Original Article

Analysis of Three-Year Temporal Trends in Antibiotic Sensitivity Patterns of Klebsiella Pneumoniae Causing Sepsis

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ABSTRACT

Klebsiella species have become increasingly prevalent in nosocomial infections, posing a significant challenge for developing and developed countries due to their resistance to commonly used antibiotics. This study assessed the changing antibiotic sensitivity patterns of Klebsiella pneumoniae isolates obtained from blood cultures in sepsis patients. This retrospective cross-sectional study was conducted at the Department of Microbiology & Immunology, Ibn Sina Medical Centers in Dhaka, Bangladesh, from January 2021 to Dece mber 2023. One hundred and nineteen Klebsiella pneumonia samples were included in the study. All the Klebsiella pneumoniae were detected by the Automated Blood Culture System. Isolate identification and antibiotic susceptibility were performed using the Vitek 2 automated system. A few conventional biochemical tests were also performed for isolate identification. Our data revealed a consistently high sensitivity (100%) of Klebsiella pneumoniae isolates to Amikacin and Tigecycline, with Colistin demonstrating a sensitivity of 75%. In contrast, cefepime and amoxicillin showed 100% resistance, and resistance to azithromycin was 94%. A detailed yearly analysis highlighted increasing resistance trends, particularly notable in azithromycin, which went from 38% resistance in 2021 to 100% in 2023. Resistance of Klebsiella pneumoniae to commonly used antibiotics is a rising trend, which demands continuous surveillance strategies to address the emerging threat.

Keywords: *Antibiotic sensitivity, antimicrobial resistance, sepsis, Klebsiella pneumoniae*

Mugda Med Coll J. 2025; 8(1): 55-59
DOI: https://doi.org/10.3329/mumcj.v8i1.82884

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INTRODUCTION

Klebsiella pneumoniae, a Gram-negative, non-motile, encapsulated bacterium within the family Enterobacteriaceae, poses a significant health threat due to its involvement in various infections, including pneumonia, urinary tract infections, bloodstream infections, wound infections, and infections in different organs and tissues[1]. Over the years, Klebsiella species have become prominent in nosocomial infections, presenting a challenge in both developing and developed countries with their resistance to commonly used antibiotics. The emergence of multidrug resistance in Klebsiella spp. is a growing global health crisis, rendering many healthcare-associated infections untreatable with the existing antibiotics[2-4]. Since the early 21st century, the rise of fluoroquinolone-resistant and extended-spectrum beta- lactamase (ESBL)-producing Klebsiella pneumoniae has become a worldwide concern, attributed to the widespread use of broad-spectrum cephalosporin and fluoroquinolone antibiotics[5,6].

Clinicians' increasing turn to carbapenems for challenging nosocomial infections is leading to the emergence of carbapenem-resistant Enterobacteriaceae (CRE)[7,8]. Specifically, Klebsiella pneumoniae carbapenemases (KPCs), a class of â-lactamases, exhibit a remarkable ability to hydrolyze various antibiotics, including penicillins, cephalosporins, monobactams, carbapenems, and â-lactamase inhibitors[9]. These enzymes have become endemic in hospitals and long-term care facilities in several regions, including southern Europe, China, South America, and specific areas of North America[10,11]. Through beta-lactamase production, Klebsiella demonstrates a high potential to develop resistance to broad-spectrum antibiotics, extending to ampicillin. Many strains acquire extended-spectrum beta-lactamases, conferring additional resistance to carbenicillin, amoxicillin, and ceftazidime. Although aminoglycosides and colistin remain effective against *K. pneumoniae*, reports of colistin-resistant strains in intensive care units (ICUs) have surfaced.

Some *Klebsiella* species produce extended-spectrum beta-lactamases (ESBL), rendering them resistant to virtually all beta-lactam antibiotics except carbapenems. Moreover, these bacteria often resist aminoglycosides, fluoroquinolones, tetracyclines, chloramphenicol, and trimethoprim/sulfame thoxazole[12].

The rapid spread of antibiotic-resistant strains of *Klebsiella pneumoniae* presents a significant challenge to effective management. While numerous studies have investigated antibiotic resistance patterns in *Klebsiella pneumoniae*, comprehensive surveillance and research are needed to assess blood culture sensitivity in diverse clinical settings, particularly in regions with varying epidemiological factors. Understanding the sensitivity patterns of *Klebsiella pneumoniae* in blood cultures is essential for tailoring empirical treatment strategies and implementing effective infection control measures.

Knowledge of antibiotic sensitivity in *Klebsiella* isolates is crucial for optimal patient management. Studying their antibiotic sensitivity helps identify trends and patterns in resistance, guiding treatment decisions for clinicians. This information aids in promptly selecting the most appropriate antibiotics, resulting in improved treatment outcomes. In recent years, inappropriate antibiotic use has fueled drug resistance in *Klebsiella pneumoniae*, associated with higher mortality rates and increased therapeutic costs. Determining antibiotic resistance patterns is essential for selecting appropriate treatments, guiding initial antibiotic treatment decisions for patients with *Klebsiella* bloodstream infections, ultimately reducing the time required to select suitable antibiotics and enhancing patient outcomes.

METHODS

This cross-sectional study was conducted at the Department of Microbiology & Immunology, Ibn Sina Medical Center, Dhaka, Bangladesh, from January 2021 to December 2023. A total of one hundred and nineteen *Klebsiella pneumoniae* were isolated and tested for antibiotic susceptibility.

Blood samples were primarily incubated using the BACTEC FX Automated Blood Culture System. Secondary incubation was done in blood agar and MacConkey agar media for 24 hours. *Klebsiella pneumoniae* isolates were identified using colony morphology on MacConkey Agar and standard biochemical tests on motility indole urea agar, Kligler iron agar, Simmons citrate media, indole test, and string test. Further confirmation of isolate identity and antibiotic susceptibility were performed using the Vitek 2 automated system. The Clinical Laboratory Standards Institute (CLSI) document determined cut-off values. The European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines were followed when required. MDR *Klebsiella pneumoniae* is defined as one that acquired non-susceptibility to at least one agent in three or more antimicrobial groups (such as aminoglycosides, antipseudomonal penicillin, carbapenems, extended-spectrum cephalosporins; any drug among of the four generations cephalosporin, fluoroquinolones, penicillin, and â-lactamase inhibitors).

The study was approved by the Institutional Review Board of Ibn Sina Medical College, Dhaka, Bangladesh.

RESULTS

This retrospective study was done on one hundred nineteen *Klebsiella pneumoniae* isolates over three years to observe their antibiotic sensitivity pattern change. 100% of isolates were sensitive to amikacin and tigecycline, while 75% were sensitive to colistin and 62% to imipenem. Meropenem, ertapenem, netilmicin, gentamicin, and cefotaxime all were almost fifty per cent sensitive. On the other hand, cefepime amoxicillin was 100% resistant, and azithromycin showed 94% resistance (Table-I). Table-II shows the changing sensitivity to antibiotics over the last three years.

Table-I: *Antibiotic sensitivity patterns (n=119)*

Antibiotic disc	Sensitive	Resistance	Moderate
Amikacin	100%	0%	0%
Ampicillin	6%	94%	0%
Azithromycin	2%	94%	4%
Amoxiclav	31%	67%	2%
Ciprofloxacin	44%	48%	8%
Ceftazidime	30%	69%	1%
Cefixime	34%	66%	0%
Cefuroxime	28%	72%	0%
Ceftriaxone	33%	67%	0%
Cotrimoxazole	31%	69%	0%
Gentamicin 10µg	52%	46%	2%
Meropenem	50%	50%	0%
Imipenem	62%	36%	2%
Ertapenem	50%	48%	2%
Netilmicin	51%	49%	0%
Aztreonam	26%	74%	0%
Cefotaxime	52%	48%	0%
Colistin	75%	25%	0%
Tigecyclines	100%	0%	0%
Cefepime	0%	100%	0%
Amoxicillin	0%	100%	0%
Chloramphenicol	45%	55%	0%
Piperacillin	25%	75%	0%

Table-II: *Changing sensitivity to antibiotics over the last three years (n=119)*

Antibiotic disk	Year	Sensitive	Resistant	Moderate resistance	P value
Amikacin	2021	100%	0%	0%	
	2022	100%	0%	0%	-
	2023	100%	0%	0%	
Ampicillin	2021	8%	92%	0%	
	2022	4.5%	95.5%	0%	0.798
	2023	0%	0%	0%	
Azithromycin	2021	38%	53%	9%	
	2022	2%	98%	0%	0.025
	2023	0%	100%	0%	
Amoxyclav	2021	65%	30%	5%	
	2022	9%	91%	0%	0.001
	2023	7%	93%	0%	
Ciprofloxacin	2021	73%	20%	7%	
	2022	34%	62%	4%	0.004
	2023	37%	60%	3%	
Ceftazidime	2021	70%	30%	0%	
	2022	13%	84%	3%	0.001
	2023	15%	85%	0%	
Cefixime	2021	70%	30%	0%	
	2022	8%	92%	0%	0.001
	2023	9%	91%	0%	
Cefuroxime	2021	70%	30%	0%	
	2022	14%	86%	0%	0.001
	2023	0%	100%	0%	
Ceftriaxone	2021	70%	30%	0%	
	2022	17%	83%	0%	0.001
	2023	15%	85%	0%	
Cotrimoxazole	2021	46%	54%	0%	
	2022	17%	83%	0%	0.054
	2023	40%	60%	0%	
Gentamicin 10	2021	73%	27%	0%	
	2022	41%	56%	3%	0.089
	2023	36%	64%	0%	
Meropenem	2021	73%	27%	0%	
	2022	75%	25%	0%	0.018
	2023	70%	30%	0%	
Imipenem	2021	77%	23%	0%	
	2022	50%	47%	3%	0.301
	2023	50%	50%	0%	
Ertapenem	2021	73%	27%	0%	
	2022	29%	67%	4%	0.017
	2023	0%	100%	0%	
Netilmicin	2021	77%	23%	0%	
	2022	39%	61%	0%	0.006
	2023	39%	61%	0%	

Table-II (Cont'd)

Antibiotic disk	Year	Sensitive	Resistant	Moderate resistance	P value
Aztreonam	2021	0%	0%	0%	
	2022	38%	62%	0%	0.345
	2023	18%	82%	0%	
Cefotaxime	2021	0%	0%	0%	
	2022	32%	68%	0%	0.345
	2023	58%	42%	0%	
Colistin	2021	0%	0%	0%	
	2022	90%	10%	0%	0.208
	2023	70%	30%	0%	
Tigecycline	2021	0%	0%	0%	-
	2022	100%	0%	0%	
	2023	100%	0%	0%	
Cefepime	2021	0%	0%	0%	
	2022	0%	100%	0%	-
	2023	0%	100%	0%	
Amoxicillin	2021	0%	0%	0%	
	2022	0%	100%	0%	-
	2023	0%	100%	0%	
Chloramphenicol	2021	0%	0%	0%	
	2022	100%	0%	0%	0.236
	2023	38%	62%	0%	
Piperacillin	2021	0%	0%	0%	
	2022	0%	100%	0%	0.537
	2023	29%	71%	0%	

DISCUSSION

This comprehensive retrospective study was done in a specialized medical centre to observe the changes in the antibiotic sensitivity patterns of *Klebsiella pneumoniae* isolated from blood culture over three years. Nowadays, strains of *Klebsiella* that are resistant to multiple drugs are of significant public health importance due to their greater potential for major hospital outbreaks. In our study, a total of 119 *K. pneumoniae* were identified, of which all isolates were sensitive to amikacin and tigecycline. Furthermore, gentamicin and colistin demonstrated substantial percentages of sensitivity (52% and 75%, respectively), indicating their high efficacy against *Klebsiella* strains. Additionally, with a 50% sensitivity rate, meropenem and ertapenem displayed a balanced sensitivity profile. These results indicate that due to the lower resistance profile, amikacin, tigecycline, gentamicin, colistin, meropenem, and ertapenem may be better options for treating *Klebsiella pneumoniae* infections. Our results are highly comparable to previous research findings, where 72.0% of the isolates were resistant to ceftazidime, nearly 69% to cefotaxime, and 67.2% to amikacin[12].

Our observed sensitivity against amikacin was 100%. This parenteral antibiotic is used less frequently. Unavailability and frequent dosing have made them less preferred agents. Another investigation on *Klebsiella pneumoniae* isolates showed 100% resistance to cefotaxime and 100% resistance to ceftazidime. On the other hand, 63% of the samples showed the highest gentamycin susceptibility[13]. However, ceftazidime resistance was 69%, and cefotaxime resistance was 50% in our study.

Compared to previous research, the resistance rate in our study is higher; cefuroxime has over 75% resistance. Meanwhile, another investigation detected only 14.3% of cefuroxime[14]. Meropenem and imipenem exhibited over 50% resistance in the carbapenem group, which is comparable to an earlier study findings, as imipenem had a high sensitivity of 74.3%, while meropenem's sensitivity was only 34.3%[14].

According to our study, 48% of *Klebsiella* showed resistance to ciprofloxacin. Another study found it in only 23.6% cases[15]. This difference may be explained by the time gap between these two studies, which is around ten years. Fluoroquinolone resistance may be linked to its overuse due to wide accessibility, availability in oral form, and preference by physicians and patients due to its lower price and convenient dosing schedule.

Several notable resistance tendencies became apparent when examining how Klebsiella's antibiotic sensitivity has changed over the past three years. Azithromycin, among them, showed a notable rise in resistance, increasing from 38% in 2021 to 100% in 2023, indicating a notable decline in efficacy over time. This can be explained by the overuse of azithromycin for the COVID-19 pandemic throughout the world.

Furthermore, there was increasing resistance to Ciprofloxacin, Ceftazidime, Cefixime, Cefuroxime, Ceftriaxone, Cotrimoxazole, Ertapenem, and Netilmicin, with varying trends over time. This result is consistent with another study, which assessed the antibiotic susceptibility profile of 1805 *Klebsiella pneumoniae*[16]. An elevated level of resistance was observed to Colistin (239.3%), meropenem (74.2%), ciprofloxacin (68%), gentamicin (35.1%), Tigecycline

(33.9%), imipenem (29.7%), ertapenem (26.8%), and amikacin (21.4%). Ertapenem stood out with remarkable change, with resistance rising from 27% in 2021 to 100% in 2023. These evolving resistance patterns need further study to modify antibiotic regimens and guarantee efficacious treatment alternatives for *Klebsiella* infections.

CONCLUSION

Klebsiella pneumoniae has become resistant to most of the commonly used antibiotics. The antibiotic sensitivity pattern of the organism has deteriorated throughout the COVID-19 pandemic. However, in our study, data regarding all antibiotics were unavailable for the whole study period due to changes in guidelines that determine the antibiotics to be tested for each isolate.

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