

# Clinical characteristics and factors associated with diagnoses of ventilator and non-ventilator associated pneumonia in Intensive care unit

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## ABSTRACT

**Introduction:** Ventilator-associated pneumonia (VAP) is a significant cause of morbidity and mortality in ventilated patients in intensive care units (ICUs) worldwide. This study was conducted to identify the proportion, associated factors and outcomes of patients who developed VAP.

**Materials and Methods:** This was a retrospective, cross-sectional study involving 111 ventilated patients admitted to the ICU at Hospital Universiti Sains Malaysia (HUSM) from 1 April 2018 to 30 June 2019. The patients were categorised into VAP and non-VAP groups using the clinical scoring for VAP at the end of the stay in ICU. Logistic regression analysis was performed to determine the factors independently associated with VAP and its outcomes.

**Results:** Thirty-three patients were categorised into the VAP group and the remaining 77 patients were categorised into the non-VAP group. The proportion of patients who developed VAP was 30.0%. The VAP rate per 1000 people according to the Johansen, Clinical Pulmonary Infection Score (CPIS), and Center for Disease Control and Prevention (CDC) criteria were 6.9, 6.1 and 0.4, respectively. There was an association between duration of mechanical ventilation (MV; odds ratio [OR] = 1.22; 95% confidence interval [CI] 1.12, 1.34;  $p < 0.01$ ) and length of ICU stay (OR = 1.213; 95% CI 1.107, 1.32;  $p < 0.01$ ) and VAP. However, there was no difference in the patients between VAP and non-VAP groups in terms of mortality.

**Conclusion:** The VAP rate differs according to the diagnostic criteria. The factors associated with VAP in our centre were increased duration of MV and increased length of ICU stay. There was no difference in the mortality rate between the VAP and non-VAP groups.

## KEYWORDS:

*Ventilator-associated pneumonia; intensive care unit*

## INTRODUCTION

Ventilator-associated pneumonia (VAP) is one of the leading causes of healthcare-associated infection (HAI) in adult

intensive care units (ICUs) and is linked to increased ICU days, mechanical ventilation (MV) days and mortality.<sup>1,2</sup> However, while there have been many proposals for a definition of VAP, there is no consensus on the meaning of this term. Furthermore, a 'gold standard' guideline to diagnose VAP or test the accuracy of the current clinical scoring and parameters used is lacking.<sup>3</sup> A new term used for ventilation-associated lung infection that does not meet the VAP criteria is ventilator associated tracheobronchitis. This encompasses infection arising in the larynx, trachea, and bronchus.<sup>4</sup> However, the diagnosis, treatment and outcome are similar to VAP.<sup>4</sup>

As the mean duration of MV and hospital stay becomes longer in the VAP group of patients, the resource utilisation burden increases to almost 1.5-fold compared with patients who do not develop VAP.<sup>5</sup> Further studies on the incidence and risk factors of VAP can help physicians minimise VAP occurrence through the implementation of simple, economically safe preventive measures. Overall, the eradication of this preventable nosocomial infection would save lives and conserve health care resources.<sup>6</sup>

The aim of this study was to determine the proportion of various definitions of VAP throughout the study period in HUSM and comparing of clinical characteristics and associated factors of three different criteria in diagnosing ventilator associated pneumonia versus non - ventilator associated pneumonia in the ICU. The number depends on the formula used to calculate and types of definition used to diagnose VAP. The denominator used in our study consisted of patients who underwent MV days in the ICU per 1000 people. Indirectly, the results will reduce unnecessary antibiotic prescriptions, which may eventually lead to decrease in antibiotic resistance in HUSM.

## MATERIALS AND METHODS

This was a retrospective, cross-sectional study approved by the Medical Research and Ethics Committee (JEPeM) of USM (JEPeM Code: USM/JEPem/18040218). Patients aged 16 years and above who were intubated and requiring MV for at least 48 hours were included. A total of patients who were

*This article was accepted: 31 March 2021*

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admitted to the General ICU and Surgical ICU at HUSM from 1 April 2018 to 30 June 2019 were screened. The sample was then narrowed by selecting patients labelled as having pneumonia in the admission and discharge ICU medical record book. The patients were excluded from the study if their medical records could not be traced at the record office or the final diagnosis was community-acquired pneumonia. A precision of 4.5–5% with a significance level ( $\alpha$ ) 0.05 and 10% dropout was used to calculate the sample size for this study.

#### *Sampling method*

The participants were divided into VAP and non-VAP groups. A data collection sheet was used to collect and record the following information: demographic data, for example, ages, sex and clinical data, including the date of ICU admission; cause of admission (medical or surgical); associated comorbidities; primary diagnosis (the reason for initiation of ventilation); level of consciousness according to the Glasgow Coma Scale (GCS); duration of MV; length of ICU stay; occurrence of VAP; causative organisms of VAP; duration of antibiotic use (up to 48 hours before MV); positioning of patients (supine or semi-recumbent); re-intubation; requirement of non-invasive ventilation (NIV); tracheostomy; and the outcome (survival or death). VAP was defined based on clinical, radiological, and microbiological criteria as described in Clinical Pulmonary Infection Score (CPIS), Johansen and Center for Disease Control and Infection (CDC) criteria. VAP was considered if pneumonia occurred after 48 hours of MV to fulfil the criteria of various definitions in our study. Those who did not fulfil these criteria were assigned to the non-VAP group. Permissions were obtained from the director of HUSM and head of the ICU.

#### *Diagnostic criteria for VAP*

Diagnosis of VAP was made using three different clinical scores, namely, the CPIS, Johansen and CDC criteria for VAP.

#### *CPIS criteria*

In the CPIS, the diagnosis of VAP was made using clinical variables. This instrument uses a score of 0–2 for the ventilation-perfusion ratio, chest radiography, tracheal secretions, tracheal aspirate culture, temperature, and leucocytosis. The maximum score that could be obtained is 12, and a score  $> 6$  is diagnostic of VAP.<sup>7</sup>

#### *Johansen criteria*

According to the Johansen criteria, VAP can be diagnosed based on a new persistent infiltrate on a chest radiograph and at least two of the following: fever of  $\geq 38$  °C, leucopenia ( $<4000$  white blood cells [WBC]/mm<sup>3</sup>) or leucocytosis ( $\geq 12\,000$  WBC/mm<sup>3</sup>) and purulent respiratory secretions, worsening gas exchange ( $\text{PaO}_2/\text{FiO}_2 < 240$ ).<sup>8</sup>

#### *CDC criteria*

The CDC's new definition of VAP consists of a hierarchical approach that identifies ventilator-associated events (VAE). The first tier is a ventilator-associated condition (VAC). This is defined as the deterioration of respiratory function for 48 hours after a period of 48 hours of stability or improvement. Subsequent tiers are infection-related ventilator-associated complications (IVACs), defined as a temperature  $>38$  °C or  $<36$  °C or a white cell count  $>12\,000$  mm<sup>3</sup> or  $\leq 4000$  mm<sup>3</sup> and

one or more antibiotics started within 2 days before or after the onset of VAC and continuing for at least 4 days. The third tier is possible occurrence of pneumonia. The patient must fulfil the VAC and IVAC criteria with purulent secretion or positive culture. The last tier is probable pneumonia, in which both purulent secretion and positive culture are present.<sup>9</sup> The probable VAP criteria can also be met by positive pleural fluid culture, lung tissue with histological evidence of infection and positive diagnostic tests for Legionella or selected respiratory viruses.<sup>9</sup>

#### *Calculations of incidence*

The VAP incidence density was calculated as follows: (Number of cases with VAP/Number of ventilator days)  $\times$  1000 = VAP rate per 1000 ventilator days.<sup>9,12</sup>

#### *Data collection*

Data were collected using a data collection sheet that was prepared and filled in by the researcher once a patient had been identified. In the HUSM, a patient is followed up for 30 days via the hospital informative system after discharge from/death in the ICU or discharge from the hospital (based on the medical record and ICU chart of the patients).

#### *Data analysis*

Statistical analysis was performed using IBM SPSS version 24.0 statistical software. The quantitative variable was expressed as mean and standard deviation (SD), while qualitative data were presented as a number with a percentage. Continuous data were compared using the Student t-test or Mann–Whitney test as appropriate. A categorical variable was compared using the Chi-square test or Fisher's exact test. A logistic regression model was performed to determine factors independently associated with risk factors for developing VAP and the related outcomes. Variables with a  $p$ -value  $< 0.25$  in univariate analysis were subjected to the multivariate regression model. The adjusted odds ratio (OR) and 95% confidence interval (CI) were calculated. A double-sided  $p$ -value  $< 0.05$  was considered statistically significant.

## RESULTS

Of the total of 796 MV patients admitted to the ICU, a total of 156 patients with the diagnosis of pneumonia were considered for the study. Another 30 patients were excluded because they were found to have community-acquired pneumonia while the remaining 15 patients were excluded because their medical records could not be traced or there were incomplete data at the records office. Therefore, 111 patients were included in the final analysis. The total ventilator days for patients who were mechanically ventilated during the study period was 4589 days. The total mean duration of mechanical ventilator days was 5.7 days. There were 73 (66.7%) male patients and 37 (33.3%) females. The mean age of the patients was 53.94 years. The main causes of admission were surgical (65.8%), and others medical (34.2%). Most patients had underlying comorbidities (70.2%), while the others (29.7%) had no underlying comorbidities. The mean GCS score for the patients was 11. Thirty-three per cent of patients with VAP presented with septic shock, while 43.6% of the non-VAP group had septic shock. The mean Acute Physiology and Chronic Health

Table I: Comparison between demographic factors associated with VAP

Variables	VAP (n = 33) n (%)	Non-VAP (n = 78) n (%)	p-value
Gender			
Male	24 (72.7)	50 (64.1)	
Female	9 (23.3)	28 (35.9)	0.378 <sup>f</sup>
Age (years) <sup>a</sup>	55.97 (13.279)	53.09 (18.868)	0.361 <sup>c</sup>
Race			
Malay	31 (93.9)	75 (96.2)	
Non-Malay	2 (6.1)	3 (3.8)	0.633 <sup>f</sup>
GCS <sup>b</sup>	12 (8)	14 (7)	0.095 <sup>d</sup>
Comorbidities			
Yes	24 (72.7)	54 (69.2)	
No	9 (27.3)	24 (30.8)	0.713 <sup>f</sup>
Admission category			
Medical	11 (33.3)	22 (66.7)	
Surgical	27 (34.6)	51 (65.4)	0.896 <sup>e</sup>
Septic shock			
Yes	11 (33.3)	34 (43.6)	
No	22 (66.7)	44 (56.4)	0.314 <sup>e</sup>
Position of patient			
Supine	3 (9.1)	3 (3.8)	
Semi-recumbent	30 (90.9)	75 (96.2)	0.360 <sup>f</sup>
APACHE II score <sup>a</sup>	14.30 (6.197)	14.064 (7.848)	0.877 <sup>e</sup>
SOFA Score <sup>a</sup>	9.455 (4.790)	8.744 (5.113)	0.494 <sup>e</sup>

<sup>a</sup> Mean (SD), <sup>b</sup> Median (IQR), <sup>c</sup> Independent t-test, <sup>d</sup> Mann-Whitney test, <sup>e</sup> Chi-square test, <sup>f</sup> Fisher exact test

Table II: Comparison between treatment-associated factors and VAP

Variables	VAP (n = 33) n (%)	Non-VAP (n = 78) n (%)	p-value
Antibiotic exposure			
Single	4 (12.1)	19 (25.7)	
Multiple	29 (87.9)	55 (74.3)	0.115 <sup>b</sup>
Duration of antibiotic (days) <sup>a</sup>	29 (23.5)	12 (12.5)	<0.001 <sup>c</sup>
Tracheal Suctioning			
Open method	31 (93.9)	75 (96.2)	
Closed method	2 (6.1)	3 (3.8)	0.633 <sup>d</sup>
Duration of mechanical ventilation (MV; days) <sup>a</sup>	21 (15.5)	5 (7)	<0.001 <sup>c</sup>
Length of ICU stay (days) <sup>a</sup>	24 (16)	7 (7)	<0.001 <sup>c</sup>
Length of hospital stay (days) <sup>a</sup>	34 (27)	14 (14.3)	<0.001 <sup>c</sup>
Adverse reaction			
Require NIV > 2 hours	7 (58.3)	9 (69.2)	
Re-intubation	5 (41.7)	4 (30.8)	0.571 <sup>b</sup>

<sup>a</sup> Median (IQR), <sup>b</sup> Chi-square test, <sup>c</sup> Mann-Whitney test, <sup>d</sup> Fisher exact test

Evaluation (APACHE) II score at admission for the VAP group was 14.3, and the non-VAP group was 14 ( $p = 0.877$ ). The mean Sequential Organ Failure Assessment (SOFA) score was 9 in the VAP group, whereas the non-VAP group had a mean SOFA score of 8 ( $p = 0.494$ ; Table I). None of the sociodemographic factors analysed showed any significant difference in terms of the development of VAP in our cohort. The three most common organisms associated with VAP in our centre were *Klebsiella pneumoniae*, *Acinetobacter* spp. and *Pseudomonas aeruginosa*.

The number of study subjects fulfilling the three types of criteria for VAP in our 111 study patients was 33, which accounted for 29.7%. As for the diagnosis of VAP, 32 out of 33 patients fulfilled the Johansen criteria (97%), 28 patients (85%) fulfilled the CPIS criteria and only 2 (6%) fulfilled the CDC criteria. The proportion of VAP according to each

diagnostic tool varied; for the CDC criteria, it is 1.8%, whereas the proportional incidences of VAP according to the CPIS and Johansen criteria were 25.2% and 28.8%, respectively. The total VAP rate was 7.1. The VAP rates for the Johansen, CPIS and CDC criteria were 6.9, 6.1 and 0.4, respectively.

The VAP population required a significantly longer duration of antibiotic therapy during the total admission days ( $p < 0.001$ ), with a median duration of 29 days. However, there was no significant difference in the requirement of single or multiple types of antibiotics ( $p = 0.115$ ). Open or closed tracheal suctioning was not associated with VAP ( $p = 0.633$ ; Table II).

Patients with a longer duration of MV were prone to developing VAP (OR 1.22; 95% CI 1.12, 1.34;  $p < 0.01$ ). Those

Table III: Factors associated with VAP using simple logistic regression

Factors	b	Adjusted OR (95% CI)	p-value <sup>a</sup>
Age (years)	-0.01	0.990 (0.954, 1.027)	0.59
Gender	-0.464	0.629 (0.239, 1.656)	0.348
Race	0.373	1.451 (0.581, 3.626)	0.425
Comorbidity	0.17	1.185 (0.48, 2.928)	0.713
Admission category	0.057	1.059 (0.448, 2.506)	0.896
GCS	-0.522	0.594 (0.236, 1.496)	0.268
Septic shock	-0.623	0.535 (0.201, 1.425)	0.211
Position	-0.667	0.513 (0.089, 2.960)	0.456
APACHE II	0.008	0.993 (0.919, 1.071)	0.847
SOFA	0.54	1.055 (0.939, 1.185)	0.367
Duration of antibiotic (days)	0.025	1.026 (0.973, 1.081)	0.346
Duration of MV (days)	0.205	1.228 (1.121, 1.344)	< 0.01
Re-intubation	1.353	3.869 (0.95, 15.75)	0.059
Requiring NIV post-intubation	0.879	2.407 (0.799, 7.267)	0.119
ICU mortality	0.689	1.991 (0.869, 4.563)	0.104
30-day mortality	-0.177	0.170 (0.009, 3.257)	0.24
Length of ICU stay (days)	0.193	1.213 (1.107, 1.328)	< 0.01
Length of hospital stay (days)	0.017	1.018 (0.971, 1.066)	0.464

OR = odds ratio, a simple logistic regression test, MV = mechanical ventilation, NIV = non-invasive ventilation

Table IV: Associated factors for VAP (n = 111) using multiple logistic regression

Factors	b	Adjusted OR (95% CI)	p-value <sup>a</sup>
Septic shock			
No		1	
Yes	-1.538	0.215 (0.044, 1.041)	0.056
Duration of mechanical ventilation (MV; days)	0.590	1.803 (1.232, 2.638)	0.002
Adverse event 1 (requiring NIV)	1.920	6.821 (1.230, 37.824)	0.028
Adverse event 2 (re-intubation)	-0.502	0.605 (0.048, 7.674)	0.698
Length of ICU stay (days)	-0.328	0.72 (0.510, 1.017)	0.063

<sup>a</sup> Multiple logistic regression, NIV = non-invasive ventilation

Constant = -3.611

Backward LR method was applied

No multicollinearity and no interaction

Hosmer–Lemeshow test, p-value = 0.241

Classification table, 86.5% correctly classified

Area under the ROC curve 93.9% (95% CI: 0.897, 0.981)

Table V: Comparison of outcomes from VAP

	VAP (n = 33) n (%)	Non-VAP (n = 78) n (%)	p-value
ICU mortality	20 (37)	34 (63)	0.10 <sup>a</sup>
30 days mortality	1 (12.5)	7 (87.5)	0.432 <sup>b</sup>

<sup>a</sup> Chi-square test, <sup>b</sup> Fisher exact test

who stayed longer in the ICU were at risk of VAP (OR 1.21; 95% CI 1.10, 1.32;  $p < 0.01$ ; Table III). The median durations of ICU stay were 24 days in the VAP group and 7 days in the non-VAP group. At the same time, the VAP population required significantly longer hospital stays ( $p < 0.001$ ). The VAP group had a median hospital stay of 34 days, and the non-VAP group had a median of 14 days. There was no significant difference in the requirement of NIV or re-intubation in either group ( $p = 0.571$ ; Table II).

A backward stepwise linear regression model was conducted to explore the significance of VAP predictors. Variables entered in the first step were the presence of septic shock,

duration of MV, requirement of NIV, re-intubation, ICU mortality, 30-day mortality, and length of ICU stay (Table III). The last step revealed that only duration of MV (OR = 1.803; 95% CI 1.232, 2.638;  $p = 0.002$ ) and post-intubation requirement of NIV (OR = 6.821; 95% CI 1.230, 37.824;  $p = 0.028$ ) were factors significantly associated with VAP (Table IV).

The next step in the analysis was checking the fitness of the model. Firstly, using the Hosmer–Lemeshow goodness-of-fit test, the p-value was found to be 0.241, which is not significant. The classification table showed that the data were 86.5% correctly classified for the model. Finally, the area



under the receiver operating characteristic (ROC) curve was 93.9%. A value in the ROC curve of less than 0.5 means that the model is of no use for discrimination. The recommended area under the ROC curve is at least 70%. These three tests supported the claim that the model fit the data. Therefore, it can best describe the association between the factors associated with the proportion of VAP in the ICUs of HUSM. Out of the 111 patients, 54 died in the ICU, and a further eight patients died after ICU discharge within 30 days of enrolment. However, there was no significant difference in ICU mortality ( $p = 0.101$ ) or 30-day mortality ( $p = 0.432$ ) between the groups (Table V).

## DISCUSSION

Our study population consisted of various surgical and medical cases in view of the sampling frame taken from both surgical and medical ICUs. The proportion of VAP in our study was 29.7%. The denominator used was the total number of study population (111). There were three established criteria used in our study, namely, the Johansen, CPIS and CDC criteria. It was crucial to differentiate among them to ensure the standardised incidence was obtained, especially for quality assessment and performance indicator evaluation in ICUs.

Many studies have been published regarding the incidence of VAP; however, there is a difference in the denominators used to calculate it. In our study, two different numbers were used as denominators. The first denominator used was the number of study populations which was 111. A total of 33 out of 111 gives a proportion or incidence of 29.7%, which was similar to that found 10 years ago in our institution by Kathereson et al.<sup>13</sup> However, the incidence of VAP per 1000 ventilator days was 7.1, which was below the national key performance indicator of 10. The incidence even differs if the individual criteria were used in the ICU. The incidences for the Johansen, CPIS and CDC criteria were 6.9, 6.1, and 0.4 per 1000 ventilated days, respectively. It is exceedingly difficult to establish a VAP diagnosis based on CDC criteria because the first tier on the hierarchy requires the patient to be maintained in a stable mechanical ventilator setting for 2 days. The Malaysian ICU registry also reveals dramatic improvement in terms the VAP rate in 2017, after implementation of the CDC criteria. The VAP rate reported in the Malaysian Registry of Intensive Care Report 2017 is 1.7, whereas it was 5.4 in 2013.<sup>14</sup> Inter-observer variability criteria such as chest radiography, should be given priority to ensure accuracy of data used to diagnose VAP. Therefore, modified CDC criteria up to the tier of IVAC represent a standardised tool to define VAP for surveillance. The advantage of CDC criteria is that no chest radiography is included in the criteria.

Traditionally, it has been acknowledged that VAP diagnosis is based on a combination of clinical, radiological and microbiological criteria. However, the diagnosis brings a challenge to physicians because there is a wide range of clinical conditions that mimic VAP in chest radiography results of ventilated patients, including acute respiratory distress syndrome, pneumonia, pulmonary oedema, pulmonary contusion, pulmonary haemorrhage, and lung carcinoma. Some of the clinical conditions used in the

diagnosis of VAP (e.g. change in the amount, consistency, and colour of tracheal secretion) are subjective and may vary according to inter-individual variation in interpretation. The combination of clinical findings, radiological findings and laboratory parameters may increase the specificity and sensitivity of VAP diagnosis, but limitations persist.<sup>10</sup> As there are no pathognomonic radiological features for VAP, the interpretation may overlap with other diseases. For obtaining microbiological specimens, invasive technique (eg. bronchoalveolar lavage [BAL]) and non-invasive techniques (i.e. tracheal aspirate [TA] culture) can be used. Both techniques are the more common sample obtaining method used when required to guide in terms of diagnosis and treatment of pneumonia in HUSM. Both reflect low sensitivity because bronchoscopic sampling cannot guarantee that the sample is taken from the lung area that is the most affected. The TA specimen may be contaminated with normal flora from the oropharyngeal area.

In a 2012 meta-analysis study comparing invasive and non-invasive techniques, it was concluded that the methods exhibited no differences in terms of survival, length of ICU stay, or duration of MV.<sup>11</sup> In 2017, the guidelines issued by the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology/Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT) expressed a preference for invasive sampling techniques, such as mini-BAL, bronchoscopic BAL or protected specimen brush (PSB) to diagnose VAP as Pneumonia-1 (PNEU-1).<sup>12</sup> In 1991, Pugin and colleagues developed the CPIS to aid the diagnosis of VAP using clinical variables.<sup>7</sup> This scale gives a score of 0–2 for each of TA culture, tracheal secretions, chest radiography, ventilation-perfusion (PF) ratio, leucocytosis and temperature. A score of more than 6 is diagnostic of VAP. The interpretation of chest radiography and tracheal secretions are prone to being affected by inter-observer variability.

The Johansen criteria from 1999 allow VAP to be diagnosed based on the presence of new or progressive infiltrates on serial chest radiographs associated with at least two of three clinical findings of infection, such as temperature  $>38^{\circ}\text{C}$ , purulent secretions or leucocytosis. Fabregas and colleagues compared the validity of the diagnosis by these criteria with immediate post-mortem lung biopsies and found that the sensitivity was only 69%, while the maximum specificity was 75%.<sup>8</sup>

In 2013, the United States of America, CDC introduced a new definition of VAP.<sup>9</sup> It was initially designed as a surveillance instrument for HAI, and it was not meant for the diagnosis of pneumonia. It has low specificity compared with bronchoscopic cultures. Neither is it specific for VAP. The agreement between VAP and VAC and IVAC was poor (less than 0.2).<sup>15</sup>

The definition of VAP was noted to be fulfilled mainly by the Johansen criteria, followed by CPIS scoring and CDC criteria in our study. Klompas, who suggested routine bedside evaluation coupled with radiographic information, provided suggestive but not definitive evidence for VAP. Clinicians should consider an additional test to provide further evidence

for VAP or establish another diagnosis.<sup>16</sup> Ventilator-associated tracheobronchitis (VAT) is a term used if chest radiograph results do not meet the criteria.<sup>17</sup> The organisms identified to be associated with VAP are similar to those in previously reported studies, namely, *Klebsiella pneumoniae*, *Acinetobacter* spp. and *Pseudomonas aeruginosa*.<sup>14,18-20</sup>

The prolonged duration of MV carried 1.8 times the risk of developing VAP in our study. A study by Trouillet et al. supported our finding that MV duration is an important risk factor for the development of VAP.<sup>21</sup>

The use of NIV prior to re-intubation in patients who fail extubation carries the greatest risk (6.8 times) of developing VAP. However, a meta-analysis and systematic review by Hess found that non-invasive weaning significantly reduced mortality and length of stay in intensive care and hospital, consistent with the observed reduction in VAP.<sup>22</sup>

In Malaysia, Katherason et al. (2009) reported that the incidence of VAP was 27.0%. Among the risk factors identified were aspiration pneumonia, cancer, leucocytosis and duration of MV.<sup>13</sup> It was found that potentially modifiable independent risk factors were aspiration and exposure to paralytic agents. In 1998, Cook et al. reported that exposure to antibiotics conferred protection, resulting in low rates of early-onset VAP.<sup>23</sup> A study by Charles et al. in 2013 showed chronic lung failure, H2 blocker usage and supine head position were significant risk factors for VAP.<sup>24</sup> In our study, positioning was not a significant factor in developing VAP; however, a total of 95% of the study subjects were in a semi-recumbent position. The study showed that supine patient positioning may facilitate aspiration, a possibility that is potentially decreased by semi-recumbent positioning. Drakulovic et al. reported a 3-fold reduction in VAP incidence in patients treated while in a semi-recumbent position compared with patients treated while completely supine.<sup>25</sup> A Spanish ICU, ventilator care bundle practice reduced the VAP rate by 50% (from 9 to 4.5) within 3 months of implementation.<sup>20</sup> However, our study did not find a significant association between supine or semi-recumbent positions and the VAP incidence.

Awareness of the various risk factors will reduce the morbidity and mortality associated with VAP. Supine head position, stress ulcer prophylaxis, surgery, burns, chronic renal failure, trauma, steroid therapy and duration of MV of more than 5 days were documented as risk factors in 2003.<sup>26</sup> The reported VAP-associated mortality ranges from 20 to 70%. In France in 2016, the mortality rate was reported as 25%.<sup>27</sup> Patients with VAP are often critically ill, with multiorgan involvement. Survival may be affected both by other underlying conditions and sepsis because of a new-onset VAP. A recent study demonstrated a relatively limited attributable (1–1.5%) ICU mortality of VAP when adjusting for the severity of co-existing diseases.<sup>19</sup>

The role of systemic antibiotics in the development of VAP remains unclear. A study by Trouillet et al. showed that recent antibiotic usage (within 15 days) predisposes patients to infection with antibiotic-resistant organisms.<sup>21</sup> In contrast, prior exposure to antibiotics protects against the development of early-onset VAP.<sup>13</sup> However, our study

showed no significant association between antibiotic exposure and VAP incidence. The VAP populations had an increased need for a longer duration of antibiotics (mean = 29 days; SD = 23.5), which may reflect an increase in the cost of treatment for patients.

#### LIMITATIONS OF THE STUDY

Since this was a retrospective study, our main limitation was tracing the patients' medical records. The medical records and ICU charts were kept separately at the record office, and this caused difficulty in obtaining some of the data needed, especially the ventilator setting and arterial blood gas results, which could not be traced elsewhere. In addition, some of the medical records of patients could not be traced because the patients were already deceased or the clinic kept the records for follow-up purposes. This caused a lower number of patients to be included in the study. We were unable to predict the new incidence of VAP due to the cross-sectional nature of the study. However, we were able to identify VAP-associated factors. Diagnosis of VAP using the new CDC definition is limited because most of the information needed relates to the daily ventilator setting, which was recorded in the ICU chart but could not be traced. Furthermore, not all intubated patients were subjected to bronchoscopy because this is an invasive procedure that requires skilful personnel and carries a risk to the patient. Thus, sputum BAL was not obtained from all patients as per the requirement to diagnose pneumonia or probable pneumonia in the new CDC definition of VAP.

#### CONCLUSION

The proportion of VAP during the study period in HUSM was 29.7%. The rate of VAP was 7.1 per 1000 ventilator days. The factors associated with VAP were increased duration of MV and length of ICU stay. There was no significant difference in mortality between intubated patients who developed VAP and those who did not in our ICU.

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