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Major Article

Multinational prospective cohort study over 18 years of the risk factors for ventilator-associated pneumonia in 9 Asian countries: INICC findings

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ABSTRACT

Background: Ventilator associated pneumonia (VAP) rates in Asia are several times above those of US. The objective of this study is to identify VAP risk factors.

Methods: We conducted a prospective cohort study, between March 27, 2004 and November 2, 2022, in 279 ICUs of 95 hospitals in 44 cities in 9 Asian countries (China, India, Malaysia, Mongolia, Nepal, Pakistan, Philippines, Sri Lanka, Thailand, Vietnam).

Results: 153,717 patients, followed during 892,996 patient-days, acquired 3,369 VAPs. We analyzed 10 independent variables.

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Using multiple logistic regression we identified following independent VAP RFs= Age, rising VAP risk 1% per year (aOR=1.01; 95%CI=1.00-1.01, *P*<.0001); male gender (OR=1.17; 95%CI=1.08-1.26, *P*<.0001); length of stay, rising VAP risk 7% daily (aOR=1.07; 95%CI=1.06-1.07, *P*<.0001); mechanical ventilation (MV) device utilization (DU) ratio (OR=1.43; 95%CI=1.36-1.51; p<.0001); tracheostomy connected to a MV (OR=11.17; 95%CI=1.95-14.27; p<.0001); public (OR=1.84; 95%CI=1.49-2.26, *P*<.0001), and private (OR=1.57; 95%CI=1.91, *P*<.0001) compared with teaching hospitals; upper-middle income country (OR=1.86; 95%CI=1.63-2.14, *P*<.0001). Regarding ICUs, Medical-Surgical (OR=4.61; 95%CI=3.43-6.17; *P*<.0001), Neurologic (OR=3.76; 95%CI=2.43-5.82; *P*<.0001), Medical (OR=2.78; 95%CI=2.04-3.79; *P*<.0001), and Neuro-Surgical (OR=2.33; 95%CI=1.61-3.92; *P*<.0001) showed the highest risk.

Conclusions: Some identified VAP RFs are unlikely to change= age, gender, ICU type, facility ownership, country income level. Based on our results, we recommend limit use of tracheostomy, reducing LOS, reducing the MV/DU ratio, and implementing an evidence-based set of VAP prevention recommendations.

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INTRODUCTION

The International Nosocomial Infection Control Consortium (INICC) was founded in 2002 as a global research network for healthcare-associated infections (HAI).¹ Its main goal is to encourage evidence-based infection prevention recommendations in order to decrease the incidence of HAIs, mortality, bacterial resistance, excessive length of stay (LOS), and expense associated with them.²

In 2006,³ 2008,⁴ 2010,⁵ 2012,⁶ 2014,⁷ 2016,⁸ 2019,⁹ and 2021,¹⁰ INICC issued international reports containing information on ventilator-associated pneumonia (VAPs) and clinical outcomes. The VAP rates in low and middle income countries (LMIC) are considerably greater than those in high-income nations, according to INICC data.³⁻¹⁰ INICC also found that the crude mortality rate in ICU patients without HAI is 17.12% (95% CI=16.93-17.32), for those with VAP it is 42.32% (95% CI=40.61-44.09), and for those with VAP plus central line associated bloodstream infection (CLABSI) plus catheter associated urinary tract infections (CAUTI) it is 63.44% (95% CI=55.99-71.60).¹⁰

Regarding the identification of risk factors (RF) for VAP, Almuneef et al (2004) conducted a prospective surveillance study of VAP among all patients receiving mechanical ventilation (MV) for 48 hours or more admitted to a pediatric intensive care unit (PICU) in Saudi Arabia. On multiple logistic regression analysis, only prior antibiotic therapy, continuous enteral feeding, and bronchoscopy were independent predictors of VAP.¹¹ Petdachai (2004) carried out a prospective observational study in a neonatal intensive care unit (NICU) of 170 infants who required MV for longer than 48 hours. Stepwise logistic regression analysis identified 3 RFs independently associated with VAP: umbilical catheterization; respiratory distress syndrome; and insertion of an orogastric tube.¹² In a cardiac surgical intensive care unit (ICU), Pawar et al. performed a prospective study at Escorts Heart Institute and Research Centre, New Delhi, India. Potential RFs were analyzed. On multivariate analysis, intermittent positive-pressure ventilation hours and steroids were independent VAP RFs.¹³ Apisarnthanarak et al. conducted a prospective cohort study. By multivariate analysis, CLABSI before VAP was an independent VAP RF after adjustment for the duration of endotracheal intubation.¹⁴

The above-mentioned studies and other studies have analyzed the impact on VAP of several variables, but as of the time of publication, no study has concurrently examined numerous nations to establish VAP RFs, nor has any study looked at any of the following factors and their relationship to VAP prospectively over an 18-year period: income level per country according to the World Bank; facility ownership; type of hospitalization; and ICU type. The main goal of this study is to identify how these variables and other variables are VAP RFs.

METHODS

Study population and design

This prospective observational cohort study was performed on patients who were admitted to 279 ICUs in 95 hospitals in 44 cities in 9 Asian countries (China, India, Malaysia, Mongolia, Nepal, Pakistan, the Philippines, Sri Lanka, Thailand, and Vietnam) between March 27, 2004 and February 12, 2022, over 18 years.

Prospective cohort in ICUs and surveillance of healthcare associated infections

Each patient's data was gathered at the time of ICU admission. Infection prevention professionals (IPP) visited each patient's bedside daily from the time of admission until discharge. This analysis prospectively included all adult and pediatric patients hospitalized in an ICU with or without HAIs, and their data was gathered utilizing the INICC Surveillance Online System (ISOS). IPPs bring a tablet to the bedside of each hospitalized patient in the ICU, sign in to ISOS, and upload the patient's data.²

The information is provided since the time of admission and includes information about the setting, such as the nation, city, name of the hospital, and the ICU type, as well as information about the patient, such as age, type of hospitalization, use of invasive devices (central line [CL], MV, urinary catheter [UC]), and presence of infection. IPPs upload information about each patient's invasive devices (CL, MV, UC) and positive cultures (blood, urine, and respiratory samples) to ISOS every day until the patient is released.²

If the patient has signs or symptoms of HAI, an infectious diseases specialist approach the patient to determine the presence of an HAI (CLABSI, VAP, or CAUTI). According to the CDC/National Healthcare Safety Network (CDC/NHSN), IPPs look at a patient's signs and symptoms, cultures, X-rays, and other described criteria to fulfill definitions of HAI.¹⁵

Over the 18 years of this study, all IPPs of all participant hospitals have been applying the current and updated CDC definition of HAIs. That is, whenever the CDC updated their definitions, our IPPs began using the new updated definitions. When IPPs upload the results of a culture to the ISOS, the ISOS immediately displays a message and directs the IPP to an online module of the ISOS where the IPP can check all the CDC/NHSN criteria to determine the presence of a HAI and the kind of HAI (CLABSI, VAP, CAUTI).²

Daily device utilization checks are performed by ISOS. When a bias in patient-days or device use is detected from admission to discharge, the ISOS notifies the IPPs. If the patient is hospitalized in the ICU without any devices in place, it is likely because IPP forgot to upload to ISOS the use of devices or forgot to upload to ISOS the

discharge of the patient. If ISOS notices a lack of use of any kind of device on any given day, it will send a message to the IPP to remind him or her to upload missing devices or upload the discharge of the patient. In other words, ISOS asks IPPs to look into why a patient in an ICU doesn't have any devices in place. This approach significantly reduces biases associated with device utilization, patient days, and discharge conditions.²

Patients with missing data were excluded from this study. The Institutional Review Boards of the participating hospitals provided their approval for this study. Patients' and hospitals' identities are treated with confidentiality.

INICC surveillance online system

Standard CDC/NSHN methodologies state that HAI denominators are gathered from all patients as pooled data without mentioning the characteristics of particular patients or the quantity of device-days associated with particular patients.¹⁵

INICC HAI surveillance is carried out through the use of an online platform, the ISOS, which includes CDC NHSN criteria and methods.¹⁵ Additionally, ISOS includes the gathering of patient-specific information on all patients, including those with and those without HAI, with several variables per patient. The VAP RFs can be estimated by being able to match data from all patients admitted to the ICU by different variables.² The CDC/NHSN criteria and methods are used to identify HAIs, estimate HAI rates, and calculate the MV device utilization ratio from the data uploaded to ISOS.¹⁵

Validation of diagnosis of healthcare associated infections

The validation of HAI is a feature of the ISOS and is useful for maximizing the sensitivity, specificity, and accuracy of surveillance data. Each HAI reported by an IPP is validated, that is, scrutinized to be certain that criteria are fulfilled to justify its recording as an HAI. All necessary corrections and additions are indicated with a clear red sign on the screen. The validation process also includes the scrutiny of data reported for putatively uninfected patients to permit detection of unreported but true HAI. To accomplish this, when the IPP uploads a culture to the ISOS but does not confirm a HAI, based on the uploaded culture, the date that the culture was taken, and the result of the culture, the ISOS automatic validation system shows an online message to the IPP asking to check CDC/NHSN criteria for that putative HAI, should the ISOS suspect a HAI. The ISOS sends an XLS file to the IPP every month with a list of biases about HAIs that haven't been confirmed.²

Study definitions

Ventilator: Any device used to support, assist, or control respiration through the application of positive pressure to the airway when delivered via an artificial airway, specifically an oral/nasal endotracheal or tracheostomy tube.

Definitions of VAP used during surveillance were those published by CDC in 1991¹⁶ and all their subsequent updates through 2022.¹⁷

Ventilator-associated pneumonia: A pneumonia where the patient is on MV for >2 consecutive calendar days on the date of event, with day of ventilator placement being Day 1, **AND** the ventilator was in place on the date of event or the day before.¹⁷

Clinically Defined Pneumonia: Two or more serial chest imaging test results with at least **one** of the following: New and persistent **or** Progressive and persistent; Infiltrate; Consolidation; Cavitation; Pneumatoceles, in infants ≤ 1 year old. For ANY PATIENT, at least **one** of the following: Fever; Leukopenia; or leukocytosis; For adults \geq 70 years old, altered mental status with no other recognized cause. And at least **two** of the following: New onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or

increased suctioning requirements; New onset or worsening cough, or dyspnea, or tachypnea; Rales or bronchial breath sounds; Worsening gas exchange; increased oxygen requirements; or increased ventilator demand.¹⁷

Pneumonia with Common Bacterial or Filamentous Fungal Pathogens and Specific Laboratory Findings: Two or more serial chest imaging test results with at least **one** of the following: New and persistent **or p**rogressive and persistent Infiltrate; Consolidation; Cavitation; Pneumatoceles, in infants ≤ 1 year old. At least **one** of the following: Fever; Leukopenia or leukocytosis; For adults \geq 70 years old, altered mental status with no other recognized cause. And at least one of the following: New onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements; New onset or worsening cough, or dyspnea, or tachypnea; Rales or bronchial breath sounds; Worsening gas exchange; increased oxygen requirements; or increased ventilator demand. At least one of the following: Organism identified from blood; Organism identified from pleural fluid; Positive quantitative culture or corresponding semi-quantitative culture result from minimally-contaminated LRT specimen; ≥5% BAL-obtained cells contain intracellular bacteria on direct microscopic exam; Positive quantitative culture or corresponding semi-quantitative culture result of lung tissue; Histopathologic exam shows evidences of pneumonia.¹⁷

World Bank country classifications by income level: The WB assigns the world's economies to 4 income groups—low, lower-middle, upper-middle, and high-income countries. The classifications are based on gross national income (GNI) per capita in the current USD. Low income are those countries with GNI less than USD 1,045. Lower-middle income those with GNI from 1,046 to 4,095. Uppermiddle income for those with GNI from 4,096 to 12,695. High income for those with GNI >12,695.¹⁸

Mechanical ventilator device-utilization ratio: Mechanical ventilator device-utilization (MV/ DU) ratio was calculated as a ratio of MV-days to patient-days for each location type. As such, the MV/DU ratio of a location measures the use of invasive devices and constitutes an extrinsic RF for VAP. MV/DU ratio may also serve as a marker for the severity of illness of patients (ie severely ill patients are more likely to require an invasive device) which is an intrinsic RF for VAP.¹⁹

Facility/institution ownership type

Publicly owned facilities owned or controlled by a governmental unit or another public corporation (where control is defined as the ability to determine the general corporate policy); *not-for-profit privately owned* facilities that are legal or social entities created for the purpose of producing goods and services, whose status does not permit them to be a source of income, profit or other financial gains for the unit(s) that establish, control or finance them; and, *for-profit privately owned facilities* that are legal entities set up for the purpose of producing goods and services and are capable of generating a profit or other financial gains for their owners.²⁰

Statistical analysis

Patients with and without VAP were compared using multiple logistic regression. Statistically significant variables were independently associated with an increased risk for VAP. The test statistic used was the Wald test, and the statistical significance level was set at 0.05. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for statistically significant variables were also given. These were calculated from the results of multiple logistic regression.

Patients with CPAP, and patients with tracheostomy not connected to a MV were excluded from this study, because sample size of them was not balanced with other types of respiratory support. 4

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We estimated variables independently associated with the outcome (VAP), adjusted to the following prospectively collected data: (1) Gender (female, male), (2) age, (3) MV-days before acquisition of VAP, (4) MV/DU ratio as a marker of severity of illness of patient, (5) type of respiratory support (endotracheal tube connected to a mechanical ventilator, tracheostomy connected to a mechanical ventilator), (6) hospitalization type (medical, surgical), (7) LOS, (8) ICU type (medical-surgical, medical, pediatric, surgical, coronary, neurosurgical, cardio-thoracic, neurologic, trauma, pediatric oncology, adult oncology), (9) facility ownership (publicly owned facilities, notfor-profit privately owned facilities, for-profit privately owned facilities, teaching hospitals),²⁰ and (10) income per country according to WB (low, lower-middle, upper-middle, high).¹⁸

The evaluated outcome was the acquisition of VAP according to CDC/NHSN definitions.¹⁵ All statistical analyses were performed using R software, version 4.1.3.

RESULTS

A cohort, prospective, multicenter surveillance study of VAPs was carried out in 279 ICUs of 95 hospitals in 44 cities across 9

Table 1

Setting and patient characteristics

participating Asian nations (China, India, Malaysia, Mongolia, Nepal, Pakistan, Philippines, Sri Lanka, Thailand, Vietnam). This is a cohort study, and the length of participation of hospitals is variable and ranged from 1.37 and 201.93 months (Mean, 40.66; SD, 41.68).

From March 27, 2004, to February 11, 2022, over the course of 18 years, data on 153,717 critical patients was gathered. They were followed from admission to discharge from the ICU during 892,996 patient-days, and they acquired 3,369 VAPs.

Table 1 shows data on setting and patient characteristics. Table 2 shows the VAP rate stratified per ICU type, income level according to the World Bank, and facility ownership.

Using multiple logistic regression, we found that the following variables are statistically significantly and independently linked to VAP (Table 3): (1) Age, rising the risk 1% per year; (2) male gender compared with female gender; (3) length of stay, rising the risk 7% per day; (4) MV/DU ratio; (5) use of tracheostomy over use of endotracheal tube; (6) public hospitals and private hospitals compared with teaching hospitals; (7) upper middle income countries. (8) The highest risk of VAP was seen in the medical-surgical ICUs, followed by neurologic, medical and neurosurgical ICUs.

Period	03-27-2004 to 02-11-2022
Years, n	18
ICUs, n	279
Hospitals, n	95
Cities, n	44
Countries, n	9
Total patients, n	153,717
Total patients-d, n	892,996
Average LOS, mean, SD	mean= 5.81, SD= 6.93
VAP, n	3,369
Survival status, n (%)	
Alive	137,616 (89.53%)
Death	16,101 (10.47%)
Number of countries, stratified per income level according to World Bank	10,101 (1011/2)
Lower middle income country	6 (66.67%)
Upper middle income country	3 (33.33%)
Number of patients admitted per facility ownership, n (%)	3 (33.35%)
Publicly owned facilities	16,231 (10.56%)
For-profit privately owned facilities	76,077 (49.49%)
University hospitals	
Not-for-profit privately owned facilities	50,459 (32.83%) 10,050 (7,12%)
	10,950 (7.12%)
Number of patients per Hospitalization type	115.004 (75.05%)
Medical hospitalization, n (%)	115,824 (75.35%)
Surgical hospitalization, n (%)	37,893 (24.65%)
Number of patients admitted per type of ICU, n (%)	
Medical-Surgical ICU	89,524 (58.24%)
Medical ICU	24,847 (16.16%)
Coronary ICU	9,846 (6.41%)
Surgical ICU	9,747 (6.34%)
Pediatric ICU	6,605 (4.30%)
Neuro-Surgical ICU	4,912 (3.20%)
Cardio-thoracic ICU	4,323 (2.81%)
Trauma ICU	2,490 (1.62%)
Neurologic ICU	1,423 (0.93%)
Gender, n (%)	
Male	97,137 (63.19%)
Female	56,580 (36.81%)
Age, mean, SD	Mean= 53.74, SD= 21.82
Device-d and device utilization ratio	
MV-utilization ratio, mean, SD	mean= 0.24, SD= 0.55
Total MV-d, n, mean, SD	225,019, mean= 1.46, SD= 4.20
Number of d using the following types of respiratory support, $n(\%)$	· · · · · · · · · · · · · · · · · · ·
CPAP	1,844 (0.82%)
Endotracheal tube with MV	213,361 (94.82%)
Tracheostomy with MV	9,103 (4.05%)
Tracheostomy without MV	711 (0.32%)
CPAR continuous pacifico airuan procuren ICU intensivo care uniti ICC length of staru M/ mechanical ventilator: CD standa	. ,

CPAP, continuous positive airway pressure; ICU, intensive care unit; LOS, length of stay; MV, mechanical ventilator; SD, standard deviation; VAP, Ventilator associated pneumonia.

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Table 2

Ventilator associated pneumonia rates stratified per ICU type, per World Bank country classifications of income level, per Facility ownership type, and per country

	Patients, n	Patient d, n	VAP, n	MV-d, n	VAP rate	95% CI
ICU type*						
Pooled	153,717	892,996	3,369	258,442	13.04	13.02 - 13.05
Neurologic	1,423	8,903	44	2,758	15.95	15.80 - 16.10
Medical-surgical	89,524	497,238	2,466	156,294	15.78	15.76 - 15.8
Medical	24,847	168,713	530	39,173	13.53	13.49 - 13.56
Neuro-surgical	4,912	31,103	95	8,468	11.22	11.14 - 11.29
Cardio-thoracic	4,323	18,591	53	6,660	7.96	7.89 - 8.02
Pediatric	6,605	40,957	64	14,472	4.42	4.38 - 4.45
Surgical	6,747	62,441	50	11,498	4.35	4.31 - 4.38
Trauma	2,490	11,548	18	4,177	4.31	4.24 - 4.37
Coronary	9,846	53,502	49	14,942	3.28	3.25 - 3.30
Lower-middle income						
Pooled	144,788	830,212	3,043	23,1674	13.13	13.12 - 13.15
Publicly owned facilities	13,235	83,149	559	29,494	18.95	18.90 - 19.00
For-profit privately owned facilities	75,370	435,584	1,922	120,032	16.01	15.99 - 16.04
University hospitals	45,233	250,807	418	66,680	6.27	6.24 - 6.28
Not-for-profit privately owned facilities	10,950	60,672	144	15,468	9.31	9.26 - 9.35
Upper-middle income						
Pooled	8,929	62,784	326	26,768	12.18	12.13 - 12.22
Publicly owned facilities	2,996	23,586	8	4,662	1.72	1.67 - 1.75
For-profit privately owned facilities	707	3,117	2	1,180	1.69	1.62 - 1.77
University hospitals	5,226	36,081	316	20,926	15.10	15.04 - 15.15

CI, confidence interval; ICU, intensive care unit; MV, mechanical ventilator; VAP, Ventilator associated pneumonia.

*ICUs are listed in order of the highest to lowest Ventilator associated pneumonia rate.

DISCUSSION

In our study, age, male gender, LOS, MV/DU ratio, use of tracheostomy, hospitalization in public hospitals and private hospitals, upper middle-income countries, medical-surgical, neurologic, neurosurgical, and medical ICUs were identified as independent VAP RFs.

The risk of VAP increased 1% per year according with our study. Beardsley et al. carried out a study to pinpoint VAP risk variables in a children's quaternary care hospital. In their study, older age was also one of the VAP RF.²¹

The current investigation found a link between VAP and male gender. Coincidentally, Kollef et al. examined 521 ICU patients who needed MV for more than 12 hours in a prospective cohort study they carried out in the ICUs of Barnes-Jewish Hospital. They proved

Table 3 Multiple logistic regression analysis of risk factors for Ventilator associated pneumonia

	aOR	95% CI	P value
	uon	55% CI	1 value
Age	1.01	1.00-1.01	<.0001
Gender, male	1.17	1.08-1.26	<.0001
LOS	1.07	1.06-1.07	<.0001
MV-d	0.96	0.95-0.96	<.0001
MV-utilization ratio	1.43	1.36-1.51	<.0001
Tracheostomy connected to a MV	11.17	9.55-14.27	<.0001
Endotracheal tube connected to a MV	6.38	5.81-7.02	<.0001
Surgical Hospitalization	1.09	0.99-1.19	.06
Publicly owned facilities	1.79	1.46-2.22	<.0001
For-profit privately owned facilities	1.57	1.29-1.91	<.0001
University hospitals	0.66	0.54-0.81	<.0001
Upper middle income country	1.86	1.63-2.14	<.0001
Medical-Surgical ICU	4.61	3.43-6.17	<.0001
Neurologic ICU	3.76	2.43-5.82	<.0001
Medical ICU	2.78	2.04-3.79	<.0001
Neuro-Surgical ICU	2.33	1.61-3.92	<.0001
Coronary ICU	0.69	0.45-1.06	.08
Pediatric ICU	1.28	0.84-1.97	.24
Surgical ICU	0.69	0.45-1.04	.07
Trauma ICU	1.15	0.65-2.02	.63

aOR, adjusted odds ratio; *CI*, confidence interval; *ICU*, intensive care unit; *LOS*, length of stay; *MV*, mechanical ventilator; *VAP*, ventilator associated pneumonia.

through the use of multivariate logistic regression analysis that the male gender was a RF independently linked to the emergence of VAP. $^{\rm 22}$

In addition, our study found a link between VAP and the MV/DU ratio. In their NICU, Geslain et al. carried out a prospective observational study. Logistic regression were used in the data analysis. Patients who developed VAP had invasive ventilation for significantly longer periods of time.²³

We found that LOS as associated with rise on the risk of VAP. Coincidentally, a prospective study was conducted by Sofianou et al to determine the VAP RF in patients requiring MV for more than 48 hours. VAP occurred in 67 (33.8%) patients. Logistic regression analysis showed a relationship between VAP and LOS in ICU,²⁴

We found a higher risk of VAP in patients using tracheostomy. Ibrahim et al conducted a prospective cohort study to identify VAP RF in a medical ICU and a surgical ICU in a 500-bed private community nonteaching hospital in US. Eight hundred eighty patients received MV. VAP developed in 132 patients receiving MV. Logistic regression analysis demonstrated that tracheostomy was also independently associated with the development of VAP.²⁵

Also, there was a link between the risk of VAP in public and private hospitals versus teaching hospitals. On the contrary, a previous study in NICUs found that the VAP rate per 1,000 MV-days was 13.2; 95% CI 11.5-15.0 at university hospitals, 4.9; 95% CI 2.5-8.6 at public hospitals, and 2.4; 95% CI 1.3-3.9 at private hospitals. University hospitals compared with private hospitals showed a higher risk for VAP at university hospitals (RR 5.56; 95% CI 3.30-9.38, P = .0001).²⁶ University hospitals compared with public hospitals showed a higher risk for VAP at university hospitals (RR 2.69; 95% CI 1.50-4.80, P = .0001).²⁶ Also a previous study conducted in PICUs found that the VAP rate per 1,000 MV-days at university hospitals was 8.3; 95% CI 7.3-9.3, at public hospitals was 4.7; 95% CI 3.9-5.7, and at private hospitals was 3.5; 95% CI 2.6-4.5.²⁷ Public hospitals compared with private hospitals showed a higher risk for VAP at public hospitals. University hospitals compared with private or public hospitals showed the highest risk for VAP at university hospitals.²⁷

In our research, we found that the risk of VAP was higher in ICU patients from upper middle-income countries than in ICU patients

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from lower middle-income countries. On the contrary, in a previous study conducted in NICUs, which discovered that the VAP rate per 1,000 MV-days in lower middle income countries was 11.8; 95% CI 10.1-13.6; and 6.7; 95% CI 5.2-8.5 in upper middle income countries. Lower middle-income countries had a higher risk of VAP when compared to upper middle-income countries (RR 1.75; 95% CI 1.32-2.32, P = .0001).²⁶ In a previous study conducted in PICUs, VAP rate per 1,000 MV-days in lower middle income countries was 9.0; 95% CI 7.5-10.6, and in upper middle income countries was 5.4; 95% CI 4.8-6.1. Lower middle income countries had a higher risk of VAP than upper middle income countries.²⁷ This finding could be explained by the probably inadequate health care quality programs in those upper middle-income countries participating in our study.

We also discovered that medical surgical, neurologic, neurosurgical, and medical ICUs had the highest risk. MV-utilization ratio, as a marker of severity of illness of patients, is the highest at those types of ICUs,²⁸ and this could explain these ICUs are associated with the highest risk of VAP.

Some of the VAP risk factors found in our study, such as the nation's economy, hospital affiliation, ICU type, age, and gender, are not expected to change. Based on the obtained results, the RFs with the highest chance to have an impact is limiting the use of tracheostomy, limiting the LOS, reducing the MV/DU ratio, and improving management of patients using MV with a set of recommendations based on evidence such as those published by APIC/IDSA/SHEA to prevent VAPs.²⁹

It has been demonstrated that it is feasible to lower the extremely high rate of VAP that is now present in Asia. This is accomplished by following the above-mentioned recommendations of APIC/SHEA/ IDSA, adding monitoring compliance with them, and giving health personnel performance feedback.³⁰⁻³⁷

Our study has some limitations. First, because this study is part of a surveillance system in which hospitals voluntarily participate for free, it is not representative of all hospitals in Asia. Second, the VAP rates in our study are probably lower than the VAP rates discovered in other hospitals that are not participating in our study, since the hospitals that take part in our surveillance system are probably the ones that have a better-quality VAP surveillance and prevention program. Third, it is possible that changes in personal or practices may have influenced risk over time. Last but not least, the IPPs of the participating hospitals did not collect information on underlying disorders and disease severity scores. Instead, we used the mechanical ventilation utilization ratio as a measure of severity of illness of patients were and adjusted the analysis to account for this independent variable.

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References

- Rosenthal VD, Maki DG, Graves N. The International Nosocomial Infection Control Consortium (INICC): goals and objectives, description of surveillance methods, and operational activities. *Am J Infect Control*. 2008;36:e1–e12.
- Rosenthal VD. International Nosocomial Infection Control Consortium (INICC) resources: INICC multidimensional approach and INICC surveillance online system. Am J Infect Control. 2016;44:e81–e90.
- Rosenthal VD, Maki DG, Salomao R, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. *Ann Intern Med.* 2006;145: 582–591.
- Rosenthal VD, Maki DG, Mehta A, et al. International nosocomial infection control consortium report, data summary for 2002-2007, issued January 2008. *Am J Infect Control*. 2008;36:627–637.

- Rosenthal VD, Maki DG, Jamulitrat S, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary for 2003-2008, issued June 2009. *Am J Infect Control*. 2010;38:95–104.
- Rosenthal VD, Bijie H, Maki DG, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004-2009. *Am J Infect Control*. 2012;40:396–407.
- Rosenthal VD, Maki DG, Mehta Y, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 43 countries for 2007-2012. Deviceassociated module. *Am J Infect Control*. 2014;42:942–956.
- Rosenthal VD, Al-Abdely HM, El-Kholy AA, et al. International Nosocomial Infection Control Consortium report, data summary of 50 countries for 2010-2015: device-associated module. *Am J Infect Control*. 2016;44:1495– 1504.
- 9. Rosenthal VD, Bat-Erdene I, Gupta D, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 45 countries for 2012-2017: Device-associated module. *Am J Infect Control*. 2020;48:423–432.
- Rosenthal VD, Duszynska W, Ider BE, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary of 45 countries for 2013-2018, adult and pediatric units, device-associated module. *Am J Infect Control*. 2021;49:1267– 1274.
- Almuneef M, Memish ZA, Balkhy HH, Alalem H, Abutaleb A. Ventilator-associated pneumonia in a pediatric intensive care unit in Saudi Arabia: a 30-month prospective surveillance. *Infect Control Hosp Epidemiol*. 2004;25:753–758.
- 12. Petdachai W. Ventilator-associated pneumonia in a newborn intensive care unit. *Southeast Asian J Trop Med Public Health*. 2004;35:724–729.
- Pawar M, Mehta Y, Khurana P, Chaudhary A, Kulkarni V, Trehan N. Ventilator-associated pneumonia: Incidence, risk factors, outcome, and microbiology. J Cardiothorac Vasc Anesth. 2003;17:22–28.
- 14. Apisarnthanarak A, Holzmann-Pazgal G, Hamvas A, Olsen MA, Fraser VJ. Ventilator-associated pneumonia in extremely preterm neonates in a neonatal intensive care unit: characteristics, risk factors, and outcomes. *Pediatrics*. 2003;112:1283– 1289.
- National Healthcare Safety Network (NHSN) Patient Safety Component Manual. 2022. https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf. Accessed November 4, 2022.
- Emori TG, Culver DH, Horan TC, et al. National nosocomial infections surveillance system (NNIS): description of surveillance methods. *Am J Infect Control*. 1991;19: 19–35.
- National Healthcare Safety Network. General Key Terms. 2022. https://www.cdc. gov/nhsn/pdfs/pscmanual/16psckeyterms_current.pdf. Accessed November 4, 2022.
- New World Bank country classifications by income level: 2021-2022. 2022. https://blogs.worldbank.org/opendata/new-world-bank-country-classificationsincome-level-2021-2022. Accessed November 4, 2022.
- Dudeck MA, Edwards JR, Allen-Bridson K, et al. National Healthcare Safety Network report, data summary for 2013, Device-associated Module. *Am J Infect Control.* 2015;43:206–221.
- World Health Organization. Glossary of Terms. WHO European Primary Health Care Impact Performance and Capacity Tool (PHC-IMPACT) Page 152019. https:// www.euro.who.int/__data/assets/pdf_file/0006/421944/Glossary-web-171219. pdf. Accessed November 4, 2022.
- 21. Beardsley AL. Ventilator-associated infections need a new approach. *Pediatr Crit* Care Med. 2016;17:587.
- Kollef MH, Von Harz B, Prentice D, et al. Patient transport from intensive care increases the risk of developing ventilator-associated pneumonia. *Chest.* 1997;112:765–773.
- 23. Geslain G, Guellec I, Guedj R, et al. Incidence and risk factors of ventilator-associated pneumonia in neonatal intensive care unit: a first French study. *Minerva Anestesiol.* 2018;84:829–835.
- Sofianou DC, Constandinidis TC, Yannacou M, Anastasiou H, Sofianos E. Analysis of risk factors for ventilator-associated pneumonia in a multidisciplinary intensive care unit. Eur J Clin Microbiol Infect Dis. 2000;19:460–463.
- Ibrahim EH, Tracy L, Hill C, Fraser VJ, Kollef MH. The occurrence of ventilator-associated pneumonia in a community hospital: risk factors and clinical outcomes. *Chest*, 2001;120:555-561.
- Rosenthal VD, Lynch P, Jarvis WR, et al. Socioeconomic impact on device-associated infections in limited-resource neonatal intensive care units: findings of the INICC. Infection. 2011;39:439–450.
- Rosenthal VD, Jarvis WR, Jamulitat S, et al. Socioeconomic impact on device-associated infections in pediatric intensive care units of 16 limited-resource countries: international Nosocomial Infection Control Consortium findings. *Pediatr Crit Care Med*. 2012;13:399–406.
- CDC-NHSN. The 2019 National and State Healthcare-Associated Infections (HAI) Progress Report. [cited 2022 February 17]. https://www.cdc.gov/nhsn/datastat/ index.html. Accessed November 4, 2022.
- Klompas M, Branson R, Cawcutt K, et al. Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 Update. *Infect Control Hosp Epidemiol*. 2022;43:687–713.
- Leblebicioglu H, Yalcin AN, Rosenthal VD, et al. Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in 11 adult intensive care units from 10 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). *Infection.*. 2013;41:447– 456.

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- **31.** Mehta Y, Jaggi N, Rosenthal VD, et al. Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in 21 adult intensive-care units from 10 cities in India: findings of the International Nosocomial Infection Control Consortium (INICC). *Epidemiol Infect.* 2013;141:2483–2491.
- 32. Rosenthal VD, Rodrigues C, Alvarez-Moreno C, et al. Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in adult intensive care units from 14 developing countries of four continents: findings of the International Nosocomial Infection Control Consortium. *Crit Care Med*. 2012;40: 3121–3128.
- **33.** Rosenthal VD, Alvarez-Moreno C, Villamil-Gomez W, et al. Effectiveness of a multidimensional approach to reduce ventilator-associated pneumonia in pediatric intensive care units of 5 developing countries: International Nosocomial Infection Control Consortium findings. *Am J Infect Control*. 2012;40:497–501.
- 34. Rosenthal VD, Rodriguez-Calderon ME, Rodriguez-Ferrer M, et al. Findings of the International Nosocomial Infection Control Consortium (INICC), Part II: impact of a

multidimensional strategy to reduce ventilator-associated pneumonia in neonatal intensive care units in 10 developing countries. *Infect Control Hosp Epidemiol*. 2012;33:704–710.

- 35. Tao L, Hu B, Rosenthal VD, Zhang Y, Gao X, He L. Impact of a multidimensional approach on ventilator-associated pneumonia rates in a hospital of Shanghai: findings of the International Nosocomial Infection Control Consortium. J Crit Care. 2012;27:440–446.
- 36. Al-Mousa HH, Omar AA, Rosenthal VD, et al. Impact of the International Nosocomial Infection Control Consortium (INICC) multidimensional approach on rates of ventilator-associated pneumonia in intensive care units of two hospitals in Kuwait. J Infect Prev. 2018;19:168–176.
- **37.** Rosenthal VD, Desse J, Maurizi DM, et al. Impact of the International Nosocomial Infection Control Consortium's multidimensional approach on rates of ventilatorassociated pneumonia in 14 intensive care units in 11 hospitals of 5 cities within Argentina. *Am J Infect Control*. 2018;46:674–679.