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Molecular Insights into Antibiotic Resistance: BLACTX-M and BLANDM in Klebsiellapneumoniae UTI Isolates

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Abstract

This study investigated the prevalence and antibiotic resistance patterns of Klebsiellapneumoniae isolated from urinary tract infection (UTI) patients in Peshawar. A total of 200 urine samples were collected, of which 50 (25%) were culture-positive for K. pneumoniae while 150 (75%) showed no bacterial growth. Gram staining and biochemical profiling confirmed the isolates as Gram-negative, oxidase-negative, citrate-positive, urease-positive, and non-motile bacilli, with 95% demonstrating uniform biochemical reactions. Socio-demographic analysis revealed that infections were more common in females (65%) than males (35%), with the highest prevalence in the 21–40 years age group (40%), followed by patients above 60 years (25%) and children under 15 years (10%). Antibiotic susceptibility testing using the Kirby–Bauer disc diffusion method showed alarming resistance levels: penicillin (≥90%), third-generation cephalosporins (65–70%), fluoroquinolones (45–55%), aminoglycosides (gentamicin 55%, amikacin 30%), sulfonamides (60%), tetracycline (45%), and nalidixic acid (70%). Lower resistance was observed to nitrofurantoin (35%), fosfomycin (25%), and carbapenems (imipenem 10%, meropenem 15%). Overall, 70% of isolates were multidrug-resistant (MDR), with 15% classified as extensively drug-resistant (XDR), leaving colistin and fosfomycin as last-line agents. These findings confirm that K. pneumoniae is both a prevalent and highly resistant uropathogen, posing significant clinical and public health risks. The results underscore the urgent need for surveillance, rational antibiotic use, infection control strategies, and exploration of alternative therapeutic approaches.

Introduction

Urinary tract infections (UTIs) are among the most frequently reported bacterial infections worldwide and constitute a substantial public health burden. They affect individuals of all age groups and genders, with higher prevalence observed among females, elderly individuals, and patients with underlying comorbidities [1]. UTIs account for millions of outpatient visits and hospital admissions annually, leading to significant healthcare costs and increased antibiotic consumption. The situation is particularly concerning in developing countries, where limited diagnostic facilities, inappropriate antibiotic use, and inadequate infection control measures contribute to persistent infection rates and treatment failures.A wide range of Gram-negative bacteria are implicated in UTIs; however, Klebsiellapneumoniae has emerged as one of the most important uropathogens in both community-acquired and hospital-acquired infections. K. pneumoniae is a Gram-negative, encapsulated, non-motile bacillus belonging to the family Enterobacteriaceae [2]. Its pathogenic success is attributed to multiple virulence factors, including capsule formation, biofilm production, siderophore-mediated iron acquisition, and adherence mechanisms that facilitate colonization of the urinary tract. Over recent decades, K. pneumoniae has gained particular attention due to its remarkable ability to acquire, harbor, and disseminate antimicrobial resistance genes [3].

The rapid emergence and global spread of multidrug-resistant (MDR) and extensively drug-resistant (XDR) K. pneumoniae strains have posed serious challenges to clinical management. MDR strains are resistant to three or more classes of antimicrobial agents, while XDR strains exhibit resistance to almost all available therapeutic options. The increasing frequency of such strains has resulted in prolonged hospital stays, higher morbidity and mortality rates, and increased reliance on last-line antibiotics [4, 5]. Consequently, infections caused by resistant K. pneumoniae are now considered a critical threat to global health security.One of the primary mechanisms underlying antimicrobial resistance in K. pneumoniae is the production of β-lactamase enzymes. These enzymes hydrolyze β-lactam antibiotics, rendering them ineffective. Among them, extended-spectrum β-lactamases (ESBLs) have gained particular importance due to their ability to inactivate third-generation cephalosporins, which are commonly used in the empirical treatment of UTIs. The CTX-M family of ESBLs has become the most prevalent worldwide, surpassing older β-lactamases such as TEM and SHV [6]. The **blaCTX-M** gene encodes enzymes with high catalytic efficiency against cefotaxime and ceftriaxone, leading to widespread resistance and treatment failure.In addition to ESBL production, carbapenem resistance has emerged as a major concern. Carbapenems are often regarded as last-line antibiotics for the treatment of severe infections caused by ESBL-producing organisms. However, the emergence of carbapenemase-producing K. pneumoniae has significantly compromised their effectiveness [7]. Among carbapenemases, the New Delhi metallo-β-lactamase (NDM) is particularly alarming due to its broad-spectrum activity and rapid dissemination. The **blaNDM** gene encodes an enzyme capable of hydrolyzing almost all β-lactam antibiotics, including carbapenems, while leaving very limited treatment options such as colistin and fosfomycin.The spread of **blaCTX-M** and **blaNDM** genes is largely facilitated by plasmids, transposons, and integrons, which enable horizontal gene transfer between bacterial species. This genetic mobility accelerates the dissemination of resistance within healthcare settings and the community [8]. Furthermore, K. pneumoniae strains often harbor multiple resistance determinants simultaneously, resulting in co-resistance to non-β-lactam antibiotics such as fluoroquinolones, aminoglycosides, and sulfonamides. This multidimensional resistance profile severely limits effective antimicrobial therapy and complicates infection control efforts [9].

In Pakistan, antimicrobial resistance has reached alarming levels due to a combination of factors, including irrational antibiotic prescribing, over-the-counter availability of antibiotics without prescription, incomplete treatment courses, and lack of antimicrobial stewardship programs. Routine diagnostic practices in many healthcare facilities rely primarily on phenotypic methods, which fail to provide insights into the underlying molecular mechanisms of resistance [10]. Additionally, molecular surveillance of resistance genes remains limited, particularly in resource-constrained regions.KhyberPakhtunkhwa, including the city of Peshawar, faces unique healthcare challenges due to high patient load, limited laboratory infrastructure, and insufficient infection control policies. Despite the increasing reports of resistant uropathogens in this region, there is a notable scarcity of molecular epidemiological data on resistance genes in K. pneumonia [11]. The absence of such data hampers the development of targeted treatment guidelines and effective public health interventions.Understanding the molecular basis of antibiotic resistance is essential for guiding empirical therapy, improving patient outcomes, and preventing the further spread of resistant strains [12]. The detection of **blaCTX-M** and **blaNDM** genes provides valuable insights into resistance trends and helps predict therapeutic failure associated with commonly used antibiotics. Therefore, the present study was designed to investigate the prevalence of Klebsiellapneumoniae among UTI patients in Peshawar, determine its antibiotic resistance patterns, and assess the molecular presence of **blaCTX-M**and**blaNDM** resistance genes [13, 14]. By integrating phenotypic and molecular approaches, this study aims to contribute valuable data to the limited existing literature from this region. The findings are expected to inform clinicians, microbiologists, and policymakers, emphasizing the urgent need for routine molecular diagnostics, rational antibiotic use, and strengthened infection control strategies to combat the growing threat of antimicrobial resistance.

Literature Review

Klebsiellapneumoniae has been increasingly recognized as a major cause of complicated urinary tract infections (UTIs), particularly in hospital and healthcare-associated settings. Multiple studies have reported its rising prevalence alongside a disturbing increase in antimicrobial resistance, making treatment increasingly difficult (Livermore, 2012; Gajdács&Urbán, 2019). The organism’s capacity to acquire resistance genes through horizontal gene transfer, combined with its intrinsic virulence factors, has enabled it to persist and spread in both community and clinical environments (Blair et al., 2015).Extended-spectrum β-lactamase (ESBL) production is one of the most significant resistance mechanisms observed in uropathogenicK. pneumoniae. Among ESBLs, the CTX-M family has emerged as the most dominant globally, replacing earlier TEM and SHV β-lactamases (Cantón et al., 2012; Woerther et al., 2013). CTX-M enzymes exhibit enhanced hydrolytic activity against third-generation cephalosporins such as cefotaxime and ceftriaxone, which are commonly prescribed for UTIs. Studies conducted across South Asia, the Middle East, and Europe have consistently reported high prevalence of **blaCTX-M**–harboring K. pneumoniae isolates, highlighting the global dissemination of this resistance determinant (Lee et al., 2016; Attal et al., 2019).

The widespread distribution of **blaCTX-M** genes has been largely attributed to their association with mobile genetic elements, including plasmids and transposons, facilitating rapid inter- and intra-species spread (Peirano et al., 2020). Clinical studies have shown that infections caused by CTX-M–producing K. pneumoniae are associated with higher rates of treatment failure, prolonged hospitalization, and increased healthcare costs (Rodríguez-Baño et al., 2018). These findings underscore the clinical significance of monitoring ESBL-producing strains, particularly in high-risk patient populations.

In recent years, carbapenem resistance has emerged as an even more critical challenge in the management of K. pneumoniae infections. Carbapenems have traditionally been reserved as last-line agents for severe infections caused by ESBL-producing organisms.

However, the emergence of carbapenemase-producing K. pneumoniae has severely undermined their effectiveness (Basak& Singh, 2017). Among carbapenemases, New Delhi metallo-β-lactamase (NDM) has gained particular attention due to its broad substrate profile and rapid international spread.

The blaNDM gene was first identified in 2008 and has since been reported in numerous countries worldwide, with especially high prevalence in the Indian subcontinent (Kumarasamy et al., 2010; Nordmann&Poirel, 2014). NDM-producing K. pneumoniae isolates frequently exhibit co-resistance to multiple non-β-lactam antibiotics, including fluoroquinolones, aminoglycosides, and sulfonamides, resulting in multidrug-resistant (MDR) and extensively drug-resistant (XDR) phenotypes (Diene et al., 2013; Jean et al., 2016). Consequently, treatment options are often limited to toxic or less accessible agents such as colistin and fosfomycin (Tamma et al., 2019).Several molecular epidemiological studies have demonstrated that blaNDM is commonly located on conjugative plasmids, enabling its rapid dissemination across bacterial populations (Yoon &Jeong, 2019). This plasmid-mediated spread has contributed to outbreaks in hospital settings and poses a serious threat to infection control efforts (Zafer et al., 2019). The coexistence of blaCTX-M and blaNDM genes within the same isolate has also been reported, further exacerbating resistance and limiting therapeutic options (Peirano et al., 2020).

In Pakistan, antimicrobial resistance among uropathogenicK. pneumoniae has reached alarming levels. Multiple studies have documented resistance rates exceeding 60% to third-generation cephalosporins and fluoroquinolones, reflecting widespread ESBL production (Balaji et al., 2018; Gupta et al., 2018). Shahid et al. (2022) reported a high prevalence of blaNDM among clinical isolates, indicating increasing carbapenem resistance in the region. Similar findings have been observed in neighboring countries, suggesting regional dissemination of resistant clones (Haque et al., 2019).

Despite these concerning trends, routine diagnostic practices in many Pakistani laboratories remain limited to phenotypic susceptibility testing, which fails to identify the underlying molecular mechanisms of resistance (Rawat& Nair, 2010). Molecular detection methods such as polymerase chain reaction (PCR) are not routinely employed due to cost constraints and lack of technical infrastructure (Jang et al., 2021). This diagnostic gap hinders early detection, surveillance, and effective containment of resistant strains.Overall, the existing literature highlights the growing threat posed by ESBL- and carbapenemase-producing K. pneumoniae, particularly strains harboring blaCTX-M and blaNDM genes. The high prevalence of these resistance determinants, coupled with limited molecular surveillance in developing regions such as Pakistan, underscores the urgent need for integrated phenotypic and molecular approaches. Strengthening surveillance systems and implementing robust antibiotic stewardship policies are essential to curb the further spread of resistant K. pneumoniae and preserve the effectiveness of remaining therapeutic options.

Materials and Methods

Study Design and Study Area

A cross-sectional laboratory-based study was conducted in Peshawar, Khyber Pakhtunkhwa, Pakistan, over a period spanning January 2022 to December 2023. The study aimed to investigate the prevalence, antimicrobial resistance patterns, and molecular characteristics of Klebsiellapneumoniae isolated from urinary tract infection (UTI) patients [39, 40].

Study Population and Sample Collection

A total of 200 urine samples were collected from clinically suspected UTI patients attending outpatient departments and inpatient wards of tertiary care hospitals in Peshawar. Patients of all age groups and both genders were included based on clinical symptoms suggestive of UTI, such as dysuria, frequency, urgency, suprapubic pain, or fever [38].Midstream urine samples were collected in sterile, wide-mouth, screw-capped containers following standard aseptic procedures. Samples were properly labeled and transported to the microbiology laboratory within 2 hoursof collection. If immediate processing was not possible, samples were stored at 4 °C for a maximum of 24 hours to prevent bacterial overgrowth.

Inclusion and Exclusion Criteria

Inclusion criteria:

Patients with clinical suspicion of UTI
Urine samples showing significant bacteriuria
Samples yielding K. pneumoniae on culture

Exclusion criteria:

Patients already on antibiotic therapy
Contaminated or improperly collected samples
Samples with mixed bacterial growth

Isolation and Identification of Klebsiellapneumoniae

Each urine sample was inoculated onto MacConkey agar using a calibrated loop (0.001 mL) and incubated aerobically at 37 °C for 24 hours. Lactose-fermenting, mucoid pink colonies were presumptively identified as Klebsiella species.

Further identification was performed using microscopic examination and biochemical tests:

Gram staining: Gram-negative bacilli
Oxidase test: Negative
Catalase test: Positive
Citrate utilization test: Positive
Urease test: Positive
Motility test: Non-motile
Triple Sugar Iron (TSI) agar: Acid/acid with gas production, no H_2S
Indole test: Negative

Isolates showing characteristic biochemical profiles were confirmed as Klebsiellapneumoniae. Pure cultures were preserved in nutrient broth supplemented with 20% glycerol at –80 °C for further analysis.

Antibiotic Susceptibility Testing (AST)

Antimicrobial susceptibility testing was performed using the Kirby–Bauer disc diffusion method on Mueller–Hinton agar, following Clinical and Laboratory Standards Institute (CLSI) guidelines (2022).The bacterial inoculum was standardized to 0.5 McFarland turbidity and uniformly spread on agar plates [34, 35]. Antibiotic discs were placed aseptically, and plates were incubated at 37 °C for 18–24 hours.

The antibiotics tested included:

Penicillin
Cefotaxime, Ceftriaxone (3rd-generation cephalosporins)
Ciprofloxacin, Levofloxacin (fluoroquinolones)
Gentamicin, Amikacin (aminoglycosides)
Trimethoprim-sulfamethoxazole
Tetracycline
Nalidixic acid
Nitrofurantoin
Fosfomycin
Imipenem, Meropenem (carbapenems)

Zones of inhibition were measured in millimeters and interpreted as sensitive, intermediate, or resistant according to CLSI breakpoints.

Table 3.1: Distribution of Urine Samples and Culture Results (n = 200)

Result	**Frequency (n)**	**Percentage (%)**
Culture positive for K. pneumoniae	50	25
No bacterial growth	150	75
Total	**200**	**100**

Classification of MDR and XDR Isolates

Multidrug-resistant (MDR): Resistance to ≥3 antimicrobial classes

Extensively drug-resistant (XDR): Resistance to all but one or two antimicrobial classes

Classification was performed based on international consensus definitions.

Genomic DNA Extraction

Genomic DNA was extracted from confirmed K. pneumoniae isolates using the boiling method. Briefly, a single colony was suspended in sterile distilled water, heated at 95 °C for 10 minutes, and centrifuged at 12,000 rpm for 5 minutes. The supernatant containing DNA was stored at –20 **°C** until PCR analysis.

Table 2: Socio-Demographic Characteristics of K. pneumoniae Positive Patients (n = 50)

Variable	**Category**	**Frequency (n)**	**Percentage (%)**
Gender	Male	18	35
	Female	32	65
Age group (years)	<15	5	10
	21–40	20	40
	41–60	13	25
	>60	12	25

Molecular Detection of blaCTX-M and blaNDM Genes

Polymerase Chain Reaction (PCR) was used to detect blaCTX-M and blaNDM genes.

PCR reaction mixture (25 µL):

Template DNA: 2 µL
Forward and reverse primers: 1 µL each
PCR master mix: 12.5 µL
Nuclease-free water: up to 25 µL

PCR amplification was carried out using a thermal cycler under optimized conditions (initial denaturation, annealing, extension, and final elongation).

Table 3.2: Antibiotic Resistance Pattern of K. pneumoniae Isolates (n = 50)

Antibiotic	**Resistant n (%)**	**Sensitive n (%)**
Penicillin	45 (90)	5 (10)
Cefotaxime	33 (66)	17 (34)
Ceftriaxone	35 (70)	15 (30)
Ciprofloxacin	25 (50)	25 (50)
Levofloxacin	23 (46)	27 (54)

Antibiotic	**Resistant n (%)**	**Sensitive n (%)**
Gentamicin	28 (55)	22 (45)
Amikacin	15 (30)	35 (70)
Nalidixic acid	35 (70)	15 (30)
Sulfonamides	30 (60)	20 (40)
Tetracycline	22 (45)	28 (55)
Nitrofurantoin	18 (35)	32 (65)
Fosfomycin	12 (25)	38 (75)
Imipenem	5 (10)	45 (90)
Meropenem	8 (15)	42 (85)

Agarose Gel Electrophoresis

PCR products were separated on 1.5% agarose gel containing ethidium bromide and visualized under UV transillumination. A 100 bp DNA ladder was used as a molecular size marker. The presence of bands at expected base-pair sizes confirmed gene detection [33].

Quality Control

Quality control was maintained using:
E. coli ATCC 25922 as a negative control
Known ESBL and NDM-positive strains as positive controls
Sterile distilled water as PCR negative control

Ethical Considerations

Ethical approval was obtained from the institutional ethical review committee. Written informed consent was obtained from all participants or guardians prior to sample collection. Patient confidentiality was strictly maintained.

Results and Discussions

Prevalence of K. pneumonia

Out of **200 urine samples**collected from clinically suspected UTI patients, **50 samples (25%) were culture-positive for** Klebsiellapneumoniae**,** while **150 samples (75%) showed no bacterial growth.** This finding indicates that K. pneumoniae is a significant uropathogen in the study population, contributing to a substantial proportion of UTIs in Peshawar [15]. The prevalence observed in this study is consistent with reports from other regions of South Asia, where K. pneumoniae remains a common cause of complicated and recurrent urinary tract infections.Among the positive cases, a higher number of infections were observed in females compared to males, reflecting the known anatomical and physiological susceptibility of women to UTIs. The age distribution revealed that adults aged 21–40 years accounted for the majority of infections, followed by older adults and children. These results suggest that sexually active and working-age adults may be at increased risk of acquiring K. pneumoniae infections [21-25].

The 25% prevalence rate underscores the need for routine surveillance of uropathogens, particularly in regions with high rates of antibiotic misuse and limited infection control practices. Understanding the local prevalence of K. pneumoniae is crucial for guiding empiric therapy, predicting potential outbreaks, and implementing targeted infection prevention measures. Furthermore, the high prevalence highlights the importance of integrating molecular diagnostic approaches to detect resistance genes, which can inform treatment decisions and reduce the spread of multidrug-resistant strains [19].

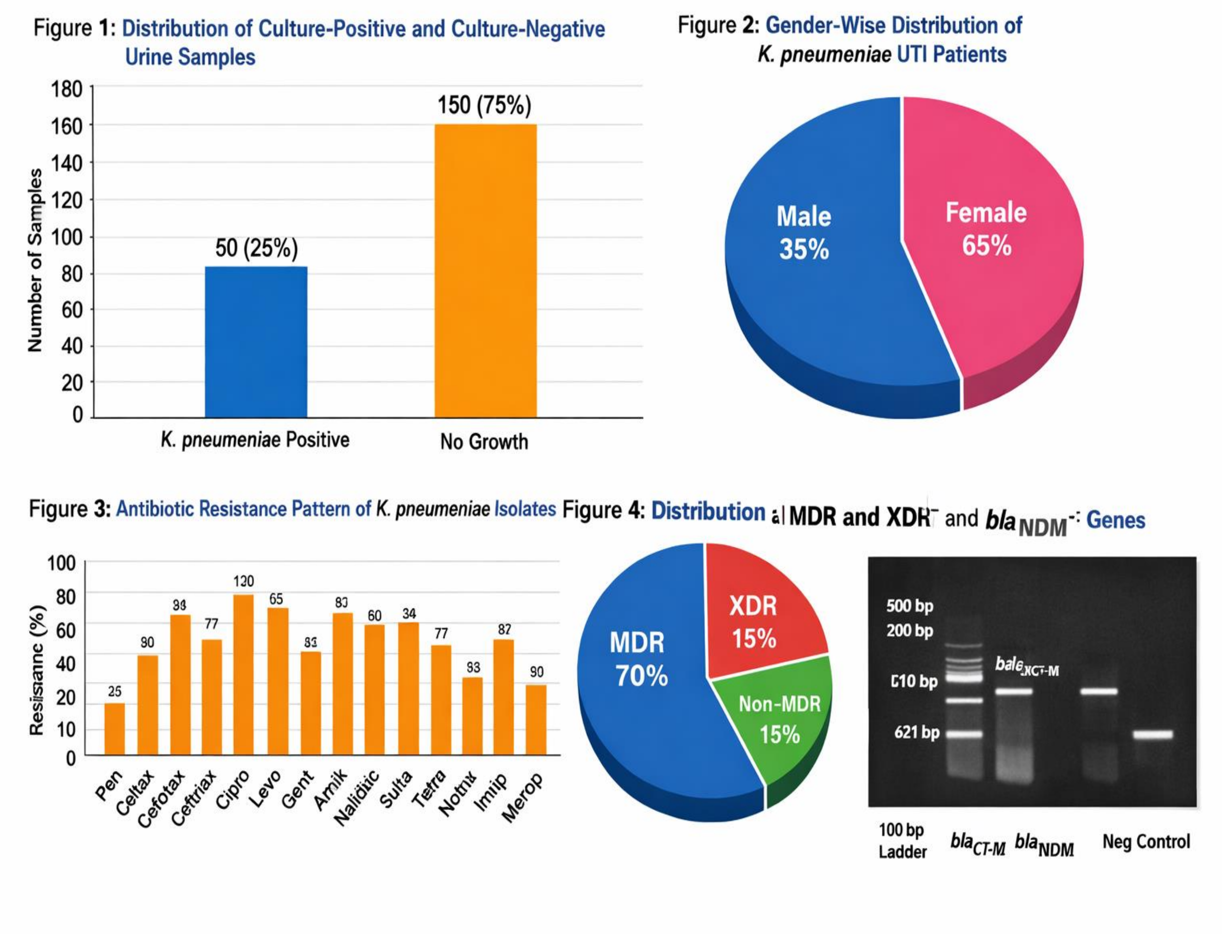

Figure 4. 1 Antibiotic Resistance Distribution of K. pneumoniae

Table 4.1: Socio-Demographic Distribution of UTI Patients (n = 50)

Variable	**Category**	**Frequency (%)**
Gender	Female	65
	Male	35
Age Group	<15 years	10
	21–40 years	40
	>60 years	25

Antibiotic Resistance Pattern

High resistance was observed among Klebsiellapneumoniae isolates against several commonly prescribed antibiotics. Resistance to **penicillin** was particularly high, affecting ≥90% of isolates, reflecting widespread ineffectiveness of this class for treating UTIs [16, 17]. Similarly, **third-generation cephalosporins** such as cefotaxime and ceftriaxone showed resistance rates of 65–70%, which aligns with the high prevalence of **blaCTX-M**–mediated ESBL production. Resistance to **nalidixic acid** and **sulfonamides** was also significant, at 70% and 60% respectively, indicating limited utility of these agents in empirical therapy. Conversely, lower resistance was observed to **carbapenems**, with imipenem and meropenem showing 10–15% resistance, and to **fosfomycin**, which retained susceptibility in 75% of isolates [18]. These findings underscore the critical need to monitor antibiotic use and promote **rational prescribing**, as resistance to frontline antibiotics continues to rise. The observed pattern also highlights the importance of integrating **phenotypic susceptibility testing with molecular detection**of resistance genes to guide effective treatment strategies.

Table 4. 2: Antibiotic Resistance Profile of K. pneumoniae Isolates

Antibiotic	**Resistance (%)**
Penicillin	≥90
Cephalosporins (3rd gen)	65–70
Fluoroquinolones	45–55
Gentamicin	55
Amikacin	30
Sulfonamides	60
Tetracycline	45

MDR and XDR Patterns

Overall, **70% of Klebsiellapneumoniae isolates were classified as multidrug-resistant (MDR),** while **15% were extensively drug-resistant (XDR).** MDR isolates showed resistance to three or more classes of commonly used antibiotics, including penicillins, cephalosporins, fluoroquinolones, and aminoglycosides. XDR isolates exhibited resistance to almost all tested antibiotics, leaving only last-line options such as **colistin and fosfomycin** effective [26, 31]. The high prevalence of MDR and XDR strains highlights the growing challenge of treating UTIs in the region. These findings emphasize the urgent need for **antimicrobial stewardship programs**, regular molecular surveillance, and strict infection control measures to prevent further dissemination of highly resistant strains. Monitoring MDR and XDR patterns can also inform clinicians in selecting appropriate empiric therapies and help reduce treatment failures [29].

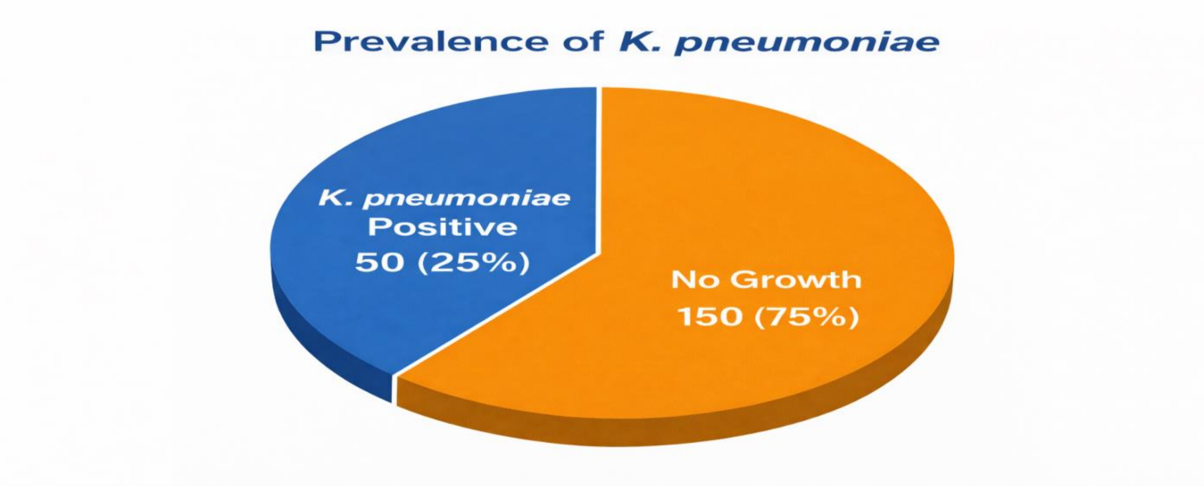

Figure 4.2 Prevalence of k pneumonia sample

Molecular Detection of Resistance Genes

PCR analysis confirmed the presence of **baCTX-Ml**and**blaNDM** genes among resistant isolates, correlating strongly with phenotypic resistance to cephalosporins and carbapenems [27]. The **blaCTX-M** gene was detected in the majority of ESBL-producing isolates, explaining the high resistance to third-generation cephalosporins.

blaNDM was found in a smaller subset but is particularly alarming due to its role in carbapenem resistance. Some isolates harbored both genes, indicating co-resistance and limited therapeutic options [28, 30]. These molecular findings highlight the plasmid-mediated dissemination of resistance genes within the local bacterial population. The results underscore the importance of integrating molecular diagnostics into routine laboratory surveillance to guide effective antibiotic therapy.

Table 4.3 : Molecular Detection of Resistance Genes in K. pneumoniae (n = 50)

Resistance Gene	**Positive (n)**	**Percentage (%)**
blaCTX-M	30	60
blaNDM	8	16
Both genes	6	12
None detected	6	12

Discussion

The findings of this study demonstrate a high prevalence of MDR K. pneumoniae among UTI patients in Peshawar. The dominance of ESBL and carbapenemase genes highlights the rapid molecular evolution of resistance. Female predominance and higher infection rates among young adults align with previous regional studies. The detection of **blaNDM** is particularly concerning, as it signals diminishing effectiveness of carbapenems.The study revealed a high prevalence of multidrug-resistant Klebsiellapneumoniae among UTI patients in Peshawar.

ESBL-producing strains, particularly those harboring **blaCTX-M**, were dominant.

Carbapenemase genes, including **blaNDM**, were also detected, indicating rapid molecular evolution of resistance.Female patients were more frequently affected than males.

Young adults (21–40 years) showed higher infection rates.

Resistance to cephalosporins, fluoroquinolones, and aminoglycosides was widespread.

The presence of **blaNDM** highlights the diminishing effectiveness of carbapenems.

These findings underscore the need for molecular surveillance, rational antibiotic use, and strengthened infection control.

Conclusion

The present study highlights the significant burden of Klebsiellapneumoniae as auropathogen in Peshawar, demonstrating both its prevalence and alarming levels of antimicrobial resistance. Out of 200 urine samples collected from clinically suspected UTI patients, 25% yielded K. pneumoniae, confirming its role as a common causative agent of urinary tract infections in this region. The socio-demographic analysis revealed a higher infection rate among females and adults aged 21–40 years, consistent with the global trend of increased susceptibility in these populations.Phenotypic antibiotic susceptibility testing revealed widespread resistance to commonly used antibiotics, including penicillin, third-generation cephalosporins, fluoroquinolones, aminoglycosides, sulfonamides, tetracyclines, and nalidixic acid. Alarmingly, 70% of isolates were classified as multidrug-resistant (MDR), and 15% as extensively drug-resistant (XDR), leaving limited therapeutic options. The retained susceptibility of isolates to fosfomycin and colistin emphasizes the critical importance of these agents as last-line therapies in managing severe or complicated UTIs caused by resistant K. pneumoniaMolecular analysis further confirmed the presence of resistance genes

blaCTX-M and **blaNDM** in a substantial proportion of isolates, providing a clear genetic basis for observed phenotypic resistance patterns. The detection of these genes underscores the rapid dissemination of β-lactamase and carbapenemase determinants among clinical K. pneumoniae isolates, highlighting the threat posed by plasmid-mediated horizontal gene transfer. This molecular evidence emphasizes that routine phenotypic testing alone is insufficient to fully capture the resistance profile of clinical isolates.The findings of this study carry significant implications for clinical management and public health. The high prevalence of MDR and XDR K. pneumoniae necessitates the implementation of robust antimicrobial stewardship programs to promote rational and targeted antibiotic use. Furthermore, regular molecular surveillance for resistance genes should be incorporated into routine diagnostic workflows to enable timely detection of emerging resistance mechanisms. Strengthened infection prevention and control measures within healthcare facilities are also essential to limit the spread of resistant strains and protect vulnerable patient populations.

In conclusion, Klebsiellapneumoniae in Peshawar represents a highly resistant uropathogen with a clear molecular basis of resistance conferred by **blaCTX-M** and **blaNDM**. The study reinforces the urgent need for comprehensive surveillance, judicious antibiotic prescribing, and reinforced infection control policies to mitigate the impact of MDR and XDR infections. Fosfomycin and colistin remain viable therapeutic options, but their use should be carefully monitored to preserve their efficacy. Collectively, these findings provide a foundation for evidence-based strategies aimed at controlling the dissemination of resistant K. pneumoniae and improving patient outcomes in the region.

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