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# THE STUDY OF THE ORGANISMS COLONIZING TRACHEA IN MECHANICALLY VENTILATED PATIENTS ADMITTED IN THE INTENSIVE CARE UNIT (ICU)

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**Abstract:**

**Objectives:** To isolate and identify the organisms colonizing trachea in mechanically ventilated patients admitted in the Intensive Care Unit (ICU). **Methods:** The present study was conducted on 265 patients were admitted in the ICU during from July 2004 to June 2005 in Government Medical College & Hospital, Aurangabad (Maharashtra). A total of 100 patients on mechanical ventilation with intubation tube fulfilling the inclusion criteria were followed-up prospectively. The patterns of tracheal colonization were studied in these patients. Patients were followed-up twice a week on day 4 and day 7. The antibiotic sensitivity testing of the isolated organisms were carried on Mueller-Hinton Agar (MHA)**. Results:** In all total 361 isolates of organisms were identified from the 229 processed samples of endotracheal aspirates (EA) of mechanical ventilation. *Pseudomonas aeruginosa* was the most commonly isolated organism, present in 135 (37.4%), followed by *Klebsiella pneumonia* in 103 (28.5%),*Staphylococcus epidermidis* in 53 (14.7%), *Staphylococcus aureus* in 10 (4.36%)among the 229 positive culture samples.The isolation rate of *Pseudomonas aeruginosa* increased with the duration of ventilation from 18.5% on day 1 to 46.7 % on day 7. **Conclusion:** One aspect been proven beyond doubt is that, the microorganisms, either exogenous or endogenous, colonize the normally sterile trachea of mechanically ventilated patients before the development of VAP. Nevertheless, the optimal management of patients with VAP requires collaboration amongst critical care specialists and microbiologists.

**Keywords:** Ventilation-associated pneumonia, endotracheal aspirates, mechanical ventilation, Microorganisms.

## INTRODUCTION:

The hospital while fulfilling its role as a health care institute, sometimes presents its patients with the unwanted gifts of Hospital-acquired infections (HAI).The common HAI are respiratory tract infection, urinary tract infection, blood-stream infection, and skin and surgical-site infections.**(1,2)**

According to the surveillance data from the National Nosocomial Infections Surveillance (NNIS) system of the Centers for Disease Control and Prevention (CDC), 'Hospital acquired pneumonia (HAP) or Nosocomial pneumonia' is the most common infection in the intensive care units (ICUs).**(3,4)**

Hospital acquired pneumonia (HAP) is more frequent in intubated patients with mechanical ventilation (MV).**(5)** The incidence of HAP varies from 9 to 78 %, depending on the severity of illness, type of patients studied, the techniques & criteria used to diagnose the pneumonia.**(6)** Hospital-acquired pneumonia is the most common nosocomial infection reported among mechanically ventilated patients admitted in the ICU, where it is labeled as 'Ventilation-associated pneumonia' (VAP), with estimated prevalence ranging from 10 to 65.**(7)**The mortality rate in VAP ranges from 24% to 80% in several studies with 2 to 10 fold higher risk of death in ICU-ventilated patients.**(8,9)**

Various organisms have been implicated in the colonization and causation of a VAP. It is possible that various organisms are introduced into the trachea through different routes.**(10)** To label the presence of organisms in the trachea as 'colonization' or 'pneumonia' is not a very simple task.**(11)**

In ICU patients, especially those who are intubated, the signs of pneumonia are relatively subtle, and thus the diagnosis often is relatively complex. **(12)** However, no single criterion has been specifically diagnostic for VAP. **(13)** Since the Accurate data on etiologic agents and the epidemiology of ventilator-associated pneumonia are limited by the lack of a "gold-standard" for diagnosis.**(14)** Laboratory investigations of microbial cause are important because in the absence of such identification of organisms, antibiotic therapy may not be optimal. Clinicians need to adapt the treatment recommendations and preventive measures to their respective institutes, as the routes of infection and agents causing pneumonia vary considerably among health-care facilities.**(15)**

Therefore, knowledge about the commonest etiological pathogens colonizing trachea in mechanically ventilated patients, developing into VAP at the institute level by prospective study will definitely be useful in formulating the optimal management of the patients.

## MATERIALS AND METHODS

The present study was conducted in 5-bedded Intensive Care Unit (ICU), Government Medical College & Hospital, Aurangabad (Maharashtra). The study period extended from July 2004 to June 2005. A total of 265 patients were admitted in the ICU during the study period.

Patients with more than 48 hours of mechanical ventilation (MV) with endotracheal tube were included in the study. Patients on mechanical ventilation for 48 hours or less or who developed pneumonia within 48 hours of MV were excluded from the study. Exclusion criteria were severe immunosuppression (organ

transplantation, AIDS) and evidence of pulmonary infection or suspicion of gross aspiration at admission.All the patients were given antibiotic prophylaxis with administration of gentamicin. A total of 100 patients on mechanical ventilation with intubation tube fulfilling the inclusion criteria were followed-up prospectively.

Informed consent was obtained from the patient or the nearest relative of the patient. The patterns of tracheal colonization were studied in these patients.

Major complaints, underlying disease, indication for intubation, general & systemic examination, and results of routine investigations with X-ray chest reporting were noted. Patients receiving antibiotics with its duration of administration was also recorded. Patients were followed-up twice a week on day 4 and day 7. During the follow-up visits, special note about the duration of Mechanical Ventilation (MV), CBC, X-ray chest, rise in temperature and extra pulmonary focus, if any was noted.

The antibiotic sensitivity testing of the isolated organisms were carried on Mueller-Hinton Agar (MHA), by modified Kirby-Bauer disc-diffusion method, using 0.5 McFarland as the turbidity standard as per NCCLS guidelines. **(16)**

## RESULTS

During the one-year study period, from July 2004 to June 2005, a total of 265 patients were admitted in the medical ICU. Out of which 100 patients mechanically ventilated (MV) with intubation tube for more than 48 hours were included in the study to evaluate the pattern of tracheal colonization and development of VAP. The study group comprised of 64 males and 36 female patients.

The study group comprised of wide range of age, the youngest being a seven-year old female and the oldest an 80 years female. The maximum numbers of patients were clustered in the age group of 21-30 years, consisting 26% of the patients. The mean age of patients was 30.7 years.

The tracheal aspirates were followed on days 1, 4 and 7 to evaluate the incidence of tracheal colonization and development of VAP. However, on day 5, total 3 patients were extubated since they showed signs of recovery. These 3 patients, one each with OPP, GBS and ARF did not yield any organism either on day 1 or day 4 of intubation.

During the study, 1 patient died on fourth day and 2 patients died each on day 5 and day 6.

In all total 361 isolates of organisms were identified from the 229 processed samples of endotracheal aspirates (EA) from 100 patients up to the seventh day of mechanical ventilation.

Average number of isolates per EA sample was 1.58. The mean colonization rate was 3.61 strains per patient. Mean colonization rate was obtained by dividing the total number of organisms isolated by the total number of patients studied.

**Table 1 : Microorganisms Isolated from Endotracheal Aspirates**

| ORGANISM | NO. OF ISOLATES | Percentage % |
|---|---|---|
| **Pseudomonas aeruginosa** | 135 | 37.4 |
| *Klebsiella pneumoniae* | 103 | 28.5 |
| *Staphylococcus epidermidis* | 53 | 14.7 |
| *Escherichia coli* | 49 | 13.6 |
| *Staphylococcus aureus* | 10 | 2.8 |
| **Proteus mirabilis** | 04 | ***1.1*** |
| *Streptococcus pyogenes* | 04 | 1.1 |
| **Streptococcus pneumoniae** | 03 | 0.9 |
| **TOTAL** | **361** | **100** |

**Table 2 : Day Wise Isolation of Organisms.**

| ORGANISM | DAY 1 | | DAY 4 | | DAY 7 | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| **P. aeruginosa *(135)*** | 25 | 18.5 | 47 | 34.8 | 63 | 46.7 |
| *Kl. pneumoniae* (103) | 19 | 18.4 | 38 | 36.9 | 46 | 44.7 |
| *S. epidermidis* (53) | 08 | 15.1 | 22 | 41.5 | 23 | 43.4 |
| *E. coli* (49) | 07 | 14.3 | 20 | 40.8 | 22 | 44.9 |
| *S. aureus* (10) | 06 | 60 | 02 | 20 | 02 | 20 |
| **P.mirabilis *(04)*** | 00 | 0 | 01 | 25 | 03 | 75 |
| **S. pyogenes *(04)*** | 01 | 25 | 02 | 50 | 01 | 25 |
| **S.pneumoniae *(03)*** | 01 | 33.3 | 01 | 33.3 | 01 | 33.3 |
| **Total Isolates (361)** | **67** | **18.6** | **133** | **36.8** | **161** | **44.6** |

Out of the total 100 patients studied, colonization with Gram-negative organisms occurred in 87 patients (i.e. 87 %).*Pseudomonas aeruginosa* was the most

commonly isolated organism, present in 135 (37.4%), followed by *Klebsiella pneumoniae,* isolated in 103 (28.5%) of the 229 positive culture samples. The total Gram-negative organisms isolated were 291 (80.6%), while Gram-positive organisms accounted to be 70 (19.4%).

*Staphylococcus epidermidis* accounted for 53 (14.7%) among the 229 positive culture samples. Out of total 10 *Staphylococcus aureus,* 4 were methicillin resistant *Staphylococcus aureus* (MRSA), while 6 were methicillin sensitive *Staphylococcus aureus* (MSSA).

*Pseudomonas aeruginosa* was the most commonly isolated organism among all other organisms throughout the duration of mechanical ventilation (MV).

*Pseudomonas aeruginosa* predominated with 37.3%, 35.3% and 39.1% isolates in the endotracheal aspirates (EA) processed on days 1, 4 and 7 respectively.

Total number of isolates increased with the duration of mechanical ventilation (MV) from 18.6% on day 1 to 44.6% on day 7.The isolation rate of *Pseudomonas aeruginosa* increased with the duration of ventilation from 18.5% on day 1 to 46.7 % on day 7. Similarly, isolation rate of *Klebsiella pneumoniae* increased with the duration of ventilation from 18.4% on day 1 to 44.7 % on day 7.

Significant increase in isolation of coagulase negative *Staphylococcus epidermidis* (CONS) was seen from 15.1 % on day 1 to 43.4% on day 7. Although, *Staphylococcus aureus* showed decrease in the isolation rate from 60% on day 1 to 40% on day 7, developed resistance to β-lactams. Two isolates each on day 4 & 7 of *Staphylococcus aureus* were MRSA.

## DISCUSSION

Mechanical ventilation is indicated to combat the fatal outcome of respiratory failure due to various causes like central nervous system dysfunction as a result of poisoning, drug intoxication, paralytic diseases, head injuries and many others.

Ventilation-associated pneumonia (VAP) is the commonest complication in patients mechanically ventilated with endotracheal intubation tube. A wide range of microorganisms causes the potential problem of VAP. **(17)** The associated large bulk of morbidity and mortality makes its early diagnosis and appropriate treatment, the right of the patient.

Various studies have studied the pattern of tracheal colonization and shown that over a period of time, the micro-organisms gradually colonize the trachea. Potentially pathogenic organisms, mostly Gram-negative bacteria, rapidly colonize airways of critically ill patients.**(17)** The organism colonizing the trachea depends on the source, either oropharynx or stomach, the length of hospital stay with duration of mechanical ventilation and the various associated risk factors.**(11)**

In the present study, colonization occurred in 97 patients out of the total 100 patients studied. Hence, total colonization rate was

found to be 97%. In a study by Ewig *et al* the trachea was initially colonized by 83% of the organisms causing VAP, whereas de Latorre *et al*, reported 83.3% colonization rate in their studies.**(17,18)**

In the present study, in almost all 57 patients developing VAP, the infecting organism had colonized the trachea. Delclaux *et al* in a study showed that in 66% of the episodes of VAP, the infecting organism had colonized the trachea. **(19)**

In the present study, the tracheal aspirates were followed up on days 1, 4 and 7 of intubation to evaluate the colonizing organisms causing VAP. Johanson *et al* found only 22% of their patients to be colonized on the first day. However, they studied only *Enterobacteriaceae* and *Pseudomonas species*.**(20)** Niederman *et al* also found only 22% of their patients colonized within the first three days of intubation. This low value could be explained by the fact that they studied only enteric Gram-negative bacilli. **(21)** Both this studies also neglected the Gram-positive organisms, which tend to colonize the trachea early during ventilation.

Francisco J de Latorre *et al* found that 80% of the patients mechanically ventilated had their trachea colonized on day 1.**(18)** In our study, on day 1, i.e. within first 24 hours of intubation, out of the total 100 endotracheal aspirates, 47 showed growth on culture indicating the early tracheal colonization rate of 47%, which increased drastically to 97.83% on day 7 of mechanical ventilation. The result of our study relates well to the study carried out by Bonten *et al* [116] where they found 96.1% of the patients, previously colonized by the organisms.**(22)**

Schwartz *et al* found the similar trend. 75% of their patients colonized on day 1 increased to 95% by the end of day 4 and subsequently to 98.6% at the end of week of intubation. **(23)** Niederman *et al* also showed a similar trend. The frequency of colonization increased over duration with only 22% of the subjects being colonized at the start of MV to 78% at the end of the week.**(21)**

Similarly, of the total 122 isolates responsible for VAP, *Pseudomonas aeruginosa* emerged as the most common pathogen with 41% followed by *Klebsiella pneumoniae* 26.2%. Of the total isolated organisms developing VAP, only 25.4% were isolated on day 4 which dramatically increased to 74.6% on day 5 of MV. Merchant *et al* [72] found that *Pseudomonas aeruginosa* made upto 44% of the total isolates, followed by *Klebsiella spp.* (34%) and *Escherichia coli* (9%).**(24)**

A large-scale study conducted in 107 ICUs in Europe demonstrated, a crude pneumonia rate observed was 9%.**(25)** The low incidence of VAP in these studies could be due to greater specificity of criteria for diagnosis, clinical criteria and quantitative culture of PSB.

Distribution of microorganisms responsible for the VAP differs according to the population studied (surgical/medical/trauma), the duration of hospital / ICU stay, duration of mechanical

ventilation (MV) and the diagnostic method used.**(10)**

Salata *et al* found Gram-negative bacilli in 62% of their pathogens incriminated in the development of VAP.**(26)**, whereas Ewig *et al* reported 54% colonization rate due to Gram-negative bacteria in their studies.**(17,)**

In the present study, out of the total 100 patients studied, colonization with Gram-negative organisms occurred in 87 % of the patients. The total Gram-negative organisms isolated were 291 (80.6%), while Gram-positive organisms accounted to be 70 (19.4%) out of the total 361 isolates identified.

The Gram-negative organisms showed increased in the colonization rate with duration of mechanical ventilation (MV) from 76.1% on day 1 to 83.2% to day 7.

The more percentage isolation of Gram-negative organisms colonizing trachea may be due to higher isolation rate of *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* among the Gram-negative bacteria, which in turn might be due to more mean duration of MV (13 days) and prior broad-spectrum antibiotics to every patient.

Niederman *et al* isolated *Pseudomonas aeruginosa* and enteric Gram-negative bacilli in 73.3% if their tracheal aspirates.**(21)** Craven *et al* studied 233 patients and found predominance of Gram-negative bacilli, which were detected in 61% of the patients developing VAP.**(27)** Baker *et al* showed that Gram-negative bacilli accounted for 63% of the isolates causing VAP.**(28)**

Johanson W G *et al* found *Klebsiella pneumoniae* to be the most common organism isolated from the respiratory tract, but not all of their patients were intubated.**(20)**

In the present study, total 361 isolates were isolated from 97 patients colonizing the trachea of the 100 patients studied. Out of these 361, total 122 isolates were responsible for VAP. *Pseudomonas aeruginosa* was the most commonly isolated organism 40% (50 of the 122), followed by *Klebsiella pneumoniae* 26.2% (32 of the 122), of the 229 positive culture samples throughout the duration of MV.

In the present study, *E.coli* was found as 12.3% of the isolates, while *Proteus spp.* even after colonizing the trachea of MV patients did not develop VAP. Trouillet *et al* found *E.coli* in 3.3% and *Proteus spp*. in 2.9% of their isolates obtained from VAP patients.**(14)**

In the present study, MRSA accounted for 3.3%, while *Streptococcus pyogenes* and *Streptococcus pneumoniae* each were 0.8% of the total isolates. Trouillet *et al* [24] found CONS and *Streptococcus species* in 1.6% and 13.9% of their samples respectively, from patients of VAP. In our study, *Staphylococcus epidermidis* accounted for 53 (14.7%). **(14)**

The decrease in the isolation of Gram-positive organisms could be attributable to effect of prophylactic antibiotic treatment,

which might have caused the disappearance of the sensitive strains and also the colonization by the Gram-negative bacteria with increase in the duration of MV.

## CONCLUSION

Thus, to conclude with ventilation-associated pneumonia (VAP), a common complication of mechanical intubation in the ICU, caused by a wide range of microorganisms with increasing resistance to empirically administered antibiotics, adding on to the large bulk of morbidity and mortality makes its accurate diagnosis and adequate treatment, the patients right towards the health care providers.

One aspect been proven beyond doubt is that, the microorganisms, either exogenous or endogenous, colonize the normally sterile trachea of mechanically ventilated patients before the development of VAP.

The need of hospital infection control should be entrenched with stress on personal cleanliness and hygiene to eliminate the sources of infection and cease the spread of microorganisms.

Nevertheless, the optimal management of patients with VAP requires collaboration amongst critical care specialists and microbiologists. This will help not only in the early recognition and management of individual VAP cases, but also may lead to early recognition of any outbreaks.

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**Ethical approval:** The study was approved by the institutional ethics committee

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