blood cell count, etc.
2. Only isolates of *K. pneumoniae* and *E. coli* that underwent phenotypic testing and were determined to be ESBL-producers.
3. The patient must be at least eighteen years old.
4. Isolates from diseases acquired in hospitals and the community

Exclusion Criteria:
1. During the study period, the same patient had duplicate isolates.
2. Isolates that exhibit resistance to every antibiotic that was examined.
3. Individuals who were on antibiotics for 48 hours before the sample was taken

Microbiological Methods:
Isolation and Identification: Blood and MacConkey agar plates were used to cultivate clinical specimens. For 24 to 48 hours, plates were incubated at 37°C. Standard biochemical tests, including the indole test, citrate utilisation test, triple sugar iron (TSI) agar test, and urease test for the differentiation of *E. coli* and *K. pneumoniae*, were used to identify the bacteria.
ESBL Detection: As advised by the Clinical and Laboratory Standards Institute (CLSI) standards, the combined disc diffusion method was used to confirm the formation of ESBLs (CLSI, 2023). On Mueller-Hinton agar plates inoculated with the test organism, discs containing 30 µg of cefotaxime and 30/10 µg of cefotaxime-clavulanic acid were positioned 20 mm apart. The generation of ESBL was indicated by a zone diameter increase of at least 5 mm surrounding the clavulanic acid combo disc as compared to cefotaxime alone.

Antibiotic Susceptibility Testing:
Using 200 µg fosfomycin discs with 50 µg glucose-6-phosphate on Mueller-Hinton agar, the disc diffusion method was used to test for fosfomycin susceptibility in compliance with CLSI standards (CLSI, 2023). The zone diameter breakpoints suggested by CLSI were used to categorise the isolates as susceptible, intermediate, or resistant.
Control Strains: Quality control for susceptibility testing was performed using *Escherichia coli* ATCC 25922 and *Klebsiella pneumoniae* ATCC 700603 (ESBL-producing strain) as control organisms.[10]

Data Collection:
Data on patient demographics (age, gender), clinical diagnosis, and the ward of admission were recorded. The source of the isolate and their antibiotic susceptibility profile were documented.

Statistical Analysis:
The SPSS version was used to analyse the data. The study population's clinical and demographic features were compiled using descriptive statistics. A percentage representing the susceptibility of K. pneumoniae and E. coli to fosfomycin was provided.

3. RESULTS

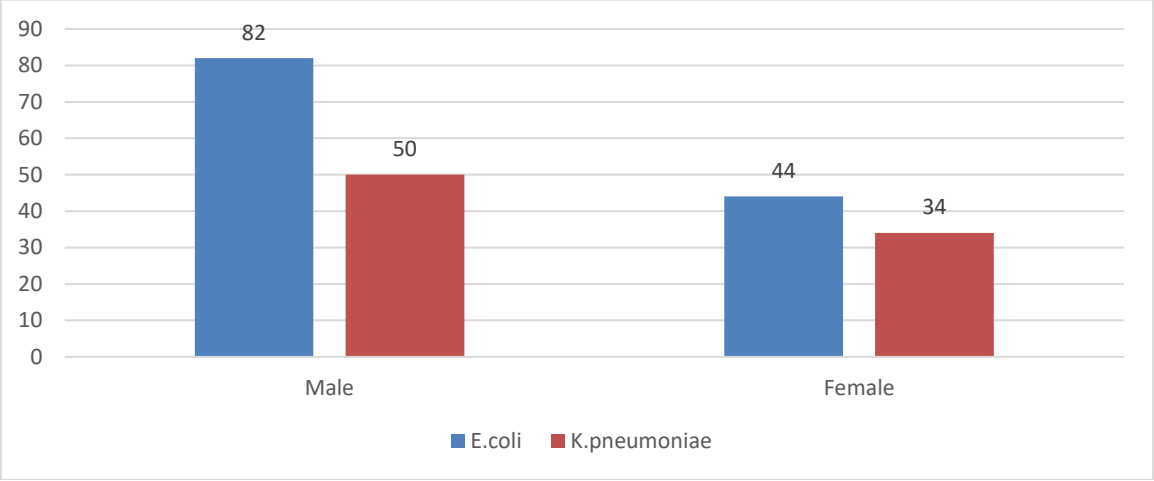
In the present study a total of 210 ESBL-producing isolates were observed comprising *Escherichia coli* and *Klebsiella pneumoniae*, were included in the study.

Table no.1 Gender Distribution of ESBL-Producing Isolates.

Gender	*E. coli* (n=126)	*K. pneumoniae* (n=84)	Total (n=210)
Male	82 (65%)	50 (59.5%)	132 (62.8%)

Female	44 (34.9%)	34 (40.4%)	78(37.1%)

Graph no.1: Gender Distribution of ESBL-Producing Isolates.

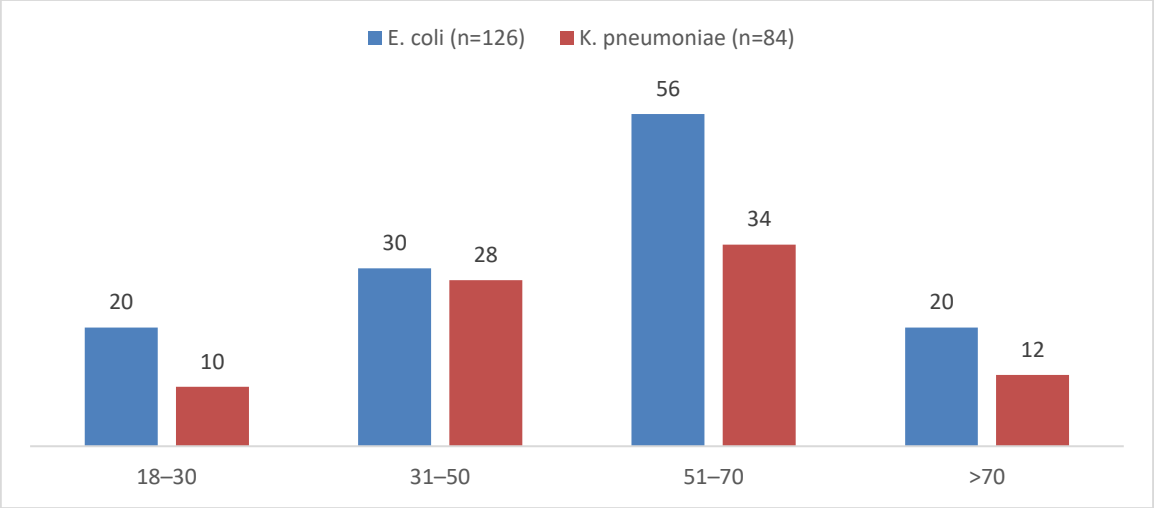


In the current study 210 ESBL-producing isolates were found out of which 62.8% were from male patients and 37.1% from female patients.Among *E. coli* isolates, 65% were from males and 34.9% from females and in *K.pneumoniae* isolates, 59.5% were from males and 40.4% from females. This indicates a higher prevalence of ESBL-producing infections among male patients compared to females in this study.

Table no.2: Age Distribution of ESBL-Producing Isolates

Age Group (Years)	*E. coli* (n=126)	*K. pneumoniae* (n=84)	Total (n=210)
18–30	20 (15.8%)	10 (11.9%)	30 (14.2%)
31–50	30 (23.8%)	28 (33.3%)	58 (27.6%)
51–70	56 (44.4%)	34 (40.4%)	90 (42.8%)
>70	20 (15.8%)	12 (14.2%)	32 (15.2%)

Graph no.2: Age Distribution of ESBL-Producing Isolates



The majority of ESBL-producing isolates were found in patients aged 51–70 years (42.8%). Among *E. coli* isolates, 44.4% were from patients in the 51–70 age group. *K. pneumoniae* was also most prevalent in patients aged 51–70 years (40.4%). The elderly group (>70 years) represented 15.2% of the total isolates, showing a relatively high burden of ESBL infections in older patients. This suggests that older adults, especially those in the 51–70 age group, are more likely to ESBL-producing *E. coli* and *K. pneumoniae*.

In the present study the distribution of these isolates, their clinical sources, and their susceptibility to fosfomycin were analyzed.

Table no.3: Distribution of ESBL-Producing Isolates

Organism	Number of Isolates (%)
Escherichia coli	126 (60%)
Klebsiella pneumoniae	84 (40%)
Total	210 (100%)

Graph no.3: Distribution of ESBL-Producing Isolates

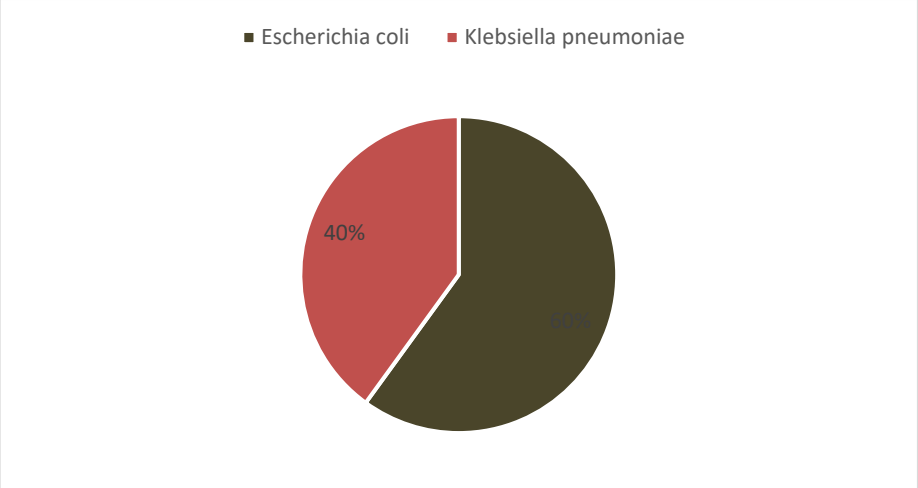


Table no.4: Clinical Source of Isolates and and Fosfomycin Susceptibility

Clinical Source	*E. coli* (n=126)	*K. pneumoniae* (n=84)	Total (n=210)
Urine	49 (38.8%)	30 (35.7%)	79 (37.6)
Pus	23 (18.2%)	19 (22.6%)	42 (20%)
Respiratory Secretions	22 (17.4%)	18 (21.4%)	40 (19%)
Sputum	20 (15.8%)	11 (13%)	31 (14.7%)
Wound Swabs	12 (9.5%)	6 (7.1%)	18 (8.5%)
Total	126	84	210

Table no.5: Fosfomycin Susceptibility by Disc Diffusion

Organism	Susceptible (%)	Intermediate (%)	Resistant (%)
***Escherichia coli* (n=126)**	114 (90.4%)	8 (6.3%)	4 (3.1%)
***Klebsiella pneumoniae* (n=84)**	66 (78.5%)	10 (11.9%)	8 (9.5%)

Fosfomycin demonstrated high in vitro activity against ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*, with 90.4% of *E. coli* and 78.5% of *Klebsiella pneumoniae* being susceptible by disc diffusion.

Table 6:Clinical Sources and Fosfomycin Susceptibility.

Clinical Source	*E. coli* (n=126)	Susceptible (*E. coli*) n (%)	*K. pneumoniae* (n=84)	Susceptible (*K. pneumoniae*) n (%)	Total (n=100)	Total Susceptible. n (%)
Urine	49	43 (87.7%)	30	14 (46.6%)	79	62 (78.4%)
Pus	23	17 (73.9%)	19	10 (52%)	42	25 (59.5%)
Respiratory/Tracheal Secretions	22	18 (81.8%)	18	9 (50%)	40	25 (62.5%)
Sputum	20	15 (75%)	11	7 (63.6%)	31	21 (67.7%)
Wound Swabs	12	8 (66.6%)	6	2 (33.33%)	18	10 (55.5%)
Total	126	101 (80.1%)	84	41 (48.8%)	210	150 (71%)

Table no. 7: Distribution and Fosfomycin Susceptibility of ESBL-producing *E. coli* and *K. pneumoniae* Isolates Across Different Clinical Sources

Study	Location	Organism	Fosfomycin Susceptibility (%)	Total Isolates
Urine	India Our Study (2024)	*E. coli*	87.7%	49
		K. pneumoniae	46.6%	30
Karageorgopoulos et al. (2012)[11]	Greece	*E. coli*	88.0%	55
		K. pneumoniae	79.0%	25
Rodríguez-Baño et al. (2014)[12]	Europe	*E. coli*	89.4%	200
		K. pneumoniae	79.0%	100
Neetu et al. (2020)[13]	India (North)	*E. coli*	85.0%	65
		K. pneumoniae	77.0%	20
Pus	**Our Study (2024)**	India	*E. coli*	73.9%
			K. pneumonia	52%
	Falagas et al. (2016)[14]	Global Review	*E. coli*	84.0%
			K. pneumoniae	74.0%
Respiratory/Tracheal Secretions	**Our Study (2024)**	India	*E. coli*	81.8%
			K. pneumoniae	50%
	Liu et al. (2020)[15]	China	*K. pneumoniae*	78.0%
Sputum	Our study (2024)	India	*E. coli*	75%
			K. pneumoniae	63.6%
	Xiang et al. (2022)[16]	China	*E.coli*	78%
			K. pneumoniae	40%
Wound Swabs	**Our Study (2024)**	India	*E. coli*	66.6%
			K. pneumoniae	33.33%
	Yahav et al. (2020)[17]	Various Regions	*E. coli*	82.0%
			K. pneumoniae	72.0%

Table No.8: Antibiotic Sensitivity Profiles of Clinical Samples

Antibiotic	*E. coli (n=126)*	*K. pneumoniae (n=84)*
Fosfomycin	114 (90.4%)	66(78.5%)
Nitrofurantoin	111 (88%)	25 (29.7%)
Tetracycline	61 (48.4%)	38 (45.2%)
Ampicillin-Sulbactam	88 (69.8%)	60 (71.4%)
Cefuroxime	45 (35.7%)	34 (40.4%)
Ciprofloxacin	76 (60.3%)	45 (53.5%)
Co-trimoxazole	63 (50%)	39 (46.4%)
Meropenem	114 (90.4%)	68 (80.9%)
Ceftazidime	77 (61%)	47 (55.9%)
Gentamicin	92 (73%)	64 (76.1%)
Tobramycin	86 (68.2%)	24 (75%)
Colistin	102 (80.9%)	66 (78.5%)

These findings indicate that fosfomycin is a viable treatment option for infections caused by ESBL-producing *E. coli* and *K. pneumoniae* in tertiary care hospitals.

4. DISCUSSION

Fosfomycin, a naturally occurring antimicrobial agent, exhibits broad-spectrum antibacterial activity against Gram-negative pathogens as it suppresses the peptidoglycan synthesis pathway, which is a major constituent of the bacterial cell wall [3].

Fosfomycin in combination with various antibiotics represents an excellent clinically efficacious regimen for the treatment of urinary tract infections (UTIs) caused by extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*. Underlying mechanisms of fosfomycin resistance remain largely uncharacterised. To investigate the antibacterial efficacy of fosfomycin against ESBL-producing *E. Coli* and *Klebsiella pneumoniae* the present study was undertaken.

Despite the development of antimicrobial resistance during anti-infective therapy, fosfomycin has regained a great deal of interest in recent years and has been increasingly used to treat infections caused by multidrug-resistant bacteria particularly under conditions of limited oxygen [4], [5].

Managing infections in hospital settings is made more difficult by the rising incidence of organisms that produce extended-spectrum beta-lactamases (ESBLs), particularly *Escherichia coli* and *Klebsiella pneumoniae*. Treatment options are complicated by these resistant infections, which frequently necessitate the use of antibiotics like carbapenems as a last resort. But the rise of bacteria resistant to carbapenem has sparked interest in substitute therapies like fosfomycin. In this investigation, we assessed fosfomycin's in vitro efficacy against 210 isolates of *K. pneumoniae* and *E. coli* that produced ESBLs and were taken from a tertiary care hospital in India. Our findings support the possible use of fosfomycin as an effective treatment option by showing high susceptibility rates for both species [11,12].

In our study, 90.4% of *E. coli* and 78.5% of *K. pneumoniae* isolates were susceptible to fosfomycin by disc diffusion. These results are in line with similar studies conducted globally. A study by Neetu et al. (2020) [13] in northern India reported a fosfomycin susceptibility rate of 89% for ESBL-producing *E. coli*, with a slightly lower susceptibility for *K. pneumoniae* (76%). Over the past decade, the resistances of Gram-negative bacteria have become one of the largest threats to public health worldwide. The severity of infections generated by these bacteria, their considerable capacity for transmission and dispersion through the environment, the difficulty in employing empiric treatment (and even appropriately targeted treatment) and the scarcity of new antibiotics against some Gram-negative bacilli (GNB) [14].

Multidrug resistance is the most important problem in antibiotic resistance due to the difficulty in treating multidrug-resistant microorganisms and the exponential increase in multidrug resistance over the last decade, not to mention AmpC production and the emergence and dissemination of extended-spectrum beta-lactamases (ESBL) and carbapenemases; these ESBL-producing and carbapenemase-producing strains are the main pathogens involved in nosocomial or healthcare-associated infections [15,16]. A considerable majority of these strains are characterized by the loss of activity against beta-lactam agents, as well as marked resistance to other families of commonly employed antibiotics, such as quinolones and aminoglycosides, due to the accumulation of numerous resistance mechanisms or the transmission of plasmids that transport genes with additional resistance [17].

The limited new options against these types of bacterial strains has meant that, over the last decade, antibiotics such as fosfomycin have gained considerable importance as rescue strategies or as combined therapy options for treating infections caused by these multidrug-resistant bacteria . Similarly, a study by Gupta et al. (2017) [18] in India, demonstrated that fosfomycin was highly effective against ESBL-producing *E. coli*, with susceptibility rates exceeding 90%. An international study [6] highlighted the broad-spectrum activity of fosfomycin, showing an average susceptibility rate of 85-95% for ESBL-producing *Enterobacteriaceae* across different regions. These findings were in support to the current study where underscoring the global relevance of fosfomycin as a viable treatment option for ESBL-producing organisms.In other study, *K. pneumoniae* exhibited slightly lower susceptibility (80%) compared to *E. coli* (92.3%), which is consistent with the findings of Grabein et al. (2017) [19]. In their systematic review, they reported that *K. pneumoniae* often displays slightly lower susceptibility rates to fosfomycin compared to *E. coli*. This may be due to the presence of chromosomal resistance mechanisms or other resistance factors unique to *K. pneumoniae*, which might reduce the efficacy of fosfomycin in some isolates.

In our study, ESBL infections were more prevalent in males 132 (62.8%) than females 78 (37.1%). The study by Prakash et al. (2019) [20] similarly reported a higher prevalence of ESBL-producing *E. coli* and *K. pneumoniae* in male patients, particularly in older age groups. This may be due to the higher incidence of comorbid conditions such as diabetes and prostate enlargement in older males, predisposing them to recurrent UTIs. There was another study which was in constrast to the current study where the female patients predominated over the male ones, with a prevalence of 51.90%, a sex ratio of 1.08 [21].

The age distribution in our study revealed that patients aged 51–70 years were most affected by ESBL-producing infections, accounting for 42.8% of the total cases. This observation is consistent with findings from a study conducted by Nair et al. (2018) [22], which reported that the majority of ESBL-producing isolates were found in older adults, particularly those with underlying chronic diseases. The high prevalence of infections in this age group can be attributed to weakened immune systems, frequent hospitalizations, and the use of indwelling devices such as catheters, which are common risk factors for ESBL colonization and infection.

Given the high susceptibility rates observed in our study, fosfomycin appears to be a viable treatment option, especially for uncomplicated UTIs caused by ESBL-producing *E. coli*, which constituted the majority of isolates in this study. The single-dose oral regimen of fosfomycin for UTIs provides a convenient and effective treatment option, particularly in outpatient settings. Study by Mataseje et al. (2016) [23] have demonstrated that fosfomycin remains highly effective in treating lower urinary tract infections caused by resistant *E. coli*, including ESBL-producing strains.
However, the slightly lower susceptibility rates observed in *K. pneumoniae* isolates highlight the need for cautious use in severe infections such as bloodstream infections or pneumonia, where combination therapy may be more appropriate. Fosfomycin has been successfully used in combination with other agents, such as carbapenems, to enhance its effectiveness in serious infections Rossi et al. (2020) [24]. Fosfomycin presents a valuable option for treating UTIs, particularly those caused by *Escherichia coli*, including strains that produce ESBLs. Given the limited number of effective antibiotics available for these cases, older antibiotics, including Fosfomycin, have been re-evaluated for their efficacy against multi-resistant bacteria. Fosfomycin has shown good in vitro sensitivity against these resistant strains [25,26].
The results of the current study indicate a variable susceptibility of gram-negative bacteria, particularly *E. coli* and *Klebsiella pneumoniae*, to commonly used antibiotics, with notable effectiveness of fosfomycin and nitrofurantoin, particularly for *E. coli* isolates (90.4%). This is consistent with findings from other studies, such as that by Neetu et al. (2021)[27], which reported a 92% susceptibility rate of *E. coli* to nitrofurantoin, underscoring its continued relevance in treating urinary tract infections caused by ESBL-producing strains. Other similar study by Faibr M et al. (2017) [28], Kalai J et al. (2023)[29] and Mohamed A.H et al.(2023) [30] .The findings for *Pseudomonas aeruginosa* showed a noteworthy susceptibility to meropenem and gentamicin , similar to study reported by Gyawali et al .(2020)[31].
In the current study fosfomycin maintained higher activity against ESBL-*Escherichia coli* than against ESBL-*Klebsiella pneumonia* with 90.4% and 78.5% respectively. This study was in support to the study performed by the other research investigator where Fosfomycin was observed to have higher activity against ESBL-*Escherichia coli* than against ESBL-*Klebsiella pneumoniae* [32].
Fosfomycin has been proposed as an adjunct antibiotic for the treatment of UTIs for several decades [33].
Fosfomycin is highly effective against uropathogenic ESBL-producing *E. coli* isolates. It could be used as an alternative treatment for both uncomplicated and complicated urinary tract infections. Since, Fosfomycin has no harmful effects on the body and its microbiota, so several clinical studies have demonstrated an excellent effectiveness of this antibiotic in the treatment of urinary infections compared to the use of other first-line antibiotics. [34-36].

5. CONCLUSION

This study confirms the high in vitro activity of fosfomycin against ESBL-producing *E. coli* and *K. pneumoniae* isolates. Given the increasing resistance to other antibiotics, fosfomycin represents a promising alternative, especially for UTIs caused by ESBL-producing *E. coli*. However, continued monitoring of resistance patterns and further clinical studies are warranted to guide its optimal use in both monotherapy and combination regimens.

6. DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study
Consent to participate: There is consent to participate.
Consent for publication: There is consent for the publication of this paper.
Authors' contributions: Author equally contributed the work.

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