CLINICAL, SUBCLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WITH COMMUNITY - ACQUIRED PNEUMONIA AT RISK OF PES INFECTION

Dang Duy Thanh[1,2], Cao Thi My Thuy[1,2], Nguyen Thi Hong Tran[1,2,] Truong Thi Nhu Hao[1], Vo Nhat Khoa[1], Nguyen Vu Hien[1,3] and Nguyen The Bao[1,✉]

[1]Can Tho University of Medicine and Pharmacy
[2]Can Tho Central General Hospital
[3]Can Tho City General Hospital

This study aims to describe the clinical and subclinical characteristics and evaluate treatment outcomes of community-acquired pneumonia (CAP) patients at risk of Pseudomonas aeruginosa, extended-spectrum beta-lactamases-producing Enterobacteriaceae, methicillin-resistant Staphylococcus aureus (PES) infection. A cross-sectional descriptive study was conducted on 90 CAP patients with potential PES infection admitted to the Respiratory Department of Can Tho Central General Hospital in 2023. Most cases presented with symptoms, including moist rales (91.1%), increased cough (90%), dyspnea (86%), purulent sputum production (77.8%), and consolidation syndrome (71.1%). More than half of the cases exhibited fever (54.4%). A white blood cell count increase was typical (13.31 x 109 cells/L) and predominantly neutrophilic (81.3 ± 19.7%). Chest radiography predominantly showed bilateral infiltration (58.9%). PES pathogens were isolated in 30 patients (33.3%). The majority of cases did not respond to initial antibiotics (56.6%), most of the cases were stable and cured (accounting for 91.1%) with an average hospital stay of 8 days. Patients with CAP at risk of PES infection exhibit typical acute symptoms and laboratory features of conventional CAP. Most responded poorly to initial treatment, but the final treatment resulted in a very high rate of stability and cure.

Keywords: Community-Acquired Pneumonia, Pseudomonas aeruginosa, Extended-spectrum beta-lactamases- producing Enterobacteriaceae, methicillin-resistant Staphylococcus aureus.

I. INTRODUCTION

Community-acquired pneumonia is a leading cause of death from infectious diseases globally, significantly associated with the burden of illness and mortality rates.[1] The estimated incidence of CAP worldwide varies from 1.5 to 14 cases per 1000 person-years.[2] Currently, *Streptococcus pneumoniae* remains the most common pathogen in community - acquired pneumonia,. However, the concept of PES has been increasingly recognized due to its association with poor initial treatment response, as well as high rates of ICU admission and mortality.[3,4]

Early identification of the causative agent is now yielding many benefits in treating respiratory tract inflammatory diseases.[5,6] However, research focused on patients with CAP at risk of PES infection has not been widely conducted, particularly in Vietnam. For these reasons, we conducted the study: "Clinical characteristics and treatment outcomes of patients with community-acquired pneumonia

Corresponding author: Nguyen The Bao
Can Tho University of Medicine and Pharmacy
Email: drntbao12345@gmail.com
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at risk of PES infection" with the following two objectives:

1. To describe the clinical and subclinical characteristics of patients with community-acquired pneumonia at risk of PES infection admitted to Can Tho Central General Hospital in 2023.

2. To evaluate treatment outcomes of patients with community-acquired pneumonia at risk of PES infection admitted to Can Tho Central General Hospital in 2023.

II. MATERIALS AND METHOD

1. Study population

All patients with community-acquired pneumonia admitted to the Respiratory Department - Can Tho Central General Hospital from April 2023 to November 2023.

Inclusion Criteria

Participants aged 18 and above, regardless of gender, who consented to participate in the study.

Patients meeting the defined criteria for community-acquired pneumonia according to the consensus conference between the American Thoracic Society and the Infectious Diseases Society of America:[7]

+ Presence of new infiltrates on chest X-ray, involving one or both lungs.

+ Patients presenting with one or more acute respiratory symptoms: cough (new or worsening), sputum production (with changes in color and consistency to purulent, green, or yellow), dyspnea, fever above 38°C or hypothermia below 36°C, pleuritic chest pain, or crackles on auscultation.

+ Patients with a PES score ≥ 2, based on criteria including age: < 40 (0 points), 40-65 (1 point), > 65 (2 points), male gender (1 point), prior antibiotic use (2 points), chronic lung disease (2 points), chronic kidney disease (3 points), altered mental status (2 points), fever (subtract 1 point).[6]

Exclusion criteria

Hospital-acquired pneumonia.

Patients who refuse treatment or transfer to another hospital.

2. Study method

Study design

Cross-sectional descriptive study.

Sample size

The sample was conveniently chosen, selecting all patients with CAP who met the criteria for hospitalization during the study period based on the data collection form. A total of 90 eligible patients were recruited and followed until the end of the study.

Study contents

General characteristics of study participants: age, gender, living circumstance (live with relatives/live alone).

Clinical characteristics: dyspnea, increased cough, fever, purulent sputum production, consolidation syndrome, crackles or moist rales (yes/no per one).

Subclinical characteristics:

- White blood cell (count, neutrophil ratio).

- Chest x-ray results (unilateral/bilateral infiltrates).

- Bacterial identification culture results (negative/positive for PES pathogens, other pathogens), pathogens were recorded exactly the name. The clinical specimens were stained and cultured on a suitable selective medium at the Department of Microbiology, Can Tho Central General Hospital. After overnight incubation, microbial colonies were observed, selected for suspension culture, and subjected to identification and antibiotic susceptibility

testing using the Vitek 2 Compact system (bioMérieux, France). Results were reported within 5 days after sample collection including bacterial identification and antibiogram.

Evaluation of treatment outcomes:

- The proportion of each initial antibiotic used.

- Initial treatment outcomes (response/poor response)[8]:

+ Respond: treatment improves and respiratory symptoms gradually decrease such as fever, sputum production and dyspnea, or chest x-ray or chest CT improves.

+ Poor respond: treatment does not improve and respiratory symptoms increase such as fever, cough, sputum production, difficulty breathing persists or chest x-ray or chest CT scan increases the damage.

Overall treatment outcomes during hospitalization:

+ Stabilization and recovery: when progress after 7 days and/or 14 days is good, the patient is discharged from the hospital.

+ Poor response: when the condition of patient does not improve after 14 days or worsens and requires resuscitation or death or family ask to go home.

Statistical analysis

The data were analyzed by Statistical Package for the Social Sciences (SPSS) software 22.0. The values of quantitative variables are presented as means, standard deviations if normally distributed, or medians, quartiles if not normally distributed. The values of qualitative variables are presented as frequencies or percentages. The results are represented in table and chart forms.

3. Ethics in research

The board of directors of Can Tho Central General Hospital and the ethics committee for biomedical research at Can Tho University of Medicine and Pharmacy approved this study.

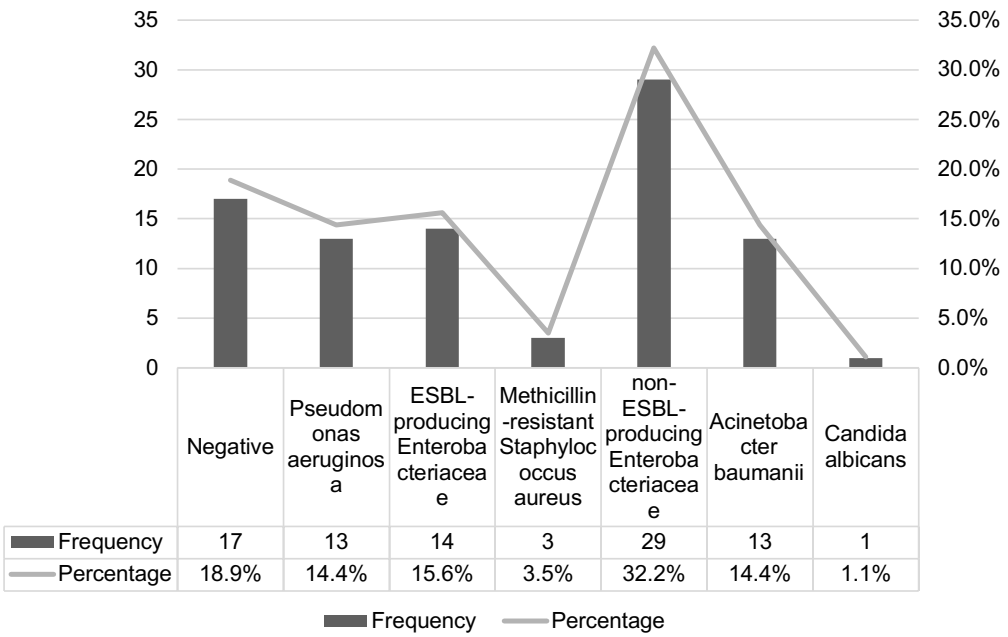
III. RESULTS

A total of 90 patients with CAP at-risk PES infection were included in the study. The age group 40-65 years old was the most common, accounting for 63%, while the age group < 40 years old had the lowest proportion at 7%. The average age in the study was 72.1 ± 14.4 years old. The male-to-female ratio was approximately 2. The majority of patients lived with family (89%), while the remaining 11% lived alone, with no cases living in nursing homes or long-term care facilities in this study.

Table 1. Clinical and subclinical characteristics (n = 90)

Characteristics	Frequency	Percentage (%)
Dyspnea, yes	78	86.0
Increased cough, yes	81	90.0
Purulent sputum production, yes	70	77.8
Consolidation syndrome, yes	64	71.1
Crackles or moist rales, yes	82	91.1
Temperature, ≥ 38°C	49	54.4
Chest radiograph, bilateral infiltration	53	58.9
White blood cell count, x 10^9 cells/L (mean ± SD)	13.3 ± 4.1	
Neutrophil, % (mean ± SD)	81.3 ± 19.7	

Regarding clinical characteristics, the majority of community - acquired pneumonia cases presented with respiratory symptoms, including dyspnea (86%), cough (90%), sputum production with color changes (77.8%), consolidation syndrome (71.1%), crackles or moist rales (91.1%). More than half of the cases had a fever (54.4%). In terms of subclinical characteristics, chest X-ray imaging revealed a higher prevalence of bilateral infiltrates compared to unilateral infiltrates (58.9% versus 41.1%). The average white blood cell counts in the study subjects increased (13.3 ± 4.1 x 10^9 cells/L), with mean neutrophil % being 81.3% ± 19.7.



	Negative	Pseudomonas aeruginosa	ESBL-producing Enterobacteriaceae	Methicillin-resistant Staphylococcus aureus	non-ESBL-producing Enterobacteriaceae	Acinetobacter baumanii	Candida albicans
Frequency	17	13	14	3	29	13	1
Percentage	18.9%	14.4%	15.6%	3.5%	32.2%	14.4%	1.1%

Figure 1. Bacterial identification culture results (n = 90)

Among the 90 study subjects, 33.3% of patients cultured positive for PES pathogens (14.4% *Pseudomonas aeruginosa*, 15.6% ESBL-producing *Enterobacteriaceae* and 3.5% methicillin-resistant *Staphylococcus aureus*), while 18.9% cultured negative. The remaining cultured pathogens were non-ESBL-producing *Enterobacteriaceae* (32.3%), *Acinetobacter baumanii* (14.4%), and *Candida albicans* (1.1%).

Table 2. Antibiogram of PES pathogens

Pathogens	Antibiotics	Level of antibiotic resistance (%)		
		Sensitive	Resistant	Intermediate
Pseudomonas aeruginosa	Ceftazidim	40	60	
	Gentamycin	50	50	
	Amikacin		80	20
	Piperacillin/tazobactam	50	50	
	Cefepim	10	50	
	Imipenem	30	60	
	Meropenem		60	
	Ciprofloxacin	30	60	
	Colistin			40
Methicillin-resistant *Staphylococcus aureus*	Oxacillin		100	
	Vancomycin	100		
	Linezolid	100		
ESBL-producing *Klebsiella pneumoniae*	Ampicilin		100	
	Amikacin	27.4	54.6	9.1
	Gentamycin	36.4	63.6	
	Imipenem	9.1	90.9	
	Ertapenem	9.1	81.8	9.1
	Piperacilin /tazobactam		100	
	Cefepime		100	
	Ciprofloxacin		100	
	Colistin			9.1
ESBL-producing *Escherichia coli*	Ampicillin		100	
	Amikacin		100	
	Gentamycin	25	50	25
	Imipenem		100	
	Ertapenem	25	75	
	Piperacilin /tazobactam		100	
	Cefepim		100	
	Ciprofloxacin		100	
	Colistin			25

Isolated PES bacteria, including *Pseudomonas aeruginosa* and ESBL-producing *Enterobacteriaceae* showed high resistance to beta-lactam, quinolone and aminoglycoside antibiotics (50-100%), but there was no resistance to colistin, with intermediate sensitivity ranging from 9.1-40%. In terms of Methicillin-resistant *Staphylococcus aureus*, there was complete resistance to oxacillin, in contrast to vancomycin and linezolid.

Table 3. The rate of initial antibiotic use (n = 90)

Initial antibiotic use	Frequency	Percentage (%)
Amoxicillin + acid clavulanic	38	42.2
Cephalosporin	45	50.0
Imipenem	4	4.4
Meropenem	3	3.4
Moxifloxacin	17	18.9
Levofloxacin	43	47.8
Ciprofloxacin	19	21.1
Amikacin	7	7.8
Vancomycin	4	4.4

In our study, the majority of initial antibiotics used were amoxicillin + clavulanic acid or cephalosporin (with proportions of 42.2% and 50.0%, respectively), combined with a quinolone (with moxifloxacin accounting for 18.9%, levofloxacin for 47.8%, and ciprofloxacin for 21.1%). Only about 7.8% utilized carbapenem (imipenem or meropenem) combined with amikacin (7.8%) or vancomycin (4.4%).

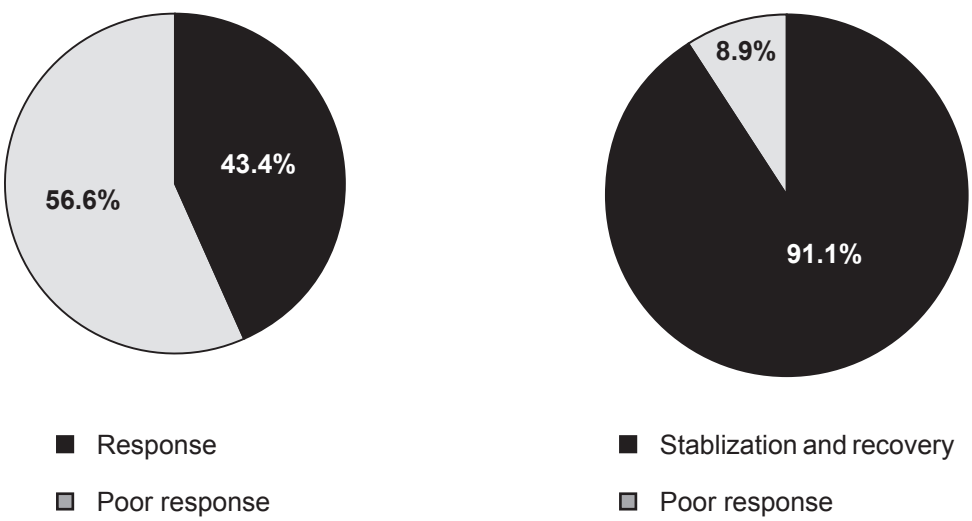


Figure 2. Evaluation of treatment results (n = 90)

Among the 90 patients admitted for CAP at risk of PES infection, a staggering 56.6% did not respond to initial treatment. However, the overall treatment outcomes revealed that the majority achieved stabilization and recovery, accounting for 91.1%. There were 8 cases with poor response, constituting 8.9%.

In addition, the median value of hospital stay of the study subjects was 8 days (ranging from a minimum of 3 to a maximum of 32 days).

IV. DISCUSSION

Among the 90 patients with community-acquired pneumonia admitted to the study, the majority belonged to the age group of 65 years and above, with the average age being 72.1 ± 14.4 years old. Among them, males predominated. Regarding clinical characteristics, we observed that cough was prevalent in CAP patients in our study, followed by dyspnea and purulent sputum production. On physical examination, crackles or moist rales were predominant, followed by consolidation syndrome and fever. These results are consistent with CAP being an acute illness typically presenting with prominent and varied respiratory symptoms.[9,10] They also align with studies by Ta Thi Dieu Ngan, conducted at the National Hospital for Tropical Diseases, Dong Da General Hospital, and Duc Giang Hospital, which reported cough as the most common symptom (93%), followed by fever (83.1%) and sputum production (76.8%).[11] Nguyen Thanh Hoi's study at the Respiratory Department of Bach Mai Hospital also noted cough (94.7%) and sputum production (86.8%) as common symptoms.[12]

In terms of subclinical characteristics, we observed that the average white blood cell count in CAP patients was often elevated, with neutrophil predominance. According to Le Van Them et al., most CAP patients have increased white blood cell counts and neutrophil predominance (66%).[13] This finding is consistent because the pathogens causing CAP are mainly bacteria, often pneumococci or PES pathogens, in high-risk populations.[3] Evaluation of chest X-ray images showed that the majority of patients had bilateral infiltrates. Ta Thi Dieu Ngan reported that only 40.8% of CAP patients had bilateral lung involvement.[11] This difference in results may be due to our study focusing on a group at risk of PES infection, which may result in more bilateral lung involvement. Similarly, we observed that 33.3% cultured positive for PES pathogens, higher than Catia Cilloniz et al.'s study (12%). This is entirely appropriate because all our subjects had a PES score ≥ 2, whereas Catia Cilloniz et al. studied elderly subjects who may or may not be at risk of PES infection.[14] The antibiotic susceptibility results for PES strains that we obtained are also similar to previous reports in Vietnam. Hung Do Tran and colleagues found that *Pseudomonas aeruginosa* and ESBL-producing *Enterobacteriaceae* exhibited strong resistance to most antibiotics (50-100%), except for colistin, amikacin, piperacillin-tazobactam, imipenem, and meropenem (0-25%). Methicillin-resistant *Staphylococcus aureus* also showed similar resistance patterns and was only susceptible to vancomycin, linezolid, doxycycline, tigecycline, and rifampin.[15] These findings raise significant concerns about the status of antibiotic resistance in CAP patients at risk of special pathogens in Vietnam.

Most CAP patients admitted to the hospital received initial antibiotic therapy with beta-lactams and quinolones (92.2% and 87.8%, respectively). This is because the 2015 Ministry of Health guidelines for CAP treatment typically recommend combination therapy with these

two antibiotics in high-risk groups.[16] Among the 90 patients hospitalized for CAP at risk of PES infection, up to 56.6% did not respond to initial treatment. This result is expected because all patients had risk factors for PES infection, which are pathogens often resistant to drugs in initial treatment protocols. However, overall treatment outcomes showed that the majority (91.1%) stabilized and recovered, with an average hospital stay of 8 days. This result is quite similar to general CAP research findings by Doan Nguyen Tra My et al., who reported a 96.4% success rate in treatment.[17] Similarly, Ta Thi Dieu Ngan's study also reported a treatment success rate of 89.4%.[11] This indicates that although PES pathogens causing CAP often respond poorly to initial treatment, if clinicians clinically identify these high-risk patients from the outset, monitor and assess initial responses both clinically and subclinically, and adjust antibiotic therapy accordingly, the ultimate success rate of treatment remains very high.

The present study is a small cross-sectional descriptive study with limitations. The limited sample size comes from a single healthcare center, making it challenging to represent the community. Moreover, we mainly focused on describing patients' clinical characteristics and treatment outcomes rather than identifying any associated factors or new management strategies. We propose conducting larger-scale studies to address these lingering issues.

V. CONCLUSION

Patients with CAP at risk of PES infection still exhibit typical acute symptoms as well as laboratory features of conventional CAP. It is noteworthy that the majority often have bilateral lung infiltrates. Common antibiotics of the beta-lactam and quinolone groups are preferred for initial treatment. Despite most showing poor response to initial treatment, overall treatment outcomes mainly indicate stabilization and recovery.

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