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Frequency and Etiology of Ventilator-Associated Pneumonia in COVID-19 Patients Presenting to Tertiary Care Hospital

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ABSTRACT

Objective: To establish the frequency and aetiology of the pathogens causing Ventilator-Associated Pneumonia in COVID patients admitted to a tertiary care hospital.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Medicine and Intensive Care, Pak Emirates Military Hospital, Rawalpindi Pakistan, from July 2021 to Feb 2022.

Methodology: Patients between 25 to 70 years of age of either gender with severe COVID pneumonia with positive RT-PCR, clinical and radiological evidence of critical disease, and needing ventilatory support due to respiratory failure were included in this study. Ventilator-associated pneumonia (VAP) was identified and confirmed by positive culture taken 48 hours after intubation, and Cultures noted organisms.

Results: Of 300, 238(79.3%) patients developed Ventilator-Associated Pneumonia (VAP) 48 hours after intubation. VAP was diagnosed by positive cultures taken from bronchial secretions and blood samples. Culture report analyses were assessed for pathogens, which revealed Klebsiella pneumonia (KP) being the most common pathogen 64(26.9%), followed by Acinetobacter baumannii 49(20.6%) and Pseudomonas aeruginosa 26(10.9%). Polymicrobial culture results were also seen, which revealed Acinetobacter+Klebsiella in 29(12.2%) subjects, Pseudomonas with KP in 33(13.9%), and Acinetobacter with Pseudomonas aeruginosa in 13(5.5%).

Conclusion: Klebsiella pneumonia is the most common pathogen found to cause VAP in COVID-19 patients. Around 30% of polymicrobial cultures were noted.

Keywords: Acinetobacter baumunni, COVID-19, Candida, Intubation, Klebsiella pneumonia, Pseudomonas aeruginosa, Ventilator-associated pneumonia, Ventilatory support.

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INTRODUCTION

Ventilator-associated pneumonia (VAP) occurs 48 hours or more after endotracheal intubation and mechanical ventilation in patients requiring airway support.[1] VAP was a foremost pressing challenging nosocomial infection in ICUs even before the COVID-19 pandemic.[2] However, now, when Hospitals and ICUs are more inundated with complicated and longer critical care of patients with COVID-19 disease, nosocomial infections like VAP are more rampant than expected, making VAP a bigger and more pressing concern.[3,4]

Studies have shown that approximately 5% of individuals affected by COVID-19 infection experience respiratory impairment, leading to severe disease with acute respiratory failure, requiring extreme management by mechanical ventilation, which exposes them to a high risk of VAP.[5,6] High-risk individuals with COVID-19 infection develop severe and critical diseases with radiological features of ground-glass opacities on the HRCT chest and a very intense Systemic Inflammatory Response Syndrome (SIRS) that leads to Multi Organ Dysfunction Syndrome (MODS).[7,8] Important contributing factors responsible for the risk of VAP incidence in mechanically intubated patients include old age, prolonged ventilation, immunosuppressant use, lapses in prevention processes, Comorbid conditions, chronic Lung pathology, & immunosuppressive status. [9,10]

This study focuses on the early diagnosis of VAP, causative pathogens, and targeted treatment options for VAP. In addition, there is a high incidence of multidrug resistance in our country due to unnecessary self-medication by patients and unjust overuse of antibiotics in COVID-19 patients. It leads to the resistant

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organism in VAP infection, leading to difficulty in choosing treatment due to multi-drug resistant pathogens and resulting in much higher mortality due to VAP in COVID-19-infected individuals. There is a dire need for antibiotic stewardship programs to limit the excessive and unjust use of antibiotics and to emphasize judicial targeted use, as it may inflict a risk of post-pandemic multi-drug resistant organisms causing HAIs like VAP.

METHODOLOGY

The cross-sectional study was conducted at the ICU of the Internal Medicine & Critical Care Medicine Department, Pak Emirate Military Hospital, Rawalpindi, Pakistan, from July 2021 to February 2022 after approval from the Ethical Committee of (certificate A/28/EC/445). The sample size was calculated using the WHO sample size calculator, taking a reported prevalence of ventilator-associated pneumonia of 40-60%.[11]

Inclusion Criteria: Patients of either gender aged 25 years to 70 years, with confirmed Severe COVID-19 infection with positive RT-PCR and radiological evidence by Ground Glass opacities (GGOs) on HRCT chest, requiring mechanical ventilation due to acute respiratory failure were included.

Exclusion Criteria: Patients with pre-existing debilitating lung pathology (chronic obstructive pulmonary disease (COPD), asthma, Tuberculosis) or terminal illness, malignancy, patients on chemotherapy or radiotherapy, and patients with HIV infection were excluded from the study.

Patients with severe COVID-19 infection requiring respiratory support were shifted to the ICU of Pak Emirate Military Hospital. Those mechanically ventilated owing to respi-ratory compromise due to critical illness were included in the study and clinically examined daily for the clinical signs of VAP. Any patients showing signs of Ventilator-associated Pneumonia (VAP) 48 hours post-intubation were diagnosed by clinical examination, laboratory findings, and chest radiograph. All COVID-19 patients, intubated and mechanically ventilated and had a fresh pulmonary infiltrate, fulfilled two or more criteria, including new-onset fever (38.5°C or higher), excessive bronchial secretions, and leukopenia or leukocytosis (WBC <4,000 or >11,000mm^3), were labe-lled as ventilator-associated pneumonia (VAP). The patient's age, gender, comorbidities, HRCT involve-ment, causative pathogen, and mortality were retrospectively analyzed.

For sampling, blood and bronchial/trans-tracheal secretions were collected and tested for confirmation of causative organisms. Blood samples were collected from all ventilated patients of COVID-19 disease with suspected VAP who showed signs of deterioration, new radiological findings, or worsening of PaO2/FiO2 ratio before changing or adding a new antibiotic. Bronchial secretions were simultaneously collected via Transtracheal aspirate (TTA) or bronchoalveolar lavage (BAL) along with blood samples and sent for culture and sensitivity.

The isolated bacteria on culture reports of the blood sample as well as BAL were classified into two categories: 1) definite pathogen if identical pathogen were seen on blood and TTA/BAL specimens; 2) probable or possible pathogen: if the culture of blood sample and BAL showed different pathogen. Causative pathogens were then segregated as per their frequency. Co-infection was considered if more than one pathogen was seen on the culture report.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency & percentages.

RESULTS

Three hundred individuals with critical COVID-19 infection of either gender were admitted to ICU requiring mechanical ventilation due to critical illness, out of which 238(79.3%) patients developed VAP after 48 hours of intubation. Among 238(79.3%) patients who developed VAP, 91(38.2%) were vaccinated for COVID-19 before getting infected with COVID-19, whereas 146(61.3%) were unvaccinated patients, representing a high percentage of the unvaccinated population developing critical illness due to COVID-19 as compared to vaccinated patients. Among 238 patients, 144(60.5%) had a history of empirical antibiotic use before admission, and 94(39.5%) had a history of steroid use for COVID-19 infection before getting admission and being shifted to ICU (Figure-1). Other contributing factors in getting VAP infection were also observed (Figure-2).

Furthermore, patients were clinically assessed daily for suspected VAP and 160(67.2%) patients had positive Blood/BAL/TTA culture on the third day of intubation. In comparison, 78(32.8%) developed VAP on the fifth day, confirmed by positive cultures.

Specific pathogens grown on culture samples of BAL and blood, *Klebsiella pneumoniae* was the most common culprit pathogen causing nosocomial infection in 64(26.9%) patients, followed by *Acinetobacter baumannii* in 49(20.6%) patients and *Pseudomonas*

aeruginosa in 26(10.9%) patients developing VAP on mechanical ventilation. A usual combination of pathogens was noticed in culture reports as Acinetobacter with *Klebsiella* in 29(12.2%), *Pseudomonas aeruginosa* with KP in 33(13.9%), and *Acinetobacter* with *Pseudomonas aeruginosa* in 13(5.5%) of patients developing VAP. Total culture results showed KP in 86(36.1%) as a single pathogen and co-infection, followed by *Acinetobacter* in 70(29.4%) & *Pseudomonas* in 53(22.2%) (Table).

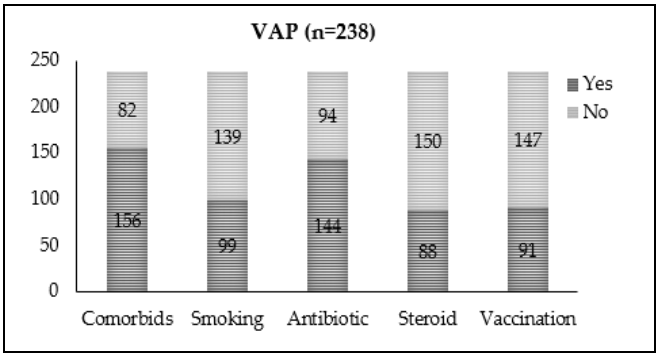

Figure-1: Factors affecting VAP frequency among patients

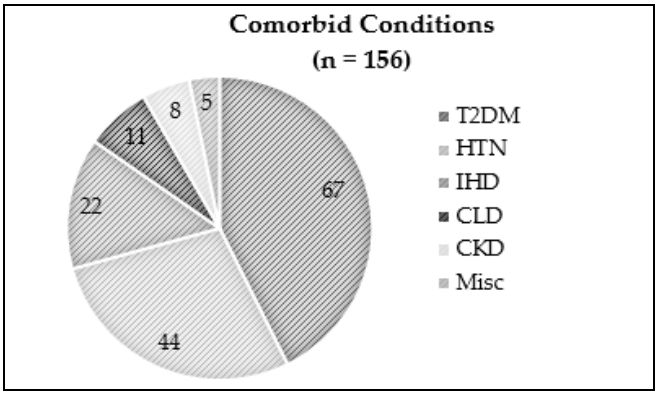

Figure-2: Comorbid Conditions

Table: Organisms causing Ventilator-Associated Pneumonia separated in Cultures (n=238)

Pathogen	n(Age%)
Klebsiella pneumoniae	64(26.9%) (Total=86(36.1%)
Acinetobactor bauminnii	49(20.6%) (Total=70(29.4%)
Pseudomonas aeruginosa	26(10.9%) (Total=53(22.2%)
Acinetobactor+Klebsiella pneumoniae	29(12.2%)
Klebsiella pneumoniae+Pseudomonas aeruginosa	33(13.9%)
Acinetobactor+Pseudomonas aeruginosa	13(5.5%)
Serritia	09(3.8%)
Candida sp.	07(2.9%)
Staph aureus	06(2.5%)
E coli	02(0.8%)

VAP has a high mortality ratio as compared to other nosocomial infections; it was noted in the study that out of 300 COVID-infected mechanically ventilated patients, only 88(69.8%) were successfully extubated. Among these 88(69.8%) extubated patients, 40 (64.5%) patients were those who did not develop VAP (n=62) and only 48(20.1%) patients developing VAP (n=238) were successfully extubated, showing a high mortality rate of VAP with superadded mortality due to COVID-19 infection (Figure-3). Pathogens causing ventilator-associated pneumonia in COVID-19 patients are shown in Figure-4.

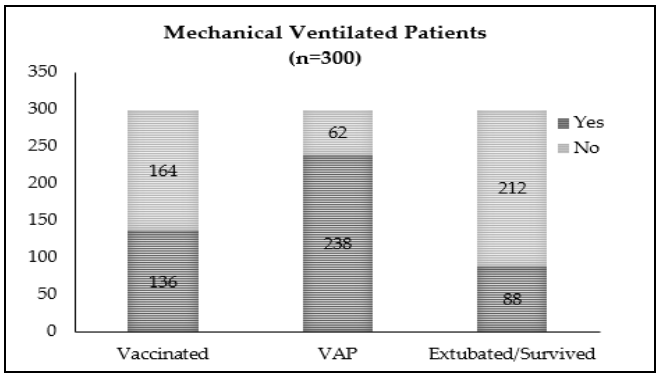

Figure-3: Status and Outcome of Mechanically Ventilated patients

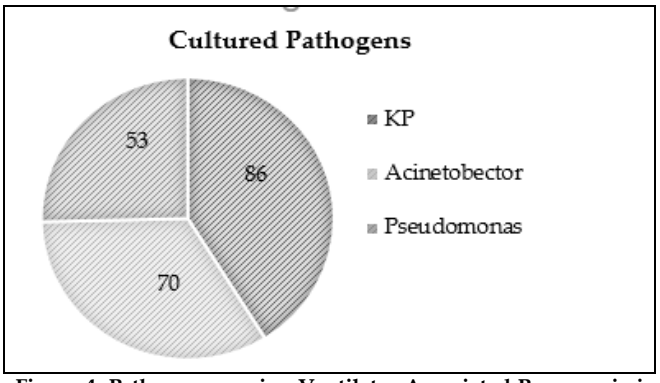

Figure-4: Pathogens causing Ventilator-Associated Pneumonia in COVID-19 patients

DISCUSSION

The result of this study revealed that VAP prevalence is significantly increased in COVID-19 infected patients, with KP (total=86(36.1%) being the most common culprit pathogenic organism followed by *Acinetobacter* (total=70(29.4%) and *Pseudomonas* (total= 53(22.2%) which was inconsistency with national and international data with increased incidence due to superadded COVID-19 infection.

This study revealed that only 136(45.3%) patients were vaccinated against COVID-19, less than half the patients getting the critical illness. In addition, the results highlight that out of a total of n=300 mechani-

cally ventilated patients owing to critical COVID-19, 238(79.3%) developed VAP. A Cohort study conducted by Papazian *et al*. in the Department of Anesthesia and Intensive Care, Hôspital Sainte-Marguerite, Marseille, France, showed that mortality of VAP was 40%.[12] Noor *et al*. conducted a surveillance study on the prevalence of VAP in intubated patients in Aga Khan Hospital Karachi, revealing that 70(28%) out of 250 mechanically ventilated patients developed VAP.[13] In another study conducted by Kumar *et al*. concluded that 84 (30.5%) out of 275 patients on ventilator support developed VAP.[13]

Ventilator-associated pneumonia represents a substantial health challenge in the difficult time of the COVID-19 pandemic in Pakistan, posing a hefty blow to our slow-growing economy.[14] It has been observed that there is an increasing trend of unjust use of empirical antibiotics by the patients and health workers as well, which leads to an increase in antibiotic resistance and resistant pathogens growing on cultures, leading to increased disease burden and longer ICU stay with difficult to treat the infection along with COVID-19.[15] Another study concluded that common pathogens of VAP included *Acinetobacter species* (31.0%), *Pseudomonas aeruginosa* (27.6%), *Staphylococcus aureus* (15.1%), *Klebsiella species* (6.5%) and *Escherichia coli* (5.6%) were culture from patients on ventilator support.[16] Worldwide, increased cases of multi-drug resistance in Gram-negative rods, especially *Pseudomonas aeruginosa* and *Acinetobacter,* especially to *Fluoroquinolones, Ceftazidime*, and *Aminoglycosides* has been observed, which is becoming a pressing health concern in treating serious infections like VAP.[17] Moreover, it is well-known that Ventilator-associated pneumonia is the most common Hospital-acquired infection in intubated patients in intensive care units (ICU), accounting for more than 25% of all ICU infections. Emerging antibiotic resistance is on the rise, becoming a global health problem, prolonging ICU stays and increasing disease burden in terms of mortality and costs.[18]

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LIMITATIONS OF STUDY

The study was carried out during the extraordinary COVID-19 pandemic with overburdened and overworked staff with limited resources and emerging new data and treatment modalities. It may have slightly more cases due to the above causes had it been conducted otherwise.

CONCLUSION

It has been observed in this study that, with COVID infection overburdening the mortality rate associated with VAP, strict adherence to ICU protocols, careful handling of ventilators, careful and proper protocol for sampling, just and targeted use of antibiotics, patient care procedures, and adequate trained staffing may reduce the incidence of VAP which subsequently reduce the mortality in ventilated patients. These precautions and measures will also minimize the overall risk of antibiotic-resistant pathogens.

Conflict of Interest: None

Author's Contribution:

Following authors have made substantial contributions to the manuscript as under:

HAS & MY: Conception, study design, drafting the manuscript, approval of the final version to be published.

MH & MUK: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MFS & UUH: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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