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Original Article

Antimicrobial Susceptibility Patterns of Carbapenem-Resistant *Klebsiella pneumoniae* Causing Lower Respiratory Infections

Shaheen Akhter Chowdhury[1*], Swarna Paul[2], Fouzia Ahmed Chowdhury[3], Muhammad Moazzem Hossain[4], Afroza Sultana[5], Showmik Paul[6], Abdul Quddus[7], Saurav Das[8]

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*Corresponding author

ABSTRACT

Introduction: Lower respiratory tract infectiosn (LRTIs) continue to be a significant health burden, and the most common bacterial causes include multi-drug resistant (MDR) bacteria like Klebsiella pneumoniae (K. pneumoniae) infections. The emergence of carbapenem-resistant K. pneumoniae (CRKP) has added to these concerns due to limited treatment options and poorer clinical outcomes. This study was aimed to find out antimicrobial susceptibility pattern and to detect mechanism of carbapenem resistance among K. pneumoniae isolates from LRTI patients. **Methods & Materials:** This cross-sectional study was performed to find out the antimicrobial susceptibility pattern of carbapenem resistant Klebsiella pneumoniae (CRKP) causing lower respiratory tract infection (LRTIs). This study was performed in the Department of Microbiology of Sylhet MAG Osmani Medical College, Sylhet, Bangladesh from July,2021 to June,2022. A total of 153 sputum samples were received from the diagnosed cases of LRTIs from adult patients (aged ≥18years). Data analysis performed by Statistical Package for Social Sciences (SPSS) version 26. **Result:** A total of 153 sputum samples were analyzed, with bacterial growth detected in 66.0% of cases. Klebsiella pneumoniae was isolated in 20.9% of samples, of which 25.0% were carbapenem-resistant. CRKP isolates showed high rates of multi-drug resistance, particularly against amoxicillin-clavulanic acid, ciprofloxacin, cefoxitin, azithromycin, meropenem, imipenem, and cefepime. Carbapenemase production was detected in 75.0% of CRKP isolates by Modified Hodge Test. **Conclusion:** This research revealed the extent of the problem of carbapenem-resistant Klebsiella pneumoniae among LRTI cases and a substantial number of isolates found to be carbapenemase producers. The isolates were multi-drug resistant to commonly used antibiotics like β-lactams, fluoroquinolones, and most of the other routinely administered drugs, and therapeutic options were almost nil.

Keywords: *Antimicrobial Susceptibility, Carbapenem Resistant, Klebsiella Pneumoniae, LRTI*

1. *Senior Clinical Pathologist, Department of Laboratory Medicine, Chittagong Medical College Hospital, Chattogram, Bangladesh (ORCID: 0009-0009-1500-7321)*
2. *Medical Officer, Department of Microbiology, Chittagong Medical College, Chattogram, Bangladesh*
3. *Assistant Professor, Department of Microbiology, Chattogram International Dental College, Chattogram, Bangladesh*
4. *Lecturer, Department of Virology, Chittagong Medical College, Chattogram, Bangladesh*
5. *Senior Medical Officer, Alif Hospital and Diagnostic Center, Chattogram, Bangladesh*
6. *Lecturer, Biochemistry, Chandpur Medical College, Chandpur, Bangladesh*
7. *Junior Consultant, Department of ENT & Head- Neck Surgery, Parshuram Upazila Health Complex, Feni, Bangladesh*
8. *Junior Consultant, Cardiology, Kutubdia Health Complex, Cox's Bazar, Bangladesh*

INTRODUCTION

Lower respiratory tract infections (LRTIs) are a common and significant cause of morbidity and mortality worldwide. They are also responsible for lots of hospital admissions, mainly amongst critically ill and immunocompromised patients. Bacterial causes of LRTI are common, and Klebsiella pneumoniae has become an increasingly significant opportunistic pathogen in the community, in hospitals, causing pneumonia, ventilator-associated pneumonia, and fulminant respiratory infections [1,2]. Klebsiella pneumoniae is a Gram-negative bacillus of the Enterobacteriaceae family. Its virulence lies in its polysaccharide capsule that helps in evading the host immune system [3]. Over the past decade, the appearance of an antimicrobial resistance pattern among the etiological agent *Klebsiella pneumoniae* has become one of the most challenging issues for global health community. Of the multiple forms of resistance developed by the organism, the production of carbapenemase enzymes and the resultant resistance to carbapenems have been raised to a much higher level than other mechanisms of antibiotic inactivation because of carbapenems are considered as drugs of choice for treatment of severe infections caused by multidrug resistant (MDR) gram-negative bacteria [4]. During this period the emergence of carbapenem-resistant *K.* pneumoniae (CRKP) has led to a dramatic decline in therapeutic options and high rates of clinical failures, prolonged hospital stays, increased healthcare costs, and high mortality [5]. The mortality rate in patients infected with CRKP has been reported to be greater than 40% which is much higher than with infections due to carbapenem sensitive strains [6]. CRKP infections have been related to high morbidity and mortality in groups of patients in the intensive care unit as well as those admitted in hospitals with APACHE II scores and having invasive procedures and prior use of antibiotics [7]. Resistance conferred by CRKP can be achieved by a number of methods including on production of a range of carbapenemase enzymes like Klebsiella pneumoniae carbapenemase (KPC), new Delhi B-lactamase (NDM), VIM (Verona integron-encoded Metallo--lactamase), OXA-48 and also by loss of porins and increased efflux [8]. These resistance determinants are frequently plasmid-mediated, facilitating rapid dissemination among bacterial populations and contributing to hospital outbreaks [9]. Global surveillance studies have demonstrated an increasing prevalence of CRKP in both developed and developing countries, emphasizing the urgent need for continuous monitoring and antimicrobial stewardship interventions [10]. Recent meta-analytic evidence estimated that approximately 28.7% of hospital-acquired *K. pneumoniae* infections globally are carbapenem-resistant. Antimicrobial susceptibility profiles may vary based on geographic location, healthcare setting and resistant genes being circulated. As a result, institution specific surveillance studies are really important in clinical management and infection control policies. Assessment of susceptibility pattern of carbapenem resistant *Klebsiella pneumoniae* from LRTIs shall give an idea about prevailing resistance trends and help to conserve antimicrobial resources. To that extent, present study was undertaken to report antimicrobial susceptibility pattern of carbapenem resistant *Klebsiella pneumoniae* from LRTIs.

METHODS & MATERIALS

This is a cross-sectional study, which was carried out in the Department of Microbiology, Sylhet MAG Osmani Medical College Sylhet Bangladesh, during the period of July, 2021 to June, 202 to determine the pattern of antimicrobial susceptibility in carbapenem resistant *Klebsiella pneumoniae*, isolated from LRTIs. One hundred and fifty-three sputum samples were collected from adult patients (≥18 years of age), with LRTIs attending the Medicine outpatient department (OPD) and the clinical wards of Sylhet MAG Osmani Medical College Hospital, Sylhet. Immunosuppressive therapy users and cases of tuberculosis were excluded. Sputum specimens were collected in sterile, clean, leak-proof, wide-necked containers and transported promptly to the microbiology laboratory for immediate processing. Macroscopic and microscopic examinations of the specimens were performed before culture on Blood agar and MacConkey agar media, followed by incubation at 37°C for 24 hours. Suspected *Klebsiella pneumoniae* isolates were identified through gram staining technique and standard biochemical tests, including indole, catalase, urease, citrate, oxidase, and triple sugar iron (TSI) tests. Antimicrobial susceptibility testing (AST) of the isolates was carried out by the Kirby Bauer Disc Diffusion method on Mueller Hinton agar media, following the Clinical and Laboratory Standards Institute (CLSI) guideline, 2021. Phenotypic detection of carbapenemase production was carried out by the Modified Hodge Test (MHT). A 0.5 McFarland suspension of *E. coli* ATCC 25922 was prepared and swarm inoculum was evenly spread using a sterile swab on the surface of Muller Hinton agar media and a disk of meropenem (10 g) was placed in the center of the plate and the test isolate streaked radially from the disk border to the edge of the plate. Plates were incubated at 37°C for 24 hours and interpreted as per CLSI 2021 guidelines. Prior Ethical approval was obtained from Ethical Review Committee Sylhet MAG Osmani Medical College for this study. All data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 26. Only descriptive statistical analyses were performed.

RESULTS

Among the 153 sputum samples collected in this study, the participants had a mean age of 52.43 ± 17.12 years, ranging from 18 to 87 years. Male participants constituted the majority (69.3%), with a male-to-female ratio of 2.3:1. (*Table I*).

Table I

Demographic Characteristics and Microbiological Findings of Study Participants (*n*=153).

Variables	Frequency (n)	Percentage (%)
Age (years)		
Mean ± SD	52.43 ± 17.12	—
Range	18–87	—
Gender		
Male	106	69.3
Female	47	30.7
Male: Female ratio	2.3: 1	—

A total of 153 sputum samples were collected from the study participants. Among them, 101 (66.0%) samples showed positive bacterial growth on culture, while 52 (34.0%) samples demonstrated no microbial growth. Of the total samples, single bacterial growth was identified in 87 (56.8%) cases, whereas mixed bacterial growth was observed in 14 (9.2%) cases (*Table II*).

Table II

Sputum Culture Findings Among the Study Participants (*n* = 153).

Sputum Culture Findings	Frequency (n)	Percentage (%)
Total sputum samples collected	153	100.0
Growth positive	101	66.0
No growth	52	34.0
Single bacterial growth	87	56.8
Mixed bacterial growth	14	9.2

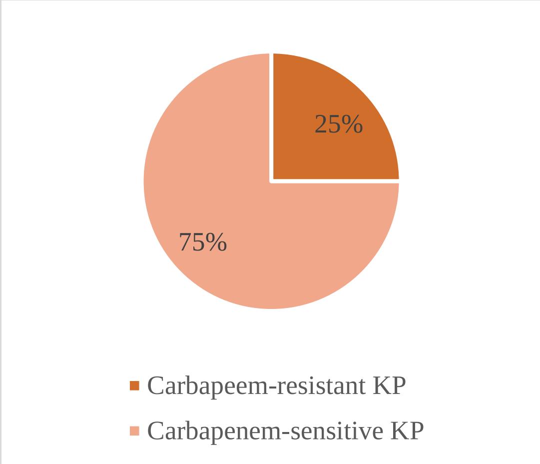

Figure 1 Pie chart showing positive Klebsiella pneumoniae (KP) isolates (*n*=32).

Among the isolated organisms, *Klebsiella pneumoniae* was detected in 32 (20.9%) cases. Of these isolates, 8 (25.0%) were identified as carbapenem-resistant *Klebsiella pneumoniae* (CRKP), whereas 24 (75.0%) were carbapenem-sensitive strains (*Figure 1*).

The highest sensitivity was observed for piperacillin–tazobactam, ceftazidime, cefotaxime, and amikacin, each showing sensitivity in 4 (50.0%) isolates. Moderate sensitivity was found for cefoxitin, meropenem, imipenem, azithromycin, and cefepime, while the lowest sensitivity was observed for amoxicillin–clavulanic acid and ciprofloxacin, with only 1 (12.5%) sensitive isolate each. High resistance rates were noted against amoxicillin–clavulanic acid and ciprofloxacin (87.5% each), followed by cefoxitin, meropenem, imipenem, and azithromycin (75.0% each). Intermediate susceptibility was identified only for piperacillin–tazobactam and amikacin in 1 (12.5%) isolate each, and for cefepime in 2 (25.0%) isolates (*Table III*).

Table III
Antimicrobial Susceptibility Patterns of Carbapenem-Resistant *Klebsiella pneumoniae* in LRTI (*n*=8).

Antimicrobials	Sensitive n (%)	Intermediate n (%)	Resistant n (%)
Piperacillin–tazobactam	4 (50.0)	1 (12.5)	3 (37.5)
Ceftazidime	4 (50.0)	0 (0.0)	4 (50.0)
Cefotaxime	4 (50.0)	0 (0.0)	4 (50.0)
Cefoxitin	2 (25.0)	0 (0.0)	6 (75.0)
Amoxicillin–clavulanic acid	1 (12.5)	0 (0.0)	7 (87.5)
Meropenem	2 (25.0)	0 (0.0)	6 (75.0)
Imipenem	2 (25.0)	0 (0.0)	6 (75.0)
Amikacin	4 (50.0)	1 (12.5)	3 (37.5)
Azithromycin	2 (25.0)	0 (0.0)	6 (75.0)
Cefepime	2 (25.0)	2 (25.0)	4 (50.0)
Ciprofloxacin	1 (12.5)	0 (0.0)	7 (87.5)

DISCUSSION

In this study, among the 32 isolated *Klebsiella pneumoniae* strains, 8 (25.0%) were identified as carbapenem-resistant *Klebsiella pneumoniae* (CRKP), which was comparable to findings reported by Shanmugam et al, Bina et al, and Aminul et al [11,12]. Among the 8 CRKP isolates, carbapenemase production detected by the Modified Hodge Test (MHT) was observed in 75.0% of cases, which was consistent with the findings of Shanmugam et al, where MHT positivity was reported in 86.6% of CRKP isolates [11]. Similar high positivity rates ranging from 71% to 84% have also been reported in other studies [13-15]. The increasing emergence of carbapenemase-producing *K. pneumoniae* in hospital settings may be attributed to several factors, including irrational and excessive antibiotic use, inappropriate dosing practices, circulation of counterfeit or substandard antibiotics, and inadequate infection control measures related to the isolation and management of multidrug-resistant pathogens. Additionally, these organisms may also be acquired from community sources, as they have been isolated from common water reservoirs [16]. Regarding antimicrobial susceptibility patterns, CRKP isolates in the present study demonstrated high resistance rates to amoxicillin-clavulanic acid (87.5%), ciprofloxacin (87.5%), cefoxitin (75.0%), azithromycin (75.0%), meropenem (75.0%), imipenem (75.0%), and cefepime (50.0%). Similar multidrug resistance patterns were reported by Bahrami et al, where CRKP isolates exhibited resistance to ciprofloxacin (96.7%), cefepime (100.0%), piperacillin–tazobactam (98.4%), ceftazidime (98.8%), and amikacin (87.0%) [17-18]. Furthermore, carbapenemase-producing *K. pneumoniae* detected by conventional PCR in the present study exhibited extensive resistance to multiple antimicrobial agents, including colistin (100.0%), amoxicillin-clavulanic acid (100.0%), cefoxitin (100.0%), ciprofloxacin (100.0%), cefotaxime (75.0%), ceftazidime (75.0%), cefepime (75.0%), azithromycin (75.0%), meropenem (75.0%), and imipenem (75.0%). Resistance among carbapenemase-producing *K. pneumoniae* frequently extends beyond β-lactams to include fluoroquinolones, aminoglycosides, and tetracyclines, creating substantial therapeutic challenges. Although optimal treatment strategies remain uncertain, some evidence suggests that appropriately administered carbapenem-based regimens may still retain clinical value in selected cases [19]. Therefore, routine implementation of the Modified Hodge Test in microbiology laboratories is important, as positive findings can provide clinicians with critical information regarding carbapenemase production. This approach offers a rapid and cost-effective method for detecting carbapenemase production in *K. pneumoniae*.

LIMITATIONS

- The study was conducted at a single tertiary care centre with a relatively small sample size, limiting the generalizability of the findings.
- Only descriptive statistical analysis was performed, which restricted the assessment of associations between variables.
- Molecular analysis should be done to detect carbapenem resistance genes among the isolates.

CONCLUSION

This study demonstrated a considerable burden of carbapenem-resistant *Klebsiella pneumoniae* among lower respiratory tract infection cases, with a notable proportion of isolates producing carbapenemase enzymes. The isolates showed high levels of multidrug resistance, particularly against commonly used antibiotics such as β-lactams, fluoroquinolones, and other routinely prescribed agents, leaving very limited therapeutic options.

RECOMMENDATION

All clinically significant isolates of *K. pneumoniae* should be subjected to routine antimicrobial susceptibility testing before administering antibiotics. Rapid identification of carbapenemase producing organisms using phenotypic and molecular methods should be strengthened in diagnostic laboratories. Strict compliance to measures for infection prevention and control and implementation of good antimicrobial stewardship programs are the necessary steps to prevent dissemination of multidrug resistant organisms.

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CONFLICT OF INTEREST

None declared.

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