

## Research Article

# Ventilator Associated Pneumonia: Incidence and Risk Factors in a University Hospital

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## ABSTRACT

**Background:** Ventilator associated pneumonia (VAP) is a type of nosocomial pneumonia associated with increased morbidity and mortality. Awareness about the risk factors can be used to implement simple and effective preventive measures.

**Objectives:** To determine the factors associated with development of VAP and its microbial profile among patients admitted to ICUs.

**Methods:** A nested case-cohort study was conducted at Al-Hussein university hospital in Cairo city, Egypt for a period of 6 months from the 1<sup>st</sup> of March 2013 to the end of August 2013. Patients who were on mechanical ventilation (MV) for more than 48 hours were monitored at frequent intervals for development of VAP. Samples obtained by endotracheal aspiration were cultured on Blood agar - Chocolate agar - MacConkey agar, plates of which were incubated at 37c for 24 hours. The isolated organism was identified by morphological and biochemical identification.

**Results:** Of the 73 samples which were taken from endotracheal tubes of the patients, 42 cases were diagnosed as VAP with an incidence rate of 57.5%. Early onset VAP occurred in 36 (85.7%), while late onset VAP was observed in the remaining 6 patients (14.3%). Escherichia coli (40.5%) followed by Klebsiella pneumoniae (23.8%) were the most commonly isolated pathogens. Univariate analysis showed that the duration of MV and ICU stay, re-intubation, supine head position, impaired consciousness, steroids use and H<sub>2</sub> blocker use were the risk factors associated with VAP (p < 0.05). Logistic regression revealed duration of MV as an independent risk factor for VAP.

**Conclusion:** The incidence of ventilator pneumonia is high in our study. VAP was significantly related to duration of MV and ICU stay, re-intubation, supine head position, impaired consciousness, steroids use and H<sub>2</sub> blocker use.

**Keywords:** Ventilator-Associated Pneumonia (VAP), intensive care unit, incidence, risk factors

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## INTRODUCTION

Ventilator-associated pneumonia (VAP) refers to nosocomial pneumonia occurring in patients receiving mechanical ventilation (MV), 48 hours or more after airway intubation (which did not appear to be incubating at the time of admission). It is a common complication of care that affects approximately one-fourth of patients receiving

mechanical ventilation<sup>(1)</sup>. Development of VAP in a time ≤ 96 hours of MV is classified as early onset; a delay of more than 96 hours is termed as late onset<sup>(2)</sup>. The incidence of VAP varies from 9% to 60% of patients, based on the definition, type of hospital or ICU, study population and levels of antibiotic exposure<sup>(2)</sup>. In Egypt, VAP was the most common type of device associated infections (DAIs) in all of the ICUs investigated (88.7%)<sup>(3)</sup>.

VAP is associated with increased mortality in ICU<sup>(4)</sup>. VAP is also associated with considerable morbidity, including prolonged ICU hospitalization, extended mechanical ventilation and increased costs of hospitalization.<sup>(5)</sup> The cost of care of such patients is significantly higher as compared with patients without this complication.<sup>(6)</sup> Many predisposing factors including age and severity of the underlying diseases are associated with developing VAP. Meanwhile, history of antibiotic exposure and duration of mechanical ventilation are involved.<sup>(7)</sup> Awareness of these risk factors can aid in identification of patients at higher risk, guide institution of appropriate preventive measures, and modulate potential intervention measures while managing such patients.

The study aimed to assess the incidence and risk factors for acquisition of VAP and its microbiological profile.

## METHODS

### *Study Setting & Design*

A nested case-cohort study was conducted in the ICU of Al-Hussein university hospital in Cairo city, Egypt. This hospital has an ICU with 36 beds. Patients admitted in ICU, requiring intubation and mechanical ventilation for more than 48 hours were considered eligible for inclusion. A total of 73 eligible patients including 42 cases and 31 controls were included. Patients who developed pneumonia after 48 hours of ventilation were selected in the case group ( $n=42$ ) and those who did not develop pneumonia constituted the control group ( $n=31$ ). The study was completed between 1<sup>st</sup> of March 2013 to the end of August 2013. VAP was diagnosed as per CDC criteria.<sup>(8)</sup> Patients who are mechanically ventilated for more than 48 hours, with occurrence of new and persistent infiltration in the chest roentgen, together with any two of the following: i) Fever, defined as temperature  $>38^{\circ}\text{C}$   $\text{mm}^3$ . ii) Leukocytosis, defined as total leukocyte count  $>10 \times 10^3$   $\text{mm}^3$ . iii) Purulent tracheal aspirate. Chest X ray was done at the time of admission and repeated every day. This diagnosis was confirmed by the presence of organisms on culture of tracheal aspirate. The tracheal aspirates were sent for microbial analysis done routinely after 48 hours of mechanical ventilation. All endotracheal aspirate was subjected to culture in: Blood agar - Chocolate agar - MacConkey agar, plates of which were incubated at  $37^{\circ}\text{C}$  for 24 hours. The isolated organism was identified by Colony morphology- Gram stained film - detection of Motility on semi-solid agar - Oxidase test - Sugar fermentation test - Indole production test - Methyl red and Vogues proskauer test - Citrate utilization test - Triple sugar iron (TSI). This was repeated at interval of 48 hours if initially

negative. The organisms detected on culture of tracheal aspirate were charted for the purpose of identifying the causative agent. Antibiotics were changed as per sensitivity pattern. Total leukocyte count was done as indicated by the admitting diagnosis or routinely at 48 hours or as indicated by chest X-ray findings. Patients with pneumonia prior to mechanical ventilation or those developing pneumonia within 48 hours, patients intubated without mechanical ventilation in ICU and patients ventilated for less than 48 hours were excluded from the study. The patients who developed VAP or met the above criteria within 96 hours of mechanical ventilation were categorized as early onset VAP and those who developed the same after this time period were categorized as late-onset VAP. Data were collected on Age, sex, duration of MV, duration of ICU stay, risk factors such as chronic obstructive pulmonary disease (COPD), diabetes, and chronic use of inhaled / oral steroids, prior use of antibiotics, re-intubation, and coma. Prior antibiotic use was defined as intravenous antibiotic administration for  $>24$  hours during any time of the patient's hospitalization prior to and during mechanical ventilation.

### **Statistical Analysis**

Data were analyzed by use of SPSS software, version 16.0 (SPSS). Univariate analysis was used to compare variables for the outcomes of interest. Continuous data were compared using the Student's t test. Either  $\chi^2$  or Fisher's exact tests were used to compare categorical variables. A multivariate analysis was also performed using multiple logistic regressions with enter approach. All  $P$  values lower than 0.05 were considered statistically significant.

### **Ethical Statement**

The study was approved by the institutional review board and the ethics committee of the Faculty of Medicine affiliated to Al-Azhar Universities, Egypt. The research complied with the international ethical research guidelines of declaration of Helsinki. An informed consent was taken from all participants' nearest relatives/care givers after explaining the aim and concerns of the study. Data sheets were coded to ensure anonymity and confidentiality of patient's data.

## RESULTS

During a 6-month period, 73 patients who received MV for  $> 48$  hours were prospectively evaluated. Of the 73 patients, 42 (57.5%) developed VAP during their ICU stay. Early onset VAP occurred in 36 patients (85.7%), while late onset VAP was observed in the remaining 6 patients (14.3%). Table (1) shows the causative organisms isolated from culture of tracheal aspirate: Among VAP patients, 36 cases were of polybacterial origin while 6 patients had monobacterial growth.

*Escherichia coli* was the most common organism (40.5%) isolated from VAP patients. It was followed by *Klebsiella pneumoniae* (23.8%), *Pseudomonas*

*aeruginosa* (9.5%), *Proteus* (9.5%), *Acinetobacter* (9.5%) and staphylococci (7.2%).

**Table 1:** Types of isolated pathogens

Isolated organism	Number	%
E.coli	17	40.5%
Klebsiella	10	23.8%
Psoudomonas ereguinosa	4	9.5%
Proteus	4	9.5%
Acinetobacter	4	9.5%
Staphylococcus	3	7.2%
Total	42	100%

Table (2) describes baseline characteristics of the study population. Regarding gender of the participants, most of the participants in the VAP group (64.3%) and non VAP group (61.3%) were males, the difference was statistically non-significant ( $P= 0.8$ ). The mean  $\pm$  SD age of patients receiving MV was  $53.8 \pm 7.2$  years for the non-VAP group and  $57.3 \pm 8.3$  years for the VAP group. No statistically significant difference was detected between VAP and non VAP groups regarding age of the participants ( $p = 0.07$ ). The mean  $\pm$  SD duration of MV was found to be  $6.3 \pm 2.2$  days for the non-VAP group and  $16.2 \pm 3.5$  days for the VAP group. Also the mean  $\pm$ SD duration of ICU stay was found to be  $11.3 \pm 3.3$  days for the non-VAP group and  $18.9 \pm 3.7$  days for the VAP group. The duration of mechanical ventilation for the VAP group was significantly high ( $p < 0.001$ ). Similarly, the VAP group also had significantly longer duration of ICU stay ( $p < 0.001$ ). Patients exposed to re-intubation were at a statistically significant ( $p = 0.001$ ) higher risk

of VAP (OR = 5.1, 95% CI = 1.8 to 16.1) compared with those not exposed. Supine head position and impaired consciousness were found to be risk factors, having a statistically significant association with VAP ( $P = 0.001$  and  $0.005$ , respectively). It was also revealed that prior steroids and H<sub>2</sub> Blocker usage were more likely to develop VAP (OR=3.1, 95% CI = 1.1 to 9.2,  $p=0.02$  and OR=3.0, 95% CI = 1.0 to 9.0,  $p=0.03$  respectively). While prior antibiotic usage was less likely to develop VAP (OR=0.9, 95% CI = 0.3 to 2.8,  $p= 0.88$ ). There was no statistical difference ( $P = 0.91$  and  $0.79$ , respectively) in the risk of development of VAP between cases and control group as regards history of diabetes and COPD. Table (3) shows the logistic regression analysis of the risk factors for VAP. Selected risk factors were entered into a logistic regression model (stepwise) to perform the multivariate analysis which revealed that duration of MV was an independent risk factor for VAP

**Table 2:** Baseline characteristics of the study population

Variables	VAP (42) No. (%)	Non VAP (31) No. (%)	OR	CI (95%)	P value
Sex (male)	27(64.3%)	19(61.3%)	1.1	0.4-3.3	0.8
Age (mean $\pm$ SD yrs)	57.3 $\pm$ 8.3	53.8 $\pm$ 7.2	---	-0.2-7.2	0.07
MV(mean $\pm$ SD )	16.2 $\pm$ 3.5	6.3 $\pm$ 2.2	---	8.5-11.3	<0.001*
ICU stay (mean $\pm$ SD )	18.9 $\pm$ 3.7	11.3 $\pm$ 3.3	---	5.9-9.2	< 0.001*
Re-intubation	31(73.8%)	11(35.5%)	5.1	1.8-16.1	0.001*
Supine head position	36(85.7%)	16(51.6%)	5.7	1.6-20.1	0.001*
Impaired consciousness	26(61.9%)	9(29.0%)	4.0	1.3-12.2	0.005*
Steroids use	29(69.0%)	13(41.9%)	3.1	1.1-9.2	0.02*
H <sub>2</sub> Blocker	23(54.8%)	9(29.0%)	3.0	1.0-9.0	0.03*
Antibiotic use	25(59.5%)	19(61.3%)	0.93	.3-2.7	0.88
Diabetes	33(78.6%)	24(77.4%)	1.1	0.3-3.7	0.91
COPD	31(73.8%)	22(71.0%)	1.2	0.4-3.7	0.79

\* Significant ( $P < 0.05$ )

**Table 3:** Logistic regression analysis of the risk factors for VAP

Variables	Adjusted OR	CI (95%)	P value
Duration of MV	6.4	1.8-22.6	0.004

## DISCUSSION

Ventilator associated pneumonia is a type of nosocomial infection acquired in the ICU. This study reported that the incidence of VAP was about 57.5%, which is not comparable. In a study conducted from four multidisciplinary intensive care units in Greece, the incidence was reported to be 32%.<sup>(9)</sup> In an evaluation made in Boston, VAP was reported at the rate of 10.2% per 1000 ventilator days. Similarly Gupta and coworkers reported an incidence of 28%.<sup>(10)</sup> In a study from South India the incidence was reported to be 18%.<sup>(2)</sup>

In this study, early onset VAP occurred in 36 patients, while late onset VAP was observed in the remaining 6 individuals. Our findings were similar to those reported by Charles *et al.*,<sup>(11)</sup> on the other hand, Gadani *et al.*,<sup>(12)</sup> reported fewer EVAP than LVAP.

The most common organism associated with VAP was E.coli, followed by Klebsiella and Pseudomonas. A study in India<sup>(12)</sup>, found that Pseudomonas (43.24%), followed by Klebsiella (18.91%), were commonly associated with VAP. While in another study<sup>(13)</sup> it was found that Acinetobacter sp. was the most common causative agent of VAP. Regarding gender of the patients there was no significant difference between VAP and non VAP groups which was similar to the findings by Ranjit and Bhattarai<sup>(14)</sup> in their study, where older age was significantly associated with increased risk of VAP. That is in agreement with another study by Giard *et al.*,<sup>(15)</sup> which revealed that, advanced age was independent risk factors for LVAP acquired in ICU.

In the present study the duration of mechanical ventilation for the VAP group was significantly high. Similarly, the VAP group also had significantly longer duration of ICU stay which is similar to the findings reported by Saravu *et al.*, in their study about the determinants of VAP<sup>(16)</sup>.

A significant association was found in this study between re-intubation and development of VAP, which is in accordance with a previous study by Saravu *et al.*,<sup>(16)</sup>. Re-intubation is associated with transfer of organisms from upper respiratory to lower respiratory tract, which could explain the higher incidence of VAP among such cases.

A significantly higher risk of supine position compared with the semi-recumbent position was found among the study groups because it may facilitate aspiration, which may be decreased by a semi recumbent positioning. This finding is similar to that reported by Saravu *et al.*, as position was considered as a risk factor in the development of VAP.<sup>(16)</sup> Also impaired consciousness was a significant risk of VAP. Findings are consistent with the study by Joseph *et al.*,<sup>(2)</sup>. This may be due to the higher chances of aspiration in comatosed patients. Steroid usage was found significantly higher in VAP group than that of non-VAP group; the results of this study coincide with the results of the stud by Saravu *et al.*,<sup>(16)</sup> this may be attributed to the suppressive effects of steroids on innate and acquired

immunity. A significant difference among the study groups regarding H<sub>2</sub> blockers usage was found. This is in agreement with the result by Saravu *et al.*,<sup>(16)</sup> but in contrast to Ranjit and Bhattarai study.<sup>(14)</sup> H<sub>2</sub> blockers usage can alter the gastric pH thereby facilitating organism multiplication which, when aspirated, can lead to occurrence of VAP. Prior antibiotic usage was higher among the cases, but the association was not statistically significant. Park revealed that previous antibiotic use decreases EVAP but markedly increases multidrug resistant (MDR) pathogens.<sup>(17)</sup> While another study by Lahoopour *et al.*,<sup>(18)</sup> showed that prior antibiotic usage was an independent significant risk factor for acquisition of VAP.

In this study, there was no statistical significance difference between VAP cases and control group as regards history of diabetes and COPD. Findings are consistent with those by Saravu *et al.*,<sup>(16)</sup> as history of diabetes and chronic obstructive pulmonary disease were not associated with acquisition of VAP.

In logistic regression, the only independent significant risk factor for VAP in the present study was the duration of MV. In another study, impaired consciousness, reintubation, were found to be independent risk factors for VAP.<sup>(2)</sup> While in the study by Charles *et al.*,<sup>(11)</sup> supine head position was found to be the only independent risk factor for VAP. On the other hand, mechanical ventilation, antibiotic exposure, duration of hospitalization and fever were found to be independent risk factors for VAP in Lahoopour *et al.* study.<sup>(18)</sup>

## CONCLUSION AND RECOMMENDATIONS

The incidence of ventilator pneumonia is high. VAP is significantly related to duration of MV and ICU stay, re-intubation, supine head position, impaired consciousness, steroids use and H<sub>2</sub> blocker use. Logistic regression analysis showed that MV was the only independent risk factor.

## CONFLICT OF INTEREST

All authors declare no conflict of interest

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