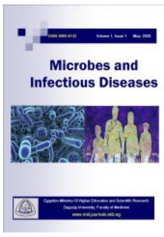
Microbes and Infectious Diseases 2025; 6(1): 299-307



Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Original article

Prevalence of multidrug-resistant *Klebsiella pneumoniae* in urinary tract infections: A retrospective observational study in eastern India

Swayamprabha Sahoo[1], Jatindra Nath Mohanty[2], Sweta Padma Routray[1], Ashirbad Sarangi[1], Debasish Swapnesh Kumar Nayak[3], Sejal Shah[4], Jayashankar Das[5], Enketeswara Subudhi[6], Tripti Swarnkar[*4]

1- *Centre for Biotechnology, Siksha 'O' Anusandhan Deemed to be University, Bhubaneswar, India.*
2- *Genetic Engineering and Genomic Laboratory, School of Applied Sciences, Centurion University of Technology and Management, Ramachandrapur, Jatni-752050, Odisha, India.*
3- *Department of Computer Science and Engineering, Siksha 'O' Anusandhan Deemed to be University, Bhubaneswar, India.*
4- *Department of Bioinformatics, Faculty of Technology, Marwadi University, Rajkot, India.*
5- *Valnizen Healthcare, Vile Parle, Mumbai, 40056, Maharastra, India.*
6- *Centre for Biotechnology, Siksha 'O' Anusandhan University, Khandagiri, Bhubaneswar, Odisha, 751003, India.*

ARTICLE INFO

Article history:
Received 13 March 2024
Received in revised form 4 April 2024
Accepted 5 April 2024

Keywords:
Multidrug-resistant
Klebsiella pneumonia
Urinary tract infection (UTI)
Healthcare management
Gram-negative bacteria

ABSTRACT

Background: Urinary tract infection (UTI) commonly affects people of different ages. It is important to explore the antibiotic susceptibility of the bacterial agents to improve the empirical antibacterial prescription to tackle the fast emerging of multi-drug resistant (MDR) bacteria. *Klebsiella pneumoniae*, a Gram-negative bacterium, is widely known for its hypervirulence, drug resistance and opportunistic nature, with significant implications for critically ill or immunocompromised patients. The study aim is to determine the prevalence of antibiotic resistance pattern among isolates from urinary tract infections (UTIs) and provide valuable insights for healthcare management. **Methods:** This is a retrospective observational study including 250 patients among 500 sample screened to have UTI at the largest hospital in eastern India from July 2020 to November 2022. All UTI patients underwent agar-based bacterium identification and antibiotic sensitivity testing using the disc diffusion method. **Results:** *Klebsiella pneumoniae* (122 cases) and *Escherichia coli* (74) were the first and second most frequent Gram-negative isolates, followed by *Pseudomonas aeruginosa* (45) and *Acinetobacter baumannii* (9). Notably, ten *Klebsiella pneumoniae* strains were resistant to five major antibiotic classes: β-lactam, aminoglycosides, fluoroquinolones, tetracyclines, and polymyxin. piperacillin/tazobactam, ceftazidime, aztreonam, and imipenem exhibited high resistance rates when tested against *Klebsiella pneumoniae* isolates. In contrast, gentamicin, levofloxacin, minocycline, fosfomycin, and colistin demonstrated relatively lower effectiveness against *Klebsiella pneumonia* isolates. **Conclusion:** Monitoring of multidrug-resistant bacteria becomes critical for prudent antibiotic use, ultimately dropping the prevalence of hospital-acquired infections and contributing to the larger fight against antimicrobial resistance.

DOI: 10.21608/MID.2024.276619.1844
* *Corresponding author:* Tripti Swarnkar
E-mail address: *swarnkar.tripti@gmail.com*

Introduction

Hospital-acquired infections are a serious concern for patients worldwide [1]. The development of multidrug-resistant (MDR) bacteria, due to the mismanagement and overuse of antibiotics in medicine and agriculture, has led to a higher risk of poor clinical outcomes, death, and increased economic burden for patients [2]. To effectively treat MDR bacterial infections and reduce their impact, it is crucial to understand their clinical characteristics, prevalence, and distribution in hospitals [3]. Common nosocomial infections seen in Indian hospitals include pneumonia, urinary tract infections (UTIs) and bloodstream infections [1,4].

A recent study conducted by Lin H *et al.* found *Klebsiella pneumoniae* as the most common organism accountable for various infectious diseases [5]. Matsumoto *et al*. investigated the prior association between extended-spectrum beta-lactamase (ESBL) producing *Klebsiella pneumoniae* and respiratory and UTI in a previous study [6]. The study showed that urinary tract infections are caused by bacterial movement from the anus to the meatus urinary tract, and that gastroesophageal reflux is brought on by intestinal colonisation of ESBL-producing *K. pneumoniae*. The global rise in resistance to carbapenem and polymyxin has heightened the risk of infections caused by resistant *Enterobacteriaceae* [7]. As a result, ESBL- producing bacteria like *Klebsiella pneumoniae* are critical priorities for the development of new antibiotics, according to the World Health Organization's (WHO) Global Action Plan (GAP) on Antimicrobial Resistance (AMR) [8,9]. The GAP's objective is to rise the investment in developing of new medicines, vaccines, diagnostic tools & other interventions to combat AMR [10]. An in-depth understanding of the implications posed by ESBL-producing *K. pneumoniae* on public health necessitates urgent and proactive measures to effectively combat and mitigate its effects [11].

To address the issue of antimicrobial resistance, the World Health Organisation (WHO) has introduced various measures, such as the implementation of the Global Antimicrobial Resistance Surveillance System (GLASS) and the Tricycle Project [12,13]. GLASS serves as a monitoring system for tracking the occurrence of antimicrobial resistance in different types of bacteria, including *E. coli* and *K. pneumoniae*. The bacterium *K. pneumoniae* is widely recognized for its role in causing pneumonia, septicemia and urinary tract infections (UTIs). A previously reported study on ESBL-producing *K. pneumonia* that is isolated from nosocomial infections found high rates of resistance to all antibiotic classes. This highlights the urgent need to develop new antibiotics to combat the growing threat of antimicrobial resistance, which has become a significant public health concern [14].

Therefore, it is crucial to determine the antibacterial susceptibility patterns of bacterial isolates to identify appropriate empirical therapy for critically ill patients. In this study, our aim is to investigate the prevailing drug resistance trends among isolates from urinary tract infections and provide valuable insights for healthcare authorities to plan, implement, and evaluate effective management programs.

Materials and Methods

The current study provides an in-depth overview of the study design, sample collection and laboratory procedures. This information is essential for understanding the study's methodology and the reliability of the findings.

Study Design

This was a retrospective study conducted in hospital ICUs. The study aimed to collect urine samples from the patients with suspected urinary tract infections for surveillance and epidemiological purposes.

Sample Size

The proposed study was conducted at IMS & SUM Hospital, Bhubaneswar over two years. Approximately 500 patients were screened for this research study. After the screening, a total of 250 eligible patients were enrolled to participate in the research. All patients with suspected UTIs who met the inclusion criteria were eligible for enrolment in the experiment.

Inclusion Criteria

- Patients admitted to the ICU.
- Patients who showed clinical symptoms of urinary tract infections, such as fever, dysuria, frequent urination, urgency, and flank pain.
- People who used a urinary catheter for at least 48 hours.

- Participants in the study who gave their consent as patients.

Exclusion Criteria

- Patients who had recently received antibiotic treatment within the previous 48 hours.
- The participants who have a history of allergic reactions to the antibiotics under investigation are not allowed to participate.
- Women who are pregnant or breastfeeding.

Sample Collection

Urine samples were collected aseptically from eligible patients using a sterile urine collection bottle. The samples were collected by trained nursing staff following standard operating procedures to minimize the risk of contamination. A total of 20 ml of urine was collected from each patient and transferred to a sterile screw-capped container. The containers were labelled with the patient's ID and transported to the microbiology laboratory for analysis within 30 minutes of collection [15].

Laboratory Analysis

Urine samples were analysed in the hospital laboratory using standard microbiological techniques. The samples were cultured on CLED, MacConkey agar and blood agar plates (HiMedia, India) and incubated for 24-48 hours at 37°C. Then identification of bacterial isolates was done using standard biochemical tests, including Urease, Citrate, Voges-Proskauer, Methyl Red, Catalase, Oxidase, and Indole tests, etc.

Antibiotic sensitivity test

After isolating and identifying pure cultures, the Kirby-Bauer disk diffusion method was employed following the guidelines of the Clinical and Laboratory Standards Institute (2019) (CLSI) to assess the susceptibility of microorganisms to various antibiotics [16,17]. A comprehensive antibiotic sensitivity test (ABST) was conducted, using up to 16 antibiotics categorized into five groups: Beta-lactam, fluoroquinolones, tetracyclines, aminoglycosides, polymyxin, and others (HiMedia, India) [18]. The ABST results were analysed to determine the antibiotic resistance pattern of the microorganism, and the findings were reported accordingly. This method provides clinicians with valuable information for selecting the best antibiotic treatment for infections caused by microorganisms.

Statistical analysis

We collected data on gender and antibiotic susceptibility in urinary tract infected *Klebsiella pneumoniae* patients. The prevalence of antibiotic resistance was determined by calculating the percentage of positive results. Statistical analysis was conducted using the R programming language to investigate the relationship between gender and antibiotic susceptibility. Chi-square tests were applied to the dataset to calculate chi-square test statistics, degrees of freedom, and p-values. These tests evaluated the observed frequencies of antibiotic susceptibility categories stratified by gender. A significance level of 0.05 was utilized to ascertain statistical significance, with antibiotics yielding p-values below this threshold signifying noteworthy associations between gender and antibiotic susceptibility [19].

Results

Sample collection and identification of multidrug resistance *Klebsiella pneumoniae*

After screening a large cohort of approximately 500 patients with urinary tract infections over two years, a total of 250 patients were enrolled in the study, with 174 (69.6%) males and 76 (30.4%) females, with the majority of patients affected falling in the age range of 41-80 years. Notably, the most prevalent isolate among all samples was *Klebsiella pneumoniae* 122 (48.8%), which affected a high number of UTI cases. *E.coli* was the second most commonly found pathogen, affecting 74 (29.6%) patients, followed by *Pseudomonas aeruginosa*, which affected 45 (18%) patients. In terms of gender, 50 male patients and 24 female patients were affected by *E. coli*, while 31 male patients and 14 female patients were affected by *Pseudomonas aeruginosa*. Interestingly, only 9(3.6%) cases of *Acinetobacter baumannii* were reported in our surveillance, of which 6 were male and 3 were female. It was observed that 69.6% of enrolled cases are male. **Figure 1** contains all the relevant patient details pertaining to the study.

Antimicrobial susceptibility of *K. pneumoniae* in UTI patients:

In this study, a panel of 16 antibiotics was used to test the susceptibility of all isolates. The results showed that some of the isolates were multidrug-resistant, with varying levels of resistance to different antibiotics. Particular, 5 (4.09%) had resistance to two antibiotics; 5 (4.09%) to three antibiotics; 13 (10.65%) to five antibiotics;

8 (6.55%) to seven antibiotics; 12 (9.83%) to eight antibiotics; 14 (11.47%) to nine antibiotics; 23(18.85%) to ten antibiotics and 2 (1.63%) to twelve antibiotics; 1 (0.81%) *et al* diseases and the development of new antibiotics **(Figure 2).**

The present study aimed to investigate the prevalence of urinary tract infections in a cohort of 500 patients. Upon screening, 250 patients were identified as UTI positive, out of which 122 patients were diagnosed with *Klebsiella pneumoniae* infection. We further analysed the antimicrobial susceptibility pattern of *K. pneumoniae* strains against various antibiotics. Our results showed a high level of resistance in *K. pneumoniae* strains against piperacillin (59.01%), ceftazidime (58.19%), aztreonam (57.37%), imipenem (57.37%), meropenem (51.63%), and tigecycline (51.63%). However, the strains were most susceptible to minocycline (73.77%) and fosfomycin (67.21%), followed by cefoperazone (50.81%), gentamicin (53.27%), ciprofloxacin (50%), levofloxacin (59.01%), and colistin (54.91%) **(Figure 3).**

Resistant *Klebsiella pneumonia* Infections: Concerns over Antibiotic Susceptibility

We revealed here that 10 out of the 122 *Klebsiella pneumonia* infections were highly resistant to three major antibiotic groups: β-lactam, colistin, and fluoroquinolones. **Figure 2** demonstrates that it is noteworthy that colistin is an antibiotic of last resort, used when other antibiotics are ineffective. The emergence of colistin-resistant bacteria is a cause for concern as it poses a significant threat to public health.

Ten strains of *Klebsiella pneumoniae* (identified as Patient ID 1411(M), 477(M), 1163(M), 814(M), 756(M), 640(F), 733(M), 662 (M), 561(F), and 1256(F)) are resistant to more than 14 antibiotics across 16 different groups. Following the Antibiotic Susceptibility Testing (ABST) performed on the ten strains, Amikacin antibiotic displayed intermediate results in seven strains (Patient ID: 1411(M), 477(M), 1163(M), 814(M), 756(M), 640(F), and 1256(F)). On the other hand, the fosfomycin antibiotic showed sensitivity to five strains (477(M), 814(M), 756(M), 561(F), and 1256(F)), and three strains displayed intermediate results (1411(M), 1163(M), and 662(M)). The remaining two strains (640(F) and 733(M)) were found to be resistant to fosfomycin (**Figure 4)**. The study observed that most patients with KPC-producing urinary tract infections showed positive clinical responses to treatment, even when active antibiotic therapy was delayed or not administered, and when urinary catheters were not removed promptly. Fosfomycin was the most frequently used treatment, and the results indicate its effectiveness. Additionally, tetracycline derivatives showed promise as potential treatment options for KPC-producing UTIs.

Statistical analysis

The Chi-square test results for multiple antibiotics unveil significant gender-related differences in antibiotic susceptibility. Chi-square tests were used to evaluate these associations, with a significance level of 0.05. For piperacillin-tazobactam, ceftazidime, and cefoperazone. Significant associations were observed between gender and antibiotic susceptibility for sulbactam, cefepime, azatreonam, imipenem, meropenem, amikacin, gentamicin, ciprofloxacin, levofloxacin, minocycline, tigecycline, fosfomycin, and colistin ($p < 0.05$). Male patients demonstrated a higher prevalence of resistance to Piperacillin than female patients. Tazobactam, ceftazidime, and cefoperazone. Sulbactam, cefepime, azatreonam, imipenem, meropenem, amikacin, gentamicin, ciprofloxacin, levofloxacin, minocycline, tigecycline, fosfomycin, and colistin. Conversely, female patients exhibited higher susceptibility rates for these antibiotics. However, for trimethoprim. sulfamethoxazole, no significant association was found between gender and antibiotic susceptibility ($p = 0.3808$). Both male and female patients demonstrated similar susceptibility patterns for trimethoprim-sulfamethoxazole. Similarly, for ceftazidime, cefoperazone. sulbactam, and tigecycline, gender-specific differences in antibiotic susceptibility were not significant ($p > 0.05$). In these cases, both male and female patients exhibited comparable susceptibility profiles. By using an analytical approach, it was possible to identify differences in antibiotic sensitivity patterns between genders. This information assisted clinicians to make decisions about the most effective ways to treat patients with antibiotics **(Table 1).**

Table 1. Gender specific antibiotic sensitivity data analysis using Chi-square tests.

Name of antibiotic	Gender	Intermediate (I)	Resistance (R)	Sensitive (S)	X-Squared	df	p-value
Piperacillin.Tazobactam	**M**	7	53	27	36.69	2	1.079e-08
	F	1	19	15	15.314	2	0.0004727
Ceftazidime	**M**	NA	56	31	7.1839	1	0.007356
	F	NA	15	20	0.71429	1	0.398
Cefoperazone.Sulbactam	**M**	4	42	41	32.345	2	9.471e-08
	F		14	21	1.4	1	0.2367
Cefepime	**M**	22	39	26	5.4483	2	0.0656
	F	2	16	17	12.057	2	0.002409
Aztreonam	**M**	17	51	19	25.103	2	3.539e-06
	F	5	19	11	8.4571	2	0.01457
Imipenem	**M**	2	52	33	43.931	2	2.887e-10
	F		18	17	0.028571	1	0.8658
Meropenem	**M**	5	47	35	32.276	2	9.804e-08
	F	3	16	16	9.6571	2	0.007998
Amikacin	**M**	20	24	43	10.414	2	0.005479
	F	7	11	17	4.3429	2	0.114
Gentamicin	**M**	2	39	46	38.552	2	4.252e-09
	F		16	19	0.25714	1	0.6121
Ciprofloxacin	**M**	4	42	41	32.345	2	9.471e-08
	F	2	13	20	14.114	2	0.0008612
Levofloxacin	**M**	9	30	48	26.276	2	1.969e-06
	F	3	8	24	20.629	2	3.316e-05
Minocycline	**M**	9	16	62	57.172	2	3.847e-13
	F	2	5	28	34.686	2	2.938e-08
Tigecycline	**M**	3	44	40	35.241	2	2.226e-08
	F	1	19	15	15.314	2	0.0004727
Fosfomycin	**M**	12	14	61	53.034	2	3.046e-12
	F	5	9	21	11.886	2	0.002625
Trimethoprim-Sulfamethoxazole	**M**	27	25	35	1.931	2	0.3808
	F	14	9	12	1.0857	2	0.5811
Colistin	**M**	34	7	46	27.517	2	1.059e-06
	F	11	3	21	13.943	2	0.0009383

Figure 1. Demographic and Pathogen Distribution: This figure visually depicts key demographics and the distribution of pathogens among 250 UTI patients in a year-long study of a total cohort of 500. It highlights gender proportions, age distribution, and the prevalence of significant pathogens, including *Klebsiella pneumoniae*, *E.coli*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* with gender-specific details.

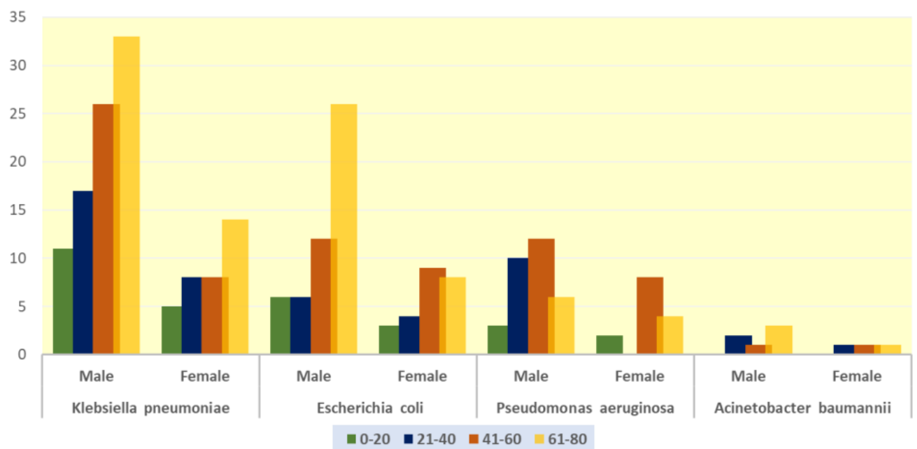


Figure 2: This figure illustrated the distribution of UTI case, with a predominance of male cases (70%) and a higher prevalence among individuals aged 61-80 years.

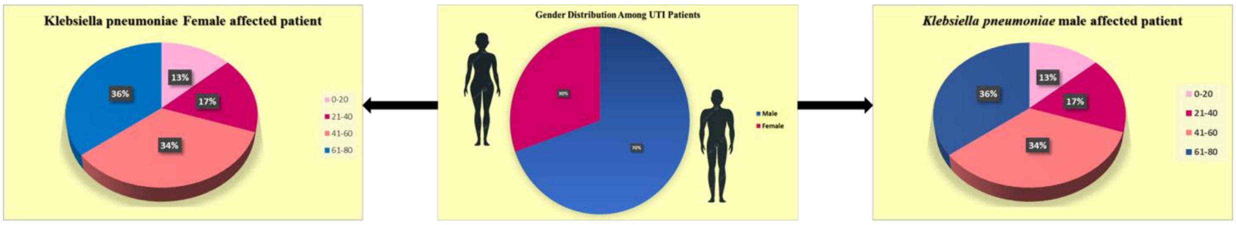


Figure 3: Describe the hierarchical clustering of *Klebsiella pneumoniae* isolates based on their phenotypical profile of antimicrobial resistance as demonstrated by the antibiotic sensitivity test. The Heatmap shows the susceptibility of the isolates to 16 types of antimicrobial agents, including Piperacillin, Ceftazidime, Cefoperazone, Cefepime, Aztreonam, Imipenem, Meropenem, Amikacin, Gentamicin, Ciprofloxacin, Levofloxacin, Minocycline, Tigecycline, Colistin, Fosfomycin, and Trimethoprim/Sulfamethoxazole. Red blocks indicate resistance, white blocks indicate intermediate susceptibility, and blue blocks indicate susceptibility.

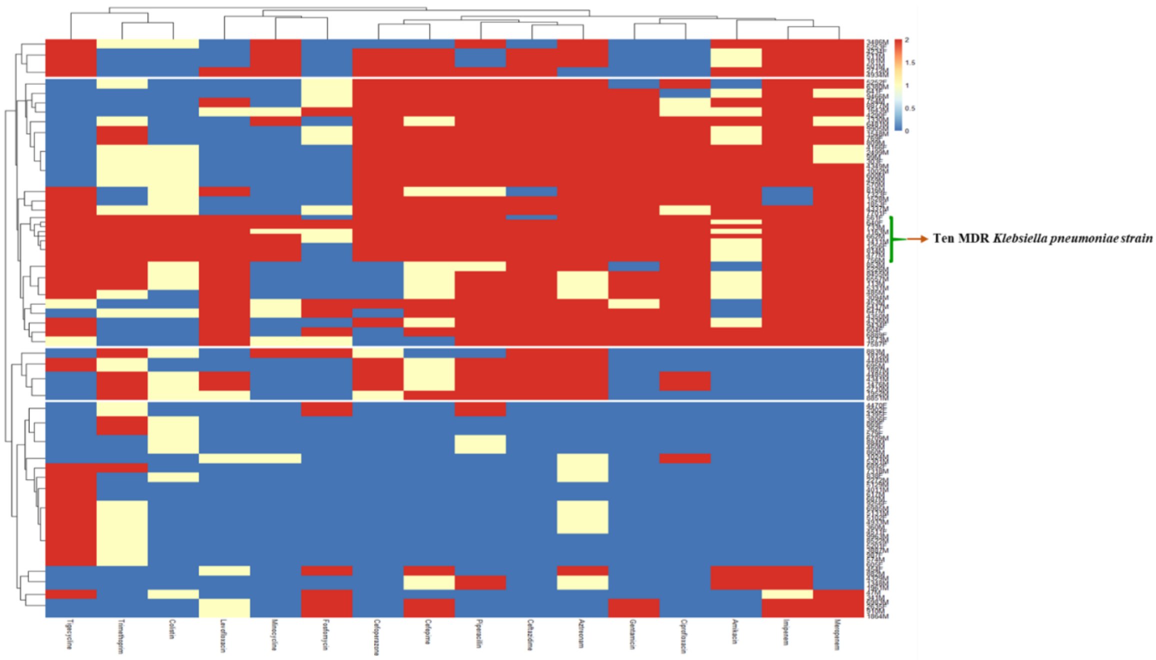
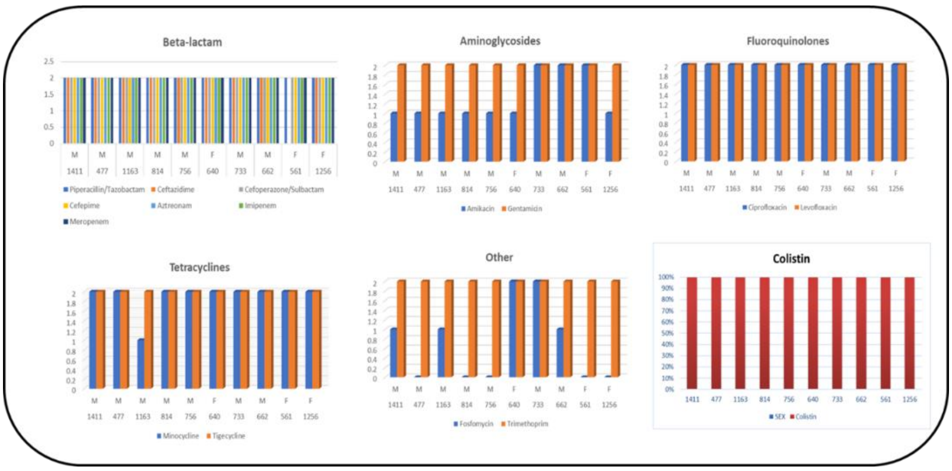


Figure 4: Antimicrobial susceptibility patterns of 16 different antibiotics



Discussion

The worldwide drug resistance rate of *Klebsiella pneumoniae* has increased to alarming levels, reaching up to 70%, accompanied by a concerning infection-related fatality rate ranging from 40% to 70% [20]. In recent years, the emergence of multidrug-resistant (MDR) *Klebsiella pneumoniae* and carbapenem-resistant *Klebsiella pneumonia* (CRKP) has become a significant and pressing global public health concern.

Urinary tract infections are a widespread and serious problem that places an immense burden on healthcare systems, especially in India [21]. Our research has shown that different microorganisms that display a range of resistance patterns to various broad-spectrum antibiotics are responsible for UTIs. The global disease burden is increasing due to the prevalence of antibiotic resistance, and treating UTIs is becoming more challenging [22,23]. Resistance to extended-spectrum beta-lactams, fluoroquinolones, and carbapenem agents is becoming an increasingly serious problem worldwide [24].

With a high prevalence rate of 48.8% (122 cases), *Klebsiella pneumoniae* emerged as the primary pathogen isolated from urine samples in our study. These findings are in accordance with other findings that a high incidence of *Klebsiella pneumoniae* frequently occurs in UTI cases. The group Wang *et al.* conducted a comprehensive 8-year study spanning and just finished before two year back at their hospital [25], and found the similar pattern of prevalence data. They intended to investigate the clinical distribution and resistance pattern of *Klebsiella pneumoniae* strains that were unaffected by carbapenems and extended-spectrum β-Lactamase (ESBL). The study found that *Klebsiella pneumoniae* strains made up 26.2% (4547/17358) of *Enterobacteriaceae*, ranking second only to *Escherichia coli*. The isolation rate of *Klebsiella pneumoniae* strains increased each year. Additionally, the authors observed that carbapenem-resistant *Klebsiella pneumoniae* (CR KP) had the highest detection rate among carbapenem-resistant *Enterobacteriaceae* (CRE). It accounted for 72.2% (431 out of 597), and this rate also increased over the study period. In contrast to the study by Wang *et al.*, where *K. pneumoniae* ranked second, our investigation focused specifically on UTI patients, where we found that *K. pneumoniae* was the most prevalent pathogen. Male patients are considerably more likely to have UTIs, highlighting the increased risk in this demographic.

In contrast to the study by Alexander *et al.*, which explored KPC-producing Enterobacteriaceae in UTIs and reported a 76% success rate despite delayed antibiotic initiation, our study aligns with their findings. It highlights the challenges posed by these infections. Aminoglycoside and tetracycline derivatives like tigecycline, minocycline and fosfomycin emerged as promising treatment options for these infections, offering valuable insights for researchers and clinicians. Furthermore, in 2019, Gopichand *et al.* investigated fosfomycin's in-vitro effectiveness against MDR strains in UTIs, particularly *Escherichia coli*, *K. pneumoniae* etc, which showed significant inhibitory effects and potential against extended-spectrum beta-lactamases and carbapenemase producers. The disruption of biofilm formation by fosfomycin indicated its potential as a valuable treatment option for challenging UTIs [26,27]. Our study further corroborates these findings by highlighting that levofloxacin, minocycline, and fosfomycin had limited effectiveness against *Klebsiella pneumoniae* isolates, emphasizing the ongoing need for research in effective UTI treatments. Here in this study *Klebsiella pneumoniae* strains are highly resistant to antibiotics like piperacillin/tazobactam and ceftazidime. However, they show less resistance to antibiotics like minocycline and fosfomycin. This suggests that minocycline and fosfomycin may be more effective in treating infections caused by these strains. At the same time, piperacillin/tazobactam and ceftazidime may not work as well due to high resistance.

Conclusion

Two year study of 500 patients with urinary tract infections, *Klebsiella pneumoniae* was found to be the most common bacteria, affecting 122 patients followed by *E.coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. The antimicrobial resistance profile of *Klebsiella pneumoniae* classified them into resistant, intermediate, and sensitive types. The study found that 10 out of the 122 *Klebsiella pneumonia* were highly resistant to three major antibiotic groups: β-lactam, colistin, and fluoroquinolones. This research endeavour provides valuable insights into antibiotic resistance profile of urinary tract infecting *Klebsiella pneumoniae* which may help combating the infections due to such resistant bacteria effectively and ultimately lowering the mortality rates. The study suggests the need for large-scale surveillance of multidrug-resistant *Klebsiella pneumonia* to direct the rational use of antibiotics and reduce the incidence of hospital-acquired infections. These resistance strains will be further subjected to genetic-level analysis to identify the prevalent resistance genes and other underlying pathogenic factors in our next study.

Disclosure of potential conflict of interest

The authors report no conflicts of interest.

Conception and design: all authors. Administrative support: all authors. Provision of study materials or patients: all authors. Collection and assembly of data: all authors. Data analysis and interpretation: all authors. Manuscript writing: all authors. Final approval of manuscript: all authors. SPS, TS, ES, JD reviewed the manuscript.

Financial disclosure: None.

References

1- Nimer NA. Nosocomial infection and antibiotic-resistant threat in the Middle East. Infection and drug resistance 2022; 1:631-9.
2- Ananda T, Modi A, Chakraborty I, Managuli V, Mukhopadhyay C, Mazumder N. Nosocomial infections and role of nanotechnology. Bioengineering. 2022;9(2):51.
3- Pacios O, Blasco L, Bleriot I, Fernandez-Garcia L, González Bardanca M, Ambroa A, et al. Strategies to combat multidrug-resistant and persistent infectious diseases. Antibiotics 2020;9(2):65.
4- Thomas D, Nair SS, Kavyanjana P, Saleed KP, Shahir KP. Assessment and Management of Hospital Acquired Infections in a Tertiary Care Hospital. Indian Journal of Pharmacy Practice 2023;16(2).
5- Lin H, Sun J, Ma J, Qin Z, Jiang B, Li W, et al. Detection and quantification of Klebsiella pneumoniae in American bullfrog (Rana catesbeiana) by Taqman MGB probe real-time fluorescence quantitative PCR. Aquaculture 2023;15;568:739339.
6- Matsumoto H, Komiya K, Ichihara S, Nagaoka Y, Yamanaka M, Nishiyama Y, et al. Factors associated with extended-spectrum β-lactamase-producing Enterobacteria isolated from respiratory samples. Internal Medicine 2023;62(14):2043-50.
7- Tilahun M, Kassa Y, Gedefie A, Ashagire M. Emerging carbapenem-resistant Enterobacteriaceae infection, its epidemiology and novel treatment options: a review. Infection and drug resistance 2021; 21:4363-74.
8- Mendelson M, Matsoso MP. GUEST EDITORIAL: The World Health Organization Global Action Plan for antimicrobial resistance. South African medical journal 2015;105(5):325-.
9- Chandra P, Mk U, Ke V, Mukhopadhyay C, U DA, V R. Antimicrobial resistance and the post antibiotic era: better late than never effort. Expert Opinion on Drug Safety 2021;20(11):1375-90.
10- Iwu CD, Patrick SM. An insight into the implementation of the global action plan on antimicrobial resistance in the WHO African region: A roadmap for action. International Journal of Antimicrobial Agents 2021;58(4):106411.
11- Fils PE, Cholley P, Gbaguidi-Haore H, Hocquet D, Sauget M, Bertrand X. ESBL-producing Klebsiella pneumoniae in a University hospital: molecular features, diffusion of epidemic clones and evaluation of cross-transmission. PLoS One 2021;16(3):e0247875.
12- Tornimbene B, Eremin S, Abednego R, Abualas EO, Boutiba I, Egwuenu A et al. Global Antimicrobial Resistance and Use Surveillance System on the African continent: Early implementation 2017-2019. African

Journal of Laboratory Medicine 2022;11(1):1-1.

13- Orubu ES, Zaman MH, Rahman MT, Wirtz VJ. Veterinary antimicrobial resistance containment in Bangladesh: Evaluating the national action plan and scoping the evidence on implementation. Journal of global antimicrobial resistance 2020;21:105-15.

14- Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathogens and global health 2015;109(7):309-18.

15- Miller JM, Miller SA. A guide to specimen management in clinical microbiology. John Wiley & Sons 2017

16- CLSI A. CLSI AST news update. Clinical and Laboratory Standards Institute 2019.

17- Hudzicki J. Kirby-Bauer disk diffusion susceptibility test protocol. American society for microbiology. 2009 ;15(1):1-23

18- Ghorbanpoor H, Dizaji AN, Akcakoca I, Blair EO, Ozturk Y, Hoskisson P, et al. A fully integrated rapid on-chip antibiotic susceptibility test–A case study for Mycobacterium smegmatis. Sensors and Actuators A: Physical. 2022;339:113515.

19- Baumann E, Czerwinski F, Reifegerste D. Gender-specific determinants and patterns of online health information seeking: results from a representative German health survey. Journal of Medical Internet Research 2017;19(4):e92.

20- Greenblatt R, Mansour O, Zhao E, Ross M, Himes BE. Gender-specific determinants of asthma among US adults. Asthma research and practice 2017;3:1-1.

21- Singh Y, Karicheri R, Nath D. The burden of catheter associated urinary tract infection by candida Albicans and non Albicans with emphasis on biofilm formation and antifungal sensitivity pattern. International Journal of Health Sciences 2022;(II):2356-63.

22- Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH et al. Antibiotic resistance: a rundown of a global crisis. Infection and drug resistance 2018;1645-58.

23- Talebi Bezmin Abadi A, Rizvanov AA, Haertlé T, Blatt NL. World Health Organization report: current crisis of antibiotic resistance. BioNanoScience 2019 ;9(4):778-88.

24- Dembélé R, Konaté A, Traoré O, Kaboré WA, Soulama I, Kagambèga A et al. Extended spectrum beta-lactamase and fluoroquinolone resistance genes among Escherichia coli and Salmonella isolates from children with diarrhea, Burkina Faso. BMC pediatrics 2020;20:1-9.

25- Wang M, Wei H, Zhao Y, Shang L, Di L, Lyu C et al. Analysis of multidrug-resistant bacteria in 3223 patients with hospital-acquired infections (HAI) from a tertiary general hospital in China. Bosnian journal of basic medical sciences 2019;19(1):86.

26- Alexander BT, Marschall J, Tibbetts RJ, Neuner EA, Dunne Jr WM, Ritchie DJ. Treatment and clinical outcomes of urinary tract infections caused by KPC-producing Enterobacteriaceae in a retrospective cohort. Clinical therapeutics 2012;34(6):1314-23.

27- Gopichand P, Agarwal G, Natarajan M, Mandal J, Deepanjali S, Parameswaran S, et al. "Is Fosfomycin As Effective As Claimed On MDR Gram-Negative Bacteria Causing UTI?" [Response To Letter]. Infection and Drug Resistance 2019 ;3:3091-2.

Sahoo S, Mohanty JN, Routray SP, Sarangi A, Nayak DSK, Shah S et al. Prevalence of Multidrug-Resistant *Klebsiella pneumoniae* in Urinary Tract Infections: A Retrospective Observational Study in Eastern India. Microbes Infect Dis 2025; 6(1): 299-307.