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Antibiotic Susceptibility Patterns among Indonesian Adults Hospitalized with Pneumonia

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ABSTRACT

Introduction: Pneumonia continues to be a global issue with significant morbidity and mortality rates. Increased multidrug-resistant (MDR) bacterial pneumonia, aging populations, chronically ill patients, and inadequate initial antibiotic therapy increase hospitalized pneumonia patients' morbidity and mortality. This study aimed to analyze the microbiological pattern and choose a therapy based on local antibiotic susceptibility patterns.

Methods: From January 2020 to December 2022, a retrospective cross-sectional study was conducted on hospitalized pneumonia patients at Haji General Hospital, Surabaya, Indonesia. Data from medical records were gathered to illustrate patient features, bacterial culture, and antimicrobial susceptibility tests. This study included 172 patients. In this study, no specific statistical analysis was performed. The data were reported as a percentage (%).

Results: The patients were mostly 56-65 years old (36.6%) and male (55.2%). The most common comorbidities were cardiovascular disease (17.3%), and the others were diabetes mellitus (14.0%), cerebral vascular attack (CVA) (10.7%), and coronavirus infection (8.9%). Based on the sputum culture, the bacteria identified were *Klebsiella pneumoniae* (25.0%), *Pseudomonas aeruginosa* (20.9%), *Acinetobacter baumannii* (15.7%), and *Escherichia coli* (11.6%). The most common bacteria isolated from sputum cultures was *Klebsiella pneumoniae*, which was more susceptible to amikacin and meropenem.

Conclusion: Only amikacin was an antibiotic susceptible to four primary pathogens. Rates of resistance to ciprofloxacin and ceftriaxone were high, and these empiric antibiotics should be used with caution in these patients.

INTRODUCTION

Pneumonia is a common respiratory infection characterized by inflammation and infection of the lungs. It affects millions worldwide and is a major source of morbidity and mortality, especially in hospitalized patients. Higher rates of pneumonia grow significantly with age.[1] According to the Basic Health Research (RISKESDAS) 2013-2018 in Indonesia, the prevalence of pneumonia increased from 1.6% in 2013 to 2% in 2018. Annual incidences of pneumonia in the United Kingdom (UK) in 2019 per 100,000 population were 591.[1] Non-SARS-CoV-2 pneumonia has not decreased substantially despite public health interventions to reduce hospitalizations. Still, compared to previous pre-pandemic UK studies, the incidence of pneumonia has been reported to increase.[2] In the United States (US), in 2022, non-ventilator-associated hospital-acquired pneumonia rates started to rise after the COVID-19 pandemic broke out in the 2nd quarter of 2020.[3] The burden of hospitalization for pneumonia among adults in China in 2022, significantly among those over 60 years old and those with underlying medical conditions, increased.[4] In Indonesia, pneumonia is an important public health problem, significantly burdening the health system.[5–9]

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Diagnosing the organism that causes pneumonia is essential for determining appropriate antibiotic therapy. A study in the UK stated only 52% of patients with radiologically confirmed pneumonia underwent microbiological testing during hospitalization.[1] Gram-negative pneumonia is on the rise worldwide.[10] Most of the bacteria that cause ventilator-assisted pneumonia patients are gram-negative bacteria.[7,8,11] *Escherichia coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* are the most commonly identified bacteria associated with severe pneumonia in hospitalized patients.[7,11,12] However, antimicrobial therapy should be applied empirically to avoid therapeutic delays, which result in considerable mortality.[13] Empirical antibiotic selection should be tailored to local microbial patterns and bacterial susceptibility to be more effective and less likely to induce bacterial resistance.[14,15]

Resistance of pneumonia-causing bacteria to several antibiotics used in the first dosage reduce treatment effectiveness and increases morbidity and mortality.[14] However, data on microbiological etiology and drug susceptibility patterns of pneumonia are still being determined in Indonesia. This study examined the most prevalent pathogenic organisms, their antibiotic susceptibility, and the most common comorbidities in pneumonia patients at Haji General Hospital, Surabaya, Indonesia. By analyzing the data from Haji General Hospital, Surabaya, Indonesia, it could provide insights into the prevalence of antibiotic resistance among these pathogens and identify the most effective antibiotics for treatment. The findings from this study will have important implications for clinical practice and public health interventions. Knowledge of antibiotic susceptibility patterns can guide healthcare workers in selecting appropriate empirical therapy, optimizing patient outcomes, and minimizing the spread of drug-resistant strains.

METHODS

This was a cross-sectional study performed at Haji General Hospital, a 298-bed secondary hospital in Surabaya, Indonesia. The diagnosis of pneumonia was based on medical record data and the finding of bacteria on the results of the sputum culture examination. The data were obtained based on bacterial susceptibility results of antibiotic and culture testing in hospitalized pneumonia patients.

Data were collected from medical records of hospitalized pneumonia patients from 2020 to 2022. Based on inclusion and exclusion criteria, 172 patients were chosen from the overall population for this study. The inclusion criteria were patients aged 18 years old or older hospitalized with a pneumonia diagnosis, had complete medical records, including medical record number, age, and gender, and culture data and susceptibility testing for bacteria were available. Patients with incomplete medical records, those under 18 years old, and those who did not have a sputum culture were excluded from the study.

Sputum samples were collected and sent to the Laboratory of Microbiology, where they were evaluated microscopically, grown on blood agar and MacConkey media, identified, and tested for susceptibility using the VITEK 2 Compact. The results were interpreted using the Clinical and Laboratory Standards Institute (CLSI) criteria. Using WHO-NET version 5.6, the antibiotics susceptibility data were processed and analyzed. In this study, no specific statistical analysis was performed. The data were reported as a percentage (%).

Pneumonia was diagnosed based on signs and symptoms of cough, purulent sputum, fever at 38°C, chest pain, crackling sounds, and leukocytes >10,000/µl. In addition, infiltrates found on the lungs of all subjects resulted in chest X-ray. Other tests used to diagnose pneumonia included sputum cultures.

This study was ethically approved by the Institutional Ethics Committee of Haji General Hospital, Surabaya, Indonesia (no. 073/75/KOM.ETIK/2023) and conducted by the general principles of observational research.

RESULTS

Patient characteristics

Patient characteristics are shown in Table 1. 172 patients were included, including 95 males (55.2%) and 77 females (44.8%). Patients were divided into age groups with an interval of 10 years. Most patients were between the ages of 56 and 65 years old (36.6%). The second largest group was patients over 65 years old (26.7%). The most common comorbidities were cardiovascular disease (17.3%), followed by diabetes mellitus (14%), cerebral vascular attack (CVA) (10.7%), and coronavirus infection (8.9%). Cardiovascular disease includes congestive heart disease, coronary heart disease, hypertension, and atrial fibrillation.

Table 1. Characteristics of hospitalized patients with pneumonia

Variables	Frequent (N = 172)	Percentage (%)
Age (years old)		
18–25	5	2.9
26–35	4	2.3
36–45	20	11.6
46–55	34	19.8
56–65	63	36.6
>65	46	26.7
Gender		
Male	95	55.2
Female	77	44.8
Comorbid		
Cardiovascular disease	37	17.3
Diabetes mellitus	37	17.3
CVA	30	14.0
Coronavirus infection	23	10.7
CKD	19	8.9
Surgery	18	8.4
COPD	16	7.5
Sepsis	9	4.2
Lung tuberculosis	9	4.2
Others	7	3.3
	46	21.5

Notes: CVA: Cerebral Vascular Attack; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease

Table 2. The results of culture examination in patients with pneumonia

Bacteria	Frequent (N=172)	Percentage (%)
Klebsiella pneumonia	43	25.0
Pseudomonas aeruginosa	36	20.9
Acinetobacter baumannii	27	15.7
Escherichia coli	20	11.6
Ent.cloacae complex	11	6.4
Unidentified	5	2.9
Sphmon.paucimobilis	4	2.3
Aci.lwoffii	3	1.7
Steno.maltophilia	3	1.7
C.tropicalis	2	1.2
Staph.aureus	2	1.2
Staph.haemolyticus	2	1.2
Aer.hydro./caviae	1	0.6
Burkhol.cepacia	1	0.6
Ent.aerogenes	1	0.6
Gem.morbillorum	1	0.6
Koc.kristinae	1	0.6
Ochrobac.anthropi	1	0.6
Prov.stuartii	1	0.6
Ralst.insidiosa	1	0.6
Rothia mucilaginosa	1	0.6
Rzb.radiobacter	1	0.6
Ser.liquefaciens	1	0.6
Ser.marcescens	1	0.6
Staph.epidermidis	1	0.6
Str.sal.salivarius	1	0.6

Bacterial distribution and antibiotic susceptibility patterns

Table 2 shows the distribution of isolated bacteria, most of which were gram-negative. *Klebsiella pneumoniae* was the highest number (25.0%), followed by *Pseudomonas aeruginosa* (20.9%), *Acinetobacter baumannii* (15.7%), and *Escherichia coli* (11.6%). Only 2.4% were gram-positive bacteria, namely *Staphylococus aureus* (1.2%) and *Staphylococus haemolyticuss* (1.2%). Additionally, up to 1.2% of pneumonia was caused by the fungus *Candida tropicalis*. This study did not find *Streptococcus pneumoniae,* a common cause of pneumonia.

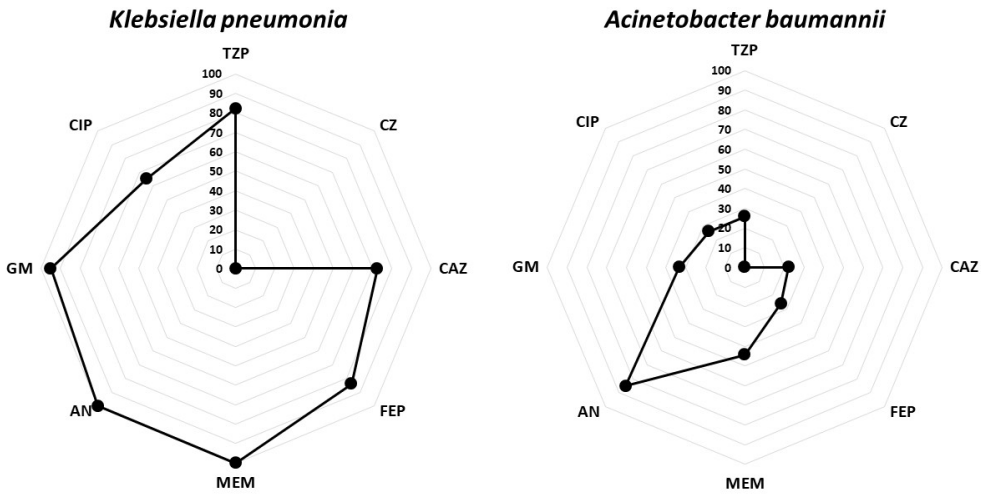
Table 3 shows the antibiotic susceptibility patterns of gram-negative bacteria isolated in this study. Of the 43 isolates of *Klebsiella pneumoniae*, 43 (100%) were susceptible to amikacin and meropenem, 95% to ertapenem and gentamicin, and 87.5% to tigecycline. *Klebsiella pneumoniae* was also susceptible to cefepime (83.8%), piperacillin-tazobactam (82.1%), ceftazidime (72.5%), aztreonam (70%), and sulfamethoxazole-trimethoprim (70%). However, all *Klebsiella pneumoniae* isolates were resistant to ampicillin, and

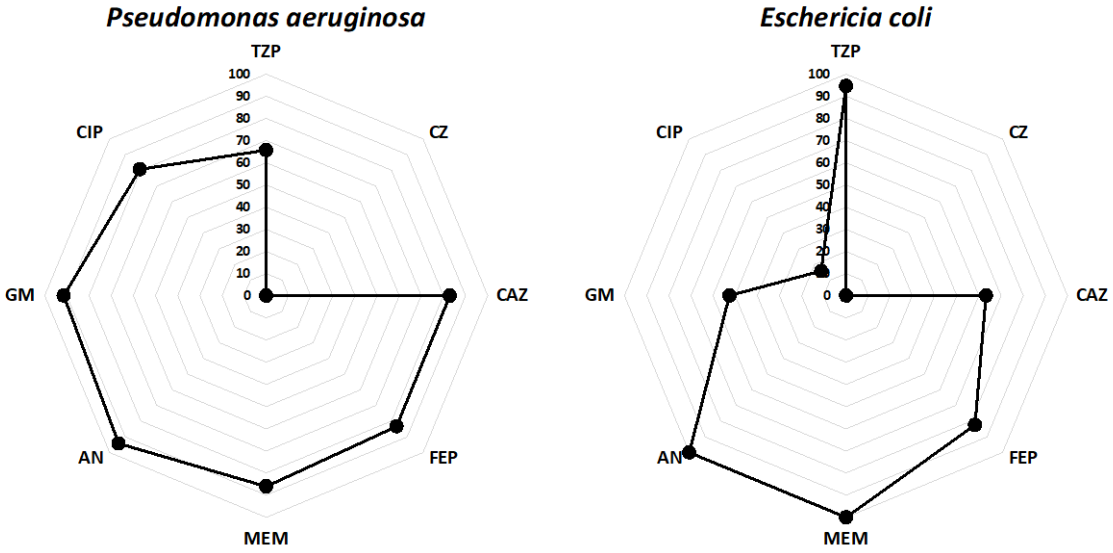
few are resistant to cefazolin (34.3%), ceftriaxone (30%), aztreonam (30%), and sulfamethoxazole-trimethoprim (30%). This study also found that 85.0% of *Acinetobacter baumannii* were susceptible to amikacin and tigecycline, and resistant to cefazolin (100%). Of the 27 isolates of *Pseudomonas aeruginosa*, they were sensitive to amikacin (94.3%), gentamicin (91.4%), and meropenem (86.1%). However, all *Pseudomonas aeruginosa* were resistant to cefazolin and tigecycline. *Escherichia coli* was 100% susceptible to amikacin, ertapenem, meropenem, and tigecycline. It was resistant to ampicillin (94.7%) and cefazolin (84.2%).

Table 3. Antibiotic susceptibility patterns of gram-negative isolates to different antibiotics

AB	*Klebsiella pneumoniae* (N=43)			*Acinetobacter baumannii* (N=27)			*Pseudomonas aeruginosa* (N=36)			*Escherichia coli* (N=20)		
	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)	R (%)	S (%)	I (%)
AM	100	0	0	-	-	-	-	-	-	94.7	5.3	0
SAM	22.5	60	17.5	51.9	44.4	3.7	-	-	-	21.1	42.1	36.8
TZP	12.8	82.1	5.1	70.4	25.9	3.7	22.9	65.7	11.4	5.3	94.7	0
CZ	34.3	0	65.7	100	0	0	100	0	0	84.2	0	15.8
CAZ	22.5	72.5	5	74.1	22.2	3.7	11.4	82.9	5.7	36.8	63.2	0
CRO	30	67.5	2.5	74.1	7.4	18.5	-	-	-	78.9	21.1	0
FEP	16.2	83.8	0	74.1	25.9	0	8.3	83.3	8.3	17.6	82.4	0
ATM	30	70	0	-	-	-	11.4	68.6	20	52.6	47.4	0
MEM	0	100	0	55.6	44.4	0	13.9	86.1	0	0	100	0
ETP	2.5	95	2.5	-	-	-	-	-	-	0	100	0
AN	0	100	0	14.8	85.2	0	2.9	94.3	2.9	0	100	0
GM	5	95	0	37	33.3	29.6	8.6	91.4	0	47.4	52.6	0
CIP	25	65	10	74.1	25.9	0	8.3	80.6	11.1	78.9	15.8	5.3
FT	25	22.5	52.5	-	-	-	-	-	-	10.5	84.2	5.3
SXT	30	70	0	37	63	0	-	-	-	73.7	26.3	0
TGC	12.5	87.5	0	7.4	85.2	7.4	100	0	0	0	100	0

Notes: AM: Ampicillin; SAM: Ampicillin-Sulbactam; TZP: Piperacillin-Tazobactam; CZ: Cefazolin; CAZ: Ceftazidime; CRO: Ceftriaxone; FEP: Cefepime; ATM: Aztreonam; MEM: Meropenem; ETP: Ertapenem; AN: Amikacin; GM: Gentamicin; CIP: Ciprofloxacin; FT: Nitrofurantoin; SXT: Sulfamethoxazole-Trimethoprim; TGC: Tigecycline





Notes: TZP: Piperacillin-Tazobactam; CZ: Cefazolin; CAZ: Ceftazidime; FEP: Cefepime; MEM: Meropenem; AN: Amikacin; GM: Gentamicin; CIP: Ciprofloxacin

Figure 1. Antibiotic susceptibility of the bacteria

In this study, the antibiotics tested for the susceptibility of bacteria were not the same. Hence, this study chose the same antibiotic to compare with the four most pneumonia-causing bacteria (Figure 1). *Klebsiella pneumonia* and *Escherichia coli* bacteria remained 100% susceptible to the antibiotic meropenem. All bacteria were not susceptible to cefazolin. Some antibiotics appeared more insensitive to *Acinetobacter baumannii* and *Escherichia coli* than *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Figure 1 shows that *Acinetobacter baumannii* had at least one antibiotic that was still susceptible. Meanwhile, *Pseudomonas aeruginosa* had the highest antibiotic sensitivity compared to other bacteria.

DISCUSSION

This cross-sectional study provided a detailed assessment of the characteristics, etiology, and antibiotic susceptibility in adult patients hospitalized with pneumonia. The significant findings were, (1) The majority of patients were males, (2) Most patients were 56-65 years old, (3) Almost all bacteria found were gram-negative, only 2.4% were gram-positive, and (4) Amikacin was the only antibiotic susceptible to four major bacteria causing pneumonia. This study looked at hospitalized patients with pneumonia but did not indicate which room they were admitted to. Some patients were admitted to the intensive care unit (ICU), cardiovascular intensive care unit, surgery, and internal medicine wards, and some to the isolation room. Some previous studies only looked at patients treated in the ICU. Therefore, the bacteria found could be considered ICU-specific.[8,11] Thus, treatment to prevent or spread infection can be made more specific.

Similar to this study, some previous studies also showed that the gender of most people with pneumonia was male.[9,16,17] In this study, the most common comorbidities were cardiovascular disease, while studies in China (2023) and Iran (2023) found cardiovascular diseases were also most common in males.[17,18] A study in Iran (2022) reported that CVA cases also mainly affected males.[19] A systematic review and meta-analysis by Abate, *et al*. (2020) stated that the incidence of symptomatic coronavirus disease was higher in males than in females.[20] In addition, a study by Hödlmoser, *et al*. (2020) found that awareness of chronic kidney disease (CKD) was consistently higher in men than in women.[21] Since most of the comorbidities in this study, according to previous studies, occurred in males, it is relevant that most hospitalized pneumonia patients were male in this study.

In a study in Indonesia (2022), among 99 hospitalized pneumonia patients, pulmonary tuberculosis (TB), human immunodeficiency viruses (HIV), and chronic obstructive pulmonary disease (COPD) were the most prevalent co-morbidities.[9] The co-morbidities of the study by Sitompul, *et al*. (2022) were different because it was conducted at the National Referral Hospital for Infectious Diseases, which treats all cases of infectious disease, including TB and multidrug-resistant (MDR) TB, even though both studies were performed in Indonesia.[9] In a study by Sahuquillo-Arce,

et al. (2016) in Spain, diabetes mellitus accounted for the highest comorbidities in 4,304 hospitalized pneumonia patients.[22] In contrast to the two previous studies, this study found cardiovascular disease to be the most common comorbidity in hospitalized pneumonia patients. This might be due to the high burden of cardiovascular disease in Indonesia. Coronary heart disease in Indonesia was 2.72%, with an incidence of 34 per 100,000 person/year.[23] This study aligns with Anderson, *et al*. (2023), who stated that cardiovascular disease was a relatively common disease in patients hospitalized with pneumonia.[24]

Pathogen growth in this study showed a predominance of gram-negative bacteria, with the most common species being *Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii*, and *Escherichia coli.* These microorganisms are closely linked to nosocomial infections. *Acinetobacter baumannii,* for example, is an aerobic gram-negative bacterium and, according to the World Health Organization (WHO), one of the most severe organisms that can escape the effects of antibiotics. It is associated with nosocomial infections worldwide and rapidly develops antimicrobial resistance through various mechanisms. These results are similar to those of several studies showing that *Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Acinetobacter baumannii* were the most common pathogens in gram-negative bacteria.[8,12,17,25,26] The study by Sitompul, *et al*. (2022) in Indonesia stated that *Klebsiella pneumonia* was primarily found in male pneumonia patients.[9] Santoso, *et al*. (2022) noted that the most common germs found in pneumonia among COVID-19 patients were *Acinetobacter baumannii*.[7] A 2019 study in France found that *Escherichia coli* was isolated from 76.5% of respiratory samples.[27] Unlike this study, several previous studies found that the most common bacterium was *Streptococcus pneumoniae*.[22,28] Another study stated that *Pneumococcus* was the most common etiology type in terms of deaths.[29] In a study in Japan (2023), there were 932 strains of respiratory tract bacteria, 21.5% *Staphylococcus aureus*, 17.5% *Pseudomonas aeruginosa*, 16.9% *Streptococcus pneumoniae*, 15.1% *Klebsiella pneumoniae*, 14.6% *Haemophilus influenzae*, and 13.6% *Moraxella catarrhalis*.[30] The detection of gram-negative bacteria in this study should be monitored. Due to their unique structure, gram-negative bacteria are more resistant to drugs than gram-positive bacteria and cause critical morbidity and mortality worldwide.[31]

In this study, *Klebsiella pneumoniae* showed the highest susceptibility (100%) to aminoglycosides (amikacin) and carbapenem β lactam (meropenem), which was higher than that reported previously (90% susceptible for amikacin and 80% for meropenem).[8] Similar to this study, Sitompul, *et al*. (2022) found that *Klebsiella pneumonia* was highly sensitive to meropenem (100%) but different from amikacin (93%).[9] The study by Santoso, *et al*. (2022) found that only 72.2% of *Klebsiella pneumoniae* were susceptible to amikacin and meropenem.[7] This study also found that *Klebsiella pneumoniae* was 100% resistant to penicillin (ampicillin), similar to a previous study by Andayani, *et al*. (2021).[8] In this study, *Pseudomonas aeruginosa* was completely (100%) resistant to 1st generation of cephalosporin (cefazolin) and tetracycline (tigecycline), most susceptible to aminoglycosides, amikacin (94.3%), and gentamicin (91.4%). In previous studies, *Pseudomonas aeruginosa* was sensitive to amikacin, gentamicin, ceftazidime, cefotaxime, imipenem, meropenem, polymyxin B, cefoperazone/sulbactam, and tobramycin.[8] This study also observed a low susceptibility rate of *Acinetobacter baumannii* to trimethoprim/sulfamethoxazole (63%), in contrast to a study in Iran, which stated that isolates of *Pseudomonas aeruginosa* exhibited the highest resistance to trimethoprim/sulfamethoxazole (93.3%).[32] Similar to the previous study by Santoso, *et al.* (2022), all *Acinetobacter baumannii* showed cefazolin resistance (100%).[7] However, susceptibility to amikacin and tigecycline was higher (85.2% vs. 57.9%, 85.2% vs. 52.6%, respectively).[7] Various mechanisms have been described to develop its resistance, β-lactamase production, increased multidrug efflux pumps, reduced membrane permeability, and altered antibiotic target sites.[33] This study found that all *Escherichia coli* were susceptible to amikacin, ertapenem, meropenem, and tigecycline, and resistant to ampicillin (94.7%), cefazolin (84.2%), ciprofloxacin (78.9%), ceftriaxone (78.9%), and trimethoprim/sulfamethoxazole (73.7%). The results of this study are similar to the study by Santoso, *et al*. (2022), who stated that all *Escherichia coli* were also susceptible to amikacin, cefotaxime, ertapenem, and meropenem.[7]

According to Sitompul, *et al*. (2022), ceftriaxone and quinolones as empiric therapy for pneumonia were very high (49.5% and 10.1%, respectively).[9] This study found that the rate of ciprofloxacin and ceftriaxone resistance was high, and these antibiotics should be used cautiously in these patients. Only amikacin was the antibiotic sensitive to the four largest pathogens. The outer membrane of gram-negative bacteria is a primary reason for resistance to various antibiotics, including β-lactams, quinolone, colistin, and other antibiotics.[31] Several attempts have been made to control gram-negative bacteria, especially resistant ones. Examples include developing antimicrobials, modifying existing antibiotics, and studying chemical structures with new

mechanisms of action and unique targets susceptible to resistant strains.[31]

This study will provide a valuable reference for treating pneumonia, especially in Indonesia, and provide evidence for improving the appropriate use of antibiotics. Since many causes of pneumonia are gram-negative bacteria, such as nosocomial infections, hospitals need to make more efforts to prevent infections, especially pneumonia. The high MDR isolation rates for *Acinetobacter baumannii* and *Escherichia coli* indicate the poor environmental conditions of the patients, poor hand hygiene, inadequate infection control practices, and failure to follow hygiene protocols.[33] Hospital administrators' efforts should include increased hand hygiene monitoring, sterilization of medical equipment, hospital environment cleanliness, and personal protective equipment use. Hand hygiene with alcohol-based hand sanitizer and fundamentals of infection prevention and control are probably the most effective measures to reduce healthcare-associated infections and the spread of antimicrobial resistance.[31]

This study has limitations. There was no information regarding the timing of isolate collection associated with patient hospitalization. Data about the onset of symptoms of pneumonia were also not available. Therefore, it was not possible to reliably distinguish between community-acquired and nosocomial infections. An additional limitation was excluding anaerobic and atypical bacteria from the current study. Further research is needed to identify the clinical symptoms associated with the type of bacteria. Hence, more appropriate empiric therapy can be applied.

CONCLUSION

This study identified gram-negative bacteria as the causative agent of pneumonia in hospitalized adult Indonesian patients. The most of patients were men between the ages of 56 and 65 years old and those with heart disease. *Klebsiella pneumoniae* was the most prevalent organism isolated from sputum cultures. It was more sensitive to amikacin and meropenem. Only amikacin was the antibiotic susceptible to the four most significant pathogens.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Authors' Contributions

Writing the manuscript, collecting data, data analysis: AFA. Supervisor, study design: MU. Data interpretation: AFA, MU, MA. All authors contributed and approved the final version of the manuscript.

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