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Original Article

Epidemiology, Microbiology, and Outcome of Ventilator-Associated Pneumonia in Medical Intensive Care Unit in a Tertiary Care Center

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Abstract

Ventilator-associated pneumonia (VAP) is considered the most common nosocomial infection in intensive care units (ICUs), with variable incidence depending on the population, type of ICU, and diagnostic criteria applied. This prolongs the need for mechanical ventilation and hospitalization and considerably increases the costs. Mortality rates are variable and are higher for multidrug-resistant pathogens.

Aims and Objectives: To study the incidence, microbiology, and outcomes of VAP in a medical ICU in a tertiary care hospital.

Type of Study: A cross-sectional observational study.

Study Duration: 1 year 9 months.

Sample Size: Minimum of 100 justified.

Materials and Methods: Once VAP was clinically diagnosed, a quantitative culture was performed. Organisms were identified and antimicrobial sensitivity was tested using standard guidelines. Data were analyzed.

Results: (1) The incidence of VAP was 22% and was independent of age, sex, alcohol intake, cigarette smoking, diabetes, hypertension, and other comorbidities. (2) The early and late VAP were 36.4% and 63.6%, respectively. Monomicrobial VAP was 86.4% and that of polymicrobial was 13.6%. (3) The most frequently diagnosed microorganisms were *Acinetobacter* spp. (27.3%) and *Pseudomonas* spp. (22.7%). (5) The multidrug-resistant/extensively drug-resistant rate was 54.5%. (6) The mortality rate of VAP patients was 45.5% compared with that of non-VAP patients (10.3%) (P = 0.05). (7) The mean duration of mechanical ventilation and ICU stay in the VAP group (15.5 days) was significantly higher than that in the non-VAP group (P = 0.05).

Conclusion: The incidence rate was 22%, with Acinetobacter and Pseudomonas being the predominant organisms. Patients with late-onset VAP have increased drug resistance, duration of mechanical ventilation, and ICU stay. Training and education should be encouraged to minimize morbidity and mortality.

Key words: Incidence, Intensive care unit, Microbiology, Mortality, Ventilator-associated pneumonia

INTRODUCTION

Ventilator-associated pneumonia (VAP) is defined as pneumonia occurring more than 48 h after the patient has been intubated and has received mechanical ventilation. Early-onset VAP was defined as pneumonia occurring after 48 h of mechanical ventilation but before day 5. Late-onset VAP was defined as VAP occurring from day 5 onward.[1] Many scoring systems have been proposed to improve diagnostic accuracy. The most common scoring system used was the clinical pulmonary infection score (CPIS) developed by Pugin *et al.*[2] In many studies, two or more serial chest X-rays or computed tomography (CT) scans were needed to suggest consolidation in patients with underlying cardiac or pulmonary disease for the

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diagnosis of VAP. In patients without underlying cardiac or pulmonary disease, a definitive chest radiograph or CT scan is sufficient.

Review of Literatures

VAP is a clinical condition with multiple factors that have a significant impact on healthcare costs. The mortality attributable to it has been found to be in the range of 0–50%.[3-5] However, the clinical epidemiology and outcomes of VAP in broad subgroups of critically ill adult populations have not been clearly defined and many aspects remain unclear. To date, a large number of primary studies have been reported, but none have been conclusive.[6] In general, early-onset VAP is caused by antibiotic-sensitive pathogens, whereas late-onset VAP is caused by multidrug-resistant pathogens that are difficult to treat. The exact prevalence of drug-resistant organisms varies among institutions. VAP is frequently caused by polymicrobial infection. Hospital-acquired pneumonia is associated with crude mortality rates of up to 70% and attributable mortality rates as high as 33–50%.[7] Many of these deaths due to VAP are believed to be the most frequent infections in patients admitted to the intensive care unit (ICU).[8] If we go through the literature to look for worldwide point prevalence studies, it is noted that nosocomial infection rates range from 6.1% to 15%. However, these rates are higher in Asia. In a recent study from Malaysia, 14% of hospitalized patients developed nosocomial infections. 21% of these infections are diagnosed as pneumonia. Ferrer *et al.* studied [9] a VAP frequency of 58% in their study. According to the Behari and Kalafatis study,[10] over a period of 6 months in all intubated and mechanically ventilated patients in the ICU, 8 (25%) out of 32 patients were diagnosed with VAP. The mean duration of mechanical ventilation in the VAP group was 249 h compared to 65.5 h in the non-VAP group (P = 0.0002). The most common bacteria isolated were *Acinetobacter baumannii*, followed by *Pseudomonas aeruginosa*. According to the Othman and Abdelazim study,[11] VAP was diagnosed in 17 patients (35.4%), and Gram-negative bacteria were the major causative pathogens (*P. aeruginosa* contributed 22.9%). According to a study by Nanthini Devi and Gomathi study,[12] the incidence rate of VAP is 36%, and more than 80% of organisms are multidrug-resistant. Ranjan *et al.* study[13] showed a VAP incidence of 57.14% and an overall mortality associated with VAP of 48.33%. A study by Sarkar *et al.* study[14] revealed that *Acinetobacter* spp., *Klebsiella pneumoniae*, and *Staphylococcus aureus* were the most frequent isolates in early-onset VAP, while *Pseudomonas* spp. and *Acinetobacter* spp. dominated late-onset VAP. VAP increases the duration of intensive care, prolongs mechanical ventilation, and increases mortality.[11,14-18] Shashikala *et al.*, study[19] found *Klebsiella* to be the most common organism isolated in VAP, whereas Kanafani *et al.*[20] and Kant *et al.*[21] found *Acinetobacter* to be the predominant organism in their studies. In Ippolito *et al.*'s[22] systematic review and meta-analysis of VAP in COVID-19 patients, the pooled estimated mortality rate was 42.7%. Moreover, the organisms causing nosocomial pneumonia may often be difficult to manage. Therefore, management guidelines are important to go ahead.

Aims and Objectives

1. Incidence of VAP
2. Causative organism of VAP
3. Outcome of VAP.

MATERIALS AND METHODS

Study Location

The study was conducted in a medical ICU in a tertiary care center.

Type of Study

This is a cross-sectional observational study.

Study Design

All patients who reach the medical ICU and remain intubated for at least 48 h will be assessed for inclusion in our study if the desired criteria are met.

Study Duration

The study will be conducted for 1-year 9-month duration.

Sample Size

The primary objective of this study was to assess the incidence, microbiology, and mortality associated with VAP in patients admitted to a medical ICU. Based on a previous study,[13] the incidence of VAP was 57.1%. Therefore, assuming the same (P) = 57.1% with a 10% margin of error, the minimum required sample size at the 5% level of significance was 94 patients.

Diagnostic Criteria

New persistent pulmonary infiltrates appearing on chest radiographs and at least two of the following: (1) fever (temperature of 38°C or higher), (2) leukocytosis (>12,000 white blood cells [WBC] mm^3 or leukopenia (<4,000 WBC/mm^3), and (3) purulent tracheobronchial secretions or worsening of hypoxia. In cases of clinically suspected pneumonia, the endotracheal aspirate was sent for microbiological examination, and the diagnosis of VAP was established with a positive quantitative culture of endotracheal aspiration.

Exclusion Criteria

(1) The study excluded ICU patients whose hospital stay was shorter than 2 days and those who showed symptoms of infection within 2 days of admission; (2) <18 years of

age; (3) Patients will be excluded if they have features of infection within 48 h of intubation; (4) Known as having chronic pulmonary disease; (5) The diagnosed VAP case shifted to another hospital from the ICU during the study. (6) Patients with clinical signs of VAP and sterile microbiological reports were excluded from the study.

Methods

A literature search was performed in PubMed and Google using the search terms 'VAP, incidence, outcome, and mortality. Consent and ethical and scientific committee approval were obtained. All the intubated and ventilated patients were screened upon admission. A total of 100 intubated patients were selected on the basis of the inclusion and exclusion criteria. A questionnaire was administered to obtain detailed information on each patient. Once the clinical features of VAP were present in these patients, a trained nurse collected endotracheal samples using a suction catheter with a mucous extractor, which was gently introduced through the endotracheal tube at a distance of approximately 25 cm. Quantitative cultures were performed immediately. Organisms were identified using standard protocols. Growth of more than 10^5 CFU/mL was used as the cut-off threshold for endotracheal aspiration. Samples showing growth below these thresholds were thought to be colonized or contaminated. When one pathogen was isolated in culture, it was termed as monomicrobial. When more than one pathogen was isolated, it was termed as polymicrobial. The antimicrobial sensitivity test was performed according to the standard guidelines. Multidrug resistance is defined as resistance to at least one antimicrobial agent in three or more antimicrobial categories. Among 100 randomly selected intubated patients, both clinical and microbiological criteria were applied to determine the number of cases that developed VAP. Patients who were diagnosed with VAP were further studied to look for microbiological patterns, and were followed up in the ICU to look for the outcome, that is, either stabilized and shifted to a step-down facility or expired in the ICU. Patients with VAP who were transferred from the ICU to another hospital for further management were excluded from the study. The ventilation days and the ICU stay duration of these VAP patients' data were compared with those of the rest of the non-VAP study patients to identify any differences in patient outcomes.

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 17.0 program for Windows (SPSS Inc., Chicago, IL, USA). We conducted a Shapiro–Wilk test to verify the distribution of the data. All data are summarized as mean ± standard deviation, whereas those with a skewed distribution are described as medians (interquartile range). The Chi-square test was used to compare differences in variables between the two groups. The Student's *t*-test was used for continuous and normal variables. The Mann–Whitney U test was used to test the independent relationships between variables that did not demonstrate normality. A two-sided $P < 0.05$ was considered statistically significant.

OBSERVATIONS AND RESULTS

In total, 100 intubated patients were included in this study based on the selection criteria. Among the 100 patients, 22 were diagnosed with VAP. 78 patients were intubated without features of VAP [Table 1]. Mean age for diagnosed VAP and non-VAP cases was 59.18 years and 56.65 years, respectively. Age was not found to be an associated factor for VAP diagnosis. We did not find any association between any age group or gender and the occurrence of VAP ($P > 0.05$). Among the 100 selected intubated patients, we found a stroke in 48%, acute coronary syndrome in 16%, non-cardiogenic pulmonary edema in 12%, intestinal obstruction in 7%, chronic liver disease in 6%, breast carcinoma in 1%, road traffic accident without stroke in 1%, brain tumor in 1%, gastrointestinal bleeding without chronic liver disease in 3%, pancreatitis in 2%, diabetic ketoacidosis in 2%, and poisoning in 1%. We did not find any association between the primary diagnosis on admission to the ICU and the diagnosis of VAP. In addition, there was no association between the occurrence of VAP and alcohol intake, cigarette smoking, diabetes mellitus, hypertension, or other comorbidities. Among 22 diagnosed VAP cases, monomicrobial VAP was 86.4% and polymicrobial was 13.6%. In monomicrobial VAP, the most frequently diagnosed organism was *Acinetobacter* (27.3%), followed by *Pseudomonas* (22.7%) [Table 2]. In VAP, the most common secondary organisms were methicillin-resistant *S. aureus* (MRSA), *Serratia* spp., and *Stenotrophomonas* species. In our study, out of 22 patients with VAP, multidrug-resistant/extensively drug-resistant (MDR/XDR) was diagnosed in 12 patients (54.5%), and organisms without MDR/XDR were diagnosed in 45.5%. The mortality rate of patients with VAP was 45.5%, which was very high compared to that of patients without VAP (10.3%). Shifting out from the ICU and discharge rates were significantly higher in the non-VAP group than in the VAP group (54.5% vs. 89.7%) [Table 3]. The mean duration of mechanical ventilation in the VAP group was

Table 1: The frequency of VAP

Is it VAP	Frequency	Percentage
VAP	22	22.0
Non-VAP	78	78.0
Total	100	100

VAP: Ventilator-associated pneumonia

15.5, which was significantly higher than that in the non-VAP group at 4.45 days [Table 4].

The mean duration of the ICU stay in the VAP group was 17.32 days which was significantly longer than that in the non-VAP group at 6.86 days [Table 5]. The frequency of MDR/XDR organisms was higher in the late VAP group than in the early VAP category [Table 6]. There was no difference in the monomicrobial or polymicrobial organisms between early versus late onset VAP ($P > 0.05$). However, the ICU stay and ventilation duration were higher in the late-onset VAP [Table 7]. We found similar mortality rates in the early and late VAP groups. We did not find any relation of duration of the ICU stay or ventilation days between monomicrobial and polymicrobial groups.

Table 2: The distribution of the first VAP organism

1st organism	VAP	
	Frequency	Percentage
Pseudomonas aeruginosa	5	22.7
Acinetobacter	6	27.3
Escherichia coli	2	9.1
Klebsiella pneumoniae	3	13.6
MSSA	1	4.5
Enterobacter	1	4.5
MRSA	1	4.5
Enterococcus	3	13.6
Total	22	100

VAP: Ventilator-associated pneumonia, MSSA: Methicillin-susceptible *Staphylococcus aureus,* MRSA: Methicillin-resistant *Staphylococcus aureus*

Table 3: The comparison of VAP and non-VAP patient mortality

Outcome	VAP		Non-VAP		*P*-value
	Frequency	Percentage	Frequency	Percentage	
Dead	10	45.5	8	10.3	<0.001
Shifted/ discharged	12	54.5	70	89.7	
Total	22	100	78	100	

VAP: Ventilator-associated pneumonia

Furthermore, we found almost similar mortality between monomicrobial and polymicrobial organism-infected groups.

DISCUSSION

Behari and Kalafatis,[10] Nanthini Devi and Gomathi,[12] Ranjan *et al.*,[13] Kant *et al.*,[21] Dey and Bairy[15] had used the CPIS, whereas Gauthier *et al.*,[16] had made a diagnosis of VAP based on the European Centre for Disease Prevention and Control Recommendation. However, we used clinical, radiological, and microbiological criteria similar to Ahmed *et al.*,[11] Ferrer *et al.*,[9] Marcio Guimaraes *et al.*,[18] study. We did not use the CPIS as a diagnostic criterion because of its poor sensitivity and specificity based on evidence to date. The incidence of VAP varies widely (between 9% and 70% almost) in different studies. The incidences reported by Ahmed *et al.* (35.4%), Dey and Bairy (45.4%), Ferrer *et al.* (58%), Gauthier Bloz *et al.* (48.9%), Nanthini Devi and Gomathi (36%), Ranjan *et al.* (57.17%), Ravi Kant *et al.* (45.12%), Sarkar *et al.*[14] (52.29%) were higher than those in our study, with an incidence of 22%. In contrast, the incidence in Behari and Kalafatis (25%) and Joao Junior *et al.*[17] (20.7%) was nearly similar to the incidence rate in our study. Such wide variations in the 51 studies are explained by the differences in multiple factors, such as the use of variable diagnostic criteria, age inclusion of the study subjects (higher incidence in older age group of patients in some studies), primary diagnosis of patients, presence of comorbid conditions during admission and immunity of the individual, study area such as medical versus surgical ICU, staff knowledge about level of hygiene and hand washing and other care, intensive care protocols for the management of patients, and multiple other factors. VAP caused by pathogens is typically caused by bacteria. Fungi and viruses are rarely involved in this process. In general, early-onset VAP is caused by organisms that are highly susceptible to antibiotics. They may include *Streptococcus pneumoniae*,

Table 4: A comparison of VAP and non-VAP patients' days on ventilator use

Outcome	VAP (*n*=22)			Non VAP (*n*=78)			*P*-value
	Mean±SD	Min-Max	Median (IQR)	Mean±SD	Min-Max	Median (IQR)	
Ventilation days	15.50±5.66	6–27	15.5 (10.5–20.25)	4.45±1.877	3–11	4 (3–5)	<0.001

SD: Standard deviation, IQR: Interquartile range, VAP: Ventilator-associated pneumonia

Table 5: A comparison of VAP and non-VAP patients' stay in the intensive care unit

Outcome	VAP (*n*=22)			Non VAP (*n*=78)			*P*-value
	Mean±SD	Min-Max	Median (IQR)	Mean±SD	Min-Max	Median (IQR)	
ICU	17.32±6.01	6–30	17 (12–22)	6.86±2.85	4–16	6 (5–8)	<0.001

SD: Standard deviation, IQR: Interquartile range, VAP: Ventilator-associated pneumonia, ICU: Intensive care unit

Haemophilus influenzae, and methicillin-susceptible *S. aureus*. In our study, the most common microorganism diagnosed in the patients with VAP was *Acinetobacter* (27.3%), followed by *P. aeruginosa* (22.7%). This finding is comparable to those of Behari and Kalafatis, Kanafani *et al.*,[21] study. In a study by Ahmed *et al.*, the most common isolate was *Pseudomonas* spp. In a study by Gauthier *et al.*, the most common isolate was *Enterobacteria* (49.8%), followed by *P. aeruginosa* (15.1%). *Acinetobacter* was the most frequently diagnosed organism in a study by Junior *et al.*, which is consistent with our findings. According to Marcio *et al.*, the most common bacteria for VAP are Gram-negative organisms, where *Pseudomonas* is most frequently found, followed by *Acinetobacter*. In a study by Ranjan *et al.*, the most common causative agent for VAP was *Acinetobacter boumani* (32.80%), followed by *Pseudomonas* (25.71%). A similar finding was also observed in a study by Kant *et al.*, where *A. boumani* was found in 25.37% and *Pseudomonas* in 17.91% of the cases. *Klebsiella* was the most common (29.5%) in Shashikala *et al.*,[19] study. In our study, early-onset VAP frequency was 36.4% and late-onset VAP was 63.6%, which was comparable with the findings of Sarkar *et al.* (early-onset VAP, 36.84%; late-onset VAP, 63.16%). In a study by Dey and Bairy, early-onset VAP and late-onset VAP were diagnosed in 47.7% and 52.3% of cases, respectively. In a study by Behari and Kalafatis, all organisms had late-onset VAP. In a study by Gauthier *et al.*, early-onset VAP was 10.7% and late-onset VAP was 89.3%; that is, late-onset VAP organisms were predominantly isolated. Gram-negative microorganisms were most frequently isolated in both early- and late-onset VAP in our study, which is similar to the findings of Sarkar *et al.* In contrast, Gauthier *et al.* found that Gram-positive bacteria were most frequently found in early VAP, and Gram-negative bacteria were predominant in late-onset VAP. In our study, monomicrobial and polymicrobial organisms were found in 86.4% and 13.6% of individuals, respectively. Hence, predominant monomicrobial growth over polymicrobial organisms seen in our study was similar to Kant *et al.*, study. In Gauthier *et al.*, study, monomicrobial VAP isolate was 60% and polymicrobial VAP isolate was 40%. In Nanthini Devi and Gomathi's study, the diagnosed monomicrobial and polymicrobial organism frequencies were 55.56% and 44.44%, respectively. The most common microorganism in both monomicrobial and polymicrobial VAP was again Gram-negative bacteria, *Acinetobacter*, which was similar to the results of Nanthini Devi and Gomathi. The most common secondary microorganisms were Stenotrophomonas (4.5%), Serratia (4.5%), and MRSA (4.5%). In a study by Ferrer *et al.*, 16% of cases of VAP had polymicrobial species, and MRSA, *H. Influenzae*, and several *Enterobacteriaceae* were the most frequently isolated polymicrobial microorganisms. Among the monomicrobial groups, *P. aeruginosa* was the most common. MDR organisms were found in 54.5% of the cases in our study. In study by Nanthini Devi and Gomathi, MDR organism was detected in more than 80% cases both in monomicrobial and polymicrobial groups. Ahmed *et al.* reported that MDR organisms are commonly diagnosed as VAP isolates. In the study group, MDR organisms were commonly isolated from VAP, with the most predominant being *Acinetobacter* (47.9%), followed by *Pseudomonas* (27%). The mean duration of ICU stay of the non-VAP patients in our study was 6.86 days. For individuals with VAP, we observed a mean duration of stay of 17.32 days ($P = 0.05$). This association was not found significant in the study of Ferrer *et al.*, group also where mean duration of ICU stays for monomicrobial and polymicrobial group was 7 and 8 days, respectively. Another different finding was noted in the study done by Gauthier *et al.*, where the mean duration of ICU stay in polymicrobial VAP group (25 days) was significantly higher than monomicrobial VAP group (5.8 days). In another study done by Dey and Bairy, ICU stay of monomicrobial and polymicrobial VAP was 23 and 25 days, respectively, i.e., association was not significant which was comparable to our study. In several studies, the duration of mechanical

Table 6: The relationship of MDR/XDR with the time of development of VAP

VAP	MDR/XDR				*P*-value
	Yes		No		
	Frequency	Percentage	Frequency	Percentage	
EARLY	0	0.0	8	80.0	<0.001
Late	12	100.0	2	20.0	
Total	12	100	10	100	

VAP: Ventilator-associated pneumonia, MDR/XDR: Multidrug-resistant/extensively drug-resistant

Table 7: A comparison between the early and late VAP groups in terms of days in the intensive care unit and mechanical ventilation

Outcome	VAP						*P*-value
	Early			Late			
	Mean±SD	Min-Max	Median (IQR)	Mean±SD	Min-Max	Median (IQR)	
ICU days	13.62±4.31	6–20	8.50 (11.25–16.75)	19.43±5.93	9–30	21 (14.50–24)	0.026
Ventilation days	11.88±3.31	6–17	2.50 (9.50–13.75)	17.57±5.75	8–27	19.50 (12.75–21)	0.022

SD: Standard deviation, IQR: Interquartile range, VAP: Ventilator-associated pneumonia, ICU: Intensive care unit

ventilation was significantly different from that of VAP. In a study by Ahmed *et al.*, VAP increased the duration of MV. A study by Marcio *et al.* also found that the mean durations of mechanical ventilation for VAP and non-VAP patients were 13 and 5 days, respectively. In a study by Kanafani *et al.*, the mechanical ventilation days in the VAP and non-VAP groups showed similar trends (24 and 11 days, respectively). Gram-negative bacteria are the prime agents responsible for increasing numbers of infections in hospitals and ICUs among immunocompromised patients, and community-acquired infections are also increasing in the current scenario. Implementation of the VAP prevention bundle along with periodic education of all healthcare staff about personal hygiene and surveillance of the ICU along with antimicrobial resistance tracking will definitely reduce VAP rates in intensive care settings.

CONCLUSION AND RECOMMENDATIONS

The incidence rate of VAP was 22%, with *Acinetobacter* and *Pseudomonas* being the predominant organisms. It increases mortality, duration of mechanical ventilation, and length of ICU stay. Late-onset VAP was associated with higher drug resistance, duration of mechanical ventilation, and ICU stay than early-onset VAP. Determining the VAP-associated epidemiology in each medical institution is important for developing effective prophylactic and therapeutic strategies aimed at decreasing the incidence of VAP-associated mortality rates and optimizing the use of antimicrobial agents.

ETHICAL COMPLIANCE

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

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