Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 03, 2022

Original research article

Predictive indications, clinical and biochemical features, and risk factors for ventilator-associated pneumonia

[1]Dr. Naga Lakshmi Katragadda, [2]Dr. D Markandeyulu, [3]Dr. G Suryanarayana Murthy, [4]Dr. Kiran Mathangi, [5]Dr. Abdul Arafath P

[1,4]Assistant Professor, Department of Pulmonary Medicine, Rangaraya Medical College, Kakinada, Andhra Pradesh, India

[2]Associate Professor, Department of General Medicine, Rangaraya Medical College. Kakinada, Andhra Pradesh, India

[3]Assistant Professor, Department of General Medicine, Rangaraya Medical College, Kakinada, Andhra Pradesh, India

[5]Post-Graduate, Department of Pulmonary Medicine, Rangaraya Medical College, Kakinada, Andhra Pradesh, India

Corresponding Author:
Kiran Mathangi (kirandr2014@gmail.com)

Abstract

Background and Objectives: Associated with the Ventilator Patients are deemed to have had pneumonia if they experience pneumonia 48 hours after being intubated. Due to factors like hospital stays and deaths, it is very troublesome and expensive. Within the first five days after being intubated, 3% of patients are thought to develop VAP.

Methods: The Department of Pulmonary Medicine and General Medicine, Government General Hospital Kakinada between August 2021 to February 2022. a tertiary referral facility for pulmonary medicine in Tamil Nadu, served as the site of this prospective observational study. This investigation took place between. August 2021 to February 2022

Results: We took these steps to ensure that none of the information we gathered was harmed in any way because we wanted to understand the clinical and biological profile of VAP in our ICUs. An average age of 45 was found among the study's participants. After intubation, pneumonia caused by the use of a ventilator usually took 7 days to manifest. They stayed in the hospital for 23 days total, on average, and averaged 14 days. Only 69 people had their levels of procalcitonin tested. In response to their request, one patient was taken out of the critical care unit (ICU) before their course of treatment was complete.

Conclusion: Patients on ventilation who had normal chest x-rays at the time of intubation are more likely to experience late-onset VAP or late VAP. The most common microbes are Acinetobacter, Pseudomonas, and Klebsiella. The results were unaffected by the prevalence of resistant species over sensitive ones.

Keywords: Ventilator assisted Pneumonia, risk factors, biochemical profiles, prognostic markers, and risk factors

Introduction

Pneumonia in a patient is referred to as Ventilator-Associated Pneumonia (VAP) after 48 hours of intubation. Due to factors like hospital stays and deaths, it is very troublesome and expensive. Within the first five days after being intubated, 3% of patients are thought to develop VAP. Late-onset VAP, which is defined as VAP that manifests after 5 days of intubation, has greater mortality rates and a higher likelihood that the underlying cause is multi-drug resistant bacteria. If a patient develops pneumonia within 48 hours of being intubated but had not previously exhibit any indications of a lung infection, they are considered to have VAP. VAP is brought on by microbial invasion of the lower respiratory tract and lung parenchyma. Endotracheal intubation and mechanical breathing undermine the body's first line of defence against microbial invasion when they compromise the oro-pharynx and airways [1, 2, 3].

Mechanical ventilation (MV), while can save lives, also puts patients at risk for a host of resource-intensive, morbid and fatal side effects include ventilator-associated pneumonia (VAP), acute respiratory distress syndrome, sepsis and atelectasis. The length of stay (LOS) in the intensive care unit (ICU), the hospital LOS and the number of ventilator days all rise by five as a result of infection-related problems. But a portion of the expenditures are due to the disease's existing inability to be systematically diagnosed at an early stage, which could result in postponed treatment or excessive use of broad-spectrum antibiotics. Current diagnostic techniques, such as signs and symptoms, microbiological cultures, and plain radiographs' visual output, as well as traditional surveillance techniques, such as manual chart reviews, prevalence surveys, discharge codes, and electronic surveillance algorithms, are often insensitive, time-consuming, and expensive. Additionally, depending on the anticipated course of the

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 03, 2022

condition, they are unable to pinpoint a person who might profit from a specific sort of treatment [3, 4, 5].
Precision medicine in intensive care units is changing as a result of artificial intelligence (AI). Using machine learning (ML) techniques, emerging technologies (such as image-based and biochemical approaches, sequencing technologies, etc.) will overcome the limitations of current diagnostic approaches. These data-intensive systems will integrate and analyse various structured and unstructured data from different sources to monitor temporal trends, identify risk factors and predict morbidity and mortality and thus, facilitate quick clinical decision making for infectious diseases [6, 7, 8].
For objective VAP detection, researchers have created automated techniques since 2014. But the diagnostic precision of VAP has not been increased by these expert systems. Additionally, automation without AI approaches is unable to foresee the likelihood or risk of difficulties developing in vulnerable people in the future. In order to produce patient-specific forecasts of VAP, we evaluated and analysed cutting-edge prediction models (such as local ecology and/or respiratory surveillance culture-based AI or ML algorithms, described as computational models able to learn from data obtained in the ICU). All diagnostic criteria were taken into consideration because there was no agreement on a "gold standard" diagnosis. We proposed that VAP probability or risk and associated effects may be forecasted. The effectiveness of existing diagnostic and prognostic models for prediction was our main goal. Our secondary goal was to evaluate the level of clinical preparedness as a component of maturity definition, as well as the risk of bias (ROB) and applicability of the prediction models [9, 10, 11].
The purpose of the study is to gather information on the incidence, prevalence, clinical and microbiological aspects of VAP. The CPIS score, APACHE-II score, MOD score, and culture results from an endotracheal aspirate, bronchoalveolar lavage, or bronchial wash will all be monitored for patients with VAP in the Medical/Surgical ICU, Surgical HDU, and Respiratory Medicine HDU. From the time a patient is admitted to the hospital until they are discharged, their progress will be monitored so that mortality and outcomes can be evaluated. The outcomes from various intensive care facilities will be compared [12, 13].
By examining their clinical and microbiological data, the researchers set out to better understand the features of patients with Ventilator-Associated Pneumonia. This study looked at how VAP presented clinically in intensive care units and hospital wards in India. in an effort to describe the VAP microbiota. This study compares the microbiologic characteristics of hospital wards and intensive care units located inside the same medical facility [14].

Material and Methods

A prospective observational study was conducted in Intensive Care Units at the Department of Pulmonary Medicine and General Medicine, Government General Hospital Kakinada between August 2021 to February 2022. a tertiary referral centre in Andhra Pradesh. This research was carried out between August 2021 to February 2022.

Inclusion criteria

1. Intensive care patients who have been intubated and admitted.
2. Pneumonia clinical and radiological evidence.

Exclusion criteria

1. Pneumonia before intubation or within 48 hours of intubation.
2. External intubation.
3. Any abnormal opacity on the chest x-ray during time of intubation.

Any patient exhibiting new symptoms, such as a fever, purulent discharges, leukocytosis, or a drop in oxygen saturation, will have a chest x-ray done. If a doctor has identified a patient as having HAP, then the patient will be taken into consideration. The diagnosis will be made based on the 2014-modified CDC Criteria. Procalcitonin levels, microbiologic outcomes of any respiratory and blood sample cultures, CPIS score, MOD score, and APACHE-II score are all going to be determined. Until they are ready to go home, patients will be observed in the ICU/HDU and throughout their hospital stay. An interval of at least 2 intensive care unit (ICU) days or 4 hospital days was considered to be a clinically relevant difference. Using logistic regression analysis, it was found that the continuous variables Procalcitonin, Modified CPIS Score, MOD Score, and APACHE-II Score at the time of diagnosis were related to the outcome in VAP. The median and mean survival periods of patients with VAP as well as their relationships to procalcitonin levels, CPIS scores, MOD scores, and APACHE II scores at the time of diagnosis were examined. Utilising the Kruskal-Wallis Test across the 3 intensive care units and the Ranksum Test across 2 groups, median values were compared. ANOVA is used to compare the means of many different variables among ICUs, whereas the T-test is used to compare the means of just one variable between two groups.

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 03, 2022

RESULTS

The average age of the patients in the surgical intensive care unit was 45. VAP typically manifested after 7 days. The average length of stay in the hospital was 22 days, and the average length of stay in the intensive care unit was 15. The median age of patients in the medical intensive care unit was 46, and they spent an average of 15 days in the intensive care unit, 6 days in the VAP, and 25 days overall in the hospital. Patients in the AICU were typically 12 days old when VAP was identified, 9 days old when they were discharged from the ICU, and 15 days old in total.

To illustrate the range of ages, the standard deviation and median ages are displayed in brackets beneath the mean ages. For the other variables-hospital days, intensive care unit days, day of developing VAP, APCHE-III, MODS, Modified CPIS and procalcitonin levels-the median was chosen due to the wide range shown throughout the scales. The minimum and maximum values are listed in parenthesis below the median value.

Ratio of early and late VAPS

Table 1: Early and late VAP comparisons between the three ICUs

	Early VAP	Late VAP
AICU	1/5	6/7
MICU	16/40	25/42
SICU	10/30	21/30
Total	30/79	50/79

All Intensive Care Units had significantly fewer early VAP incidence cases than late VAP cases. To compare the data from each ICU, an analysis of variance (ANOVA) was utilised. There was no statistically significant difference between the early and late VAP rates in the three ICUs.

Sex Distribution

Table 2: Distribution of sex in different arm

Sex	AMCU	MICU	SICU	Total
Female % (n)	18.00	38.00	54.00	35.00
Male % (n)	85.00	66.00	49.00	65.00

There were no discernible changes between the sex distributions in the three arms when the ANOVA test was applied to analyse them. The cohort was made up of 47 males and 31 women.

For the most part, study participants' immune systems were in good shape. 11.54% of the study participants were immunocompromised. Haematological malignancies, cancers treated with chemotherapy that spread and failure of the liver and kidney cells all contributed to immunosuppression.

Mortality

Table 3: Rate of deaths in ICU

Mortality	AMCU	MICU	SICU	Total
Death (n)	100	22	38.00	39.00
Alive (n)	0	31	62.00	61.00

The ANOVA test was used to assess patient mortality in different ICUs who had developed VAP. The AICU's fatality rate was high at 100%, in contrast to the medical and surgical ICU's lower mortality rates.

Bacteriological profile

In the ET aspirate culture, there was evidence of the growth of many organisms in significant numbers in 58 out of 81 patients.

Table 4: Common microorganisms in different ICUs

	Pseudomonas	Klebsiella	Acinetobacter
AICU	3/9	2/7	2/7
MICU	14/64	6/64	31/64
SICU	9/42	5/43	17/43
Total	20/125	16/125	50/125

The bacterial profile was substantially the same whether or not the ICU patients had undergone surgery. Ainetobacter species were the most frequently discovered, followed by pseudomonas and Klebsiella. Both the early and late VAP had the same bacterial profile. An analysis of variance (ANOVA) test was

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 03, 2022

used to look for statistically significant differences in the prevalence of resistant pathogens among intensive care units (ICUs).

Mortality, hospital stay and ICU

To illustrate the range of ages, the standard deviation and median ages are displayed in brackets beneath the mean ages. Due to the wide range of the APCHE-III, MODS, Modified CPIS, and Procalcitonin levels, the median was chosen for the other variables. The minimum and maximum values are listed in parenthesis below the median value. The Ranksum Test was used to compare median scores and procalcitonin levels, and the T-test was used to compare the mean 'age' of those who died with those who survived. For those who failed, the median APACHE-III score was 96; for those who succeeded, it was 66. The median MOD for those who died was 10, while the median MOD for those who survived was 7. The scores on the APACHE-III and MOD substantially varied between the two groups. The modified CPIS score and procalcitonin concentrations did not show any statistically significant connection.

Procalcitonin

Table 5: Levels of procalcitonin in living and dead

	Mean	95% CI
Mortality (n=29)	35.48	15.78-55.22
Alive (n=40)	19.29	7.12-26.14

The mean procalcitonin levels between those who passed away from their illness and those who survived were 19.29 and 38.48, respectively. But no statistically significant findings were discovered.

Table 6: Procalcitonin predictive value at 4ng/dl

Procalcitonin (ng/dl)	Mortality	Alive	Total
<4	11	18	29
>4	18	22	40
Total	29	40	69

The possibility of using a procalcitonin level of 4 ng/dl as a predictor of death was investigated by the researchers. However, no notable incidents were noted. Other fatality risks could not be distinguished from the protein procalcitonin.

Discussion

Patients who had been admitted to and intubated in various ICUs during the study period and showed symptoms of ventilator-associated pneumonia were evaluated. We modified the CDC's criteria to arrive at the diagnosis of VAP. This analysis excluded individuals who exhibited pulmonary opacities at the time of arrival or who required intubation; it only included patients with verified instances of VAP. The actual number of VAP instances may have therefore been overestimated. The patient's APACHE-III score, MODS score, Modified CPIS score, and procalcitonin level were noted at the time of VAP diagnosis. The participants in the study were followed up with until the day of their release or their demise. The study population's microbiological and clinical features were thoroughly examined and studied. Procalcitonin levels and a number of other scores have been examined to determine whether they can be used as indicators of clinical outcome, such as death and, for those who do survive, the length of stay in the intensive care unit and the hospital. A difference of 2 intensive care unit (ICU) days and 4 total hospital days was chosen at random as the threshold for clinical significance. The patients in the study were on average 45 years old. The symptoms of ventilator-associated pneumonia (VAP) frequently appear seven days after intubation. They stayed in the hospital for a total of 23 days, with an average stay of 14 days. The procalcitonin levels of only 69 people were measured. In defiance of their better judgement, the ICU personnel sent one patient home before their therapy was complete. As a result, he was disqualified from the study's main objective, which was to find factors that predict the outcome [15, 16, 17].

An analysis of variance (ANOVA) was used to compare the death rates of patients with VAP in various ICUs. The 100% death rate in the AICU stands out as particularly high when compared to the mortality rates in the medical and surgical ICU. All six of the patients who were moved from the AICU were critically unwell, required intensive care and many of them were having chemotherapy due to disseminated or haematological malignancies. Because their APACHE III values are greater, patients in AICU have a higher mortality rate than those in other ICUs. The mortality rate across the board was 30.96%. A drug-resistant organism, according to this definition, is one that has become resistant to three or more drug classes that would typically be successful against that species. The cohort's ET aspirate revealed a 91.03% growth rate for resistant bacteria. An analysis of variance (ANOVA) test was used to look for statistically significant differences in the prevalence of resistant pathogens among intensive care

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 03, 2022

units (ICUs) [18, 19].

The clinical outcome (death rate, length of intensive care unit stay, and overall hospital stay for those who survived) was calculated, along with the median age, mean age, APCHE-III score, Modified Combined Severity Index score and procalcitonin levels. The median was utilised since the range of scores and procalcitonin levels was so wide. The Ranksum Test was used to compare median scores and procalcitonin levels, and the T-test was used to compare the mean 'age' of those who died with those who survived. For those who failed, the median APACHE-III score was 96; for those who succeeded, it was 66. The median MOD for those who died was 10, while the median MOD for those who survived was 7. The scores on the APACHE-III and MOD substantially varied between the two groups. The modified CPIS score and procalcitonin concentrations did not show any statistically significant connection.

The mean procalcitonin level in those who survived the illness was 17.47, whereas the level in those who passed away was 35.36. However, no statistically significant differences were discovered. The possibility of using a procalcitonin level of 4 ng/dl as a predictor of death was investigated by the researchers. However, no notable incidents were noted. Procalcitonin did not perform well as a mortality indicator on its own. The median survival analysis, as well as the number of days spent in the intensive care unit and the hospital, were carried out using an arbitrary threshold of 4ng/dl due to the inability to produce a definitive ROC curve. This threshold was significantly higher than the cutoff of 1.5ng/dl in the earlier research. Patients with a median ICU survival of 37 days had a procalcitonin level of less than 4 ng/dl, compared to 16 days for those with a procalcitonin level of 4 ng/dl or more. However, the contrast was apparent from a medical perspective [19, 20].

The difference between individuals who spent a median of 9.5 days in the critical care unit and those who spent a median of 13 days there when their procalcitonin level at diagnosis was 4ng/dl or above was not statistically significant. Patients' median hospital admissions were both 26 days, with no statistically significant difference between those whose procalcitonin levels were below 4ng/dl at diagnosis and those whose levels were 4ng/dl or higher. Except for the median survival in terms of ICU days, our study was unable to establish procalcitonin as a predictor of prognosis in VAP patients. A more precise prediction might have been possible if procalcitonin levels and any ensuing trends towards rises or declines had been monitored in real time [20, 21].

The difference in hospital duration of stay between patients with an APACHE III score of 80 or above and those with a score of less than 80 was clinically significant but not statistically significant. Patients with lower APACHE III scores at diagnosis had shorter hospital stays (19 days vs. 28.5), albeit this difference was not statistically significant. An effective predictor of survival in patients with ventilator-associated pneumonia was found to be a high APACHE III score. The mean mod CPIS score for patients who succumbed to their illness was 5.5, while the mean mod CPIS score for patients who survived was 5.26. Neither group was significantly different from the other. The information was examined to determine whether a modified CPIS score of 6 or above might be used to predict death. Patients with ventilator-associated pneumonia whose CPIS score is under 6 may stop receiving antibiotics. No statistically significant correlation was discovered, though [22, 23, 24].

Conclusion

In ventilated patients who had healthy chest x-rays at the time of intubation, late-onset VAP—also known as late VAP-is more likely. Pseudomonas, Klebsiella, and Acinetobacter are the three most common microbes. It had no impact on the outcomes that resistant species outnumbered sensitive ones. When VAP is diagnosed, the APACHE III score is a highly accurate predictor of mortality, the length of time spent in the critical care unit, and the total length of hospitalisation. The modified CPIS score a patient had at the time of the diagnosis of VAP can be used to forecast how long they will survive on average in the intensive care unit. The median survival time in the intensive care unit is shortened in patients with a high MODS score at the time of VAP diagnosis. A person's chance of dying rises after age 45. A polymicrobial infection will lengthen the ICU and hospital stay, but it had no effect on mortality whether the ET aspirate culture grew a single resistant bacterium or several. The likelihood of death from VAP increases as people age. Despite the fact that the majority of Acinetobacter infections were resistant to more than three classes of first-line antibiotics, they had a better outcome in terms of average ICU and hospital lengths of stay.

Funding: None.

Conflict of Interest: None.

References

1. Ventilator-Associated Pneumonia: Overview of Nosocomial Pneumonias, Epidemiology of VAP, Clinical Presentation of VAP, 2015 Jun. Available from: http://emedicine.medscape.com/article/304836-overview
2. Joseph NM, Sistla S, Dutta TK, Badhe AS, Parija SC. Ventilator-associated pneumonia: A review.

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 03, 2022

Eur J Intern Med. 2010 Oct;21(5):360-8.
3. Melsen WG, Rovers MM, Koeman M, Bonten MJM. Estimating the attributable mortality of ventilator-associated pneumonia from randomized prevention studies. Crit Care Med. 2011 Dec;39(12):2736-42.
4. Luyt CE, Guérin V, Combes A, Trouillet JL, Ayed SB, Bernard M, *et al*. Procalcitonin Kinetics as a Prognostic Marker of Ventilator-associated Pneumonia. Am J Respir Crit Care Med. 2005 Jan;171(1):48-53.
5. Joseph NM, Sistla S, Dutta TK, Badhe AS, Parija SC. Ventilator-associated pneumonia in a tertiary care hospital in India: incidence and risk factors. J Infect Dev Ctries. 2009;3(10):771-7.
6. Nasia Safdar CJC. The pathogenesis of ventilator-associated pneumonia: its relevance to developing effective strategies for prevention. Respir Care. Discussion. 2005;50(6):725-39; 739-41.
7. Herzig SJ, Howell MD, Ngo LH, Marcantonio ER. Acid-suppressive medication use and the risk for hospital-acquired pneumonia. JAMA. 2009 May;301(20):2120-8.
8. Duszyńska W, Barteczko B, Kübler A. [Monitoring of nosocomial infections using the HELICS network]. Anestezjol Intensywna Ter. 2008 Mar;40(1):17-21.
9. Zilberberg MD, Shorr AF. Ventilator-Associated Pneumonia: The Clinical Pulmonary Infection Score as a Surrogate for Diagnostics and Outcome. Clin Infect Dis. 2010 Aug;51(1):S131-5.
10. Park DR. The Microbiology of Ventilator-Associated Pneumonia. Respir Care. 2005 Jun;50(6):742-65.
11. Koenig SM, Truwit JD. Ventilator-associated pneumonia: diagnosis, treatment, and prevention. Clin Microbiol Rev. 2006 Oct;19(4):637-57.
12. Craven DE. Epidemiology of ventilator-associated pneumonia. Chest. 2000 Apr;117(4-2):186S-187S.
13. Goel V, Hogade SA, Karadesai S. Ventilator associated pneumonia in a medical intensive care unit: Microbial aetiology, susceptibility patterns of isolated microorganisms and outcome. Indian J Anaesth. 2012;56(6):558-62.
14. Iregui M, Ward S, Sherman G, Fraser VJ, Kollef MH. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. Chest. 2002 Jul;122(1):262-8.
15. Niederman MS. The clinical diagnosis of venti-lator-associated pneumonia. Respiratory Care. 2005;50:788-796.
16. Huang KT, Tseng CC, Fang WF, Lin MC. An early predictor of the outcome of patients with ventilator-associated pneumonia. Chang Gung Med J. 2010 May-Jun;33(3):274-82.
17. Marshall JC, *et al*. Crit Care Med. [Cited by: De Campos T, *et al*. JOP. J Pancreas (Online). 1995;23:1638-52; 2008;9(6):690-697.
18. The Diagnostic and Prognostic Value of Serum Procalcitonin among Ventilator Associated Pneumonia Patients* [Internet]. [cited 2015 Jul 1]. Available from: http://www.scirp.org/journal/PaperInformation.aspx?PaperID=32033#.VZRIDUazkcc
19. Klompas M, Branson R, Eichenwald EC, Greene LR, Howell MD, Lee G, *et al*. Strategies to prevent ventilator-associated pneumonia in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol. 2014 Sep;35(2):S133-54.
20. Muscedere J, Rewa O, McKechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. Crit. Care Med. 2011 Aug;39(8):1985-91.
21. McClave SA, Lukan JK, Stefater JA, Lowen CC, Looney SW, Matheson PJ, *et al*. Poor validity of residual volumes as a marker for risk of aspiration in critically ill patients. Crit Care Med. 2005 Feb;33(2):324-30.
22. Chan EY, Ruest A, Meade MO, Cook DJ. Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis. BMJ. 2007 Apr;334(7599):889.
23. Kollef MH, Morrow LE, Niederman MS, Leeper KV, Anzueto A, Benz-Scott L, *et al*. Clinical characteristics and treatment patterns among patients with ventilator-associated pneumonia. Chest. 2006 May;129(5):1210-8.
24. Kollef MH, Afessa B, Anzueto A, Veremakis C, Kerr KM, Margolis BD, *et al*. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. JAMA. 2008 Aug;300(7):805-13.