นิพนธ์ต้นฉบับ

ปัจจัยที่สัมพันธ์กับการเสียชีวิตของผู้ป่วยโรคปอดอักเสบที่เกิดในโรงพยาบาลและโรคปอดอักเสบจากการใช้เครื่องช่วยหายใจในโรงพยาบาลระดับตติยภูมิ: การศึกษาแบบย้อนหลังจากสถาบันเดียว

สโรชา พิพิธแสงจันทร์[1]

บทคัดย่อ

โรคปอดอักเสบที่เกิดขึ้นในโรงพยาบาล (HAP) และโรคปอดอักเสบที่เกี่ยวข้องกับเครื่องช่วยหายใจ (VAP) เป็นหนึ่งในสาเหตุการเสียชีวิตของผู้ป่วยในโรงพยาบาลระดับตติยภูมิ การระบุปัจจัยพยากรณ์การเสียชีวิตมีความสำคัญต่อการวางแผนการรักษาและการจัดสรรทรัพยากรให้มีประสิทธิภาพ นำมาซึ่งวัตถุประสงค์ของงานวิจัยนี้ คือ เพื่อระบุปัจจัยที่สัมพันธ์กับการเสียชีวิต ศึกษาอัตราการเสียชีวิต และเชื้อก่อโรคที่พบบ่อยในผู้ป่วย HAP/VAP ในโรงพยาบาลระดับตติยภูมิ โดยรูปแบบการวิจัยเชิงวิเคราะห์แบบย้อนหลัง (Retrospective Cohort Study) ในผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็น HAP หรือ VAP ณ หอผู้ป่วยอายุรกรรม โรงพยาบาลขอนแก่น ระหว่างเดือนมกราคม 2566 ถึงธันวาคม 2567 และนำมาวิเคราะห์ข้อมูลด้วยสถิติ Multivariable binary logistic regression เพื่อหาปัจจัยที่สัมพันธ์ต่อการตาย จากการศึกษาผู้ป่วย 252 ราย (ดีขึ้น 70 ราย ตาย 133 ราย ปฏิเสธการรักษา 49 ราย) พบอัตราการเสียชีวิตร้อยละ 52.8 ผลการวิเคราะห์พหุตัวแปร พบว่าปัจจัยที่สัมพันธ์กับการเสียชีวิตอย่างมีนัยสำคัญทางสถิติ ได้แก่ ระดับอัลบูมินในเลือด (aOR 0.29 per 1-unit increase) โรคมะเร็งระบบโลหิตวิทยา (aOR 16.17) และระดับความรู้สึกตัวที่ลดลง (aOR 4.69) โดยเชื้อก่อโรคที่พบบ่อยที่สุดคือเชื้อแบคทีเรียแกรมลบที่ดื้อยา โดยเฉพาะอย่างยิ่ง *Acinetobacter baumannii* และ *Klebsiella pneumoniae* จากผลงานวิจัยนี้แสดงให้เห็นว่าอัตราการเสียชีวิตจาก HAP/VAP ยังอยู่ในระดับสูง ซึ่งสัมพันธ์กับปัจจัยที่เกี่ยวข้องกับตัวผู้ป่วยและชนิดเชื้อที่ก่อโรค การระบุกลุ่มผู้ป่วยที่มีความเสี่ยงสูงตั้งแต่ต้น จะช่วยให้แพทย์สามารถตัดสินใจเลือกรักษาได้อย่างเหมาะสมและลดโอกาสการเสียชีวิต

คำสำคัญ: โรคปอดอักเสบที่เกิดขึ้นในโรงพยาบาล, โรคปอดอักเสบที่เกี่ยวข้องกับเครื่องช่วยหายใจ, โรงพยาบาลระดับตติยภูมิ, ประเทศไทย, ปัจจัยพยากรณ์การเสียชีวิต, เชื้อก่อโรคปอดอักเสบในโรงพยาบาล

[1]นายแพทย์ชำนาญการโรคระบบการหายใจและภาวะวิกฤตระบบการหายใจ หน่วยงานอายุรกรรม โรงพยาบาลขอนแก่น

[1]Corresponding Author: สโรชา พิพิธแสงจันทร์, mmsspp.2772@gmail.com

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Mortality predictors of Hospital acquired pneumonia (HAP) and Ventilator associated pneumonia (VAP) in tertiary hospital: A Single Center Retrospective Cohort Study

Sarocha Phiphitsaengjan[1]

Abstract

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) remain significant causes of morbidity and mortality in a tertiary care hospital. Identifying specific mortality predictors is essential for optimizing clinical management resulting in better treatment outcomes. Leading to objective of this study which was to identify independent predictors associated with mortality and determine the mortality rate and common pathogens in HAP/VAP patients. A retrospective cohort study was conducted on patients diagnosed with HAP or VAP in the internal medicine wards of Khon Kaen Hospital between January 2023 and December 2024. Data were analyzed using univariable and multivariable binary logistic regression. The results found that a total of 252 patients were studied (70 improved, 133 deaths and 49 AMA) with a mortality rate of 52.8%. Multivariable analysis identified several independent predictors of mortality, including serum albumin (aOR 0.29 per 1-unit increase), hematologic malignancy (aOR 16.17), and impaired consciousness at the time of diagnosis (aOR 4.69). The most common pathogens identified were carbapenem-resistant Gram-negative bacteria, particularly *Acinetobacter baumannii* and *Klebsiella pneumoniae*. This study emphasized that mortality in HAP/VAP is high and influenced by both host factors and severe pathogen profiles. Early detection of high-risk patients, particularly those with low albumin levels, underlying malignancies and impaired level of consciousness at diagnosis, is essential for decreasing morbidity and mortality.

Keywords: Hospital acquired pneumonia, Ventilator associated pneumonia, Thai public tertiary care hospital, Mortality rate, Mortality predictors, HAP/VAP pathogen

[1]Pulmonary and pulmonary critical care medicine, Internal medicine department, Khon Kaen hospital

Introduction

Pneumonia was defined as new or worsening lung infiltration on chest imaging plus clinical evidence of infection, which are new onset of fever, purulent sputum, leukocytosis, and decline in oxygenation. Hospital Acquired Pneumonia (HAP) is defined as a pneumonia occurring 48 hours or more after admission. Ventilator Associated Pneumonia (VAP) is defined as a pneumonia occurring >48 hours after endotracheal intubation and receiving mechanical ventilation[1].

HAP/VAP are one of the most common and serious infection, especially in tertiary care setting where patients often have complex comorbidities, prolonged hospital stays and higher exposed to broad spectrum antibiotics leading to high mortality and morbidity. Thailand has set the direction for the internal medicine service plan for 2025, one of the key goals is to reduce the mortality rate of sepsis patients cause by HAP. However, there are varieties of predictor among each study and still no reliable predictor that could be used as independent indicator for HAP/VAP mortality in local public tertiary care hospital.

Despite global research, predictors of mortality and clinical outcomes in HAP/VAP have been studied but their ability in predicting mortality still inconsistent due to variation of study design, population and resource limit. Leading to author's concern and research question of what are the independent predictors of mortality among patients diagnosed with HAP/VAP in a tertiary care setting

In Thailand, the burden of HAP/VAP is one of the major challenges, a 2019 multi-center retrospective cohort study conducted in Bangkok tertiary care hospitals, including King Chulalongkorn Memorial Hospital and Siriraj Hospital, analyzed 240 patients with nosocomial pneumonia found that VAP accounted for 62.9% of cases, while HAP was 36.7% and ventilated HAP (vHAP) (0.4%)[2]. Other from Siriraj Hospital's surgical ICU reported a VAP incidence of 8.21 cases per 1,000 ventilator-days[3], while from King Narai Hospital found an incidence of 13.65 occurrences per 1,000 days[4].

The culprit nosocomial pathogens in Thailand and Asia quite differs from other global literature which identified *Staphylococcus aureus* as common pathogen[1] while in Asia, the incidence of carbapenem-resistant *Acinetobacter baumannii* are more predominated[2]. A multi-center study in Bangkok identified the three most common pathogens of nosocomial pneumonia as *Acinetobacter baumannii* (44.2%), *Pseudomonas aeruginosa* (34.6%), and *Klebsiella pneumoniae* (28.3%)[2]. The dominance of these pathogens is also showed a high rate of antimicrobial resistance which remain a significant burden on healthcare resources and complicated in empiric treatment decisions.

Crude world's all-cause mortality for HAP/VAP are varied, for HAP, reported crude mortality rates span a wide range from 14.4% to 70%[5]. The crude mortality for VAP is also broad which fall between 25% and 50%[6]. A study at Siriraj Hospital found that the VAP group had a hospital mortality rate of 33.33%, which was significantly higher than the 12.07% rate observed in the non-VAP group[3]. While the study from King Narai Hospital documented a VAP mortality rate of 62.5%[4]. In Khon Kaen province, there was a cross-sectional research from Srinagarind Hospital studied about early and late onset VAP which showed mortality rate 16.7% in early onset and 35.1% in late onset VAP[7].

There were several factors associated with HAP/VAP mortality rate. Global researches were done but with variety of population and clinical setting. One large cohort with 8,182 VAP patient from USA database found that lung cancer, septicemia, FiO_2 level, high SAPS II and SOFA score were independent factor related VAP mortality[8]. While other retrospective cohort studies from European countries and Thailand showed that AKI (aOR 5.93), hematologic diseases (aOR 11.45), mechanical ventilation dependency (aOR 3.58)[9], advanced age (CI 1.003–1.047, P=0.023), unconsciousness (CI 1.674–6.547, P=0.001)[10], initial inappropriate empirical and antibiotic treatment (OR 2.16)[11] are all strong mortality risk factors. According to Thai prospective study[12] in adult HAP/VAP revealed that all-cause mortality was 42.5% with the significant factors

associated with mortality were septic shock, multilobar involvement, previous carbapenem ATB usage within 72 hours, BUN > 20 mg/dL and pneumonia caused by MDR A. baumannii or P. aeruginosa.

Objective

1. Identify independent predictors of mortality in HAP/VAP patients at a tertiary hospital when compare between patient in dead group and improved group
2. Determine mortality rates and common pathogens of HAP/VAP.

Methodology

This study design was Single Center Retrospective Cohort study

Population

In-patients admitted in internal medicine ward, Khon Kaen Hospital, Thailand between January 2023 to December 2024

Inclusion criteria adult patients age ≥ 18 years old diagnosed with HAP or VAP according to standard clinical and radiological criteria [1]

Exclusion criteria Patients who was already under terminal disease and denied any treatment before HAP/VAP diagnosis and patients who died within 24 hours after diagnosis (to minimize bias from non-modifiable baseline severity and pre-hospital factors, ensuring a more accurate evaluation of modifiable clinical predictors)

Method

The author reviewed the electronic medical records (EMR) and laboratory database of the In-patients who were diagnosed with HAP or VAP admitted in internal medicine ward, Khon Kaen Hospital, Thailand between January 2023 to December 2024 and recorded in the case record form which had been review and approved by senior institutional experts during the research proposal stage

Data collection Epidemiological information, underlying disease, vital signs and clinical status at time of diagnosis of HAP VAP, lab test and culprit pathogen

Data Analysis and Statistics Numerical data were reported as mean ± standard deviation, while categorical data were reported as frequencies and percentages. Categorical variables were compared between groups using Pearson chi-square test and independent t-test (or One-way ANOVA) for continuous

variables. To identify independent predictors of mortality, variables with a p-value < 0.05 in the univariable analysis were entered into a multivariable binary logistic regression model using the enter method. Based on the Peduzzi et al. (1996)[13] events per variable (EPV) framework, our calculated minimum sample size (n=118) was configured to accommodate a maximum of 5 independent predictor variables (k=5) to ensure parameter stability and prevent model overfitting. Prior to finalizing the regression model, standard multicollinearity diagnostics were performed using Tolerance (>0.1) and the Variance Inflation Factor (VIF <10). Additionally, multivariate outliers were screened and controlled using Mahalanobis distance calculations at a significance threshold of 0.001. Model calibration, overall goodness-of-fit, and predictive reliability were formally evaluated using the Omnibus test, -2 Log Likelihood, Nagelkerke R^2, and the Hosmer-Lemeshow test, with statistical significance defined as a p-value < 0.05. IBM SPSS Statistics for Windows, Version 22.0 were used to analyze.

Sample size and calculation To calculate the sample size for identifying dependent risk factors related to HAP or VAP mortality, the commonly used method is based on the events per variable (EPV) rule proposed by Peduzzi et al. (1996)[13]. This approach recommends a minimum of 10 outcome events for each predictor variable. The formula is: n = 10 × k / p, where *n* is the minimum required sample size, *k* is the number of predictor variables, and *p* is the proportion of patients experiencing the event. According to the HAP/VAP study in Thai hospital[2] showed that there were 5 factors (k) related to HAP/VAP mortality which was 42.5% (p). Upon calculation, the minimum required sample size was 118.

Ethical consideration The author respects patient's privacy, confidentiality and the importance of ethical principles of human research. All patient data in this retrospective cohort study will not have any identifier that can identify the patient. And the obtained analyzed data will be used to maximized its benefits. This research has been ethically approved by the Institutional Review

Board Khon Kaen Hospital with research number KEXP68075.

Results

The study showed 252 patients with treatment outcome of 70 improved (27.8%), 133 deaths (52.8%), and 49 patients who left against medical advice (AMA) (19.4%). The mortality rate in this study was 52.8%. For the mortality predictor analysis, the author would like to focus only patients with clear outcome, which was 203 cases, as the AMA cases' status were unknown (the outcome could be improved if the reason of AMA was patient's desire of changing hospital or could be dead if the reason of AMA was the desire of dead at home). The mean age across both improved and dead groups was 61.2 ± 15.6 years, showing no significant difference in age between survivors and dead group (p=0.584) as well as BMI and gender. However, there were several baseline clinical factors at diagnosis which significantly associated with mortality as follow; patients in dead group had significant lower mean SBP (115.5 vs 132 mmHg, p<0.001), lower DBP (67 vs 73 mmHg, p=0.019) and higher heart rates (112 bpm vs 105 bpm, p=0.01) compared to the improved group and when focused on the severity scores, NEWS-2 score was significantly higher in the dead group (10.6 ± 3.3) compared to the improved group (7.5 ± 3.0, p<0.001). Besides, level of consciousness was a major factor as impair in consciousness which was defied as neurological status graded in NEWS score that is not fully awake and aware (GCS < 15 or any new-onset V, P or U on the AVPU scale) was found to be 75% of the dead group compared to only 28% of the improved group (p<0.001). Lastly, Comorbidities factors showed that Cancer (p=0.016) especially hematologic malignancy and being bedridden (p=0.004) were significantly more prevalent in dead group (Table1). Full report of result was showed in supplement.

Table 1 Demographic Characteristics

Demographic Characteristics	Overall (N=203)	Improved (N=70)	Dead (N=133)	χ^2, *t-test*	*P-value*
Gender, N (%)				0.5[x]	0.375[a]
Female	103 (50.7)	39	64		
Male	100 (49.2)	32	68		
Age (years), mean±s.d.	61.2±15.6	62.0±14.3	60.7±16.2	0.55[t]	0.584[b]
BMI (kg/m^2), mean±s.d.	22.5±4.8	22.2±4.6	22.7±4.9	0.59[t]	0.556[b]
Systolic blood pressure, mean±s.d.	121.2±31.7	132.1±28.4	115.5±31.9	3.91[t]	<0.001[b]
Diastolic blood pressure, mean±s.d.	69.6±18.4	73.8±18.2	67.4±18.1	2.37[t]	0.019[b]
Heart rate (bpm), mean±s.d.	109.8±18.9	105.1±19.5	112.3±18.2	2.5[t]	0.010[b]
Respiratory rate, mean±s.d.	24±6.3	23.4±4.6	24.5±7.4	4.14[t]	<0.001[b]
Impaired consciousness, N (%)	119 (58.6)	19 (27)	100 (75)	45.21[x]	<0.001[a]
NEWS-2 scores, mean±s.d.	9.5±3.5	7.5±3.0	10.6±3.3	5.23[t]	<0.001[b]
Underlying disease of				5.79[x]	
Cancer	39 (19)	7 (10)	32 (24)		0.016[a]
- Solid	13	2	11		
- Hematology	26	5	21		
- Bedridden	14 (7)	0 (0)	14 (11)	8.16[x]	0.004[a]

a=Chi-square test, b = One-way ANOVA, c = Kruskal-Wallis test

x = Pearson Chi-Square (χ^2,), t= Independent Samples T-Test

Table 2 Diagnosis and event

Diagnosis and event	Overall (N=203)	Improved (N=70)	Dead (N=133)	χ^2	P-value
Inotropic drugs used at diagnosis,				9.07	
N (%)	55 (27)	10	45		0.003[a]
AKI, N (%)	98 (48)	24	74	7.56	0.006[a]
Diagnosis, N (%)				6.95	0.008[a]
-Hospital acquired pneumonia					
(HAP)	89 (43)	39	50		
-Ventilator associated pneumonia	114				
(VAP)	(56)	30	84		
Intensive care unit (ICU), N (%)				3.84	0.050[a]
No (Normal Ward)	98 (48)	34	64		
ICU	64 (32)	16	48		
Semi-ICU	41 (20)	20	21		

Note: a = Chi-square test, b = One-way ANOVA, c = Kruskal-Wallis test

From diagnosis and hospital events outcome according to Table 2, the type of pneumonia influenced outcomes significantly (p=0.008) as 84 cases of total 133 dead cases (63%) were diagnosed with VAP, while 49 of total 133 dead cases were HAP (37%). Furthermore, the need for inotropic drugs (34% in the dead group vs 14% in the improved group, p=0.003) and the development of AKI (58% in the dead group vs 37% in the improved group, p=0.006) were also significantly associated with mortality. However, 36% of the dead group admitted in the Intensive Care Unit which significantly associated with mortality compared to other wards (p=0.05).

Laboratory findings outcome in Table 3 showed that platelets of patients in the improved group had significantly higher median platelet counts compared to those who died (p=0.027). As well as albumin and bicarbonate level were also

significantly higher in improved group compared to dead group with median albumin level of 3 g/dL (p<0.001) and bicarbonate level of 23 mmol/L (p=0.018) in improved group vs 2 g/dL of albumin and 21 mmol/L of bicarbonate level in dead group. While higher AST and Creatinine level significantly related with dead outcome as in dead group had median AST level of 68 U/L VS 43 U/L in improved group (p=0.017) and Creatinine level in dead group was 2 mg/dL which is higher in improved group which was 1 mg/dL (p=0.048).

Table 3 Laboratory

Laboratory finding median (IQR)	Overall (N=203)	Improved (N=70)	Dead (N=133)	Z	*P-value*
Platelet count (cells/mm^3)	207,500 (96,000-318,000)	254,000 (118,000-353,000)	175,000 (75,000-286,000)	-2.21	0.027[c]
Creatinine (mg/dL)	1 (1-3)	1 (1-2)	2 (1-3)	-1.98	0.048[c]
Bicarbonate (mmol/L)	22 (19-26)	23 (20-27)	21 (18-25)	-2.36	0.018[c]
Albumin (g/dL)	2 (2-3)	3 (2-3)	2 (2-3)	-4.73	<0.001[c]
AST (U/L)	57 (33-102)	43 (29-72)	68 (35-134)	-2	0.017[c]

Note: Calculated using the Mann-Whitney U test, where the test statistic is reported as a Z-statistic. Statistical significance is defined as $p < 0.05$

a=Chi-square test, b=One-way ANOVA, c=Kruskal-Wallis test

Table 4 Pathogens

Pathogen	Overall	Improved	Dead	χ^2	P-value
Escherichia Coli (E. Coli), N (%)	10 (5)	2	8	0.67	0.413[a]
Pseudomonas aeruginosa, N (%)	19 (9)	10	9	1.56	0.211[a]
Klebsiella pneumoniae, N (%)	81 (40)	22	59	5.51	0.019[a]
Drug Susceptible	33 (16)	11	12		
Drug Resistant	65 (32)	10	46		
Acinetobacter baumannii, N (%)	114			2.31	
	(56)	34	80		0.129[a]
Drug Susceptible	22 (11)	10	12		
Drug Resistant	90 (44)	23	67		
Stenotrophomonas maltophilia, N	18 (9)	3	15	2.11	
(%)					0.146[a]
Staphylococcus aureus, N (%)				Fisher's	
	5 (2)	3	2	Exact	0.491[a]

Note: a = Chi-square test, b = One-way ANOVA, c = Kruskal-Wallis test

Focus on pathogen Distribution (Table 4) showed that drug-resistant *Acinetobacter baumannii* was the most prevalent pathogen in all group (44%), followed by drug-resistant *Klebsiella pneumoniae* (32%). The presence of *K. pneumoniae* was statistically significant with mortality (p=0.019). In the initial screening, a total of 39 clinical, demographic, and laboratory variables were evaluated using univariable binary logistic regression. Variables demonstrating statistical significance at a threshold of $p < 0.05$, comprising 13 potential risk factors were entered into the multivariable binary logistic regression model using the enter method. While our calculated sample size allowed a maximum threshold of 5 variables under the traditional Peduzzi et al. EPV framework, the final parsimonious model successfully optimized these candidates into 3 significant independent predictors. Prior to finalizing the model,

standard linear diagnostics confirmed the absence of multicollinearity among the predictors, with acceptable Tolerance and Variance Inflation Factor (VIF) values across all parameters. Furthermore, multivariate outlier evaluation via Mahalanobis distance showed no highly influential case anomalies affecting the regression coefficients. The final model demonstrated adequate goodness-of-fit and predictive reliability, as evidenced by a statistically significant Omnibus test ($p < 0.001$) and a non-significant Hosmer-Lemeshow test. Only serum albumin level (aOR 0.29, p=0.008), underlying cancer (aOR 16.17, p=0.001) and impaired consciousness (aOR 4.69, p=0.017) remained strong, independent predictors of HAP/VAP mortality (Table 5).

Table 5 Univariate and Multivariate analysis of factors associated with Mortality of HAP/VAP: Dead vs Improved

Factors	Univariate analysis		Multivariate analysis		
	OR (95%CI)	P	aOR (95%CI)	Wald	P
SBP (mmHg)	0.98 (0.97-0.99)	0.001	0.98 (0.96-1.00)		0.091
DBP (mmHg)	0.98 (0.97-1.00)	0.021	1.01 (0.97-1.04)		0.727
Heart rate (bpm)	1.02 (1.00-1.04)	0.012	1.01 (0.98-1.05)		0.545
Respiratory rate	1.36 (1.22-1.51)	<0.001	-		
Conscious	8.06 (4.15-15.63)	<0.001	4.69 (1.32-16.70)	5.71	0.017*
NEWS-2 scores	1.32 (1.19-1.47)	<0.001	1.19 (0.91-1.55)		0.206
Cancer	2.83 (1.18-6.81)	0.020	16.17 (3.29-79.61)	11.66	0.001*
Inotropic drugs used at diagnosis	3.05 (1.43-6.53)	0.004	0.48 (0.10-2.21)		0.343
AKI	2.34 (1.27-4.33)	0.007	1.65 (0.46-5.91)		0.439
Diagnosis of HAP	1		1		
Diagnosis of VAP	2.20 (1.22-3.98)	0.009	1.58 (0.53-4.74)		0.410
Ventilator needed at diagnosis	3.11 (1.30-7.43)	0.011	3.01 (0.59-15.40)		0.186
Platelet count (cells/mm^3)	1.00 (1.00-1.00)	0.014	1.00 (1.00-1.00)		0.466
BUN (mg/dL)	1.01 (1.00-1.02)	0.024	1.01 (0.99-1.04)		0.309
Albumin (g/dL)	0.24 (0.13-0.45)	<0.001	0.29 (0.12-0.73)	7.11	0.008*

Note: p-values were determined using multivariable binary logistic regression (Enter method). Wald statistics were used to test the significance of individual predictors.

Variables marked with a dash (—) under multivariate analysis were excluded during model reduction. Statistical significance was defined as $p < 0.05$.

Omnibus $\chi^2 = 68.42$, $p < 0.001$; -2Log Likelihood = 195.12; Nagelkerke $R^2 = 0.402$;

Hosmer and Lemeshow Test $\chi^2 = 4.13$, $p = 0.845$.

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

Discussion and Conclusion

This study highlights the significant clinical burden and high mortality rate associated with HAP/VAP in a Thai tertiary care setting. The observed overall mortality rate of 52.8% and if focused only among patient with clear outcome (improved or death, not include AMA), the mortality rate was spiked to 64.8% which is very high compare to previous study reported in Southeast Asia (25%–54.5%) and notably exceeds the local mortality rate reported in previous Thai surgical ICU studies[2, 3] (33.33%) and Srinagarind Hospital, Khon Kaen provice[7](35.1%). This disparity likely reflects the complex comorbidities as baseline of patients in internal medicine field which already had high prevalence of chronic underlying diseases before diagnosis and high prevalence of multidrug-resistant pathogens. Other possible reason was from a tertiary center referral bias and disease severity, as Khon Kaen Hospital serves as referral destination for critically ill patients transferred from community hospitals, the patient that was admitted in our hospital were already severe showed as high AKI event (51%) and high NEWS.

Consistent with Asian epidemiological trends, drug-resistant *Acinetobacter baumannii* was the most prevalent pathogen (44%), followed by drug-resistant *Klebsiella pneumoniae* (32%). Our findings reinforce the observation that Asia faces a much higher burden of carbapenem-resistant Gram-negative bacilli compared to Western countries[1, 2]. Notably, the *K. pneumoniae* was statistically significant in its association with mortality, corresponding to previous Chinese multicenter retrospective study in tertiary hospitals investigating the clinical outcomes and etiologies of VAP.[14] *Klebsiella pneumoniae* was one of the predominant isolated pathogens (23.58%) and demonstrated a

significantly higher prevalence among VAP non-survivors compared to survivors. Highlighting the critical challenge in controlling these pathogens.

The multivariate analysis identified three primary independent predictors of death which were serum albumin level, underlying of malignancy, and impaired consciousness. Serum albumin showed to be a strong independent protective factor (aOR 0.29), for every unit increase in albumin, the odds of death decreased significantly. Low albumin level often relates to poor nutritional status and chronic inflammation, both of which impair the immune response to severe infection[15].

Patients with an underlying diagnosis of cancer, particularly hematologic malignancies, faced a 16-fold increased risk of death (aOR 16.17). This is consistent with previous literature identifying hematologic disease as a major risk factor (OR 11.45)[8]. The profound immunosuppression in these patients likely limits their ability to clear high-virulence nosocomial pathogens.

The third factor was decreased level of consciousness (aOR 4.69). This aligns with previous studies[10] and likely reflects both the severity of the systemic infection (sepsis-associated encephalopathy) and compromised ability to protect the airway, leading to worse clinical outcomes.

Interestingly, this study found that ICU admission event was high among the dead group, this might be from disease evaluation as the more severe patient tends to get access to ICU than the less severe. This suggests the importance of proper case selection to maximizing treatment success and minimizing resource wasting.

The high mortality rate observed in this study emphasized the urgent need of early identification and management of HAP/VAP patients especially who had cancer. Monitoring albumin levels or nutritional and clinical status, specifically consciousness also provides prognostic information. Furthermore, the dominance of MDR *A. baumannii* and *K. pneumoniae* need aggressive antimicrobial empirical treatment and infection control strategies to meet the goals for reducing the mortality.

Limitation

First and most important, 49 AMA patients (19%) were excluded. As

AMA discharge is often associated with poor prognosis, this likely represents informative censoring that underestimated mortality and biased estimates, sensitivity analyses (AMA as deaths/survivors) or a competing-risk approach are warranted. Second, as a retrospective EMR-based study, missing data and unmeasured confounders (timing/appropriateness of empirical antibiotics, baseline severity, resistance patterns) could not be controlled. Third, mortality was modelled with logistic regression, which ignores time-to-event; survival analysis may be more appropriate. Another limitation was the high number of predictors included in the final multivariable regression model. While a total of 13 variables met the $p < 0.05$ threshold from the univariable screening and were entered into the final model, our study recorded 133 mortality events. This yields an events-per-variable (EPV) ratio of approximately 10.2, which satisfies the minimum recommended threshold of 10 events per predictor to maintain model stability. Nevertheless, entering 13 variables simultaneously into a single model may still elevate the risk of model overfitting and limit our statistical power to detect independent associations for variables that became non-significant in the multivariable analysis. Finally, this single-center study of internal-medicine patients at a tertiary referral hospital may not be generalizable to surgical, ICU, or other settings. Future prospective multicenter studies with larger sample sizes and a greater absolute number of outcome events would provide significant beneficial and precise information

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