Original Research

Antimicrobial Susceptibility Pattern of *Klebsiella pneumoniae* Isolated from Various Clinical Specimens in Ujjain City, Madhya Pradesh, India

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Klebsiella pneumoniae is an important opportunistic pathogen that commonly causes nosocomial infections and contributes to substantial morbidity and mortality. This study aimed to look at the sensitivity pattern of *K. pneumoniae* isolated from a variety of clinical samples.

Methods: This cross-sectional study was conducted at Ruxmaniben Deepchand Gardi Medical College and Ujjain Charitable Trust Hospital in Ujjain City from March 2021 to September 2021 on total 463 culture-positive isolates from various clinical specimens. The VITEK-2 compact bacterial identification and monitoring system was used to identify *K. pneumoniae* and perform antibiogram testing (bioMerieux, US). NCSS statistical software 2021 was used to evaluate the data.

Results: A total of 83 positive *K. pneumoniae* cultures were investigated from diverse clinical samples. The isolates were more prevalent in females (n = 45; 54.2%) than in men (n = 38; 45.8%). The rate of antibiotic resistance in *K. pneumoniae* differed amongst distinct clinical sample sources. Ampicillin (100%), amoxyclav (81.48%), piperacillin/tazobactam (73.68%), cefuroxime (94.74%), ceftriaxone (91.2%), cefotaxime (91.2%), and cefepime (91.2%) all had substantial resistance rates (73.68%). 75 of the 83 *K. pneumoniae* isolates produced ESBL (90.36%). However, colistin (100%) showed the highest susceptibility rate against the isolates.

Conclusion: The wide variety of MDR *K. pneumoniae* harboring β-lactams and virulence genes strongly suggests a necessity for implementing effective strategies to prevent and control the spread of antibiotic-resistant infections.

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Introduction

Klebsiella pneumoniae is a Gram-negative bacillus that is non-motile, capsulated, aerobic, and non-sporing. It is a significant pathogen that can cause hospital-acquired pneumonia, urinary tract infections, digestive tract infections, bacteremia, skin and soft tissue infections, bacteremia, and septicaemia.[1-3] *K. pneumoniae* is one of the most common enteric bacteria, accounting for up to 10% of nosocomial infections and causing significant morbidity and mortality.[4] Antibiotic resistance is a serious public health concern worldwide and a major cause of infectious disease treatment failure.[5-7] Infections induced by this organism are frequently associated with significant morbidity and fatality rates, prolonged hospitalization, and expensive costs.[8] Multidrug resistance (MDR) and drug-resistant infections have become much more common in recent years.[10]

MDR *K. pneumoniae* development is considered a global public health issue.[11] It could be because hospitalized patients are frequently given broad-spectrum antibiotics.[12] Due to extended-spectrum beta-lactamase (ESBL), it is the most common pathogenic bacteria to develop resistance to broad-spectrum beta-lactam antibiotics.[5] *K. pneumoniae* is currently resistant to a wide range of antibiotics, including beta-lactams, aminoglycosides, and fluoroquinolones.[13] Due to this resistance pattern, treatment failure for hospital-acquired illnesses occurs. Carbapenems are the medicine of choice for treating infections caused by bacteria that produce extended-spectrum beta-lactamase, such as *K. pneumoniae*. These antibiotic classes are also the last option for treating life-threatening healthcare-associated illnesses. Unfortunately, bacterial resistance to carbapenems has developed worldwide, and this, combined with beta-lactamase production and efflux pump mutations, makes managing drug-resistant infectious illnesses more difficult. Antibiotic resistance is on the rise in various microorganisms, according to several studies.[14-17]

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As a result, in Ujjain City, Madhya Pradesh, India, regular monitoring of antibiotic sensitivity patterns is critical for controlling and preventing many infectious diseases. As a result, the current research sought to examine the antibiotic susceptibility pattern of *K. pneumoniae* isolated from various clinical specimens in Ujjain, India.

Materials and Methods

This cross-sectional study was conducted at Ruxmaniben Deepchand Gardi Medical College and Ujjain Charitable Trust Hospital in Ujjain City from March 2021 to September 2021 on 463 culture positive isolates from various clinical specimens. Clean-catch midstream urine samples were collected and used in sterile disposable plastic containers. Patients' blood samples were taken aseptically in blood culture bottles, and their sputum was collected in sterile plastic containers. In a sterile screw cap tube, other bodily fluids were gathered. Pus and clinical wound specimens were taken by using sterile cotton swabs. This study included male and female patients of all ages and patients with positive microbiological evidence of *K. pneumoniae*. This study did not include any infectious diseases that were not linked to *K. pneumoniae*. Patient permission was not necessary for this study because the data presented was not personal to any one person.

The clinical isolates of *K. pneumoniae* were identified using the MacConkey agar plate's cultural features. The gramme stain confirmed that the massive mucoid lactose fermenting colonies recovered from MacConkey agar plate were gram-negative and rod-shaped. The VITEK-2 compact bacterial identification and monitoring system (bioMerieux, US) was used to identify *K. pneumoniae* and perform antibiogram testing, as directed by the manufacturer (Identification and antimicrobial sensitivity testing Vitek GNID cards and 280 cards were used, respectively). The data were analyzed using NCSS statistical software 2021, with a Chi-square test and a p-value of 0.05 with a 95% confidence interval.

Results

Of 463 culture positive samples, 83 were confirmed as *K. pneumoniae* (18%) from various clinical specimens. The distribution of *K. pneumoniae* was higher in females (54.2%) compared to male patients (45.8%). The p-value of 0.025 indicates strong evidence against the null hypothesis and is statistically significant. Mostly affected age group was below 18 years (36.1%), followed by above 60 years (24%). The chi-square analysis showed 19.10 degrees of freedom 4 and a p-value calculated 0.0007, so differences were statistically significant (Table 1). The highest number of *K. pneumoniae* isolates were obtained from blood specimens (38.5%), followed by urine (22.9%), pus (21.7) and sputum (13.25%) samples. The chi-square test result showed 27.7831, degrees of freedom of 4 and a p-value of 0.0000, which means there was a significant difference between the data (Table 2). The overall susceptibility profile of *K. pneumoniae* from

Table 1: Distribution of *K. pneumoniae* isolated from various clinical specimens in terms of gender and age group (n= 83).

Characteristics	*Total no. of cases*	*P value*
Male	38 (45.8%)	0.025
Female	45 (54.2%)	
Age groups		
<18	30 (36.1%)	
18- 29	7 (8.4%)	
30- 49	11 (13.25%)	0.0007
50- 60	15 (18%)	
>60	20 (24%)	

Table 2: Distribution of *K. pneumoniae* isolated from various clinical samples (n= 83).

Source of isolation	*Total (%)*	*P value*
Urine	19 (22.9%)	
Pus	18 (21.7%)	
Blood	32 (38.5%)	0.0000
Sputum	11 (13.25%)	
Other	03 (3.6%)	

*Chi-square= 27.7831, degrees of freedom= 4, and p value = 0.0000

Table 3: Overall antibiotic sensitivity pattern of *K. pneumoniae* isolated from various clinical samples.

Antimicrobials	*Resistant (%)*	*Sensitive (%)*
Ampicillin	100	0
Amoxyclav	81.48	18.5
Piperacillin/tazobactam	73.68	26.31
Cefuroxime	94.74	5.26
Ceftriaxone	91.2	8.8
Cefotaxime	91.2	8.8
Cefepime	73.68	26.31
Cefoperazone/sulbactam	68.42	31.57
Imipenem	66.66	33.3
Meropenem	66.66	33.3
Ertapenem	66.66	33.3
Amikacin	52.63	47.37
Gentamicin	54.4	45.6
Ciprofloxacin	78.94	21
Cotrimoxazole	56.14	43.8
Colistin	0	100

various clinical specimens is shown in Table 3. Of 83 *K. pneumoniae* isolates, 75 were ESBL (90.36%) producers. According to the sensitivity pattern, 100% *K. pneumoniae* strains were resistant to ampicillin drug, followed by 94.74% resistant to cefuroxime and 91.2% resistant to ceftriaxone. Other drugs like amoxyclav showed 81.48%, piperacillin tazobactum and cefepime reported 73.68% were resistant to strains of *K. pneumoniae*. Carbapenem group of drugs showed 66.7% were resistant to *K. pneumoniae* clinical isolates. Ciprofloxacin, amikacin, gentamicin, and cotrimoxazole had resistance patterns of 78.94%, 52.63%, 54.4%, and 56.14%, respectively. However, only colistin was found to have the highest percentage of sensitivity (100%).

Discussion

K. pneumoniae is rapidly gaining notoriety for its resistance to most commonly used last-line antibiotics. It is particularly problematic in the health-care system, which has been linked to several serious diseases.[2,3,,19] The rise of antibiotic resistance genes in *K. pneumoniae* isolates, such as ESBL and carbapenemase genes, raises the risk to public health worldwide. This is because carbapenems have long been employed as a last-resort treatment for multidrug-resistant gram-negative bacterial infections. The fast global rise of *K. pneumoniae* strains resistant to beta-lactams, particularly carbapenems, puts public health at risk. One of the main reasons for the rise of plasmid-mediated carbapenemase, which can hydrolyze all beta-lactams, including the last line carbapenems,[20,21] is the widespread use and misuse of carbapenems.

Due to widespread use and misuse of antibiotics, this is also a serious problem in poor and wealthy countries. In this investigation, 83 isolates of *K. pneumoniae* were obtained from diverse clinical specimens. *K. pneumoniae* was the most commonly isolated pathogen from all clinical samples (38.55%), followed by urine samples (22.9%) and Pus (21.7%). The chi-square analysis data revealed a p-value less than 0.05, indicating a significant difference in *K. pneumoniae* isolation between clinical specimens. However, multiple additional research[3,6,14,16,17] found that urine is the most common source of *K. pneumoniae* infections. In terms of gender, female patients had a greater overall frequency of *K. pneumoniae*-associated infections than male patients. The t-test revealed a significant difference, with a p value less than 0.05 and a 95% confidence interval. These findings were in line with those of Shilpa K *et al.* that *K. pneumoniae* was the most common bacterium detected in female patients.[9] Male patients were more susceptible to *K. pneumoniae* infections, according to Akter J *et al*.[7] This variance could be caused by differences in the sample population, geographical dispersion, personal hygiene, and environmental factors.

The efficiency of currently available antibiotics is decreasing due to the advent of resistance bacteria.[11,19,20] *K. pneumoniae* was shown to be highly resistant to routinely used antibiotics in this investigation. Furthermore, *K. pneumoniae* was found to be 66.6% resistant to the carbapenem category of antibiotics, a serious problem for the healthcare system. Other investigations[20,21] also found high resistance to beta-lactams, including carbapenems. However, in a study by Ibrahim A N. *et al*., *K. pneumoniae* isolates were found to be extremely effective against ertapenem (97.7%) and imipenem (96.5%), but 100% resistant to meropenem and amikacin.[22] These differences in sensitivity patterns can be attributed to environmental variables or to the widespread misuse of antibiotics to treat infectious infections. All of the *K. pneumoniae* isolates in this investigation were ampicillin-resistant, consistent with Chakraborty S. *et al.* and Ibrahim A.N. *et al*.[11,22] All isolates were ampicillin-resistant, which could be attributable to chromosomally encoded beta-lactamases that cause intrinsic resistance. Overall, *K. pneumoniae* strains were extremely resistant to cefuroxime (94.74%), cefotaxime (91.2%), ceftriaxone (91.2%), and cefepime (73.7%) in our analysis, while colistin sensitivity was the highest (100%).

Gentamicin demonstrated 45.6% sensitivity to multidrug-resistant *K. pneumoniae* bacteria, compared to 47.4% for amikacin. Another study found Amikacin, gentamicin, and ciprofloxacin to be the most effective antimicrobial drugs for treating *K. pneumoniae* infections.[23,24] The prevalence of ESBL *K. pneumoniae* was reported to be 90.36% in this investigation. Another study found 31.8% of ESBL-producing *K. pneumoniae* in clinical samples.[25] The high frequency of ESBL isolates in our investigation could be due to the small sample size used; therefore, larger sample size is needed to obtain more precise data on the prevalence of ESBL *K. pneumoniae* in this region.

As a result, it is possible to conclude from this study that there are some variances in antibiotic sensitivity patterns compared to prior studies, which could be related to differences in sample size, geographical distributions, environmental factors, personal hygiene, and antibiotic use. Furthermore, the high rate of

resistance to ceftriaxone, cefotaxime, and cefepime in the current study compared to other nations is a concerning issue in terms of antibiotic resistance spreading among clinical isolates in our region. This data indicates that the use of these antibiotics for empirical therapy of patients with *K. pneumoniae* infections is restricted. The study's main limitation was the limited sample size (n=83) and sample population. To overcome these limitations and offer more accurate results, more study is needed using new molecular approaches to identify and analyze the sensitivity pattern of K. pneumoniae.

In conclusion, *K. pneumoniae* infection was more common in female patients, and colistin, followed by ciprofloxacin and carbapenems, was the most effective antibiotic. However, ampicillin, amoxyclav, cefuroxime, ceftriaxone, cefotaxime, and cefepime were all extremely resistant to the isolates. The rise of antibiotic-resistant strains of *K. pneumoniae* has necessitated regular regional assessment of empirical, first-line antibiotic treatment.

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