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Ventilator Associated Tracheobronchitis – Etiology and Outcome at an Intensive Care Unit of a Tertiary Care Center in North India

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ABSTRACT

Background and Aim: Ventilator associated Tracheobronchitis (VAT) is a common nosocomial respiratory tract infection which develops in intubated critically ill patients. Their etiology changes with time, hospital and ICU setting and duration of hospital stay. This study was aimed at detecting the microbiological etiology of VAT, reporting the antimicrobial susceptibility pattern and impact on outcome.

Materials and Methods: This observational study was conducted for 12 months in the Microbiology Department and intensive care unit of a tertiary care center. A total of 39 endotracheal secretions from suspected cases of VAT were subjected to routine bacterial culture and antimicrobial susceptibility testing. The outcome of the patients with VAT was measured in terms of duration of ventilation, hospital stay and mortality.

Results and Conclusion: VAT was found to occur most commonly between 60-69 years of age and among the male population (79%). A total of 47 isolates were recovered from 39 samples. Monomicrobial growth was obtained from 34 (87.18%) of endotracheal samples, while 5 (12.82%) showed polymicrobial growth of at least two pathogens. The predominant organism isolated was *Acinetobacter baumannii* (27.65%), followed by *Klebsiella pneumoniae* (23.40%) and *Pseudomonas aeruginosa* (21.27%) and all were found to be multidrug resistant. The mean duration of ventilation, ICU Stay and hospital stay for VAT was 10.87 days, 12.20 and 16.27 respectively. It is imperative to timely diagnose and monitor cases of VAT as this would help in deriving an effective early therapeutic intervention and in implementing timely preventive strategies that could help reduce progression of VAT to Ventilator associated pneumonia (VAP).

Keywords: Endotracheal secretion, Multidrug resistance (MDR), Ventilator associated Pneumonia (VAP), Ventilator associated Tracheobronchitis (VAT)

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1. Introduction

Life-sustaining interventions such as mechanical ventilation (MV) have improved the scope of modern and sophisticated intensive care medicine significantly (1). However, as a complication of long-term ventilator support, Healthcare-associated pneumonia (HAP) develops in these critically ill

patients (2). HAP is the second most common hospital-acquired infection (HAI) accounting for 15-20% of all healthcare-associated infections (2). One such HAIs, Ventilator-associated respiratory infections (VARIs) have ever since been recognized as the most common infective complication of mechanical ventilation in intensive care unit (ICU) patients (2).

Ventilator-associated Tracheobronchitis (VAT) is an inflammatory pathology occurring in patients put on prolonged mechanical ventilation. It represents a process in-between the colonization by bacteria of the respiratory tract and the subsequent development of VAP (3). It is often described as a continuum between the two and regarded as a significant risk factor for pneumonia development in such patients (4). It is reported to have an incidence between 1.4% and 19% among critical patients put on ventilator support (3). VAT belongs to the spectrum of VARIS.

There are no standard guidelines for the diagnosis of VAT, one of the most usually accepted defining criteria to diagnose suspected cases includes the following: clinical symptoms and signs of a fever (>38°C) of no other recognizable causal origin, production of purulent sputum, altered leukocyte counts; positive cultures with moderate to heavy growth along with Polymorphonuclear Leukocytes (PMN) on Gram's staining and absence of any radiological signs (2, 3).

The etiology of VAT can change over time; vary with hospitals and ICUs and most strikingly with the duration of ICU stay (5). Most commonly isolated bacteria in aerobic cultures of endotracheal secretions of VAT patients were found to be the multidrug-resistant Acinetobacter species, followed by extended-spectrum beta-lactamase-producing Escherichia coli, *Klebsiella pneumoniae*, and Pseudomonas aeruginosa (6). A rise in multi-drug resistance poses a global challenge in the management of these critically ill patients (6). Carbapenems have been used extensively and effectively to treat these cases and have provided a better patient prognosis. However, increasing carbapenem resistance is limiting the treatment options for effective management as well as subjecting the patients to extend and continued financial, emotional, and physical draining (7).

Keeping the above in mind this study was aimed at identifying the microbiological etiology in suspected cases of ventilator-associated tracheobronchitis, their antimicrobial susceptibility profile, and reporting the impact on clinical outcome.

2. Materials and Methods

This observational study was conducted for 12 months from January 2019 - December 2019 in the

Microbiology department and ICU of the Himalayan Institute of Medical Sciences, after obtaining the patient's informed consent. Ethical approval was obtained from the institutional ethics committee. "Ventilator-associated Tracheobronchitis (VAT)" was suspected upon the development of infection of the respiratory tract beyond 48 hours of artificial ventilation. A lack of radiological evidence of persistent infiltrate on chest x-rays was used to differentiate it from VAP (2). All clinically suspected cases of VAT who were above the age of 18 years were included in this study. Diagnosis of VAT was confirmed based on clinical symptoms and signs, microbiological, and radiological criteria (2). All the patients who developed pneumonia within 48 hours of ICU admission or those who were admitted with any respiratory tract infections were excluded from the study.

Sample processing for etiological identification of VAT:

Endotracheal aspirates from suspected cases of VAT were subjected to staining methods such as gram staining and aerobic bacterial culture. Samples showing polymorphonuclear cells on gram staining with bacteria were processed. Routine laboratory media such as blood and McConkey agar were used for this. Culture plates were incubated at 35° C for 18-24 hours. A colony count of $\geq 10^5$ cfu/mL obtained from endotracheal secretions was considered significant. Phenotypic identification of isolated bacterial pathogens and determination of their antimicrobial susceptibility pattern was done using VITEK-2 automated systems (8). The outcome of the patients with VAT was measured in terms of duration of ventilation, hospital stay, and mortality.

3. Results and Discussion

The most common age group which developed VAT belonged to the ages of 60-69 years. Figure 1 shows the age-wise distribution of cases of VAT.

VAT was predominantly found among the male gender in our study 31(79%). Figure 2 depicts the gender-wise distribution of cases of VAT.

The single organism was isolated among 34 (87.18%) of the endotracheal samples, while 5 (12.82%) showed polymicrobial growth of at least two pathogens. The predominant organism isolated was *Acinetobacter baumannii* (27.65%), followed by *K. pneumoniae* (23.40%) and *Pseudomonas aeruginosa* (21.27%). Figure 3 depicts the microbial etiology of VAT in our study.





Figure 2. Gender-wise distribution of cases of Ventilatorassociated tracheobronchitis

Etiology of VAT



Figure 3. Microbial etiology of Ventilator associated tracheobronchitis

Antimicrobial susceptibility profile for isolates recovered from endotracheal secretions of VAT cases:

Almost all isolates of *A. baumannii, K. pneumoniae* and *P. aeruginosa* commonly isolated were multidrug-resistant.

MDR isolates of *A. baumannii* were found resistant to more than three classes of antimicrobials such as penicillins, cephalosporins, and fluoroquinolones. These isolates were however found to be sensitive to colistin, glycylcyclines such as tigecycline (46%), tetracyclines (36.4%), and β lactam/ β lactamase inhibitors such as ampicillin-sulbactam (23%).

MDR isolates of *K. pneumoniae* were resistant to antibacterial drugs such as penicillin (100%) and cephalosporins (86-98%) and sensitive to colistin (100%), chloramphenicol (43%), gentamicin (25%), carbapenems (25%), tetracycline (25%) and piperacillin-tazobactam (23%).

Figure 1. Age-wise distribution of the cases of Ventilator-associated tracheobronchitis

All MDR isolates of *P. aeruginosa* were sensitive to colistin (100%). Other antimicrobials to which they were found sensitive included amikacin (62%), piperacillin-tazobactam (56%), carbapenems (56%), and piperacillin (46).

Outcome of VAT

The duration of mechanical ventilation, stay at ICU, and Hospital for VAT was 10.87 days, 12.20, and 16.27 respectively. A mortality of 30.76% was seen in the VAT

In our study, VAT was found most commonly to occur among patients belonging to the ages of 60-69 years. In this study, most commonly males were affected (79%). In a similar study by Ray *et al*, **(3)** a male: female ratio of 3:1 was reported. In this study, endotracheal secretions (ET) were used as suitable samples for the isolation and identification of the etiological agent of VAT. The reason is the ease of collection. In a study conducted by Rajashekhar *et al*, the cultures of ET samples were found to be in agreement with bronchoscopic samples **(9)**. In our study, significant growth of more than 10⁵ cfu/mL was isolated from all samples, therefore, satisfying the microbiological criteria for diagnosis of VAT and also differentiating them from colonizers.

In our study, a total of 47 isolates were obtained from 39 samples of suspected cases of VAT. The single organism was isolated among 34 (87.18%) endotracheal samples, while 5 (12.82%) showed polymicrobial growth of at least two pathogens. The predominant organism isolated was A. baumannii (27.65%), followed by K. pneumoniae (23.40%) and P. aeruginosa (21.27%). Ray et al, (3) also reported gram-negative bacilli such as MDR A. baumannii (40%) and P. aeruginosa (40%) as the most commonly isolated bacterial pathogens. Nseir et al (10) also observed a gram-negative preponderance, the most common isolates being P. aeruginosa (34%) and A. baumannii (18%). This is found in line with the data available for VAT in India. As drug resistance mechanisms among these gram-negative bacilli have found a permissive niche in ICU settings among susceptible patients coupled with their ability to survive in such hospital settings, it leads to an opportunity increased for colonization and

transmission among these nosocomial gram-negative bacilli.

In our study, the mean duration of ventilation, ICU Stay, and hospital stay was 10.87 days, 12.20, and 16.27 for VAT. In a similar study by Phu *et al* inhospital mortality of 7.4% in VAT, with mortally being higher among carbapenem-resistant isolates was reported (2).

A limitation of our study was that the genotypic characterization of these MDR pathogens could not be performed. This would have enabled us to gain a better understanding of the mechanism of drug resistance which would further help us in improving and tailoring our hospital antimicrobial stewardship program for a more effective empirical and timely management of these critical cases.

5. Conclusion

Ventilator-associated tracheobronchitis is considered a pathology intermediate between bacterial colonization and the development of pneumonia among ventilated patients. In our study, we obtained a significant growth from endotracheal

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secretions of cases of VAT who had not yet progressed to pneumonia. These isolates were found to be multidrug resistant. A prolonged ICU and hospital stay and high mortality rates among these cases were also noted. It is thus imperative to timely diagnose and monitor cases of VAT so that an effective empirical therapeutic intervention can be started and development and progression to VAP can be controlled.

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Conflict of Interest

The authors declare no conflict of interest.

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