A prospective study of ventilator-associated tracheobronchitis: Incidence and etiology in intensive care unit of a tertiary care hospital

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ABSTRACT

Context: Ventilator-associated tracheobronchitis (VAT) is an infective complication of mechanical ventilation and is a part of the spectrum of ventilator-associated respiratory infections. In the Intensive Care Units (ICUs), VAT is a relatively common problem but in comparison to ventilator-associated pneumonia (VAP), much less data are available on VAT and its management. Materials and Methods: Patients ventilated for more than 48 hours were screened daily for the development of VAT. Patients were followed up daily until they were extubated, died or discharged from the hospital. The patient demographics, underlying condition, causative organism and resistance patterns were observed. Results: 13.2% of patients developed VAT. The majority patients who developed VAT had underlying neurological problems. The mean time to develop VAT from the time of mechanical ventilation was 7.3 days and from time of ICU admission was 10 days, respectively. Multidrug-resistant (MDR) Acinetobacter sp. and Pseudomonas aeruginosa were the most frequently isolated organisms. Conclusions: VAT is a common healthcare-associated infection caused mostly by MDR Gram-negative bacteria. Monitoring and active surveillance are required to detect VAT at the earliest to institute appropriate isolation measures and therapy.

KEY WORDS: Healthcare-associated infection, multidrug resistant bacteria, ventilator-associated pneumonia, ventilator-associated tracheobronchitis

INTRODUCTION

Mechanical ventilation epitomizes intensive care medicine. Ventilator-associated respiratory infections (VARIs) are a major cause of concern in the intensive care units (ICUs) worldwide, especially in developing countries. VARI includes patients with ventilator-associated tracheobronchitis (VAT) and ventilator-associated pneumonia (VAP). Mechanical ventilation increases the risk of pneumonia by 6–20 fold among patients and is associated with crude mortality rates of 20%–40%.[1,2] VAT is a common ICU-acquired infection and the reported incidences of VAT range from 1.4% to 19% in patients receiving invasive ventilation.[3] VAT may represent an intermediate process between the colonization of the respiratory tract and development of VAP. The pathogenesis of lower respiratory tract infections often begins with tracheal colonization that may progress to VAT and in certain cases to VAP. There are no standardized guidelines to diagnose VAT. The information regarding VAT incidence is lacking and complicated in parts since the definition remains controversial. In fact, American
Thoracic Society/Infectious Disease Society of America do not address this entity. However, the most accepted and frequently used definition of VAT includes the following criteria: fever (>38 degrees C) with no other recognizable cause, purulent sputum production, positive culture of respiratory specimen at significant threshold, and no radiographic signs of new pneumonia. Medical literature is replete with information regarding VAP – its etiology, diagnosis, treatment, outcome, and preventive measures. In contrast, VAT as an entity has been studied less often and there are no studies from the Indian ICUs. Several studies have reported prolonged duration of mechanical ventilation and consequently increased length of ICU stay in patients who develop VAT. Recent data suggest that VAT appears to be an important risk factor for the development of the serious and life-threatening VAP and that early appropriate antibiotic therapy for VAT reduced transition to VAT thereby improving patient outcomes.

In this context, we conducted a study on VAT prospectively in a mixed medical and surgical ICU of a tertiary care unit in order to generate base line date.

Aims
The purpose of the study was to determine the incidence and etiology of VAT in a mixed medical and surgical ICU of a tertiary care hospital.

Settings and design
This was a prospective study conducted in a tertiary care ICU which manages both medical and surgical patients. The study was carried out for 10 months. VAT was diagnosed based on a combination of clinical and microbiological criteria. 212 participants fulfilled the study criteria and were included in the study.

MATERIALS AND METHODS
Patients ventilated for more than 48 h were followed up daily for the development of VAT. Patients were followed up daily until they were extubated, died, or discharged from the hospital. The patient demographics, underlying condition, causative organisms, and their antibiotic profile were recorded.

Study subjects
The study was carried out in a 60-bedded medical/surgical ICU for 10 months.

All patients who were ventilated for >48 h were included in the study. The patients were followed up daily till they were extubated or died/discharged from hospital.

Patients were excluded if they:
- Had a history of severe immunosuppression (leucocyte count <1000/µl or neutrophil count <50/µl) or HIV infection (CD 4 count <50)
- Those with nosocomial pneumonia without prior VAT were excluded.

Diagnosis of ventilator-associated tracheobronchitis
The diagnosis is based on clinical signs and symptoms, radiological, and microbiological criteria. Clinical signs and symptoms include temperature >38°C, leukocyte count >12,000 leukocytes/mm, or leukopenia (leukocyte count <4000 leukocytes/mm) plus new onset of purulent endotracheal (ET) secretions or change in character of sputum or increases in respiratory secretions or suctioning requirements with a ET aspirate (ETA).

Radiological criteria included no new or worsening infiltrates.

Microbiological criteria include ETA Gram-stain demonstrating polymorphonuclear lymphocytes with or without bacteria and semiquantitative ETA culture showing moderate to heavy growth of a potentially pathogenic microorganism. VAT cases were identified by prospective surveillance of nosocomial infections. Patients ventilated for more than 48 h were followed up daily for clinical signs of lower respiratory infections such as fever and change or increase in respiratory secretions. Relevant investigations such as complete hemogram, chest X-ray or computed tomography scan, and semiquantitative cultures of ETAs were done as per clinical judgment. For the purpose of this study, only the first episodes of VAT were taken into account.

Data collection
VAT cases were identified by prospective surveillance of nosocomial infections. Patients ventilated for more than 48 h were followed up daily for clinical signs of lower respiratory infections such as fever and change or increase in respiratory secretions. Relevant investigations such as complete hemogram, chest X-ray or computed tomography scan, and semiquantitative cultures of ETAs were done as per clinical judgment. For the purpose of this study, only the first episodes of VAT were taken into account.

Statistical analysis used
Mean and median were calculated using standard formulas.

RESULTS
Incidence
During the study period, 212 patients satisfying the study criteria were followed up. Out of the 212 patients, 28 patients (13.2%) developed VAT. In the same period, VAP developed in 24 patients (11.32%) [Table 1].

Patient profile
The majority of the patients (58%) who developed VAT were patients with neurological or neurosurgical problems, 14% of the patients had gastrointestinal disease, 7% of the patients had extensive burn lesions, 7% had cardiorespiratory problems, another 7% were patients of chronic renal failure, and the rest had medical conditions such as diabetic gangrene and systemic lupus erythomatosus [Chart 1].

The male:female ratio was 3:1.

Table 1: Incidence of ventilator-associated respiratory infection (ventilator-associated respiratory infections)

| Patient profile | Number (%) |
|-----------------|------------|
| Total number of patients intubated for >48 h | 212 |
| Total number of patients who developed VAT (%) | 28 (13.2) |
| Total number of patients who developed VAT (%) | 24 (11.32) |

VAT: Ventilator associated tracheobronchitis, VAP: Ventilator associated pneumonia
Mean time to develop VAT from the time of mechanical ventilation was 7.3 days. The mean time from ICU admission to onset of VAT was 10.7 days.

**Microbiological results**
Thirty organisms were isolated from semiquantitative ET secretion culture of patients with VAT. Three of the 28 VAT cases were polymicrobial. The most common bacteria isolated from ET secretion of VAT patients were *Acinetobacter* sp. (40%) and *Pseudomonas aeruginosa* (40%), followed by *Enterobacteriaceae* (*Klebsiella pneumoniae* and *Escherichia coli* 13%). *Staphylococcus aureus* and *Stenotrophomonas maltophilia* were isolated in one case each [Chart 2].

**Antibiotic profile of the bacterial isolates**
All the *Acinetobacter* sp. were multidrug-resistant (MDR) strains in that they were resistant to three or more classes of antibiotics. 100% of the strains were sensitive to polymyxin B and 92% were sensitive to tigecycline and 25% were susceptible to doxycycline.

Thirty-three percent of the *P. aeruginosa* were MDR strains.

The *Klebsiella pneumonia* and *E. coli* strains were extended-spectrum beta-lactamase-producing strains [Table 2].

**DISCUSSION**
VAT is an entity, which has not been well studied and there are very few publications on this subject and to the best of our knowledge, this is the first one from India. A recent meta-analysis had taken into account five studies for determining the incidence of VAT.[9] The overall incidence of VAT was found to be 11.5% based on these studies. However, most of the studies included in the meta-analysis were not prospective in nature, did not follow the standard definition of VAT, and was conducted in a selected patient population (head injury; postcardiac surgery, tertiary peritonitis). Another recent publication by Dallas *et al.*, which is one of the first from North America on this subject, however, has detected a significantly lower incidence of VAT. They have reported an incidence of 1.4% with similar incidences in surgical and medical patients.[5] *Nseir et al.* have published the only other study, which has prospectively evaluated VAT and they found an incidence of 10.6%.[5] In comparison,
A recent meta-analysis has shown the

The majority of patients in our study had

All ESBL strains

33% MDR strains

The reason for the higher device-associated rates in

Ventilator-associated tracheobronchitis (VAT) is mostly caused by drug-resistant

Antibiotic profile

Pseudomonas aeruginosa

40

All MDR strains

All sensitive to polymyxin

B, 92% sensitive to
tigecycline, 25% sensitive
to doxycycline

Enterobacteriaceae (Klebsiella

pneumoniae and Escherichia coli)

13

All ESBL strains

Staphylococcus aureus

3.5

MRSA

Stenotrophomonas maltophilia

3.5

Sensitive to co-trimoxazole

Table 2: Antibiotic susceptibility of bacteria isolated from ventilator-associated tracheobronchitis cases

Type of bacteria Percentage of isolates

Acinetobacter spp.

40

All MDR strains

Pseudomonas aeruginosa

40

Enterobacteriaceae (Klebsiella

pneumoniae and Escherichia coli)

13

Staphylococcus aureus

3.5

Stenotrophomonas maltophilia

3.5

MDR: Multidrug resistant, ESBL: Extended-spectrum beta-lactamase,

MRSA: Methicillin-resistant Staphylococcus aureus

our prospective study in a mixed medical-surgical ICU revealed an incidence of 13.7%.

The results of the recently concluded TAVeM international study done across 114 ICUs which included 2960 patients requiring mechanical ventilation revealed similar incidences for VAP and VAT (320 [11%; 10-2 of 1000 mechanically ventilated days] vs. 369 [12%; 6-8 of 1000 mechanically ventilated days].

The incidence of VAT in our ICU may be attributed to inappropriate suctioning techniques leading to suction trauma over tracheal wall resulting in localized infection of the trachea and consequently VAT. Improper suctioning techniques include deep suctioning, using catheters without blunt tip, and excessive suction pressure. These are our hypotheses and we have not looked into these aspects while doing the study. Lack of monitoring of routine cuff pressure may also result in tracheal mucosal necrosis.

Our patient profile included both surgical and medical patients. The problem with rates related to VAT is that there is no consensus on diagnostic criteria of VAT and so there is difficulty in comparing different clinical studies on VAT and establishing treatment guidelines. However, recent studies on VAT have used a more updated definition, which we have adopted in our study.

This higher incidence is not unexpected as incidence of all device-related infections in the developing countries is higher. The study by Rosenthal et al. had clearly shown that in the International Nosocomial Infection Control Consortium (INICC) which included India, the rates of VAP were as high as 22/1000 ventilator days. This is in contrast to the western data of VAP rates of <4/1000 ventilator days. A recent meta-analysis has shown the burden of healthcare-associated infections in ICU’s of developing countries were as high as 47.9/1000 patient days as compared to western data of 13.6/1000 patient days. The reasons for the higher device-associated rates in developing country are multifactorial, but the prime factor being lack of strict implementation of infection control practices, overcrowding, and poor nursing to patient ratios. However, when we reviewed our data for VAP, we found the rate of VAP in our hospital during the study period was around 7/1000 ventilator days, which is far less than the INICC reports. We have very stringent infection control practices and implement VAP bundles strictly. Therefore, breach in infection control practices is not the sole reason for the development of ventilator-associated infections. Thus, in this study, VAT seems to be an independent entity occurring mostly in patients with underlying neurological problems. The higher incidence of VAT in our study is similar to Nseir’s et al. study in France, wherein the incidence in surgical patients especially was as high as 15.3%. The majority of patients in our study had neurological conditions resulting in coma, which leads to higher incidence of ventilator-associated infections. VAT rates in dedicated neuro-ICUs have been reported to be higher at ranges of 18/1000 ventilator days.

The time to acquisition of VAT from initiation of ventilation was 7.3 days and 10 days from ICU admission as compared to 10 days and 11 days in the study by Nseir et al. The mean time was approximately 8 days as reported by Dallas et al.

The most common causative organisms were MDR Gram-negative bacilli. In our study, MDR Acinetobacter sp. and P. aeruginosa were the most frequently isolated organism. Nseir et al. also demonstrated similar findings, wherein P. aeruginosa, Acinetobacter baumannii, and methicillin-resistant S. aureus were the most frequently isolated organisms. This is well in keeping with data for VAP in India, which point to a preponderance of Gram-negative bacteria (GNB). The high incidence of MDR organisms in these GNB is also well in line with high levels of resistance in GNB in India.

A recent study by Nseir et al. has shown that appropriate antibiotic therapy for VAP reduced transition to VAP. The present study and similar studies reported in literature have revealed VAT is mostly caused by drug-resistant bacteria. Therefore, in this context, it becomes extremely important to monitor patients for the development of VAT so that appropriate antibiotics can be instituted at the proper time, thereby improving patient outcomes.

The strength of our study is the prospective nature of the study, which included daily assessment of the nature of
secretions and clinical evidence of respiratory tract infections, with radiology and microbiological examinations prompted by clinical signs and symptoms. Routine cultures were not done and semiquantitative cultures were useful in distinguishing colonization from infection. The study by Nseir et al. had a predominance of COPD patients and use of surveillance cultures may have resulted in the inclusion of some colonizers. However, in our study, cultures were done on a clinical need basis rather than a routine weekly basis; hence, our data reflects the true incidence of VAT.

One big limitation of our study was the lack of outcome data in terms of total duration of ventilation, length of stay, and antibiotic usage. Previous studies had assumed VAT is a continuum between colonization and VAP. Hence, treatment of VAT with appropriate antibiotics had been proposed as a means to decrease progression to VAP and improve outcomes by several groups. Two clinical trials investigating the effect of such treatment have shown lower rates of progression to VAP and decreased duration of mechanical ventilation. Further prospectively designed studies are required to characterize this entity and establish treatment protocols. The other limitation of our study is the lack of severity of illness score in this cohort of patients which would have enabled us to understand more about the reasons for developing VAT in this group.

CONCLUSIONS

It can be said that VAT is a common healthcare-associated infection caused mostly by MDR bacteria in mechanically ventilated patients. Diagnosis of VAT is based on a combination of clinical and microbiological criteria. Patients who develop VAT have prolonged duration of mechanical ventilation and consequently increased length of stay and health care costs. Moreover, these patients have a higher chance of progressing to VAP. Hence, it is of utmost importance to prevent these complications by practicing proper suction techniques and instituting VAP bundles strictly. It is also essential to monitor patients for the development of VAT so that appropriate infection control measures and targeted antibiotic therapy can be instituted at the proper time to prevent VAT cases from progressing to the more life-threatening VAP. Further studies are required to document outcomes in terms of duration of mechanical ventilation, length of ICU stay, antibiotic usage, routes of antibiotic administration (nebulized vs parenteral), and progression to VAP.

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Conflicts of interest
There are no conflicts of interest.

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