Journal of Clinical Microbiology and Infectious Diseases (*JCMID*) 2025, Volume 5, Number 1: 12-16 E-ISSN: 2808-9405



Prevalence and antibiotic sensitivity patterns of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* in pneumonia patients at Ngoerah Hospital from 2020 to 2022



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ABSTRACT

Background: Pneumonia remains a major global cause of mortality, with Klebsiella pneumoniae recognized as a significant pathogen. The emergence of antibiotic resistance, particularly due to Extended-Spectrum Beta-Lactamase (ESBL) production by K. pneumoniae, complicates treatment efforts. This study aimed to determine the prevalence of ESBL-producing K. pneumoniae in pneumonia patients and assess its antibiotic sensitivity profile.

Methods: A descriptive cross-sectional study was conducted retrospectively using secondary data from VITEK 2 Compact (bioMérieux) laboratory results on sputum samples collected from pneumonia patients at Ngoerah Hospital from 2020 to 2022. A total of 515 samples met the inclusion criteria out of 1,350 tested.

Results: ESBL-producing K. pneumoniae was identified in 305 isolates (59.2%), with yearly prevalence rates of 63% in 2020, 52% in 2021, and 61% in 2022. Most patients were male (66.6%), aged 60 years or older (40%), and treated in non-ICU settings (69.2%), with expectorated sputum as the most common specimen type (63%). Antibiotic sensitivity testing revealed high susceptibility of ESBL-producing isolates to ertapenem (100%), meropenem (100%), amikacin (93%), and tigecycline (81%).

Conclusion: ESBL-producing K. pneumoniae accounted for over half of pneumonia cases, with fluctuating prevalence across the study period. The infection predominantly affected older male patients treated in non-ICU wards. Despite resistance to many beta-lactam antibiotics, high sensitivity to carbapenems and other specific agents highlights their continued relevance in treatment. Surveillance of antibiotic resistance patterns remains essential for effective clinical management.

Keywords: *Klebsiella pneumoniae*, Extended-Spectrum Beta-Lactamase, Antibiotic Sensitivity, Antibiotic Resistance, ESBL-producing *Klebsiella pneumoniae*.

Cite This Article: Arikandini, D.A.P.A.R., Budayanti, N.N.S., Fatmawati, N.N.D., Mayura, I.P.B. 2025. Prevalence and antibiotic sensitivity patterns of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* in pneumonia patients at Ngoerah Hospital from 2020 to 2022. *Journal of Clinical Microbiology and Infectious Diseases* 5(1): 12-16. DOI: 10.51559/jcmid. v5i1.86

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Received: 2024-12-29 Accepted: 2025-02-20 Published: 2025-03-18

INTRODUCTION

Pneumonia is a leading cause of death worldwide, particularly among vulnerable groups such as infants, the elderly, and individuals with weakened immune systems. It is characterized by an acute respiratory infection that causes the alveoli to fill with fluid, restricting oxygen intake. According to the 2019 Global Burden of Disease (GBD) study, lower respiratory tract infections, including pneumonia, affected approximately 489 million people worldwide. In intensive care units, pneumonia has been reported to cause mortality rates as high as 23%.

Klebsiella pneumoniae is a major

bacterial pathogen responsible for severe pneumonia, particularly in hospitalacquired infections. This opportunistic gram-negative bacterium can cause various diseases and is the fourth leading cause of severe pneumonia worldwide.3 A growing concern is the rise of antibiotic resistance, particularly through the production of Extended-Spectrum Beta-Lactamase (ESBL), which inactivates beta-lactam antibiotics and severely limits available treatment options. This form of resistance, predominantly seen in gram-negative bacteria such as Klebsiella pneumoniae, represents a major threat to global public health. It has been linked to a significant number of deaths, with

estimates suggesting over 1.27 million deaths annually due to infections caused by resistant organisms.⁴

Research shows that infections caused by ESBL-producing bacteria result in higher morbidity and mortality compared to non-ESBL infections.⁵ This issue is particularly concerning in Indonesia, where the rising prevalence of ESBL resistance continues to pose a significant threat to public health.⁶ The increasing resistance complicates treatment options and underscores the need for continued surveillance and the development of targeted strategies to address this growing challenge. Therefore, this study aimed to investigate the prevalence and antibiotic

resistance patterns of ESBL-producing *Klebsiella pneumoniae* in sputum samples from pneumonia patients at Ngoerah Hospital, Bali, between dbetween 2020 and 2022.

METHODS

This study retrospectively collected data from the clinical microbiology laboratory of Ngoerah Hospital, Bali, from 2020 to 2022. The data were obtained from all sputum specimens from pneumonia patients with Klebsiella pneumoniae isolates identified using VITEK 2 Compact (bioMérieux). The study included only isolates with a ≥90% probability of ESBL production, along with their corresponding antibiotic sensitivity test results. Isolates with incomplete or terminated sensitivity test results were excluded. Data were grouped by sex, age, ward, and type of sputum specimen. The prevalence of ESBL-producing Klebsiella pneumoniae was assessed during the study period, and the findings are presented in both percentage and absolute numbers.

RESULTS

This study obtained a total of 515 sputum sample data from pneumonia patients, which were tested for antibiotic sensitivity using the VITEK 2 Compact (bioMérieux) system at the Clinical Microbiology Laboratory Installation of Ngoerah Hospital, Denpasar during the period from 2020 to 2022. Of the total sputum samples tested with the VITEK 2 Compact (bioMérieux), 305 cases (59.2%) were found to be infected with ESBL-producing Klebsiella pneumoniae. These cases met the study's inclusion criteria, with Klebsiella pneumoniae identified at a rate of≥ 90% and producing ESBL, along with antibiotic sensitivity data.

Figure 1 illustrates the prevalence rate of ESBL-producing *Klebsiella pneumoniae* from 2020 to 2022, highlighting notable fluctuations over the three years. In 2020, the prevalence rate was recorded at 63%, indicating a relatively high burden of ESBL-producing strains. This rate decreased significantly to 52% in 2021, marking the lowest prevalence during the observed period. However, in 2022, the prevalence increased again to 61%,

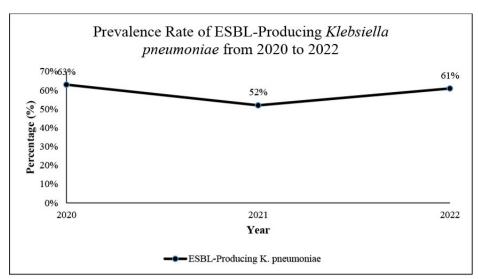


Figure 1. Prevalence Rate of ESBL-Producing *Klebsiella pneumoniae* at Ngoerah Hospital from 2020 to 2022.

Table 1. Sample characteristics

| Table 1. Sample characteristics | | |
|---------------------------------|---------------|-----------------|
| Variables | Total (n=305) | Percentages (%) |
| Gender | | |
| Male | 203 | 66.6 |
| Female | 102 | 33.4 |
| Age (year) | | |
| 0-1 | 16 | 5.2 |
| 1-5 | 2 | 0.7 |
| 5-10 | 0 | 0.0 |
| 10-19 | 11 | 3.6 |
| 19-44 | 57 | 18.7 |
| 44-59 | 97 | 31.8 |
| 60+ | 122 | 40.0 |
| Ward | | |
| Intensive Care Unit | 102 | 33.5 |
| Non-Intensive Care Unit | 203 | 66.5 |
| Type of Sputum Specimen | | |
| Expectorated Sputum | 192 | 63.0 |
| Non-Expectorated Sputum | 113 | 37.0 |

indicating a rebound but not returning to the initial level reported in 2020. Overall, the data reveal a downward trend from 2020 to 2021, followed by an upward trend in 2022, indicating dynamic changes influenced by variations in sample size over the three years.

In this study, the evaluation of sample characteristics, as shown in Table 1, revealed that 203 patients (66.6%) were male and 102 patients (33.4%) were female, indicating a higher prevalence of infection in male patients. In this study, the care units were categorized into two main types: intensive care units, which included specialized units such as cardiac care, pediatric intensive care,

neonatal intensive care, and burn units, and non-intensive care units, which referred to general wards that did not require intensive monitoring. Of the 305 sputum samples from patients with ESBL-producing Klebsiella pneumoniae, 102 patients (33.5%) were treated in intensive care units, while 203 patients (66.5%) were treated in non-intensive care units, indicating a predominance of cases in non-intensive care settings. The age distribution varied significantly, with 16 patients (5.2%) aged 0-1 year, 2 patients (0.7%) aged 1-5 years, no patients (0%) aged 5-10 years, 11 patients (3.6%) aged 10-19 years, 57 patients (18.7%) aged 19-44 years, 97 patients (31.8%)

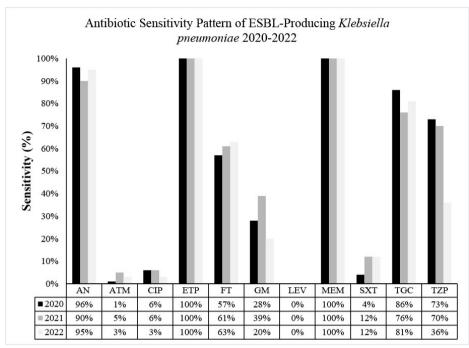


Figure 2. Antibiotic Sensitivity Pattern of ESBL-Producing *Klebsiella pneumoniae* at Ngoerah Hospital from 2020 to 2022. The antibiotics tested include Amikacin (AN), Aztreonam (ATM), Ciprofloxacin (CIP), Ertapenem (ETP), Nitrofurantoin (FT), Gentamicin (GM), Levofloxacin (LEV), Meropenem (MEM), Trimethoprim/sulfamethoxazole (SXT), Tigecycline (TGC), Piperacillin/tazobactam (TZP).

aged 44-59 years, and 122 patients (40%) aged 60 years and older. Additionally, of the sputum specimens used, 192 (63%) were expectorated sputum, while 113 (37%) were non-expectorated specimens obtained from endotracheal tubes (ETT) and orotracheal tubes (OTT) (Table 1).

Based on the antibiotic sensitivity test results, as shown in Figure 2, ESBLproducing Klebsiella pneumoniae showed high susceptibility to Ertapenem (ETP) and Meropenem (MEM) with 100% effectiveness. The bacteria also showed strong susceptibility to Amikacin (AN) (90-96%). In contrast, susceptibility Piperacillin-tazobactam (TZP) declined from 73% to 36%, while Levofloxacin (LEV) consistently showed susceptibility. Low susceptibility was observed to Ciprofloxacin (CIP), Aztreonam (ATM), and Trimethoprimsulfamethoxazole (SXT). Susceptibility to Gentamicin (GM) fluctuated, peaking at 39% in 2021 but dropping to 20% in 2022. Overall, carbapenems remained the most effective antibiotics, with varying or declining susceptibility to beta-lactam antibiotics and others (Figure 2).

DISCUSSION

This study found that 59.2% of pneumonia cases from sputum samples infected with ESBL-producing Klebsiella pneumoniae, indicating a high prevalence. Similar findings were reported in studies conducted at other tertiary referral hospitals in Indonesia, such as Zainul Abidin Hospital, Banda Aceh (79.84%) by Suhartono et al. and Dr. M Djamil Padang Hospital (70.9%) by Muztika et al.7,8 Differences in antimicrobial stewardship programs (ASP) likely contribute to variations in resistance rates, as hospitals with stricter programs may have better control over antibiotic use. In contrast, lower prevalence rates were observed in studies by Zhang et al. in China (31.8%) and Siriphap et al. in Thailand (30.2%).9,10 This is likely due to differences in hospital types, with secondary referral hospitals having fewer complex cases. These variations are also influenced by factors such as differences in antibiotic usage practices, infection control measures, hospital sanitation, patient population characteristics, and diagnostic methods.¹⁰

The prevalence of ESBL-producing *Klebsiella pneumoniae* fluctuated between

2020 and 2022, with rates of 63% in 2020, 52% in 2021, and 61% in 2022. The fluctuation in the prevalence of ESBLproducing Klebsiella pneumoniae between 2020 and 2022 can be attributed to several factors, including increased antibiotic use, hospital infections, global travel, variations in infection control practices, and improvements in surveillance.11 The higher prevalence in 2022 may be attributed to the largest number of samples collected that year, resulting in increased detection rates. These fluctuations underscore the importance of ongoing surveillance and antimicrobial stewardship in controlling the spread of drug-resistant Klebsiella pneumoniae.

The evaluation of sample characteristics revealed that the majority of patients were male, comprising 66.6% of the total sample. This finding suggests that biological and social determinants may influence susceptibility to infection. Hormonal, genetic, and anatomical differences are known to modulate infection risk between sexes, while health-related behaviors and gender roles may impact pathogen exposure and therapeutic outcomes.¹²

In terms of age distribution, most patients were over 60 years old, with 122 individuals (40%) falling into this category. This finding aligns with results from PKU Muhammadiyah Hospital Yogyakarta by Cinta Rahma et al., where the highest prevalence of ESBL-producing Klebsiella pneumoniae was observed in elderly patients (64.7%).13 The increased vulnerability in this age group may be attributed to a decline in immune system function, a higher prevalence of nutritional deficiencies, and a high burden of comorbidities in the elderly population, which collectively exacerbate the risk of infection and related complications.14

In this study, more cases were found in non-ICU wards, with a predominance of patients treated in general care units over intensive care units. These findings differ from previous studies. Research by Sinanjung et al. at Dr. Soeradji Tirtonegoro Hospital reported the highest prevalence of infection in intensive care patients (41.57%). Similarly, a study at Cipto Mangunkusumo National Hospital by Lestari et al. recorded a high prevalence of 71.4% in intensive care settings. This

high prevalence in intensive care units may be attributed to the critical condition of the patients, weakened immune systems, use of invasive devices such as ventilators, and the use of broad-spectrum antibiotics, which can promote the selection of resistant bacteria.¹⁷ In contrast, patients in non-ICU wards may exhibit distinct risk factors. Underlying health conditions, prolonged hospitalization, and prior antibiotic exposure can all increase the likelihood of colonization and infection with bacteria that are resistant to antibiotics. However, statistical analysis from a previous study by Ahmad et al. revealed no significant difference in the prevalence of ESBL-producing Klebsiella pneumoniae between intensive care units and non-intensive care units.18

Patients in this study were categorized based on sputum type, with expectorated samples being more dominant than those collected via suctioning. These results are consistent with findings from a Northern Thailand hospital, where sputum was the most common specimen for isolating ESBL-producing *Klebsiella pneumoniae* (44.2%).¹⁹ Expectorated sputum is typically collected in the morning, while non-expectorated sputum is obtained via suctioning from patients unable to produce sputum naturally.²⁰

This study found that Klebsiella pneumoniae exhibited high sensitivity to carbapenems and moderate sensitivity to certain other antibiotics while showing significant resistance to betalactams and fluoroquinolones. These results align with other studies that have noted the high resistance of Klebsiella pneumoniae to common antibiotics. A at Ulin General Hospital, Banjarmasin, by Elmawati et al. found that Klebsiella pneumoniae exhibited low sensitivity to beta-lactam antibiotics, such as Ceftazidime and Ceftriaxone. At the same time, the bacteria showed high sensitivity to Ertapenem (95.2%) and Meropenem (96.2%). This study also found that Klebsiella pneumoniae showed high sensitivity to Amikacin and Tigecycline (100%), while it exhibited significant resistance to other betalactams.21 Similarly, research at Dr. M Djamil Padang Hospital by Muztika et al. found Klebsiella pneumoniae to have high sensitivity to Meropenem (96.4%) and

Amikacin (98.9%), but 100% resistance to Ceftriaxone and only 31.5% sensitivity to Ciprofloxacin.⁸ A Nigerian study by Enyinnaya et al. reported similar findings, with *Klebsiella pneumoniae* showing high sensitivity to Meropenem (97.4%) and Amikacin (88.6%) but resistance to Ciprofloxacin (0%) and Levofloxacin (1%), and higher sensitivity to Tigecycline (84.2%).²² These studies highlight the treatment challenges of *Klebsiella pneumoniae* ESBL infections despite minor differences in antibiotic sensitivities.

This sensitivity pattern indicates that, although some antibiotics, such as carbapenems, remain effective, significant challenges persist in managing infections caused by Klebsiella pneumoniae ESBL producers. Resistance to beta-lactam antibiotics underscores the need for careful selection of antibiotic therapy. Factors influencing this resistance pattern include the inappropriate and excessive use of antibiotics in clinical practice. The research highlights the importance of proper management, prudent antibiotic use, and consideration of alternative therapies to effectively address these infections while minimizing the risk of further resistance.23 Strengthening antibiotic stewardship programs (ASP) by prioritizing narrow-spectrum antibiotics and reserving carbapenems for multidrugresistant infections is essential to reduce reliance on carbapenems. Improving infection prevention and control (IPC) measures, including strict hand hygiene, environmental disinfection, and patient cohorting, will also aid in preventing transmission. Additionally, bolstering AMR surveillance, regulating the sale of over-the-counter antibiotics, and implementing education programs for clinicians and the public are crucial to reducing resistance and maintaining effective treatment options.

CONCLUSION

Of the 515 sputum samples from pneumonia patients tested, 59.2% (305 cases) were infected with ESBL-producing *Klebsiella pneumoniae* and met the inclusion criteria. The prevalence fluctuated over the years, reaching 63% in 2020, 52% in 2021, and 61% in 2022. Evaluation of sample characteristics

revealed a higher prevalence of infection in male patients, with the highest prevalence in those aged 60 and above. Most patients were treated in non-intensive care unit (non-ICU) wards, compared to those in intensive care unit (ICU) wards. Additionally, sputum specimens were predominantly expectorated. The study found that *Klebsiella pneumoniae* exhibited the highest sensitivity to Ertapenem and Meropenem, as well as high sensitivity to Tigecycline and Amikacin, while demonstrating significant resistance to several beta-lactam antibiotics.

CONFLICT OF INTEREST

The authors affirmed that no conflicts of interest were present in this study.

ETHICAL CLEARANCE

Ethics approval was granted by Ngoerah Hospital, Denpasar, through document number 0436/UN14.2.2.VII.14/LT/2024.

FUNDING

All research funding was provided by the authors, with no external financial support.

AUTHOR CONTRIBUTION

Conceptualization, DAPARA; Design, DAPARA; Definition of intellectual content, DAPARA, NNSB, and NNDF; Literature search, DAPARA, NNSB, and NNDF; Clinical studies, DAPARA, NNSB, and NNDF; Experimental studies, DAPARA, NNSB, and NNDF; Data acquisition, DAPARA, NNSB, and NNDF; Data analysis, DAPARA, NNSB, and NNDF, and IPBM; Statistical analysis, DAPARA, NNSB, and NNDF, and IPBM; Manuscript preparation, DAPARA and NNSB; Manuscript editing, DAPARA and NNSB; Manuscript review, DAPARA, NNSB, and NNDF; Guarantor, DAPARA and NNSB. All authors have read and agreed to the published version of the manuscript.

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