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Clinical and microbiological evaluation of ventilator-associated pneumonia in an intensive care unit in Vietnam

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SUMMARY

Background: The increasing incidence of multidrug-resistant Gram-negative bacteria causing ventilator-associated pneumonia (VAP) is a global concern. A better understanding of the epidemiology of VAP in Southeast Asia is essential to optimise treatments and patient outcomes.

Methods: VAP epidemiology in an intensive care unit in Vietnam was investigated. A prospective cohort study was conducted. Patients who were ventilated for >48 hours, diagnosed with VAP, and had a positive respiratory culture between October 2015 and March 2017 were included. Whole-genome sequencing (WGS) was performed on *Acinetobacter baumannii* isolates.

Results: We identified 125 patients (137 episodes) with VAP from 1,699 admissions. Twelve patients had 2 VAP episodes. The median age was 60 years (interquartile range: 48—70), and 68.8% of patients were male. Diabetes mellitus was the most frequent comorbidity (*N*=35, 28%). *Acinetobacter baumannii* was most frequently isolated in the first VAP episode (*N*=84, 67.2%) and was multiply resistant to meropenem, levofloxacin, and amikacin.

Abbreviations: AMK, Amikacin; ATM, Aztreonam; FEP, Cefepime; CMZ, Cefmetazole; CAZ, Ceftazidime; CRO, Ceftriaxone; CST, Colistin; DOR, Doripenem; GEN, Gentamicin; LVX, Levofloxacin; MER, Meropenem; MIN, Minocycline; TZP, Piperacillin-tazobactam; TOB, tobramycin; SXT, Trimethoprim-sulfamethoxazole.

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The 30-day mortality rate was 55.2% (*N*=69) and higher in patients infected with *A. baumannii* (*N*=52, 65%). WGS results suggested a complex spread of multiple clones.
Conclusions: In an intensive care unit in Vietnam, VAP due to *A. baumannii* had a high mortality rate, and *A. baumannii* and *K. pneumoniae* were multidrug resistant, with carbapenem resistance of 97% and 70%, respectively.

Introduction

Ventilator-associated pneumonia (VAP) is one of the most common infections affecting patients in intensive care units (ICUs) [1] and is associated with increased mortality [2,3]. During the COVID-19 pandemic, the importance of intensive care management in ICUs increased, as did the frequency of VAP [4].

Microorganisms known to cause VAP include aerobic Gram-negative rods such as *Klebsiella pneumoniae* (*K. pneumoniae*) and *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), and *Acinetobacter baumannii* (*A. baumannii*), and Gram-positive cocci such as methicillin-resistant or susceptible *Staphylococcus aureus* [5]. The incidence of multidrug-resistant (MDR) Gram-negative bacteria causing VAP is increasing and is an emerging global concern [6]. In the Southeast Asian region (excluding Vietnam), an increased prevalence of multidrug-resistant (MDR) *E. coli* and *K. pneumoniae* was reported by WHO, compared to other areas [7]. MDR *A. baumannii* healthcare-associated infections are also increasing in this region [8]. Despite the significant burden posed by healthcare-associated infections, including VAP, detailed clinical and microbiological characteristics of VAP in Southeast Asia are currently lacking [2].

As new antimicrobial agents against MDR bacteria become available [9], treatment options for VAP caused by MDR organisms are increasing. However, understanding the epidemiology of VAP in Southeast Asia is essential to identify and improve treatment strategies. Further characterisation of MDR organisms may also provide useful insights into the mechanisms of antimicrobial resistance, which could aid controlling the spread of MDR organisms. This study aims to identify the clinical, epidemiological, and microbial characteristics of VAP in an ICU in Vietnam before the COVID-19 pandemic.

Methods

Study design and patient population

We conducted a prospective cohort study at Bach Mai Hospital (BMH), Hanoi, Vietnam, between 1st October 2015, and 31st March 2017. BMH has 2000 beds and is a tertiary care hospital. The study was approved by the BMH institutional review board. Adult patients (aged 18 years and over) who were admitted to the ICU, received mechanical ventilation for >48 hours, and were diagnosed with VAP were included in the study. Patients with multiple VAP episodes (episodes >7 days apart) caused by different organisms were counted separately. Patients without a positive respiratory culture were excluded.

VAP was diagnosed based on chest X-ray findings, clinical signs and symptoms, and respiratory culture results according to the National Healthcare Safety Network (NHSN) criteria and multiple physicians' evaluations [10]. Organisms were considered as "causative organisms" if isolated from respiratory samples (sputum and bronchoalveolar lavage) or blood without any other foci of infection.

Microbiology

The identification and susceptibility testing of clinical isolates was performed at the centralised microbiology laboratory at BMH. Strains were collected during two periods: from October 2015 to May 2016 (1st period) and from July 2016 to March 2017 (2nd period). Bacterial isolates were further investigated at the clinical microbiology research laboratory of the National Center for Global Health and Medicine, Tokyo, Japan. Minimal inhibitory concentrations (MICs) of bacterial isolates were determined by broth microdilution (BMD) as per Clinical and Laboratory Standards Institute criteria [11]. BMD to determine colistin MIC was performed as follows. The strains were cultured overnight in a liquid medium (tryptone soya broth, Kanto Chemical Co. Ltd., Tokyo, Japan). The culture medium was adjusted to McFarland No. 0.5 with 0.85 % NaCl solution and diluted 10 times. The diluted solution (5 μL) was inoculated into 96-well plates containing 100 μL of Mueller Hinton broth II (cation-adjusted) (Becton Dickinson, Tokyo, Japan) and various concentrations of colistin. A colistin MIC of >2 μg/mL was defined as resistant [12]. *E. coli* ATCC 25922 (0.25–0.5 mg/L) and *E. coli* NCTC 13846 were used as control strains to verify assay accuracy.

Several different methods of colistin susceptibility testing for *A. baumannii* and *K. pneumoniae* were evaluated by comparison with BMD, including the MicroScan WalkAway system (Beckman Coulter Inc, Tokyo, Japan), C323 Panel Broth microdilution method (Kyokuto Pharmaceuticals, Tokyo, Japan), BC Plate (EIKEN Chemical Co., Ltd., Tokyo, Japan), Etest (BioMérieux Japan, Tokyo, Japan), and disk diffusion methods (colistin 10 μg, BD Sensi-disc, Becton, Dickinson, Tokyo, Japan). A "very major" categorical error was defined as an event in which isolates were susceptible to colistin in each of the evaluated test methods but resistant using BMD. A "major" categorical error was defined as an event in which isolates were resistant to colistin in each of the evaluated test methods but susceptible using BMD.

Whole-genome sequencing (WGS) and data analysis

WGS was conducted for *A. baumannii* isolates only. Molecular analysis was conducted at the Pathogenic Microbe Laboratory, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan. The strains were cultured overnight in Luria–Bertani broth (Nacalai Tesque, Kyoto, Japan),

and genomic DNA was purified using a DNeasy Blood & Tissue Kit (Qiagen, Venlo, Netherlands). The DNA samples were subjected to MiSeq sequencing using Nextera XT Library Prep kits (Illumina, San Diego, CA), according to the manufacturer's instructions. Approximately 1 million paired-end reads (301 bp × 2) were obtained for each sample and were analysed using the CLC Genomics Workbench software (CLC Bio, Aarhus, Denmark).

Low-quality reads (quality score < 0.05; reads that contained more than two ambiguous nucleotides or reads <15 bp in length) were removed [13]. De novo contig assembly and single-nucleotide polymorphism (SNP) calling were performed using CLC Genomics Workbench. The contigs were analysed using the BLAST algorithm [14]. Using ResFinder [15], drug-resistance genes in the genomes were identified based on a >90% sequence identity, and the distribution of acquired drug-resistance genes was determined. Nucleotide sequences corresponding to the multilocus sequence typing (MLST) allelic profile (cpn60, fusA, gltA, pyrG, recA, rplB, rpoB) were downloaded from EnteroBase (http://mlst.warwick.ac.uk/mlst/) and compared to the WGS data using BLAST [14].

Data collection

The following parameters were retrieved from the patient's medical records: demographics, background conditions, comorbid conditions, immunocompromised status, recent healthcare-associated exposures, polymicrobial isolation; parameters regarding treatment and outcomes, including 7-day and 30-day mortality, and length of ICU stay.

Definition

Multidrug-resistant organisms (MDRO) were defined as previously reported [16]. *Stenotrophomonas maltophilia* (*S. maltophilia*) was included in the MDRO category [9].

Statistical analysis

All analyses were performed using SPSS® 20 (IBM, Armonk, NY). Univariate analyses were performed using Fisher's exact test, the Chi-square test for categorical variables, and the Mann–Whitney U test for continuous variables. All *P*-values were two-sided; $P<0.05$ was considered significant.

Ethical approval

The study was approved by the Bach Mai Hospital institutional review board (Approval No. 38).

Results

Summary of the study cohort

Out of a total of 1,699 ICU admissions during the 18-month study period (i.e., 73.6 patients [80.6 episodes]/1,000 ICU admissions), we identified 125 patients (137 episodes) with VAP. Twelve patients had two episodes of VAP.

Patient characteristics

The characteristics of the patients with VAP (*N*=125) are summarised in Supplementary Table I. The median age was 60 (interquartile range: 48–70), and 68.8 % (*N*=86) of the patients were male. Most patients (74.4 %) had at least one comorbidity before ICU admission. Diabetes mellitus was the most common comorbidity (*N*=35, 28 %), followed by chronic cardiac disease (*N*=31, 24.8 %) and chronic kidney disease (*N*=17, 13.6 %). *A. baumannii* was the most frequent species detected in respiratory samples in the first episode (*N*=84, 67.2 %), followed by *K. pneumoniae* (*N*=21, 16.8 %) and *P. aeruginosa* (*N*=17, 13.6 %) (Table I). In the second episode, *P. aeruginosa* and *S. maltophilia* were the most frequently detected species. Gram-positive bacteria were detected less frequently. The 7-day and 30-day mortality rate was 48 % (*N*=60) and 55.2 % (*N*=69), respectively.

Antimicrobial susceptibility of the bacterial isolates associated with VAP

A. baumannii isolates demonstrated poor susceptibility to beta-lactam antibiotics, including carbapenems and levofloxacin (Table II). Susceptibility to amikacin and sulfamethoxazole/trimethoprim was 8.2 and 35.3 %, respectively. Susceptibility to minocycline and colistin remained at 74.1 and 100 %, respectively. No significant change in susceptibility was observed between the 1st and 2nd periods of the study. *K. pneumoniae* susceptibility to meropenem and cefmetazole was approximately 30 %, whereas levofloxacin susceptibility was low, at 4.3 %. Susceptibility to colistin was 87 %, and amikacin susceptibility was the highest at 91.3 %. *P. aeruginosa*

Table I
Bacterial isolates from respiratory samples of the patients with ventilator-associated pneumonia (VAP)

Bacterial isolates from respiratory samples	N (%)
1st episode	
Acinetobacter baumannii	84 (67.2%)
Klebsiella pneumoniae	21 (16.8%)
Pseudomonas aeruginosa	17 (13.6%)
Stenotrophomonas maltophilia	7 (5.6%)
Escherichia coli	4 (3.3%)
Serratia marcescens	2 (1.6%)
Enterobacter cloacae	2 (1.6%)
Enterococcus faecalis	1 (0.8%)
Methicillin-sensitive *Staphylococcus aureus*	1 (0.8%)
Methicillin-resistant *S. aureus*	1 (0.8%)
Elizabethkingia meningoseptica	1 (0.8%)
Polymicrobial isolation	15 (12%)
2nd episode	
A. baumannii	1 (0.8%)
K. pneumoniae	2 (1.6%)
P. aeruginosa	4 (3.3%)
S. maltophilia	4 (3.3%)
S. marcescens	1 (0.8%)
Elizabethkingia meningoseptica	1 (0.8%)
Methicillin-resistant *S. aureus*	1 (0.8%)
Polymicrobial isolation	3 (2.4%)

Table II
Antimicrobial susceptibility of bacterial isolates in ventilator-associated pneumonia (VAP)

	TZP	CRO	CAZ	FEP	CMZ	ATM	DOR	MEM	GEN	TOB	AMK	MIN	LVX	SXT	CST[a]
A. baumannii	-	-	1	1	-	-	1	3	3	5	7	63	1	30	85
(N=85)			(1.2%)	(1.2%)			(1.2%)	(3.5%)	(3.5%)	(5.9%)	(8.2%)	(74.1%)	(1.2%)	(35.3%)	(100%)
1st period[b]	-	-	0	0	-	-	0	0	0	2	3	30	0	17	37
(N=37)										(5.4%)	(8.1%)	(81%)		(45.9%)	(100%)
2nd period[b]	-	-	1	1	-	-	1	3	3	3	4	33	1	13	48
(N=48)			(2.1%)	(2.1%)			(2.1%)	(6.3%)	(6.3%)	(6.3%)	(8.3%)	(68.8%)	(2.1%)	(27.1%)	(100%)
K.pneumoniae	2	1 (4.3%)	1	2	7 (30.4%)	1	-	7	14	-	21	-	1	-	20
(N= 23)	(8.7%)		(4.3%)	(8.7%)		(4.3%)		(30.4%)	(60.9%)		(91.3%)		(4.3%)		(87%)
P. aeruginosa	14	-	11	11	-	8	10	8	9	10	11	-	10	-	21
(N=21)	(66.7%)		(52.4%)	(52.4%)		(38.1%)	(47.6%)	(38.1%)	(42.9%)	(47.6%)	(52.4%)		(47.6%)		(100%)
S. maltophilia	-	-	1	-	-	-	-	-	-	-	-	12	12	12	-
(N=12)			(8.3%)									(100%)	(100%)	(100%)	

Data are presented as the number (%) of susceptible isolates according to CLSI criteria, as described in the Methods.
[a] Colistin susceptibility was calculated based on intermediate (as there is no standard for susceptibility) using the broth microdilution method (BMD). BMD to determine colistin MIC was performed as follows. The strains were cultured overnight in a liquid medium (tryptone soya broth, Kanto Chemical Co. Ltd., Tokyo, Japan). The culture medium was adjusted to McFarland No. 0.5 with 0.85% NaCl solution and diluted ten times. The diluted solution (5 μL) was inoculated into 96-well plates containing 100 μL of Mueller Hinton broth II (cation-adjusted; Becton Dickinson, Tokyo, Japan) and various concentrations of colistin. A colistin MIC of >2 μg/mL were defined as resistant (WHO, 2021).
[b] 1st period: October 2015 to May 2016, 2nd period: July 2016 to March 2017.

susceptibility to piperacillin/tazobactam and cephalosporins with anti-*P. aeruginosa* activity was higher than its susceptibility to carbapenems. Susceptibility to levofloxacin and colistin was 47.6 and 100 %, respectively. *S. maltophilia* showed high susceptibility to all therapeutic options other than ceftazidime (8.3 %).

Comparison of patients with and without MDRO

Eighty-three (97.6%) *A. baumannii*, 22 (95.7%) *K. pneumoniae*, and 12 (57.1%) *P. aeruginosa* isolates met the definition of MDRO. In total, 105 (84%) patients were detected with one or more of these organisms. *S. maltophilia* was detected in 6 of the 20 patients in whom MDR-*A. baumannii*, MDR-*K. pneumoniae*, or MDR-*P. aeruginosa* was not detected. In addition, four patients were found to have Enterobacterales that met the MDRO definition (*Escherichia coli*: 2, *Enterobacter cloacae*: 1, *Serratia marcescens*: 1) and one patient was detected with methicillin-resistant *Staphylococcus aureus* meeting the MDRO definition. In total, 115 patients were categorised in the MDRO group.

Patients without MDRO tended to have more alcoholism and malignancies, especially haematologic malignancies, than patients with MDRO. However, other characteristics and prognoses were not significantly different (Table III).

Comparison of different methods of colistin susceptibility testing for A. baumannii and K. pneumoniae

The drug susceptibility results revealed a limited number of drugs other than colistin that can be expected to be effective against *A. baumannii* and *K. pneumoniae*. We compared the results of colistin susceptibility testing using different assays (Supplementary Table II). The MIC of *A. baumannii* was slightly higher when using the MicroScan and C323 panels and lower when using the E-test than when using BMD. As for *K. pneumoniae*, major category errors were detected in 8.7 % of the C323 panel tests, and very major category errors in 4.3 % of the E-test and disk methods.

Empirical VAP treatment with antimicrobial agents with activity against Gram-negative bacteria

As MDR Gram-negative organisms accounted for most VAP events in this cohort, antimicrobial agents with activity against Gram-negative organisms were frequently used as empiric VAP therapy (Supplementary Table III). Glycopeptide antimicrobials such as vancomycin and teicoplanin were used as empiric agents against MDR Gram-positive bacteria in 26 (20.8%) patients, and linezolid was used in two patients. Colistin-containing regimens were used in 43 (34.4%) patients, mostly as part of a two-drug combination with a carbapenem (20.8 %, *N*=26). Treatment regimens containing amikacin without colistin were used in 7 (5.6 %) patients, and a combination with carbapenem was the most commonly used. Treatment regimens containing carbapenem without amikacin or colistin were used in 49 (39.2%) patients. Treatment regimens containing fluoroquinolone without amikacin, colistin, or carbapenem were used in 7 (5.6%) patients, and an antipseudomonal

Table III
Comparison of characteristics of the patients with ventilator-associated pneumonia with and without multidrug-resistant organisms (MDRO)

	Patients with MDRO (*N*=115)	Patients without MDRO (*N*=10)	*P*-value
Demographics			
Age (years), median (IQR)	60 (48–71)	55 (47–64)	0.310
Male	79 (68.1%)	7 (77.8%)	0.719
Healthcare-associated risk prior to hospitalisation	95 (83.3%)	8 (88.9%)	>0.999
Home therapy within 1 month	32 (28.1%)	3 (33.3%)	0.713
Hemodialysis or chemotherapy within 1 month	72 (63.2%)	6 (66.7%)	>0.999
Hospitalisation within 3 months	81 (71.1%)	7 (77.8%)	>0.999
Nursing home residence	3 (2.6%)	1 (11.1%)	0.265
Two episodes of VAP	12 (10.3%)	0	0.598
Comorbidities			
Diabetes mellitus	34 (29.3%)	1 (11.1%)	0.443
Chronic kidney disease	17 (14.7%)	0	0.609
Chronic heart disease, including ischemic heart disease	31 (26.7%)	0	0.111
Chronic obstructive pulmonary disease	13 (11.2%)	0	0.596
Cerebrovascular disease	12 (10.3%)	1 (11.1%)	>0.999
Hypertension	13 (11.2%	0	0.596
Cirrhosis	6 (5.2%)	2 (22.2%)	0.103
Alcoholism	4 (3.4%)	3 (33.3%)	0.008
Connective tissue disease/autoimmune disease	6 (5.2%)	0	>0.999
Haematologic malignancy	3 (2.6%)	2 (22.2%)	0.041
Solid malignancy	6 (5.2%)	1 (11.1%)	0.415
Any malignancy	9 (7.8%)	3 (33.3%)	0.041
Use of steroids within 1 month	7 (6%)	0	>0.999
Immunocompromised status	12 (10.3%)	3 (33.3%)	0.076
Outcomes			
Median length of ICU stay after VAP (days, IQR)	8 (2–15)	11 (3–19)	0.818
Median length of ICU stay after VAP excluding deaths within 7 days (days, IQR)	8 (2–15)	3 (2-NA)	0.582
7-day mortality	54 (47.4%)	6 (66.7%)	0.316
30-day mortality	64 (59.3%)	5 (55.6%)	>0.999

cephalosporin was the treatment of choice in 7 (5.6 %) patients.

Comparison of 30-day mortality for bacteria causing VAP

Patients infected with *A. baumannii* tended to be approximately 1.4 times more likely to die within 30 days than those infected with other species (Supplementary Table IV) (*N*=52, 65% vs. *N*=17, 45.9%); however, the difference was not statistically significant (*P*=0.069). There was no tendency toward higher mortality in patients infected with *K. pneumoniae*, *P. aeruginosa*, or *S. maltophilia*.

Relationships between A. baumannii isolates and distribution of drug resistance genes based on WGS data

As *A. baumannii* was MDR and the prognosis of VAP patients infected with *A. baumannii* tended to be poor, we analysed *A. baumannii* strains isolated in the 1st period (*N*=37) for genetic relatedness and drug resistance genes using WGS (Supplementary Table V, Figure 1). First, the 37 isolated strains were classified into four sequence types based on MLST. Next, they were subdivided into 13 groups according to their drug resistance genes (Supplementary Table V), and then further subdivided based on common and unique SNPs (Figure 1). Even though SNP-based subgrouping did not reveal a single cluster, several smaller subgroups were closely related. Ac105 and Ac113 likely represented a mixture of at least two closely related strains. The drug resistance genes armA (89.1 %) and beta-lactamase encoding genes (TEM-1D, 86.5 %; OXA-23/66/166/169, 100 %; A1, 94.6 %; and A2, 100 %), mphE (91.9 %), and msrE (91.9 %) were highly prevalent.

Discussion

This study analysed the clinical, epidemiological and microbiological characteristics of VAP in an ICU in Vietnam. Although the epidemiological characteristics of VAP in Vietnam have been reported previously [17], to the best of our knowledge, this is the first report of detailed microbiological data.

We could not determine the incidence of VAP in the ICU based on ventilator days as we did not collect the denominator data. When calculated per admission, the incidence was 73.6 patients (80.6 episodes)/1,000 ICU admissions, which is higher

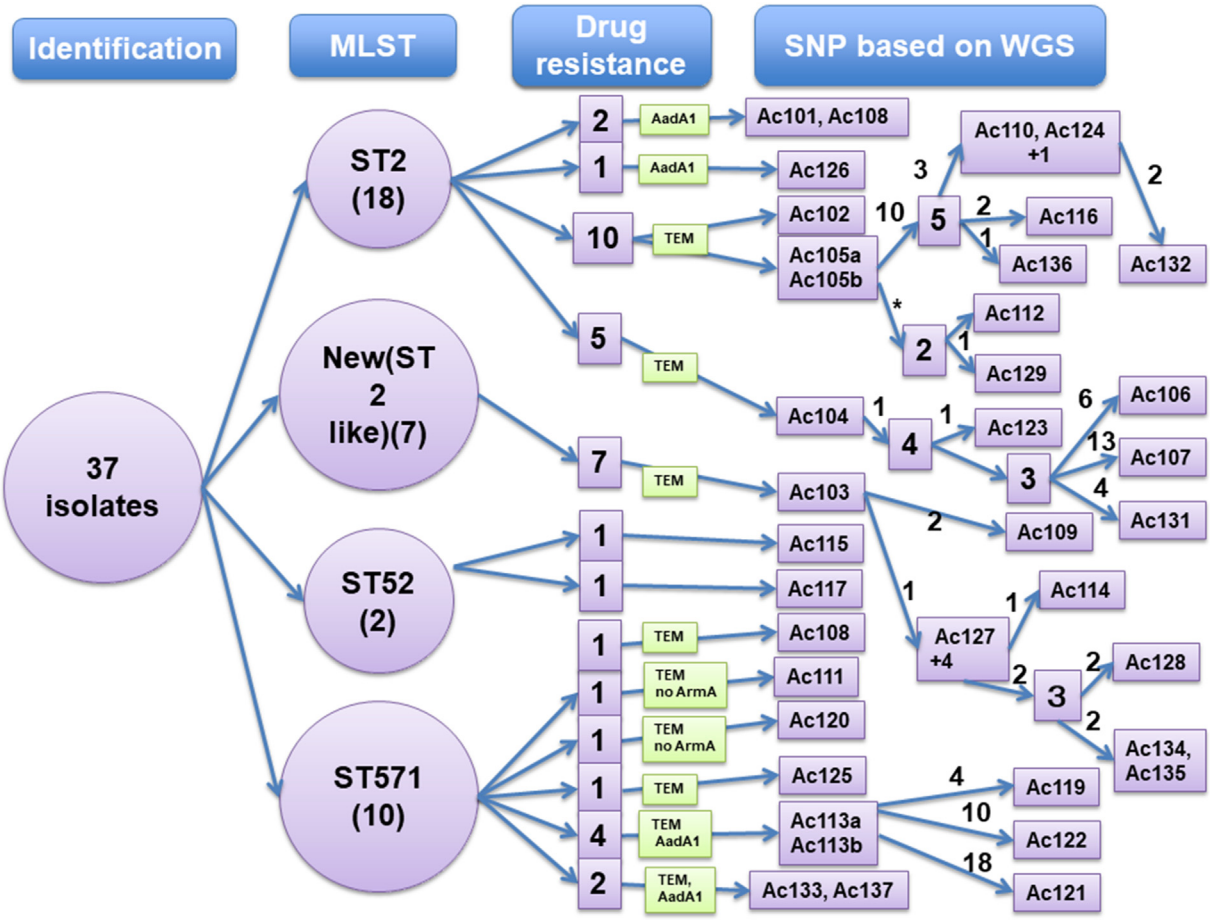

Figure 1. Genetic relatedness of the *A. baumannii* isolates in this study as determined by whole-genome sequencing (WGS). Thirty-seven strains isolated during the 1st term of the study were subdivided based on MLST, MLST plus drug resistance genes, and common and unique SNPs. The numbers above arrows at the branches under SNPs indicate the numbers of newly emerged SNPs. As for the branches from Ac105 to Ac112 and Ac129, the number of SNPs was too high to count and is therefore indicated as *.

than the incidence in Japan reported using the same denominator (about 13/1,000 admissions) [18]. The previously reported incidence of VAP in Vietnamese ICUs during 2013—2015 was 8.7/1,000 ventilator days (ventilator-associated respiratory infections, 21.7/1,000) [17], which was higher than that in the US in 2012 (1/1,000 ventilator days in medical teaching ICUs in acute care hospitals) [19], and that in Japan in 2009—2017 (3.3/1,000 ventilator days in critical care ICUs) [20]. However, it aligns with previous data from the Southeast Asian region (2.1—116/1,000 ventilator days) [21], and data from ICUs in Latin America, Europe, the Eastern Mediterranean region, Southeast Asia, and the Western Pacific region (13.1/1,000 ventilator days), reported by the International Nosocomial Infection Control Consortium (INICC) [22]. In this study, many individuals had a history of medical exposure before ICU admission. In addition to reducing the incidence in the ICU, infection control efforts outside the ICU are required to limit the acquisition of MDR bacteria.

Gram-negative bacteria, especially *A. baumannii*, *K. pneumoniae*, and *P. aeruginosa*, were the main causative organisms of VAP in our study, consistent with previous reports from Southeast Asia. [2,17,21]. *S. maltophilia* remained susceptible to levofloxacin, minocycline, and sulfamethoxazole/trimethoprim. The resistance rates of *P. aeruginosa* to carbapenems, amikacin, and fluoroquinolones were higher in this cohort than in other countries included in the INICC surveillance [22]. The carbapenem resistance rates of *A. baumannii*, *K. pneumoniae*, and *P. aeruginosa* were higher in this study than in the previous study of VAP in Vietnam [17].

Potential therapeutic interventions require precise determination of the colistin susceptibility of major causative organisms of VAP, especially highly drug-resistant *A. baumannii*. Even though BMD is the recommended method [12], it remains a challenge in resource-limited settings. Therefore, we evaluated variation in susceptibility results due to differences in the measurement methods. The E-test and disk method showed very major errors for *K. pneumoniae* when isolates were found to be susceptible when resistant. Our results are partially consistent with those reported for *A. baumannii* susceptibility by Arroyo *et al*. However, major inconsistensies between BMD and the E-test results were rare in their study [23]. The MIC tended to be lower in the E-test than in BMD in this study. Thus, care should be taken when interpreting colistin MICs obtained by the E-test.

The genetic relatedness of different *A. baumannii* strains, the major causative organism of VAP in this study, were evaluated using WGS and SNP analyses. The results suggested

complex molecular epidemiology with small-scale spread and mixing of multiple strains rather than a single clone spreading within the ICU.

In a previous study of VAP in the Southeast Asian region, mortality ranged from 16—74 %, which aligns with the mortality observed in this cohort (48%) [21]. The mortality rate of VAP due to *A. baumannii* in this cohort was 65%, which is higher than the all-cause mortality rate of VAP of 20—50% reported in the 2016 North American guidelines for managing adults with hospital-acquired and ventilator-associated pneumonia [24].

The contribution of MDR *A. baumannii* to increasing excess mortality has been reported previously [8]. The choice of empiric therapy involves complex decisions that consider the patient's background and organ damage. Carbapenem- and fluoroquinolone-based empiric regimens without amikacin or colistin were more likely to result in inadequate antimicrobial coverage. Therefore, regularly reviewing the antibiograms will be essential to guide treatment strategies considering locally available drugs in the future. The drug susceptibility results in our cohort suggest that minocycline may be an important treatment option, as previously reported [25]. In addition, novel antimicrobial agents, such as eravacycline and cefiderocol, might provide potential treatment options in the future.

This study had several limitations. First, VAP was diagnosed according to the NHSN criteria but the diagnosis may not have been 100% accurate. Secondly, we did not evaluate drug susceptibility to tigecycline, another therapeutic option for *A. baumannii*. Lastly, the study was not designed to compare the impact of interventions to decrease the incidence of VAP.

Conclusions

Even though the mortality of VAP in Vietnam is similar to the rates reported in previous studies with possible resource limitations, VAP due to *A. baumannii* had a particularly high mortality rate, and *A. baumannii* and *K. pneumoniae* were MDR.

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Authorship contribution statement

KH, NGB, and NO conceived the study. MN, DMP, and MLH contributed to the microbiological analysis, and TMA contributed to the WGS. NGB, DXC, PTT, PTPT, NQC, DVT contributed the data collection. KH drafted the original manuscript. All authors reviewed the manuscript draft and approved the final version of the manuscript.

Disclosure statement

The authors declare that there are no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.infpip.2023.100318.

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