Original Research Report

BACTERIAL PROFILES AND ANTIBIOTIC RESISTANCE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH EXACERBATION AND TYPE 2 RESPIRATORY FAILURE AT ADAM MALIK GENERAL HOSPITAL

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a prevalent condition characterized by persistent respiratory symptoms and airflow limitation. Bacterial infections may trigger COPD exacerbations, leading to more severe symptoms as well as increased morbidity and mortality rates. This study aimed to investigate the bacterial profiles and antibiotic resistance in COPD patients who had experienced exacerbation and type 2 respiratory failure at Adam Malik Central General Hospital, Medan, Indonesia. This retrospective study utilized medical records spanning from January 1, 2020, to December 1, 2022. The sample included patients aged 40–90 years who had experienced COPD exacerbation and type 2 respiratory failure. The exclusion criteria were patients who had received antibiotic therapy within 48 hours before admission, were severely immunocompromised, and had severe malignancy. The analysis results were presented in the form of means, standard deviations, and frequency distributions. Additionally, an analysis of the relationship between the categorical variables was performed using the Chi-squared test ($p<0.05$). The study analyzed 25 subjects with an average age of 63.6 years, primarily consisting of men (84%). It was shown that severe exacerbations were prevalent (92%), accompanied by the presence of common comorbidities including pneumonia (52%), diabetes mellitus (32%), and other non-communicable diseases (44%). Bacterial growth was observed in 76% of the subjects, predominantly involving Gram-negative bacteria (89.4%). *Klebsiella pneumoniae* (26.3%) and *Pseudomonas aeruginosa* (21.1%) were the most frequently isolated species. The antibiotic resistance patterns indicated that meropenem and amikacin had the highest resistance rates (100%). Cefepime, ertapenem, and gentamicin exhibited notable resistance rates of 66.7%, 66.7%, and 75.0%, respectively. This study highlights the high prevalence of Gram-negative bacteria and significant antibiotic resistance in COPD patients who exhibit exacerbation and type 2 respiratory failure.

Keywords: Chronic obstructive pulmonary disease (COPD); chronic respiratory diseases; infectious disease

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Highlights:
1. This study provides a comprehensive analysis of various factors such as age, sex, education, occupation, BMI, and comorbidities, and their relationship with bacterial infections in COPD patients experiencing exacerbation and type 2 respiratory failure.
2. While the COPD patients experiencing exacerbation did not exhibit resistance to linezolid and vancomycin, they demonstrated specific antibiotic resistance patterns characterized by high resistance rates to commonly used antibiotics such as meropenem and amikacin.
3. The findings enhance the understanding of the complex interplay of factors influencing infection patterns in this patient population.

INTRODUCTION

As a commonly found condition, chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation. This condition is often caused by significant exposure to harmful particles or gases (MacLeod et al. 2021). Patients with COPD are at a heightened risk of experiencing comorbid conditions. Subsequently, these patients may exhibit poor outcomes and increased mortality rates (Peltola et al. 2020, Bender et al. 2024). The typical symptoms of COPD include dyspnea, chronic cough, and sputum production. A comprehensive assessment of the patient's medical history is essential for identifying any risk factors associated with these symptoms (Vogelmeier et al. 2020).

Exacerbations of COPD, particularly those resulting in hypoxemic hypercapnic respiratory failure, are a significant cause of morbidity and mortality. Changes in the ventilation-perfusion (V/Q) ratio, increased respiratory load, and nutritional deficiencies are the defining characteristics of these exacerbations, which ultimately lead to type 2 respiratory failure (Neder et al. 2021). Managing COPD exacerbations requires intensive medical intervention, emphasizing the importance of understanding the bacterial patterns underlying these episodes. Bacterial infections may trigger COPD exacerbations, leading to more severe symptoms, prolonged hospitalizations, and increased rates of morbidity and mortality. Gram-negative bacteria frequently pose a challenge due to their notorious resistance to multiple antibiotics (Moghoofei et al. 2020, Bassetti et al. 2021).

Effective management strategies are crucial given the significant role of bacterial infections in COPD exacerbations, particularly in light of the frequent presence of antibiotic-resistant strains. The rise of antibiotic-resistant strains further complicates the management of COPD, highlighting the need for targeted antimicrobial strategies to effectively treat these infections (Gupta et al. 2020). Successful management of COPD exacerbations not only requires the prompt identification and treatment of bacterial infections, but also an understanding of the demographic and clinical factors that influence infection patterns. Variables such as age, sex, education, occupation, BMI, and comorbidities can significantly impact the prevalence and severity of bacterial infections in COPD patients (Buttery et al. 2021, Ma et al. 2021). The objective of this study was to analyze the bacterial patterns in COPD patients experiencing exacerbation and type 2 respiratory failure at Adam Malik Central General Hospital, Medan, Indonesia.

MATERIALS AND METHODS

This research was a retrospective analytical study conducted at Adam Malik Central General Hospital, Medan, Indonesia. Secondary data were obtained from medical records over a three years period, from January 1, 2020, to December 1, 2022. The research sample included patients with COPD exacerbation and type 2 respiratory failure. The exacerbation of COPD was defined as a sustained increase in cough, sputum production, and/or dyspnea lasting for more than 24 hours (Celli et al. 2021). Meanwhile, the condition of type 2 respiratory failure was signified by the inability of the respiratory system to adequately remove carbon dioxide from the body. This condition is referred to as hypercapnia (Lius & Syafaah 2022). The total sampling method was employed to gather patients who met specific criteria. Additionally, the selected patients needed to have type 2 respiratory failure, confirmed by hypercapnia test results. The eligible patients fell within the age range of 40 and 90 years. These research subjects provided comprehensive available data, including age, sex, comorbidities, education level, occupation, weight, and height. The exclusion criteria were patients who had received antibiotic therapy within 48 hours prior to admission, those who were severely immuno-compromised due to conditions such as human immunodeficiency virus/acquired immuno-deficiency syndrome (HIV/AIDS), and individuals diagnosed with severe malignant diseases.

The medical records obtained from Adam Malik Central General Hospital, Medan, Indonesia, provided detailed demographic information, including age, sex, comorbidities, education level, occupation, weight, and height. The diagnosis of COPD exacerbation and type 2 respiratory failure was confirmed by sustained increases in cough, sputum production, dyspnea, and hypercapnia as determined by blood gas analysis. Height and weight data were retrieved, and then the body mass index (BMI) was calculated. A thorough review of the respiratory system was conducted to assess the severity of symptoms and physical manifestations of COPD. Accurate diagnosis of COPD and assessment of its severity were confirmed following the 2017 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, using spirometry results. The COPD severity was classified into four stages by measuring the forced expiratory volume in 1 second (FEV1): GOLD 1 (mild, FEV1 $\geq$80% predicted), GOLD 2 (moderate, 50% $\leq$ FEV1 <80% predicted), GOLD 3 (severe, 30% $\leq$ FEV1 <50% predicted), and GOLD 4 (very severe, FEV1 <30% predicted) (Roversi et al. 2017). The chest X-ray data were reviewed to identify any additional respiratory conditions.

A thorough review was also conducted on purulent sputum samples according to the microbiological test results from medical records. All microbiological tests were conducted in the hospital laboratory following standard procedures. Samples were collected in a clean sputum pot in the morning after the patient had cleared debris from the mouth and throat and taken a deep cough. For each expectorated sputum sample obtained, a Gram smear was performed to determine whether the bacteria were Gram-positive or Gram-negative. Additionally, epithelial cells and polymorpho-nuclear leukocytes (PMN) counts were examined according to Bartlett's criteria, which are based on neutrophil and squamous cell counts. The samples were considered acceptable if they had more than 25 neutrophils and fewer than 10 squamous epithelial cells per low power field. Samples meeting Bartlett's criteria were then divided into two parts. One part of the samples was cultured on blood agar media and incubated at a temperature of 30°C for 24–48 hours. During incubation, colony growth was monitored, and bacterial types were identified by Gram staining. Gram-positive bacteria were grown on mannitol salt agar (MSA), while Gram-negative bacteria were cultured on McConkey media and subjected to biochemical examinations for further identification. The other part of the samples was planted on chocolate agar media, placed in a candle jar containing 5–10% carbon dioxide (CO_2), and incubated at a temperature of 37°C for 18–24 hours. Identification was made by examining colony morphology, Gram staining, and conducting biochemical tests. After identifying the bacteria, they were tested for antibiotic sensitivity using the VITEK 2 method, an automated bacterial identification and susceptibility testing system that uses fluorescence-based technology. The VITEK 2 method was used in this study, as previous investigations have shown that the testing system provides reliable identification and susceptibility results with pure bacterial cultures (Zhou et al. 2018, Kavipriya et al. 2021).

All data collected in this study were subjected to statistical analysis using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics, including means, standard deviations, and frequency distributions, were used to provide a clear and concise summary of the characteristics of the study subjects and the bacterial patterns identified in their sputum samples. For the bivariate analysis, the Chi-squared test ($p<0.05$) was employed to assess the relationship between categorical variables (Rana & Singhal 2015). The ethical clearance for this study was issued by the Research Ethics Committee of Universitas Sumatera Utara, Medan, Indonesia, with registration No. 08/KEPK/USU/2023 dated 05/01/2023.

RESULTS

This study analyzed 25 subjects with an average age of 63.6 years who were predominantly male (84%). The subjects had varied educational backgrounds, with 8% having an elementary school degree, 36% having a junior high school degree, 40% having a high school degree, and 16% having a university degree. A wide range of occupations was also reported by the participants, including unemployment (4%), civil service (16%), self-employment (48%), farming (12%), and labor (20%). The mean BMI was 20.6 kg/m², and the average hospital stay lasted 9 days. A total of 92% of the subjects experienced severe exacerbations. Additionally, various comorbidities were present, including pneumonia (52%), tuberculosis (12%), hypertension (20%), diabetes mellitus (32%), and other non-communicable diseases (44%). Most of the subjects (76%) showed bacterial growth, emphasizing the high incidence of bacterial infections and the importance of focusing on bacterial management in this patient group (Table 1).

Table 1. Characteristics of the study subjects.

Characteristics	n (%) or mean±SD
Age (y.o.)	63.6±10.7
Sex	
Male	21 (84)
Female	4 (16)
Education levels	
Elementary school	2 (8)
Junior high school	9 (36)
Senior high school	10 (40)
University	4 (16)
Occupations	
Unemployed	1 (4)
Civil servant	4 (16)
Self-employed	12 (48)
Farmer	3 (12)
Labor	5 (20)
BMI (kg/m^2)	20.6±2
Length of stay (days)	9±2.8
Exacerbation severity	
Moderate	2 (8)
Severe	23 (92)
Comorbidities	
Pneumonia	13 (52)
TB	3 (12)
Hypertension	5 (20)
Diabetes mellitus	8 (32)
Other non-communicable diseases	11 (44)
Bacterial growth	6 (24)
No	19 (76)
Yes	

Legends: y.o.=years old; BMI=body mass index; TB=tuberculosis.

Table 2. Factors related to bacterial growth in the study subjects.

Characteristics	Bacterial growth		OR	P
	No n (%)	Yes n (%)		
Age (y.o.)				
<60	3 (23.1)	10 (76.9)	0.9	1
≥60	3 (25)	9 (75)		
Sex				
Men	5 (23.8)	16 (76.2)	0.94	1
Women	1 (25)	3 (75)		
Education levels				
Elementary–junior high school	1 (9.1)	10 (90.9)	0.18	0.18
Senior high school–university	5 (35.7)	9 (64.3)		
Occupations				
Civil servant, self-employed	5 (31.3)	11 (68.8)	3.64	0.36
Farmer, labor, unemployed	1 (11.1)	8 (88.9)		
BMI				
<20 kg/m^2	3 (30)	7 (70)	1.71	0.65
≥20 kg/m^2	3 (20)	12 (80)		
Length of stay				
<10 days	2 (16.7)	10 (83.3)	0.45	0.65
≥10 days	4 (30.8)	9 (69.2)		
Exacerbation severity				
Moderate	1 (50)	1 (50)	3.6	0.43
Severe	5 (21.7)	18 (78.3)		
Pneumonia				
No	2 (16.7)	10 (83.3)	0.45	0.65
Yes	4 (30.8)	9 (69.2)		
TB				
No	5 (22.7)	17 (77.3)	0.59	1
Yes	1 (33.3)	2 (66.7)		
Hypertension				
No	6 (30)	14 (70)	4.93	0.29
Yes	0 (0)	5 (100)		
Diabetes mellitus				
No	4 (23.5)	13 (76.5)	0.92	1
Yes	2 (25)	6 (75)		
Other non-communicable diseases				
No	3 (21.4)	11 (78.6)	0.73	1
Yes	3 (27.3)	8 (72.7)		

Legends: y.o.=years old; BMI=body mass index; TB=tuberculosis; OR=odds ratio

The analysis of factors influencing bacterial growth in the patients included age, sex, education, occupation, BMI, hospital stay length, exacerbation severity, and the presence of comorbidities such as pneumonia, tuberculosis, hypertension, diabetes mellitus, and other non-communicable diseases. Notably, differences in bacterial growth rates across age and sex were not statistically significant. The education and occupation variables showed varied bacterial growth rates, despite being statistically inconclusive. Similarly, there were no statistically significant differences in bacterial growth rates among patients with a lower BMI or longer hospital stays. The severity of COPD exacerbations varied, with the moderate cases showing higher growth rates compared to the severe ones. However, these results were also not statistically significant (Table 2).

Table 3. Bacterial patterns in COPD patients with exacerbation and respiratory failure (n=19).

Bacterial species	Classification	n (%)
Acinetobacter baumannii	Gram-negative	1 (5.3)
Enterobacter aerogenes	Gram-negative	1 (5.3)
Enterobacter cloacae	Gram-negative	1 (5.3)
Escherichia coli	Gram-negative	3 (15.8)
Klebsiella pneumoniae	Gram-negative	5 (26.3)
Pseudomonas aeruginosa	Gram-negative	4 (21.1)
Pseudomonas putida	Gram-negative	1 (5.3)
Staphylococcus epidermidis	Gram-negative	1 (5.3)
Staphylococcus haemolyticus	Gram-negative	1 (5.3)
Stenotrophomonas maltophilia	Gram-negative	1 (5.3)

Table 3 presents the bacterial patterns observed in 19 COPD patients with exacerbation and respiratory failure. The bacterial species identified were predominantly Gram-negative, accounting for 89.4% of the isolates. Specifically, *Acinetobacter baumannii*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, and *Stenotrophomonas maltophilia* were all classified as Gram-negative. Among these Gram-negative bacteria, *Klebsiella pneumoniae* was the most frequently isolated, representing 26.3% of the total bacteria identified. This was followed *by Pseudomonas aeruginosa* at 21.1% and *Escherichia coli* at 15.8%. Each of the other Gram-negative species constituted 5.3% of the isolates. In contrast, the presence of Gram-positive bacteria was less common, with *Staphylococcus epidermidis* and *Staphylococcus haemolyticus* each accounting for 5.3% of the isolates.

Table 4. Antibiotic resistance patterns in *K. pneumoniae*, *P. aeruginosa*, and *E. coli* specimens (n=12).

Antibiotics	n (%)
Amikacin	12 (100)
Ampicillin-sulbactam	4 (41.7)
Aztreonam	5 (41.7)
Cefazolin	2 (16.7)
Cefepime	8 (66.7)
Ceftazidime	6 (50)
Ceftriaxone	2 (16.7)
Ciprofloxacin	2 (16.7)
Cotrimoxazole	3 (25)
Ertapenem	8 (66.7)
Gentamicin	9 (75)
Linezolid	0 (0)
Meropenem	12 (100)
Nitrofurantoin	1 (8.3)
Piperacillin-tazobactam	7 (58.3)
Rifampicin	0 (0)
Tetracycline	0 (0)
Tigecycline	6 (50)
Vancomycin	0 (0)

All specimens underwent antibiotic sensitivity tests. However, to account for the frequency of species found, any species that was identified only once in the following analysis was not reported. The analysis of antibiotic resistance patterns was conducted by including a total of 12 specimens, including *Klebsiella pneumoniae, Pseudomonas aeruginosa, and Escherichia coli*. Table 4 presents interesting findings from this analysis. All 12 specimens (100%) expressed resistance to meropenem and amikacin, indicating the highest resistance rates. Conversely, no resistance to linezolid, vancomycin, tetracycline, or rifampicin was detected. Notable antibiotic resistance patterns were observed in the testing of cefepime, ertapenem, and gentamicin, with resistance rates of 66.7%, 66.7%, and 75.0%, respectively. In contrast, the testing of other antibiotics such as cefazolin, ceftriaxone, ciprofloxacin, and nitrofurantoin exhibited lower resistance rates, ranging from 8.3% to 16.7%.

DISCUSSION

The 25 subjects in this study had an average age of 63.6 years. The majority of these subjects were male (84%). The research subjects had various educational attainments, including elementary school (8%), junior high school (36%), high school (40%), and university (16%). These demographics reflect a typical COPD patient population, which is more common in older adults and men. A higher incidence in men is often attributed to greater exposure to risk factors, such as smoking and occupational hazards (Grahn et al. 2021). The diversity in educational backgrounds suggests a broad socio-economic representation among the research subjects. This variation potentially impacts health literacy and management of the disease (Poureslami et al. 2021). The participants also had a wide range of occupations, including unemployment (4%), civil service (16%), self-employment (48%), farming (12%), and labor (20%). The prevalence of self-employment and labor-intensive jobs may indicate higher exposure to environmental pollutants, which are known as risk factors for COPD (Vlahovich & Sood 2021).

The mean BMI of the subject was 20.6 kg/m², indicating that the majority of patients were underweight or had a normal weight. These data are significant because low BMI in COPD patients is often associated with poorer outcomes and higher exacerbation rates (Ji et al. 2020). Most of the subjects (92%) suffered severe exacerbations, underscoring the critical nature of their condition. Additionally, the subjects exhibited the presence of a wide range of comorbidities, including pneumonia (52%), tuberculosis (12%), hypertension (20%), diabetes mellitus (32%), and other non-communicable diseases (44%). These comorbidities further complicate the management of COPD. This is because comorbidities can exacerbate symptoms and increase the risk of hospitalization (Westerik et al. 2017, Spece et al. 2018).

This study found that 76% of the subjects presented with bacterial growth, indicating high incidence of bacterial infections among the patients. This finding supports the need to prioritize bacterial management in COPD patients, particularly those experiencing severe exacerbations (MacLeod et al. 2021). The high prevalence of bacterial infections necessitates effective antibiotic stewardship to manage these infections and prevent resistance (Bassetti et al. 2022). In this study, various factors influencing bacterial growth, including age, sex, education, occupation, BMI, hospital stay length, exacerbation severity, and comorbidities, were analyzed. However, differences in bacterial growth rates across these factors were not statistically significant. This suggests that bacterial growth in COPD patients may be influenced by a complex interplay of factors rather than by a single demographic or clinical characteristic (Dima et al. 2019, Dicker et al. 2021).

The bacterial patterns analyzed in this study showed that Gram-negative bacteria were the most commonly identified species in the 19 COPD patients with exacerbation and respiratory failure. This finding highlights the need for targeted antibiotic therapy against these pathogens (Gupta et al. 2020). The antibiotic sensitivity tests revealed the highest resistance rates to meropenem and amikacin,

with all 12 specimens (100%) demonstrating resistance. Conversely, the testing of linezolid, vancomycin, tetracycline, and rifampicin revealed the absence of any antibiotic resistance. The testing of other antibiotics demonstrated notable resistance patterns for cefepime, ertapenem, and gentamicin, with resistance rates of 66.7%, 66.7%, and 75.0%, respectively. These results indicated the necessity of administering these antibiotics judiciously to prevent further resistance development (Kaleem Ullah et al. 2022). High rates of resistance to commonly used antibiotics, such as meropenem and amikacin, underscore the need to explore alternative treatments and develop new antibiotics. The absence of resistance to linezolid, vancomycin, tetracycline, and rifampicin provides potential therapeutic options. However, the use of these antibiotics should be carefully monitored (Avery & Nicolau 2018, Liu et al. 2019). Clinicians must consider local resistance patterns when selecting empirical antibiotic therapy for COPD exacerbations.

Strength and limitations

One of the key strengths of this study is its comprehensive analysis of a wide range of demographic and clinical factors, including age, sex, education, occupation, BMI, hospital stay length, exacerbation severity, and comorbidities. This broad scope allows for a thorough understanding of the complex interplay of factors influencing bacterial growth and antibiotic resistance in COPD patients. Additionally, the focus of this study on a diverse patient population with varied educational and occupational backgrounds enhances the generalizability of the findings to a broader COPD patient population. A notable limitation of this study is the relatively small sample size of 25 subjects, which may limit the statistical power and the ability to detect significant differences among the various factors analyzed. The cross-sectional nature of this study also limits the ability to draw causal inferences regarding the factors influencing bacterial growth and antibiotic resistance in COPD patients. Despite these limitations, the localized focus of this study provides valuable insights for tailoring treatment strategies in specific clinical settings, offering practical implications for improving patient care at the hospital level.

CONCLUSION

This study provided valuable insights into the demographic and clinical characteristics of COPD patients with bacterial infections, highlighting the high prevalence of Gram-negative bacteria and significant antibiotic resistance patterns in cases of COPD with exacerbation and type 2 respiratory failure. The findings underscored the importance of tailored antimicrobial therapy and the need for effective antibiotic stewardship to manage infections and prevent resistance in this vulnerable patient population. Despite its limitations, this study emphasized the necessity for ongoing research and surveillance to better understand and address the challenges of bacterial infections and antibiotic resistance in COPD patients. Additionally, fostering interdisciplinary collaboration among pulmonologists, infectious disease specialists, pharmacists, and primary care providers is essential for ensuring a comprehensive approach in the management of COPD patients with bacterial infections.

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Conflict of interest

None.

Ethical consideration

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Author contribution

LMA contributed to the conception and design of the study, performed data analysis and interpretation, drafted the article, provided statistical expertise, and provided final approval of the article. FS contributed to the drafting of the article, critically revised the article for important intellectual content, and provided final approval of the article. AP contributed to the drafting of the article, critically revised the article for important intellectual content, and provided final approval of the article. EM contributed to the interpretation of the data, drafted the article, provided statistical expertise, and gave final approval of the article.

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