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RESEARCH ARTICLE
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TO ASSESS THE RISK FACTORS AND TO IDENTIFY THE CAUSATIVE ORGANISM AND OUTCOME ASSOCIATED WITH VENTILATOR ASSOCIATED PNEUMONIA IN A TERTIARY CARE RESPIRATORY ICU

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Abstract:
Background: Mechanical ventilation is a crucial intervention in intensive care units (ICUs) to save lives of critically ill patients. However, Ventilator Associated Pneumonia (VAP) remains a prevalent infection among patients intubated for over 48 hours.
Aim: To assess the risk factors and to identify the causative organism and outcome associated with Ventilator associated Pneumonia.
Materials & methods: This study was conducted in a 10-bedded Respiratory Intensive Care Unit (RICU) at S.C.B Medical College and Hospital, Cuttack, Odisha, from June 2021-Oct 2022. The study included 50 patients aged over 18 years and those on mechanical ventilation for over 48 hours. Patients were monitored for VAP diagnosis and classification into Early onset pneumonia and Late onset pneumonia. The Modified Clinical Pulmonary Infection Score was used to diagnose VAP, and APACHE II scores were calculated within 24 hours of ICU admission. Endotracheal aspirate samples were collected from patients requiring mechanical ventilation for over 48 hours.
Results: Steroid therapy before intubation and emergency intubation are associated with a high incidence of VAP, with most patients undergoing reintubation. Type 2 Diabetes Mellitus and coronary artery disease are risk factors for VAP. Mortality associated with VAP is 64.5%, with total recovery in 44% of patients. Common organisms isolated were Klebsiella, Acinetobacter, Pseudomonas, Citrobacter, E. coli, Acinetobacter Klebsiella, Enterococcus, and methicillin sensitive staphylococcus aureus. Out of 19 patients, 57.9% recovered, while 35.5% were recovered in the VAP group. Mortality in early onset VAP was 57.2%, while late onset VAP had a higher mortality rate. **Conclusion:** The study reveals that VAP increases with mechanical ventilation duration, with late-onset cases and

highly resistant strains being common. Males have higher mortality rates. Future research should guide antibiotic therapy to reduce mortality and prevent resistant strains.

Key words: Klebsiella; Acinetobacter; Pseudomonas; Type 2 Diabetes Mellitus; Coronary artery disease; Ventilator associated pneumonia.

Introduction:

Mechanical ventilation is a crucial intervention in intensive care units (ICUs) to save lives of critically ill patients. However, Ventilator Associated Pneumonia (VAP) remains a prevalent infection among patients intubated for over 48 hours. VAP is caused by the presence or incubation of infectious organisms that were not present at the time mechanical ventilation was initiated [1-3]. There are two types: early onset VAP, which occurs within the initial four days of breathing, and late onset VAP, which occurs more than four days after mechanical ventilation [4]. The prevalence of VAP varies between 6% and 52%, with a maximum of 76% observed in some contexts [5].

Causative factors of VAP include duration of hospitalization, prior antibiotic use, and comorbidities. Gram-negative organisms are the predominant bacterial pathogens linked to VAP [6]. Despite advancements in antibiotic regimens, death rates associated with VAP remain high, ranging from 24% to 50% [4]. In some cases, high-risk bacteria can result in a death rate of up to 76% [4]. VAP remains a significant concern in ICU patients, and understanding its occurrence, risk factors, and pathogens can contribute to the formulation of effective preventive strategies [1-3]. This can lead to reduced mortality and morbidity rates, as well as decreased treatment and hospitalization duration associated with VAP [4-6]. The study aimed to determine VAP prevalence, evaluate risk factors, and analyze local microbiological flora to inform the better application of empirical antimicrobial drugs. Hence the present study was to assess the risk factors and to identify the causative organism and outcome associated with Ventilator associated Pneumonia.

Materials & methods:

This was a prospective observational study carried out in a 10-bed respiratory intensive care unit (RICU), S.C.B Medical College and Hospital, Cuttack, Odisha, for a period of one year, i.e., from June 2021-Oct 2022, and the ethical committee clearance has been obtained from the institutional ethical committee, SCBMC, Cuttack. Inclusion criteria: consenting patients aged >18 years of both genders and patients admitted to RICU who are on mechanical ventilation for >48 hours. Exclusion criteria: refusal of consent; patients who were already on ventilation before admission to the RICU or died within 48 hours; and patients who had pneumonia on admission.

The study included a total of 50 patients who met all inclusion and exclusion criteria from the population of patients receiving mechanical ventilation in our respiratory intensive care unit at the Department of pulmonary medicine. After clearly explaining the study procedure, we obtained written informed consent from the legally authorized patient representative. We monitored the patients on the third day of mechanical ventilation to diagnose VAP based on clinical criteria, and on the seventh day, we classified them into early-onset and late-onset pneumonia. We considered Day 0 to be the date of intubation and the start of mechanical ventilation. To clinically diagnose VAP, we used the Modified Clinical Pulmonary Infection Score. We noted a detailed history of each patient, which included their name, age, sex, underlying clinical condition, date of ICU admission, the treatment they were receiving, and their clinical outcome. The VAP diagnosis was based on clinic-radiological and microbiological criteria. We developed a clinical suspicion of VAP in patients with a modified CPIS score less than 6. Within 24 hours of ICU admission, we calculated the APACHE II score for each patient to evaluate the incidence and outcome of VAP. We confirmed the diagnosis when we observed significant growth in the culture sample. We collected an endotracheal aspirate (ETA) sample from all patients admitted to the ICU requiring mechanical ventilation for more than 48 hours on the 2nd, 4th, and 7th days, and took a BAL whenever necessary.

As the bronchoscope advances through the tracheal tubes and upper respiratory tract, aspirating secretions through it can lead to false-positive cultures due to contamination. We developed a specialized brush, known as a protected specimen brush (PSB), to collect uncontaminated secretions from the distal airways during bronchoscopy. We advance the brush from the inner cannula to collect samples from the distal airways whenever necessary.

All aspirate samples underwent Gram stain preparations within the first hour. We inoculated the samples onto 5% blood agar and MacConkey agar, reconstituted according to the manufacturer's specifications, and sterilized them at 121°C for 15 minutes. We incubated the plates at 37°C for 18–24 hours. If there was no bacterial growth within 24 hours, we extended the reading of the plates to 48 hours. We subjected the isolated colonies to Gram staining and biochemical tests for identification. We carried out identification according to standard biochemical tests.

Statistical analysis:

The present study was an observational study and a randomized simple sampling method is used. Sample size calculated using the Population (N). Confidence level is 95% and z score is 1.96. SPSS version 27 and MS Excel were used for data analysis. The variables in non-normal form number (n) and percentage (%) are presented. P value <0.05 considered as statistically significant.

Results:

Table 1: Risk factor and underlying comorbidities in patients on mechanical ventilation

Risk Factor/Comorbidity	Total Cases	NVAP	VAP			Significance
			EVAP	LVAP	Total	
Emergency Intubation	41	19	11	11	22	<0.0001
Reintubation	9	0	3	6	9	0.024
T2DM	11	3	4	4	8	0.01
Steroid Therapy	33	9	12	12	24	0.02
CAD	4	0	1	3	4	<0.0001
Smoker	23	8	6	9	15	0.001
Alcoholic	12	3	3	6	9	<0.0001
HTN	15	5	4	6	10	<0.0001
ARDS	4	2	1	1	2	0.012
Sepsis	8	4	3	1	4	0.032

Table 1 reveals that steroid therapy before intubation and emergency intubation both were associated with high incidence of VAP. The patients undergoing reintubation majority were associated with LVAP. In patients with T2DM 8 out of 11 developed VAP. similarly in patients with CAD as a risk factor associated with high incidence of VAP.

Figure 1: indicates that majority of organisms isolated in gram stains among VAP group were GNB i.e,90.3% and GPC were seen in 9.7%.

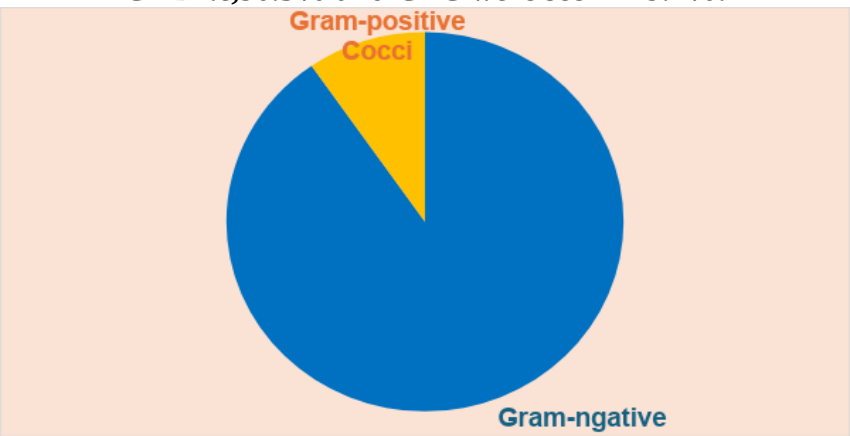

Figure 2 illustrated that the most common organism isolated was found to be klebsiella (35.5%) followed by Acinetobacter (32.3%), Pseudomonas (9.6%), Citrobacter (3.2%), E coli (3.2%), Acinetobacter Klebsiella (6.4%), Enterococcus (6.4%), and MSSA (3.2%).

Figure 2: Illustration of the most common organism isolated from the study population.

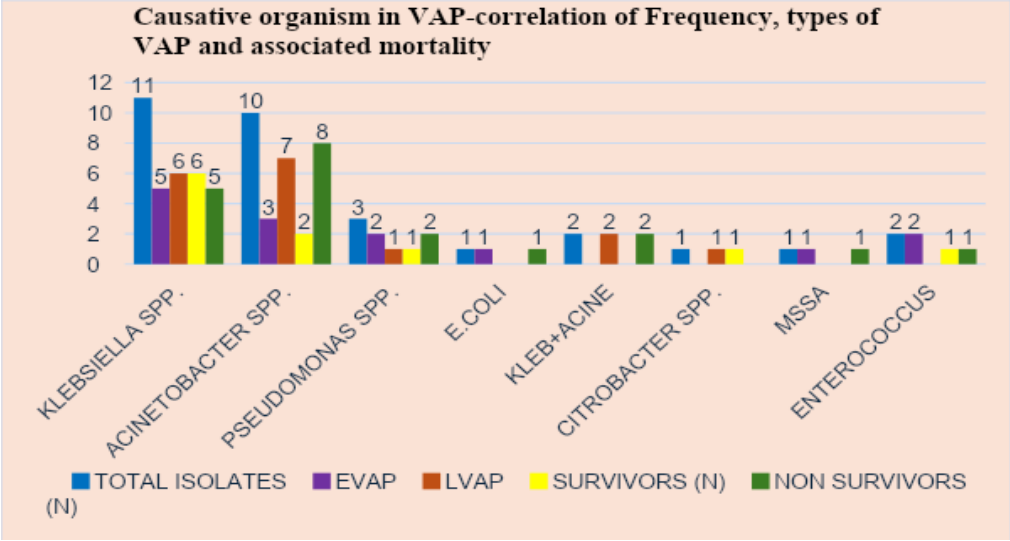

Figure 3: illustrates that the mean APACHE II score among non survivors in the VAP and Non-VAP group was 27.7 and 23.5 respectively and was statistically significant.

Figure 3: Comparison of APACHE II score and outcomes in non-VAP and VAP group.

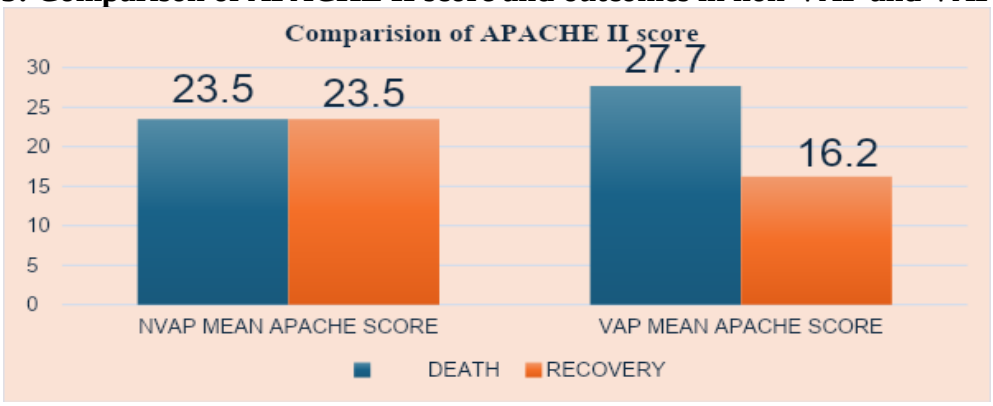

Figure 4: Outcomes in Patients with NVAP And VAP group

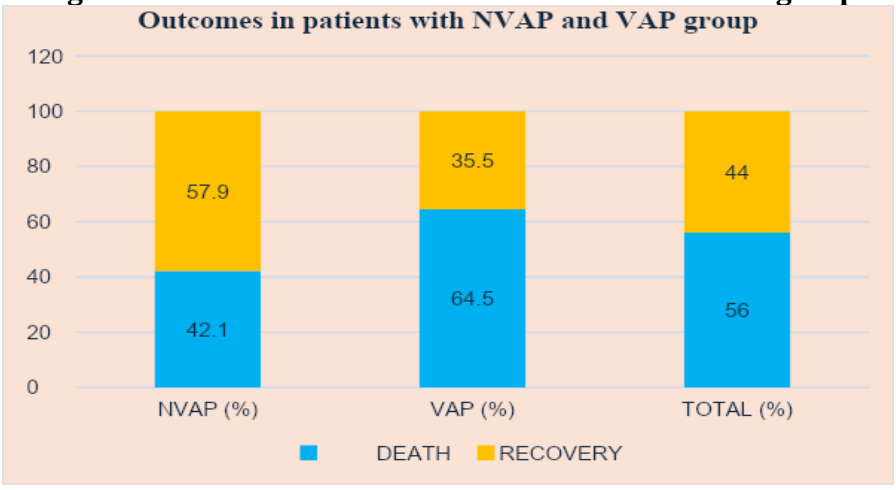

Figure 4 shows that out of 50 patients, overall mortality was seen in 28 (56%) patients. Mortality associated with VAP was 64.5%. Total recovery was seen in 22(44%) patients. In the Non-VAP group 11 out of 19 (57.9%) patients were recovered and 35.5% were recovered in the VAP group of patients. Among the VAP group more no of deaths occurred in males as compared to females i.e. out of 14 males died in the whole study 12 were associated with VAP. Mortality associated with early onset VAP was 57.2% and 64.5% in late onset VAP. The mortality in late onset VAP was more as compared to early onset VAP.

Discussion:

A prospective observational study was done on 50 mechanically ventilated patients who had been on invasive mechanical ventilation for more than 48 hours. The goal was to look at the number of cases, risk factors, and percentages of different bacterial pathogens found in the tracheal aspirate of patients with VAP, as well as how well they responded to antibiotics and the outcomes of the condition. The endotracheal aspirate's Gram staining revealed gram-negative bacilli in 56% of the 50 cases, gram-positive cocci in 6%, and no bacteria in 38% of the cases. In our study, we isolated no organism from 19 (38%) patients. We found that Klebsiella spp. was the most isolated organism in endotracheal aspirate culture, accounting for 22%, followed by Acinetobacter spp. (20%), pseudomonas (6%), Acinetobacter + Klebsiella spp. (4%), Enterococcus (4%), E. coli (2%), and Citrobacter (2%). Enterococcus spp. were the most isolated gram-positive cocci, accounting for 4% of the total organisms.

In our study, many risk factors were found to be significantly different between the VAP and NVAP groups of patients. These included emergency intubation, reintubation, T2DM, steroid therapy before intubation, CAD, smoking, drinking, high blood pressure, ARDS, and sepsis. On univariate analysis, Joseph et al., [7] found that impaired consciousness, reintubation, emergency intubation, and nasogastric tube were all significantly associated with VAP, whereas steroid therapy was not.

In our study, we performed re-intubation on 9 patients, all of whom were associated with VAP. Of these, 6 (66.7%) had late-onset VAP, and we found a statistically significant difference. This is similar to Gupta et al., [8], who found that reintubation was done in 8 patients, of whom 7 (87.5%) developed VAP, clearly indicating that reintubation is an important predisposing factor in the development of VAP ($p<0.001$). Our study aligns with the findings of Othman et al., [9], who discovered a significant association between sepsis and ARDS in the VAP group ($p = 0.01$). Patil et al., [10] found that being unconscious, needing to be re-intubated or intubated in an emergency, having a tracheostomy or tracheotomy, being older, and having problems with more than one organ were all things that put people at risk for developing VAP ($p = 0.02$).

In our study, 31 patients had purulent tracheal secretions, out of which 29 (90.3%) had gram-negative organisms and 9.7 % had gram-positive cocci. Klebsiella was the most common organism found in GNB (35.5%), followed by Acinetobacter (32.3%), pseudomonas (9.6%), Acinetobacter + Klebsiella (6.4%), E. coli (3.2%), and Citrobacter (3.2%). Among GPC, Enterococcus (9.6%) was the most common organism, followed by methicillin-sensitive Staphylococcus aureus (3.2%). Klebsiella was the most common organism associated with VAP. Joseph et al., [7] observed that Gram-negative bacteria, accounting for 80.9% of causative organisms, caused most cases of VAP. Pseudomonas aeruginosa (21.3%) and Acinetobacter baumannii (21.3%) were the most common gram-negative bacteria associated with VAP, and Staphylococcus aureus (14.9%) was the most common gram-positive bacteria among patients with VAP. Shit et al., [11] discovered that Klebsiella pneumoniae caused the majority of 10 (37%) cases of VAP, with Gram-negative organisms being the predominant pathogens. This study found that VAP was also caused by Acinetobacter baumani (72.6%), pseudomonas aeruginosa (41.5%), staphylococcus aureus (31.1%), Escherichia coli (7.2%), and stenotrophomonas maltopholia (4%). Ranjan et al., [12] discovered that Gram-negative bacilli accounted for 95.7% of the bacterial isolates. Acinetobacter spp. accounted for 34.28% of VAP cases, followed by pseudomonas aeruginosa, which was responsible for 25.71% of cases. Klebsiella, Citrobacter, Enterobacter spp., and E. coli were the other gram-negative bacteria isolated. Among

gram-positive cocci, 2 were Staphylococcus aureus and 1 was Enterococcus spp. Our study aligns with the findings of Othman et al., [9] who found that Klebsiella was the most frequently isolated organism in 31.8% of patients.

We stratified the overall risk of mortality by the APACHE II score during the first 24 hours of admission. In our study, the mean APACHE II score among the NVAP group of patients was 19.5±5.8, while 23.6±7.04 among the VAP group of patients was found to be statistically significant ($p = 0.007$). We also found that the mean APACHE II score in recovered patients in the NVAP group was 16.5 and 23.5 in non-survivor groups. Similarly, in the VAP group of patients, the mean APACHE II was 16.2 for survivors and 27.7 for non-survivors. Our study matches with Mohanty et al., [13] in their study found that the mean APACHE II score of the patients who developed VAP was 21±7.02, while those who did not develop VAP were 15.88±5.57. The mean APACHE II score among survivors was 14.11±3.49, and 24.43±5.56 among non-survivors. Another study by Gupta et al., [8] observed that the mean APACHE II score of the patients who developed VAP was 22.47±8.382, while that of patients who did not develop VAP was 14.74±7.491. According to a study by Sutino et al., [14] patients with VAP had a higher APACHE II score than patients without VAP.

In this study, 35.5% of patients had Klebsiella isolates, of which 45.5% died and 54.5% survived. 32.3% of patients had isolated Acinetobacter, of which 80% died and 20% survived. 9.6% of patients had isolated Pseudomonas spp., of which 66.7% died and 33.3% survived. 6.4% of patients tested positive for Acinetobacter+Klebsiella, and all of them died. In 6.4% of cases, we isolated Enterococcus, resulting in 50% death and 50% survival. Gupta et al., [8] who observed that we isolated Klebsiella in 23.33% of cases, 71.42% of which died and 28.57% of which survived, support our study. We isolated Acinetobacter in 20% of cases, of which 83.33% died and 16.67% survived. Similarly, we isolated pseudomonas in 30% of cases, of which 33.33% died and 66.67% survived. Sadigov et al., [15] also support our study, showing that Acinetobacter baumannii infection increased the hospital mortality rate in VAP patients ($p = 0.01$); in non-survival VAP patients, the incidence of Acinetobacter baumannii isolation was significantly higher compared to survival patients.

Among patients with VAP, COPD (68%) was associated with the highest mortality, i.e., 45.2%, followed by Bronchiectasis (6.4%). Nseir et al. [16] found that the mortality associated with VAP among COPD patients was 34%. Badaway et al., [17] observed that the mortality was 48% among COPD patients diagnosed with VAP, which is similar to our study.

Our study revealed an overall mortality rate of 56%, with 64.5% of deaths linked to VAP and 42.1% in the NVAP category. In the VAP group, the patient's mortality associated with EVAP was 57.1% and 70.5% in late-onset VAP, respectively. Our study shares similarities with Gadani et al., [18] reported an overall mortality rate of 46% and a VAP-associated mortality rate of 54%. The mortality EVAP showed a mortality rate of 20%, while late-onset VAP showed a mortality rate of 66.67%. by Gupta et al., [8] found that the overall mortality in their study was 32.71%. The mortality associated with the VAP group was 46.67%, and mortality in the NVAP group was significantly low at 27.28%. The difference between the two groups was statistically significant. Mortality in EVAP and LVAP was 25% and 50%, respectively. A study by Ranjan et al., [12] found that the overall mortality in patients with VAP was 48.33%, while in NVAP patients the mortality was 20%. This study revealed a high mortality rate due to the inclusion of critically ill patients with high APACHE II scores upon ICU admission.

Conclusion:

The study found that VAP occurrence increases with mechanical ventilation duration, with the majority being late-onset cases with highly resistant strains. Males have higher mortality rates due to VAP, with Klebsiella and Acinetobacter being the most common organisms. The APACHE II score is a useful parameter for predicting mortality and VAP development. Male gender and early-onset VAP were associated with survival in VAP patients. VAP remains a common complication of ventilator support for COPD patients, with high morbidity and mortality. Future research should guide initial antibiotic therapy to reduce mortality and prevent resistant strains.

Conflict of interest:
There is no conflict of interest among the present study authors.

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