

Research Article

Hospital-acquired pneumonia in an intensive care unit in Vietnam: clinical characteristics and pathogenic bacteria

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ABSTRACT

The increase in the number of multi-drug resistant bacteria causing nosocomial infections at the hospital's intensive care unit (ICU) is a major worldwide problem. This leads to the need for research on clinical characteristics and pathogenic bacteria of hospital-acquired pneumonia (HAP) patients. Our research aimed to describe the clinical characteristics and identify the patterns of causative agents in HAP patients. We conducted a cross-sectional descriptive study on 103 HAP patients treated in ICU of a major hospital in Can Tho City, Vietnam from May 2017 to May 2018. The identification and antimicrobial susceptibility of cultures were determined using an automated microbiology analyzer; the Bauer–Kirby disk diffusion method was used. Of 103 patients met the inclusion criteria, 95 patients were confirmed as presenting with HAP caused by MDR bacteria. The overall prevalence was higher in men than in women and increased with age. There was some evidence of a correlation between prior broad-spectrum antibiotic use and the incidence of HAP. The sputum color change and hyperthermia were common clinical symptoms in HAP diagnosing. Notably, the proportion of multiple-antibiotic-resistant bacteria causing HAP was 92.5%. High rates of most common antibiotic resistance were observed in *Acinetobacter baumannii*, *Klebsiella*, *Pseudomonas aeruginosa* and also *E. coli*. The success rate of treatment for HAP caused by MDR bacteria accounted for 49.5%. The resistance rates of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* to most common antibiotics were increasing substantially. The initial treatment for HAP ought to comply with combined antibiotic therapy or a new treatment strategy.

1. INTRODUCTION

Hospital-acquired pneumonia (HAP) and multi-drug resistant (MDR) bacteria in the intensive care unit (ICU) are developing countries' problems with high mortality rates (30 – 70%)^{1,2}. HAP is a lower respiratory infection that was not incubating at the time of admission and presents after more than 48 hours since hospitalization. HAP prolongs the duration of treatment, increases the costs of lab tests, and requires costly broad-spectrum antibiotics. According to WHO studies in high-income countries,

the attributable costs at 10,000 – 25,000 US dollars per VAP case³. The costs of HAP is a massive financial burden for healthcare systems, especially Vietnam—a lower-middle-income country (LMICs)^{1,3}.

A systematic review and meta-analysis of VAP in adults in Asia indicated that resistant gram-negative bacteria were the major cause of VAP in Asia. The most common organisms were *Acinetobacter baumannii* (26%), *Pseudomonas aeruginosa* (22%) and *Klebsiella pneumonia* (14%), in which *A. baumannii* was the most common agent in the LMICs and tropical regions⁴. Other studies have demonstrated that *Acinetobacter baumannii* (24.4%), *Pseudomonas aeruginosa* (13.8%), and *Klebsiella pneumonia* (11.6%) were the most common bacteria in ICU in Vietnam¹. In Can Tho, 2016, the percentage of mentioned gram-negative bacteria were 44.7%, 15.4%, and 9.8%, respectively. Those figures changed to 48.9%, 19.8% and 6.5% in 2017⁵.

Recently, it is difficult to treat HAP due to the increase of antibiotic resistance and the lack of new antibiotic generations⁶. The number of reports about bacterial etiology and MDR bacteria is increasing. Now, ICUs in Asia are highly resistant to antibiotics by methicillin-resistant *Staphylococcus aureus*, MDR *P. aeruginosa* and *A. baumannii*^{1,4}. In Asia, the resistance rates of *A. baumannii*, *P. aeruginosa* to carbapenem were 58% and 41% for LMICs, respectively. According to research in ICU in Vietnam, carbapenem resistance was predominant in *A. baumannii* (89.2%) and *Pseudomonas aeruginosa* (55.7%). Whilst, 14.9% *Klebsiella pneumonia* were carbapenem-resistant and more than 75% of the *Staphylococcus aureus* isolates were methicillin-resistant¹.

Studying about clinical characteristics and bacteria antibiotic resistance becomes urgent and necessary. However, causative agents and antibiotic resistance alter in accordance to ICU and period of time. Therefore, it is complicated to apply a general treatment guideline. From mentioned clinical difficulties, our research was conducted to determine clinical characteristics and pathogenic bacteria and other related factors and assess the treatment results on HAP patients in an ICU in Vietnam.

2. MATERIALS AND METHODS

2.1. Study population

The study had been conducted on all patients diagnosed with HAP and aged 32 to 94 years old in ICU of one of the top-tier hospitals of Can Tho City, Vietnam from May 2017 to May 2018. The hospital underwent a more-than-120-year-of-existence history, providing leading health care services to Mekong Delta dwellers. The hospital admits about 1,700 patients a day and currently has 700 beds, but it is also constantly overloaded with patients. The bed occupancy rate often reaches at 113% and the number of visitors entering hospital peaks at 148% of the planned target. With first-class facilities, cutting-edge equipment and a team of highly skilled doctors, the hospital is increasingly improving the quality of diagnosis and treatment for patients. The study was approved for implementation by the Research Ethics Committee of Can Tho University of Medicine and Pharmacy according to the minutes No. 20170417/CTUMP.

2.2. Study design

We carried out this cross-sectional descriptive study on a sample of 103 ICU patients and had the informed consents from them and their relatives if the patients could not sign.

2.3. Inclusion and exclusion criteria

Inclusion criteria were patients who had 48 hours of hospital admission and presented a new or progressive radiographic infiltrate with at least two of four clinical features⁶: (1) hyperthermia (i.e., fever) greater than 38 °C or hypothermia less than 36 °C, (2) leukocytosis (circulating leukocyte count greater than 11 G/L) or leukopenia (less than 4 G/L), (3) increased sputum or changes in the properties, (4) decline in oxygenation (emergence of acute respiratory failure in patients with stable respiratory conditions). Patients, with bronchoalveolar lavage fluid over 1 x 10⁴ cfu/mL, bacteria isolated from blood cultures or pleural fluid, or present bacteria and antibiogram in bacteria culture results, were also included in the study.

Patients were excluded if they met one of the following criteria: diagnosed with community-acquired pneumonia, terminal cancer, AIDS, pregnant women or being treated with pulmonary tuberculosis (+).

2.4. Sample size and sample selection

The sample size is calculated by the formula:
$$n = \frac{Z_{(1-\alpha/2)}^2 p(1-p)}{c^2}$$

Where: n: the number of studied patients (n = 103 after calculating)

α : probability of type 1 errors ($\alpha = 0.05$)

Z: normal distribution value (Z-score = 1.96 for $\alpha = 0.05$)

c: allowable error = 0.05

p: The rate of multi-resistant bacteria causing HAP (p = 92.8% according to research by Nguyen Ngoc Dai Trang⁷)

We used the non-probability convenient sampling technique to select patients to participate in the study.

2.5. Data collection

The data including demographics, intrinsic and extrinsic risk factors for pneumonia, clinical signs and symptoms, isolated pathogens with antibiogram results, and outcome on discharge from the hospitals (i.e., the results of recovery, degeneration or death) were collected by structured questionnaires and medical records.

2.6. Examination and sample collection procedure

The initial examinations and laboratory tests, including routine biochemistry and specialized tests, were done when patients were first admitted to ICU. The daily follow-up examinations were performed to diagnose HAP on all ICU patients, including patients from other departments or route admitted within 48 hours. When the patients met the inclusion criteria, they would have clinical examinations to detect risk factors and severe prognostic signs. An empiric antibiotic therapy based on hospital's protocol was used when the sputum cultures and antibiogram results were available.

In the treatment of MDR pathogens, the empirical antibiotic therapy (Appendix 1), the duration of treatment and the dosage of antibiotics (Appendix 2) were based on Vietnam Association Against Tuberculosis and Lung Diseases (VAT-LD)'s guideline⁷. If the initial antibiotic agent was appropriate, or the pathogen was not *Pseudomonas aeruginosa* or *Acinetobacter baumannii*, or there was the patient's clinical symptom improvement, the duration of treatment was from 7 to 10 days. The duration would be longer (from 14 to 21 days) in case the MDR bacteria were *Pseudomonas*

aeruginosa or *Acinetobacter baumannii*, with prolonged clinical symptoms such as fever (greater than 38°C), circulating leukocyte count greater than 10,000 / mm³, purulent sputum, and there was no improvement in chest X-ray results⁷.

We recorded the following clinical symptoms on patients: fever, and increased sputum or changes in the properties. All sputum specimens were collected by expectoration and stored in sterilized vials. Specimens were considered as standard if there were more than 25 polymorphonuclear leukocytes or less than 10 epidermal cells. The results were considered as positive when the number of observed bacteria was more than 10⁶ per 1mL of sputums.

The bronchoalveolar lavage (BAL) fluid was collected from all intubated patients by bronchoscopy procedure and then transferred to the microbiology department within 10 minutes after collection. A sample was considered as positive and statistical significant if there were more than 10⁴ cfu per milliliter of BAL⁹. The routine identification of bacteria by the Department of Microbiology of the study hospital, identification of bacteria by Vitek 2 Compact machine, cultured by quantitative methods using a 10 μ L implant, results considered to be significantly positive with a threshold of $\geq 10^4$ bacteria/mL of the sample. The disk-diffusion agar method was based on the Clinical and Laboratory Standard Institute guidelines (CLSI, 2014). The diameter of sterile ring around the antibiotic paper disks was measured and compared with the inhibition zone diameter standard. The bacteria was defined as MDR when the antibiogram result showed resistance to at least one agent in three or more different classes of antibiotics¹⁰ (Appendix 3).

2.7. Data analysis

Descriptive statistics were used to conduct statistical analyses in our study. The qualitative variables were described by frequency, percentage, and 95% confidence interval; the quantitative variables were described by mean (or median), standard deviation (or quartile), minimum and maximum. The averages were compared by the T-test (if there was a normal distribution) or Wilcoxon (if there was no normal distribution); the difference between groups' ratios was compared by a chi-square test and corrected by Fisher's exact when the expected frequency is <5. The Odds Ratio (OR) was estimated to find the effect of variables on the outcome of multiple antibiotic resistance in bacteria.

2.8. Statistical analysis

All analyses were conducted using SPSS version 22.0. The difference between groups was considered as significant if the p-values were < 0.05.

3. RESULTS AND DISCUSSION

3.1. Clinical characteristics and the association between baseline characteristics and multi-drug resistance

Of 103 patients met the inclusion criteria, 95 patients were confirmed as presenting with HAP

caused by MDR bacteria. Fifty-seven percent of the patients were women. The overall prevalence was higher in men than in women and increased with age. For the oldest patients (>80 years old), we found a prevalence of 42.7% versus 1.9% for the youngest patients (16 – 39 years old) (Table 1). Similar to the other study in Vietnam, old age is related to the occurrence of HAP¹¹. The elderly usually suffers from chronic diseases, e.g., diabetes, hypertension, chronic obstructive pulmonary disease, which are risk factors causing immunodeficiency and secretion stagnation. However, there was no statistical difference between the incidence of MDR HAP and patient characteristics (i.e., gender, age, and types of pneumonia with $p=0.07$, 0.651, and 0.468, respectively) (Table 1).

The risk factors for HAP are also shown in Table 1. According to the research from Seligman *et al.*, prior broad-spectrum antibiotic usage within 10 days was an independent risk factor (OR=3.45, 95% CI: 1.56 – 7.61, $p = 0.002$)¹². In our study, patients who used broad-spectrum antibiotics prior to the time of diagnosis had a higher incidence risk (98.1%) than those who did not (86.3%). This difference reached a statistical significance ($p=0.031$). However, there was no significant difference between MDR and non-MDR HAP in the viewpoint of factors as follows: previous antibiotic administration, re-hospitalization and blood filtration, immunodeficiency ($p>0.05$) (Table 1).

Table 1. The association between baseline characteristics and HAP caused by bacteria

Baseline characteristics	HAP caused by MDR bacteria n(%)	HAP caused by non-MDR bacteria n(%)	OR 95% CI	p-value*
Gender				
Male	38 (86.4)	6 (13.6)	0.222 (0.04-1.16)	0.07
Female	57 (96.6)	2 (3.4)		
Age				
16 – 39	2 (100.0)	0 (0.0)	0.651	
40 – 59	13 (86.7)	2 (13.3)		
60 – 79	38 (90.5)	4 (9.5)		
≥ 80	42 (95.5)	2 (4.5)		
Types of pneumonia				
HAP	52 (94.5)	3 (5.5)	0.222 (0.04-1.16)	0.468
VAP	43 (89.6)	5 (10.4)		

Table 1. The association between baseline characteristics and HAP caused by bacteria (cont.)

Baseline characteristics	HAP caused by MDR bacteria n(%)	HAP caused by non-MDR bacteria n(%)	OR 95% CI	p-value*
Time of onset of HAP				
Late	59 (95.2)	3 (4.8)	2.73	0.26
Early	36 (87.8)	5 (12.2)	(0.6-12.1)	
Antimicrobial therapy in the preceding 90 days				
Yes	20 (95.2)	1 (4.8)	1,87	1.00
No	75 (91.5)	7 (8.5)	(0.3-16.1)	
Residence in a nursing home				
Yes	6(100.0)	0 (0.0)	-	1.00
No	89 (91.8)	8 (8.2)		
Re-hospitalization in the preceding 90 days				
Yes	31 (96.9)	1 (3.1)	3.4	0.43
No	64 (90.1)	7 (9.9)	(0.4 – 28.8)	
Blood filtration in the preceding 90 days				
Yes	7 (100.0)	0 (0.0)	-	1.00
No	88 (91.7)	8 (8.3)		
Immunodeficiency				
Yes	6 (100.0)	0 (0.0)	-	1.00
No	88 (91.8)	8 (8.2)		
Broad-spectrum antibiotics used before				
Yes	51 (98.1)	1 (1.9)	8.1	0.031
No	44 (86.3)	7 (13.7)	(0.96 – 68.5)	

Abbreviations: HAP, hospital-acquired pneumonia; MDR, multi-drug resistant; OR, odds ratio; CI, confidence interval.

The increase and color change of sputum usually indicates the causes of HAP, which are bacteria. The increase was observed in 82 cases (86.3%). The most common color is off-white (41.1%), followed by yellow (32.6%) and green (12.6%) (Table 2). Our result is comparable to that of the research in Vietnam (with the proportion of the first two kinds is 47.7% and 36.4%, respectively)¹¹. This change is a crucial clinical symptom in HAP diagnosing⁶.

Fever is another clinical symptom, but in our research, this symptom appeared in 63% of patients, with more than 58% of cases have body temperature above 38.5 °C (Table 2). The figure for hyperthermia was slightly lower than other studies. This may be related to the characteristics (i.e., old age) of our study population. The elderly with a degradative health condition and using prior combined antibiotic therapy might not present fever symptoms, sometimes experienced hypothermia.

Table 2. The features of fever and sputum symptom in HAP patients

Features	Number of patients (n=95)	Percentage (%)	Notes
Temperature			Mean ± SD: 38.2°C ± 1.06 SD
Hyperthermia (≥38 oC)	60	63.2	Lowest temperature: 36.5°C
No fever	35	36.8	Highest temperature: 40°C
Increase of sputum			
No	13	13.7	
Yes	82	86.3	
<i>Off-white</i>	39	41.1	
<i>Yellow</i>	31	32.6	
<i>Green</i>	12	12.6	

Abbreviations: SD, standard deviation.

3.2. The proportion of antibiotic-resistant bacteria

Of 107 isolated bacteria causing HAP, the percentage of MDR bacteria was 92.5% and the rest was non-MDR bacteria. Gram-negative bacteria accounted for the largest proportion of MDR bacteria (95%; Table 3). This high rate of gram-negative bacteria was similar to that of other

Vietnam's researches¹³⁻¹⁵.

Out of the 99 MDR bacteria, *Acinetobacter baumannii* accounted for the highest proportion of 47.5%. The percentage of *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *E. coli* was 16.2%, 12.1%, and 10.1%, respectively. *Staphylococcus aureus* is the only gram-positive bacteria that accounted for a low proportion (5.05%) (Table 4).

Table 3. The percentage of isolated multiple-antibiotic-resistant bacteria

Variable	Frequency (n)	Percentage (%)
MDR bacteria	99	92.5
Gram-negative bacteria	94	95
Gram-positive bacteria	5	5
Non-MDR bacteria	8	7.5
Total	107	100

Abbreviations: MDR, multi-drug resistant.

Table 4. The percentage of multiple antibiotic resistance based on classes of bacteria

Strains of isolated bacteria	MDR		Non-MDR	
	n	%	n	%
<i>Staphylococcus aureus</i>	5	100.0	0	0.0
Total of gram-positive bacteria	5	100.0	0	0.0
<i>Acinetobacter baumannii</i>	47	100.0	0	0.0
<i>E. coli</i>	10	90.9	1	9.1
<i>Klebsiella pneumonia</i>	16	72.7	6	27.3
<i>Proteus spp</i>	2	100.0	0	0.0
<i>Pseudomonas aeruginosa</i>	12	92.3	1	7.7

Table 4. The percentage of multiple antibiotic resistance based on classes of bacteria (cont.)

Strains of isolated bacteria	MDR		Non-MDR	
	n	%	n	%
<i>Sphingomonas paucimobilis</i>	1	100.0	0	0.0
<i>Stenotrophomonas maltophilia</i>	2	100.0	0	0.0
<i>Enterobacter spp</i>	3	100.0	0	0.0
<i>Citrobacter freundii</i>	1	100.0	0	0.0
Total of gram-negative bacteria	94	92.2	8	7.8

Abbreviations: MDR, multi-drug resistant.

3.2.1. The antibiotic resistance of *Acinetobacter baumannii*

The current study found that all of isolated *Acinetobacter baumannii* strains resisted to carbapenems, third-and-fourth-generation cephalosporins, and second-and-third-generation fluoroquinolones. In addition, all samples were resistant to several common antibiotics: combination of penicillin/beta-lactamase inhibitors (over 95%), aminoglycosides (78-85%), and co-trimoxazole (63.8%) (Table 5). Similarly, the resistance rate

to carbapenem, beta-lactam, cephalosporin was highly increasing according to other research in Vietnam¹¹. This may be related to the widespread use of broad-spectrum antibiotics in ICU patients.

The susceptibility rates to colistin in Can Tho and Ho Chi Minh City were more than 90% and 80%, respectively^{5,16}. In our study, colistin was the only drug that showed 100% sensitivity against all the species of *A. baumannii*, similar to research in ICU of Bach Mai Hospital that there was no emergence of colistin-resistant species reported¹⁷.

Table 5. The proportion of bacteria resistant to common antibiotics

Bacteria \ Antibiotics*	<i>Acinetobacter baumannii</i>	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	<i>E. coli</i>	<i>Staphylococcus aureus</i>
Amikacin	78.7	75	66.7	30	80
Gentamicin	83	75	91.7	40	60
Tobramycin	85.1	87.5	83.3	50	60
Ampi/Sul	100	75	75	70	-
Cefepime	100	87.5	83.3	80	80
Cefotaxime	100	-	100	-	-
Ceftriaxone	100	81.2	91.7	90	-
Ceftazidime	100	87.5	83.3	90	-
Piper/Tazo	97.9	75	75	80	-
Ticar/Clavu	95.8	81.2	91.7	100	-
Imi/Cilastatin	100	43.8	50	40	100
Meropenem	100	43.8	50	30	100
Co-trimoxazole	63.8	87.5	-	70	-
Colistin	0	18.2	16.7	0	-
Ciprofloxacin	100	62.8	83.3	70	100
Levofloxacin	100	62.5	75	90	80
Ampicillin	-	100	-	-	-
Tigecycline	-	0	-	0	0

Table 5. The proportion of bacteria resistant to common antibiotics (cont.)

Bacteria Antibiotics*	<i>Acinetobacter baumannii</i>	<i>Klebsiella pneumonia</i>	<i>Pseudomonas aeruginosa</i>	<i>E. coli</i>	<i>Staphylococcus aureus</i>
Ertapenem	-	-	16.7	40	-
Amox/Clavu	-	-	-	-	80
Clindamycin	-	-	-	-	-
Oxacillin	-	-	-	-	80
Vancomycin	-	-	-	-	20
Nelitimicin	-	-	-	-	0
Linezolid	-	-	-	-	0
Teicoplanin	-	-	-	-	0

Abbreviations: Ampi/Sul, ampicillin and sulbactam; Piper/Tazo, piperacillin and tazobactam; Ticar/Clavu, ticarcillin and clavulanate; Imi/Cilastatin, imipenem and cilastatin; Amox/Clavu, amoxicillin and clavulanate.

*The isolated bacteria were assessed for their susceptibility to all suitable antibiotics available at the study hospital. All antibiotic agents appropriate for each type of bacteria isolated are shown in Table 5.

3.2.2. The antibiotic resistance of *Klebsiella*

The study demonstrated that *Klebsiella* was virtually resistant to broad-spectrum antibiotics: ampicillin (100%), third-and-fourth-generation cephalosporins (over 80%), a combination of penicillin/beta-lactamase inhibitors, e.g., piperacillin/tazobactam (75%), ticarcillin/clavulanic (81,2%) (Table 5). Our research revealed that the cephalosporin and carbapenem resistance rate was higher than when compared to the research conducted in Asia and Europe^{4,18}. These geographic differences in the rates of resistance may be in connection with national income, healthcare management systems and different patterns of antibiotic use.

Extended-spectrum β -lactamase (ESBL)-producing *Klebsiella* was reported that having a cross-resistance between aminoglycoside and fluoroquinolone. This becomes a severe worldwide concern. Thus, carbapenem was a suitable choice for severe sepsis caused by ESBL-producing bacteria. However, *K. pneumonia* was highly resistant to carbapenem (nearly 50%) when compared to it across Vietnam⁴. We couldn't explain a paradox that non-ESBL-producing *Klebsiella* rate was 68.7%, it had low sensitivity to imipenem and meropenem (lower than 50%). To answer, we need the genetic analysis of pathogenic bacteria in the future.

3.2.3. The antibiotic resistance of *Pseudomonas aeruginosa*

Pseudomonas aeruginosa ranked 3rd (92.3%)

in the microbiological isolation results of our study (Table 5). A high prevalence of *Pseudomonas aeruginosa* resistant to third-and-fourth-generation cephalosporins, second-and-third-generation fluoroquinolones (over 83%), and carbapenems (50%) was reported. Similar to a research in LMICs generally and in Vietnam particularly, the carbapenem resistance rate was 41% and 55.7%, respectively^{1,4}. Previously, the imipenem resistance rate in India was only approximately 10% and was having upward trends in resistance rate in either imipenem and cefoperazone-sulbactam, tazobactam, amikacin¹⁹. The sharply increased in resistance rates were reported as a result of antibiotic abuse, inappropriate antibiotic use strategies, and genetic mutation. Notably, all of the *Pseudomonas aeruginosa* strains were resistant to cefotaxime (100%). Only a small fraction was resistant to all tested antibiotics.

3.2.4. The antibiotic resistance of *E. coli*

Similar to *Klebsiella*, *E. coli* is one of the common ESBL-producing strains. A high percentage of resistance to common antibiotics was found in the *E. coli* strains: third-and-fourth-generation cephalosporins (80 – 90%), and second-and-third-generation fluoroquinolones (over 70%). *E. coli* was also resistant to the combination of penicillin/beta-lactamase inhibitors with the proportion of 80%. The present study showed a higher resistance rate of *E. coli* in comparison with the result from the study in Vietnam¹⁴. In that study, *E. coli* was

virtually resistant to cephalosporins, fluoroquinolones (over 71%) and was susceptible to the combination of penicillin/beta-lactamase inhibitors (e.g., piperacillin/tazobactam, ticarcillin/clavulanic) with the rate of 53%.

Notably, *E. coli* was susceptible to tigecycline and colistin (resistance rate was 0%) (Table 5), as same as what they found in Nepal²⁰. The cephalosporin and carbapenem resistance in our study was quite similar to that in Asia. (77% and 27%, respectively)⁴. The present study showed a similar resistance rate of *E. coli* in comparison with the result from the study of India, except for cephalosporin and carbapenem resistance rate¹⁹. In that study, the resistance rate was nearly 30% for ceftazidime and more than 10% for imipenem.

3.2.5. The antibiotic resistance of *Staphylococcus aureus*

Although *Staphylococcus aureus* strains accounted for a low proportion of MDR-bacteria (5%) (Table 4), the bacteria were virtually resistant to common antibiotics (e.g., amoxicillin/clavulanic, cefepime, oxacillin). This high rate (80%) was

similar to other studies in Vietnam, in India and Asian countries^{7,15,19,21}. However, there was an downward trend in resistance during 3 years. Our result was also consistent with the spread of antibiotic resistance in Asian countries. The MDR rate was 83.7%. We found that all of the *Staphylococcus aureus* strains were sensitive to teicoplanin, linezolid, and tigecycline (Table 5). The resistance rates to almost antibiotics were high, but totally sensitive to vancomycin and teicoplanin²¹.

3.3. The treatment results' assessment

The results were assessed at the end of antibiotic treatments and classified into three groups. Group I was improvement cases using the initial antibiotics, group II was the number of recovered patients with alternative antibiotics, and the rest was no recovered cases, including failure cases with initial or alternative antibiotics. The figures for group II and group III were higher, at 34.7% and 35.8%, respectively. The success rate of treatment for HAP caused by MDR bacteria accounted for only 49.5% (Table 6).

Table 6. Clinical improvement status with alternative antibiotics and the treatment results of HAP patients

Results	Number of patients (n = 95)	Percentage (%)
Clinical status		
Recovered (no alteration)	28	29.5
Recovered	33	34.7
No recovered	34	35.8
Treatment results		
Success	47	49.5
Failure	48	50.5

HAP's assessment and treatment are complicated tasks. The treatment must be taken immediately after clinical diagnosing based on patient's conditions. From the results of the clinical and paraclinical assessments, the proportion of recovered patients without changing antibiotics was 29.5% (Table 6). By contrast, 34.7% of patients recovered after alteration and the rest had degenerative clinical symptoms due to baseline or respiratory diseases, e.g., septic shock. Identical with other research from Chung, Luna et al., and Alvarez-Lerma, our results indicated inappropriate initial

antibiotic treatment leads to higher fatal rate²²⁻²⁴.

3.4. Limitations and strengths

Our research has several limitations as follows. Firstly, the sample size was modest because the study was conducted in a local hospital; in addition, some cases were not recorded due to hospital referral or giving up treatment. We suggest that future research should be based on larger sample size and hence may take more years to complete. Lastly, in the disk diffusion test, only

a few millimeters of difference in zone diameter separating susceptible from resistant strains resulted in a potentially ambiguous reading. Therefore, the experiment was conducted repeatedly to minimize the error rate. We suggest another testing method, in particular, minimum inhibitory concentration (MIC), should be applied for a better result.

One of the strengths is that our method (i.e., descriptive cross-sectional study) was appropriate to comprehend the MDR bacteria and influential factors in HAP at local scale. This method was used to figure out the predominant characteristics in a population at a specific period and provide an overall correlation between the incidence of HAP and risk factors that might exist. Besides, our method could be conducted in a short period of time with minimal resources, which is suitable for testing a new research hypothesis and paving the way for further experimental study. Finally, investigating the antibiotic resistance and clinical characteristics of HAP patients simultaneously provided practical and constructive information for medical practitioners as an internal guideline.

3.5. Clinical application and future research

Antimicrobial therapy plays an essential role in HAP treatment. Hence, grasping the resistance rate of bacteria in a specific community is necessary to initiate community-specific antibiotic treatment strategies. In fact, early and appropriate empirical antibiotic therapy is associated with an improvement in treatment outcomes and reduction in mortality. As an internal guideline, our research will guide the clinicians in choosing appropriate antibiotic strategies for the emergency treatment of severe sepsis. Because there was no record of colistin-resistant bacteria, colistin usage or colistin-tigecycline combined therapy are potential treatments for MDR HAP in the future.

4. CONCLUSIONS

In conclusion, these data suggested that coughing up sputum and the color change were crucial clinical symptoms in HAP diagnosing. Notably, the results of this study indicated an increasing

trend in common antibiotic resistance of the *Acinetobacter baumannii* and *Pseudomonas aeruginosa* species, which are the major causes of MDR HAP. Aminoglycosides, cephalosporins, fluoroquinolones, and the combination of penicillin/beta-lactamase inhibitors were drastically ineffective.

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Conflict of interest

There are no interest conflicts during the study of this research.

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