# Risk Factors Associated with Ventilator-associated Pneumonia Incidence in the Intensive Care Unit at Haji Adam Malik General Hospital, Medan, Indonesia

Miranda[1*], Achsanuddin Hanafie[2], Rina Yunita[3]
[1]Tropical Medicine Program Faculty Medicine, Universitas Sumatera Utara, Jl Dr. Mansur No 5 Medan 20155,
[2]Departement of Anesthesiology and Intensive Therapy, Haji Adam Malik General Hospital, Medan, Indonesia.
[3]Departement of Mycrobiology, Faculty of Medicine, Universitas Sumatera Utara, Medan Indonesia.

Keywords: Ventilator-Associated Pneumonia, pneumonia, nosocomial, risk factors, Indonesia

Abstract: *Ventilator-associated pneumonia* (VAP) is defined as nosocomial pneumonia that occurs 48 hours after using mechanical ventilation. The primary objective of this study is to investigate the risk factors associated with the incidence of VAP. The secondary objective is to identify the pattern of bacterial sensitivity in confirmed VAP cases. A retrospective study was conducted in the intensive care unit at Haji Adam Malik General Hospital, Medan. Data of 60 patients with and without VAP diagnosis between March 2017 and October 2018 were evaluated. The most common cause of infection was *Klebsiella pneumonia* (36.7%), with 90.9% were sensitive to Amikacin. Majority of patients were (76.6%, 46/60) aged < 60 years, used ventilator longer than 5 days (68.3%, 41/60) and with the smoking habit (53.5%, 32/60). We found no association between age, duration of ventilator and smoking habit with the increased incidence of VAP. Further study with a larger sample size may be needed to find the associations.

## 1 INTRODUCTION

Ventilator Associated pneumonia (VAP) is defined as pneumonia occurring 48 hours after the initiation of endotracheal intubation and mechanical ventilation (MV) (PDPI, 2003; Goel E et al., 2012; Widyaningsih R and Buntaran L, 2012; Hezati M E et al., 2015). The use of endotracheal tube increased the risk of infectious agents to gain direct access to the lower respiratory tract leading to pneumonia (Kalanuria A et al., 2014). VAP is classified into early onset (<5 days) and late onset (≥5 days). Early onset is usually caused by sensitive pathogens, while late onset is due to multidrug resistance microbial (Sedwick M B et al., 2012). Clinical assessment, physical examination and radiographic images incorporated in the clinical pulmonary infection scoring (CPIS) is the most common tool used to predict the occurrence of VAP.

A systematic review of 51 prospective randomized trial described the incidence of VAP was 22,8% (Yunita R and Rondhianto W,2015), and 86% of all cases were due to nosocomial infections (Wahyuning Tyas et al., 2013). VAP was associated with increased morbidity and mortality, prolonged hospital stay and patient cost (Koenig S M and truwit J D, 2006). The incidences of VAP in other countries varied from 9% to 27% (Chawla, 2008) while there are no definite incidence rates reported from Indonesia. High mortality ranging from 24% to 50% has been associated with the presence of antimicrobial resistance particularly in cases of *Pseudomonas aeruginosa*, *Acinetobacter baumanii*, *Klebsiella,* and *Enterobacter* spp. The wide use of antimicrobials, the presence of comorbidity and prolonged used of mechanical ventilator facilitated the development of antimicrobial resistance (Resende M et al.,2013). Studies have reported factors including prior intravenous antibiotic use within the previous 90 days, septic shock at time of VAP diagnosis, acute respiratory distress syndrome (ARDS) preceding VAP, hospitalization ≥ 5 days prior to the occurrence of VAP, and acute renal replacement therapy prior to VAP onset to be the main factors associated with VAP.

There are several risk factors affecting the development of VAP. Some of these risk factors may have already been presented at admission to the Intensive Care Unit (ICU), such as advanced age,



Miranda, ., Hanafie, A. and Yunita, R.
Risk Factors Associated with Ventilator-associated Pneumonia Incidence in the Intensive Care Unit at Haji Adam Malik General Hospital, Medan, Indonesia.
DOI: 10.5220/0009863902370242
In *Proceedings of the 2nd International Conference on Tropical Medicine and Infectious Disease (ICTROMI 2019)*, pages 237-242
ISBN: 978-989-758-469-5

presence of respiratory or cardiovascular system disease, organ failure, burns, trauma, acute respiratory distress syndrome (ARDS), gastric colonization, sinusitis, high volume gastric aspiration, and seasonal change (Ziyaettin K R I et al., 2018) . Age is one of the main factors influencing the VAP events. Susanti et al. described that the older the age of the patients treating by a ventilator, the greater the risk to develop VAP. This is because the age older than 60 years old has a greater risk of suffering pneumonia in the use of a mechanical ventilator in the ICU and there is a decrease in the body's immune function (Susanti E et al., 2013)

Another factor influencing VAP events is the duration of mechanical ventilator used. Mechanical ventilation is a machine to perform some or all of the work of breathing and an essential aspect of critical patient care (Clare M V and Dacvecc H K, 2005). Therefore, identification of risk factors associated with VAP is needed to implement preventive measures and to reduce mortality as the outcome of VAP. In this study, we aimed to evaluate the association between risk factors and the incidence of VAP among intensive care unit patients in Haji Adam Malik General Hospital in Medan, Indonesia.

## 2 METHODS

Data from 60 ICU patients admitted at Haji Adam Malik Hospital between March 2017 and October 2018 was collected (see table 1). CPIS form was used to assess risk factors and information on VAP. VAP diagnosis was made by the ICU doctors based on the following criteria: at least two of the following points, fever of ≥ 38°C, leukocytosis of 10.000/mm$^3$ or more, and purulent respiratory secretions; with chest radiograph showing new, persistent pulmonary infiltrates. The diagnosis was confirmed by sputum culture at the microbiology laboratory (see table 2).

Inclusion criteria were patients aged more than 18 years old and intubated and mechanically ventilated for more than 48 hours. Exclusion criteria included patients with underlying diseases (tuberculosis, malignancy, chronic obstructive pulmonary diseases, and pneumonia).

The study was reviewed and approved by the ethics committee at the Faculty of Medicine, Universitas Sumatera Utara.

Table 1: Demographic characteristics of research subjects in ICU

| **Characteristics** | **n = 60 (%)** |
|---|---|
| Gender, n (%) | |
| Male | 35 (58.3) |
| Female | 25 (41.7) |
| Age (years) | |
| <60 | 46 (76.7) |
| ≥60 | 14 (23.3) |
| Duration of ventilator used (days) | |
| > 5 | 41 (68.3) |
| ≤ 5 | 19 (31.7) |
| Education level, | |
| Primary school | 12 (20.0) |
| Junior high school | 7 (11.7) |
| High school | 38 (63.3) |
| University | 3 (5.0) |
| Occupation | |
| Private sectors | 28 (46.7) |
| Midwife | 16 (26.7) |
| Farmer | 6 (10.0) |
| Trader | 3 (5.0) |
| Fisherman | 2 (3.3) |
| Government officers | 2 (3.3) |
| Student | 2 (3.3) |
| Retired | 1 (1.7) |
| Smoking habits | |
| Yes | 32 (53.3) |
| No | 28 (46.7) |

Table 2 : Clinical Pulmonary Infection Score (CPIS)

| **Component** | | **Score** |
|---|---|---|
| Temperature ($^0$ C) | 36,5 - 38,4 | 0 |
| | 38,5 - 38,9 | 1 |
| | ≤36 and ≥39 | 2 |
| Blood Leukocytes (/mm$^3$) | 4000-11000 | 0 |
| | < 4000 atau > 11000 | 1 |
| | ≥ 500 cells band | 2 |
| Tracheal secretions | None | 0 |
| | Few or non purulent | 1 |
| | Purulent | 2 |
| Oxygenation $PaO_2$ /$FiO_2$mmHg | >120 or ARDS | 0 |
| | ≤ 240 and absence of ARDS | 2 |
| Chest radiograph | No, infiltrate | 0 |
| | Patchy or diffuse infiltrate | 1 |
| | Localized infiltrate | 2 |

# 3 RESULTS

Sixty patients were enrolled in the study. Of those, 30 was patients diagnosed with VAP and 30 was not identified as VAP cases. Baseline characteristics are shown in Table 1. Thirty-five patients (58.3%) was male, and 46 (76.7%) aged younger than 60 years old. The duration of mechanical ventilation use longer than 5 days occurred in 41 patients (68.3%). None of the risk factors assessed in this study increased the risk of VAP incidence in the ICU (Table 3); being male (OR 1.115, 95% CI 0.364-3.628, *P*=0.793), aged ≥ 60 years old (OR 0.688, 95% CI 0.168-2.695, *P*=0.542), ventilator used longer than 5 days (OR 1.592, 95% CI 0.465-5.573, *P*=0.405), and had smoking habit (OR 1).

Furthermore, 30 patients confirmed with VAP had bacterial growth in culture (See table 4) with *Klebsiella pneumonia* (*N*=11) as the most common organism, followed by *Acinetobacter baumannii* (*N*=8) and *Pseudomonas aeruginosa* (*N*= 4). Sensitivity test showed amikacin to be sensitive to *K. pneumonia* infection (90.9%).

The evaluation of sensitivity and antibiotic resistance on the pathogens are described in Table 5. Nine antibiotics were still sensitive against *P. aeruginosa* including ceftazidime, amikacin, ceftriaxone, meropenem, ertapenem, cefazoline, cefixime, ciprofloxacin, and aztreonam. While there were 14 antibiotics that were highly resistant to *P. aeruginosa*.

Sensitivity analysis on *K. pneumoniae* showed 12 antibiotics were still sensitive including amikacin, ertapenem, meropenem, gentamycin, ciprofloxacin, cefoperazone/sulbactam, ceftazidime, amoxicillin/ clavulanic acid, levofloxacin, tetracycline, tigecycline, and polymixin B. Fourteen antibiotics showed resistance to *K. pneumoniae* (see table 5).

The analysis also showed that amikacin, ertapenem, meropenem, polymixin B, ceftazidime, ciprofloxacin and piperacillin/tazobactam to be sensitive to *A. baumannii* (see table 5)

Table 3: Relationship between risk factors with VAP in the ICU at Haji Adam Malik General Hospital, Medan, Indonesia

| Variables | VAP | | OR (95% CI) | *P* |
|---|---|---|---|---|
| | Cases (n=30) | Controls (n=30) | | |
| Age, (Year) | | | | |
| ≥ 60 | 6 (20.0) | 8 (16.7) | 0.688 (0.168-2.695) | 0,542 |
| < 60 | 24 (80.0) | 22 (73.3) | | |
| Duration of ventilator used, (days) | | | | |
| > 5 | 22 (73.3) | 7 (63.3) | 1.592 (0.465-5.573) | 0,405 |
| ≤ 5 | 8 (26.7) | 3 (36.7) | | |
| Smoking habits | | | | |
| Yes | 16 (53.3) | 16 (53.3) | 1 (0.322-3.109) | 1,000 |
| No | 14 (46.7) | 14 (46.7) | | |
| | | | | |

Table 4: Bacterial profile of patients diagnosed with VAP

| Bacterial isolated | N | % |
|---|---|---|
| *Klebsiella pneumonia* | 11 | 36,7 |
| *Acinetobacter baumanii* | 8 | 26,7 |
| *Pseudomonas aeruginosa* | 4 | 13,3 |
| *Staphylococcus aureus* | 3 | 10.0 |
| *Enterobacter cloacae* | 2 | 6,7 |
| *Elizabethkinqia meni* | 1 | 3,3 |
| *Raoultella ornithine* | 1 | 3,3 |
| **Total** | **30** | **100,0** |

Table 5: Antibiotic sensitivity and resistance to bacteria caused VAP in ICU Haji Adam Malik General hospital

| Antibiotic | KP | | | AB | | | PA | | |
|---|---|---|---|---|---|---|---|---|---|
| | S | I | R | S | I | R | S | I | R |
| Amikasin | 90,9 | 9,1 | 0 | 75 | 0 | 25 | 50 | 0 | 50 |
| Ampicillin | 0 | 54,5 | 45,5 | 0 | 87,5 | 12,5 | 0 | 100 | 0 |
| Ampicillin/Sulbaktam | 0 | 54,5 | 0 | 0 | 87,5 | 12,5 | 0 | 100 | 0 |
| Cefazolin | 0 | 36,4 | 63,6 | 0 | 50 | 50 | 25 | 25 | 50 |
| Cefixim | 0 | 45,5 | 54,5 | 0 | 75 | 25 | 25 | 75 | 0 |
| Ceftazidime | 9,1 | 36,4 | 0 | 12,5 | 12,5 | 75 | 100 | 0 | 0 |
| Ceftriaxone | 0 | 27,3 | 72,7 | 0 | 25 | 75 | 50 | 50 | 0 |
| Ertapenem | 81,8 | 0 | 18,2 | 25 | 12,5 | 62,5 | 50 | 0 | 50 |
| Meropenem | 81,8 | 0 | 18,2 | 25 | 12,5 | 62,5 | 50 | 0 | 50 |
| Ciprofloxacin | 27,3 | 0 | 18,2 | 12,5 | 62,5 | 25 | 25 | 75 | 0 |
| Erithromycin | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Gentamycin | 36,4 | 45,5 | 18,2 | 0 | 100 | 0 | 0 | 75 | 25 |
| Lefofloxacin | 9,1 | 81,8 | 9,1 | 0 | 87,5 | 12,5 | 0 | 100 | 0 |
| Netilmicin | 0 | 90,9 | 9,1 | 0 | 100 | 0 | 0 | 100 | 0 |
| Tetracycline | 9,1 | 81,8 | 9,1 | 0 | 100 | 0 | 0 | 50 | 50 |
| Vancomycin | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Trimthoprime/Sulfamethoxazole | 0 | 90,9 | 9,1 | 0 | 87,5 | 12,5 | 0 | 50 | 50 |
| Aztreonam | 0 | 90,9 | 9,1 | 0 | 100 | 0 | 25 | 75 | 0 |
| Fosfomycin | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Amoxicillin/Clavulanic Acid | 9,1 | 90,9 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Polymixin B | 9,1 | 90,9 | 0 | 25 | 75 | 0 | 0 | 100 | 0 |
| Linezolid | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Tigecycline | 9,1 | 90,9 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Cefotaxime | 0 | 63,6 | 36,4 | 0 | 37,5 | 62,5 | 0 | 100 | 0 |
| Cefuroxime | 0 | 90,9 | 9,1 | 0 | 87,5 | 12,5 | 0 | 100 | 0 |
| Cotrimoxazole | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Cefoperazone/Sulbactam | 18,2 | 81,8 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |
| Nitrofurantoin | 0 | 81,8 | 18,2 | 0 | 100 | 0 | 0 | 75 | 25 |
| Piperacillin/Tazobactam | 0 | 90,9 | 9,1 | 12,5 | 87,5 | 0 | 0 | 75 | 25 |
| Clindamycin | 0 | 100 | 0 | 0 | 100 | 0 | 0 | 100 | 0 |

KP *Klebsiella pneumoniae*, AB *Acinetobacter baumanii*, PA *Pseudomonas aeruginosa*, S sensitive, I intermediate, R resistance

# 4 DISCUSSIONS

VAP has been associated with mortality, and this study evaluated the risk factors associated with the incidence of VAP in order to implement preventive measures in order to reduce mortality in ICU patients.

In this study, we found age not to be a risk factor for VAP in contrast to other studies. This can be explained by the age distribution among our patients. The majority of patients hospitalized in the ICU were aged less than 60 years old with the most common diagnosis of post-craniotomy with a history of traffic accidents. Similar results were shown in studies from Kurdistan Iran which described the majority of patients exposed to VAP was younger than 60 years old, as also in a study reported in Indonesia (Riatsa A et al., 2013).

VAP has also been reported to likely occur in the first week of mechanical ventilation due to the interaction of more risk factors at the beginning of admission (Putri Y and Budiono, 2014). However, in this study, the length of ventilator use was not significantly associated with the development of VAP. Neither the longer use of a ventilator (>5 days), as determined to be the cutoff for longer use of a ventilator, nor shorter us increased the risk of VAP. This is also supported by the results of a study from the ICU of Dr. Kariadi General Hospital Semarang Indonesia (Santoso B, 2015).

In addition, we also did not find a significant association between smoking habit and the incidence of VAP, similar to the findings in other studies

(Santoso B, 2015; Maria YS, 2011; Othman HA et al, 2017).

This retrospective study had several limitations. First, this study was conducted in a single medical center and there may have been patient selection bias. Second, this study was a retrospective survey, which not only resulted in incomplete data for some patients. Third, the disproportion of the samples in the collecting stage. This disproportion may result in different findings from others, including age, duration of ventilator used and smoking habits.

VAP remains an important nosocomial infection especially among the critically ill patients admitted to the ICU in our setting. Further study involving more detailed risk factors, diagnosis at admission, and presence of high-risk microorganisms need to be conducted to determine the risk factor for this event.

# 5 CONCLUSIONS

1 The risk factor that has no significant related with VAP infection in ICU patient at Haji Adam Malik General hospital Medan are age (OR= 0.688, 95% CI 0.168-2.695, P=0.542)

2 There was no significant association between duration of ventilator used with VAP incidence but the duration of ventilator used more than 5 days are more 1.592 at risk for VAP than ≤ 5 days OR 0.592, 95% CI 0.465-5.573, P=0.405)

3 There was no significant association between smoking habits with VAP incidence. The risk value cannot be assessed because the group of cases exposed and the control group exposed to the same number. (OR=1, 95% CI 0.322-3.109, P=1,000)

4 There are seven bacteria cause VAP found in this study: Klebsiella pneumonia, Acinetobacter baumanii, Pseudomonas aeruginosa, Staphylococcus aureus, Enterobacter cloacae, Elizabethkinqia meni, and Staphylococcus aureus.

5 The results of sensitivity test for K.pneumoniae, Amikacin, Ertapenem, Meropenem, Gentamycin, Ciprofloxacin,Cefoperazone/Sulbactam, Ceftazidime Amoxycillin/Clavulanic acid, Levofloxacin, Tetracycline, Tigecycline and Polymixin B. The results of sensitivity test for A.baumanii Amikacin, Ertapenem, Meropenem, Polymixin B, Ceftazidime, Ciprofloxacin, and Piperacillin/Tazobactam. The results of a sensitivity test for P.aeruginosa Ceftazidime, Amikacin, Ceftriaxone, Meropenem, Ertapenem, Cefazoline, Cefixime, Ciprofloxacin, and Aztreonam.

# REFERENCES


Chawla, R. M., 2008. *Epidemiology, Etiology and Diagnosis of Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia in Asian Countries*. 36(4), pp. S93-S100.

Clare, M. V., & DACVECC, H. K. Mechanical ventilation: Indication, goals, and prognosis. 2005.p.195-208.

Goel, V., A Hogade, S. & Karadesai, S., 2012. *Ventilator Associated Pneumonia in a Medical Intensive Care Unit: Microbial Aetiology, Sesceptibility Pattern of Isolated Microorganism and Outcome*,. Indian journal of Anaesthesia. 2012:56(6) : 558-562.

Hezati, M. E., Nazamiyeh, M., Seifar, F. & Beheshti, F., 2015. *Polymicrobial Ventilatoe Associated Pneumonia and Antibiotic Susceptibility of Bacterial Isolates in a University Hospital*, Tabriz, Iran. *African Journal of Bacteriology Research.*2015 : 7(5), p. 52-55.

Kalanuria, A. A., Zai, W. & Mirski, M. *Ventilator Associated Pneumonia in the ICU.*2014: 18(2), p. 1-8.

Koenig, S. M. & Truwit, J. D. *Ventilator-A ssociated Pneumonia: Diagnosis, Treatment, and Prevention. Clinical microbiology reviews.*2006: 19(4), p. 637-657.

Lahoorpour, F., Delpisheh, A., & Afkamzadeh, A. Risk factors for acquisition of ventilator associated pneumonia in adult intensive care unit.2013:*29* (5), 1105-1107.

Maria Yosephine Sutiastuti. faktor-faktor yang Berhubungan dengan Kejadian Pneumonia pada Pasien pada unit Unit Intensif di Rumah Sakit Pondok Indah Jakarta Selatan, Skripsi, Universitas Pembangunan Nasional, Jakarta.2011.

Othman, H. A., Gamil, N. M., Elgazzar, A. E., & Fouad, T. A. (2017). Ventilator associted pneumonia, Incidence and risk factors in emergency intensive care unit Zagazig university hospital . *Egyptian journal of chest diseses and tuberculosis*.2017: *66*. 703-708.

PDPI . Pneumonia Nosokomial. Dalam: *Pedoman Diagnosis & Penatalaksanaan Pneumonia Nosokomial di Indonesia.* Jakarta.2003 : p 1-17.

Putri, Yolanda, D., & Budiono. (2014). Hubungan antara Lama penggunaan ventilator mekanik dengan Kejadian Ventilator Associated Pneumonia (VAP) Pada pasien Nonsepsis di ICU RSUP Dr Kariadi Semarang . *E-Journal Undip.*2014: 1-16.

Resende,Marilia M. et al. *Epidemiology and outcomes of ventilator associated pneumonia in northern Brazol: an analytical descriptive prospective cohort study .Biomed Central*.2013:13(119) p.1-6

Riatsa, A., Nana, R. & Nur, K. Faktor-faktor yang berhubungan dengan kejadian ventilator associated pneumonia (VAP) pada pasien yang menggunakan

ventilator mekanik di ICU RSUD Tugurejo Semarang. *Ners widya husada Semarang.*20152(1), p. 1-14.

Santoso Budi. Faktor-faktor yang Berhubungan dengan Kejadian Pneumonia pada Pasien di Intensive Care Unit (ICU) Rumah Sakit Islam Surakarta.2015.file.///C/User/perpustakaan /Downloads/42-83-2-PB%20(1).pdf

Sedwick,M.B.,et al. Using evidence based practise to preven Ventilator Associated Pneumonia. 2012:32(4).p.41-52

Susanti, E., Utomo, W. & Irvani D, Y. Identifikasi Faktor Resiko Kejadian Infeksi Nosokomial Pneumonia pada Pasien yang Terpasang Ventilator di Ruang Intensive Care.2015:2(1).p. 590-598

Wahyuning Tyas, M., Suprapti, B. & Hardiono. *Analysis of Antibiotic use in VAP (Ventilator Associated Pneumonia) Patients*. *Folia Medica Indonesiana.2013:*49(3), p. 168-172.

Widyaningsih, R. & Buntaran, L. Pola Kuman Penyebab Ventilator Associated Pneumonia (VAP) dan Sensitivitas terhadap Antibiotik di RSAB Harapan Kita. *Sari Pediatri.*2012*:*13(6), pp. 384-390.

Yunita, R. & Rondhianto, W., 2015. Pengaruh Open Suction System terhadap Kolonisasi Staphylococcus Aureus pada Pasien dengan Ventilator Mekanik di Ruang Intensive Care Unit (ICU) RSD dr. Soebandi Jember. 3(1), pp. 103-110.

Ziyaettin, K., R, I., H, A., Girgin, N. K., F, K., & M, S. Prognostic risk factors in Ventilator Associated Pneumonia. *ISI Journal Master List* .2018: *24*, 1321-1328.