

## Incidence and Risk Factors of Ventilator Associated Pneumonia (VAP) in Palestine Hospitals

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### Abstract

**Background:** Pneumonia is a serious complication of mechanical ventilation in intensive care units (ICUs) patients around the world. If it develops 48 hours after the start of ventilation, it's called ventilator-associated pneumonia (VAP).

**Objectives:** The purpose of this study was to determine the incidence and risk factors of ventilator-associated pneumonia (VAP) in Palestine.

**Settings:** A prospective cohort study was conducted. It involved six intensive care units (ICUs) and one cardiac care unit (CCU) in six hospitals distributed in four cities in Palestine in a period of five months.

**Participants:** Patients who were ventilated for 48 hours or more.

**Results:** 134 patients were involved in the study. VAP was present in 29 patients (21.6%). Patients with VAP were more likely to have sepsis, neuromuscular disorders and chronic pulmonary obstructive disease (COPD), (P value: <0.001, 0.009 and 0.01), respectively.

**Conclusion:** VAP represents a common problem in Palestine and should not be neglected. Its epidemiologic profile in terms of incidence, length of stay and clinical course resembles the general pattern described everywhere.

### Background

Ventilator-associated pneumonia develops in a mechanically ventilated patient more than 48 hours after intubation. It's due to the presence of the endotracheal tube, not to the ventilation person [1]. Microaspiration is the main culprit in acquiring VAP [2].

The incidence of VAP ranges between 6% and 52% worldwide. However, the daily risk of developing VAP ranges from 1%-3% [3]. The diagnosis of VAP is based on the Criteria of the Centers for Disease Control and Prevention [4].

### Methodology

A prospective cohort study was conducted between November 2011 and March 2012 and performed at six different multidisciplinary ICUs and one CCU in 6 hospitals in Tulkarm, Jenin, Nablus and Ramallah, which represent VAP patients in Palestine referral hospitals.

Inclusion criteria were patients who required mechanical ventilation for more than 24 hours. Patients with Pneumonia prior to admission or who developed pneumonia in the first 48 hours of ventilation were excluded from our study. The research protocol was approved by the local institutional review board.

A clinical and epidemiological questionnaire was filled by medical doctors who are able to review the patient tests and investigations. VAP was diagnosed according to the modified Centers for Disease Control and Prevention criteria [4]. Risk factors examined included patient age, gender, duration of intubation, COPD, sepsis, neuromuscular disease, use of H2 Blockers, previous antibiotic use and enteral feeding. Univariate analysis was used to identify factors with significant unadjusted effects on VAP. Logistic regression was then applied to control for confounders and determine significantly related variables with VAP. The level of significance was set at 0.05.

### Results

During the study period, 134 patients were ventilated for 48 h or more and free of pneumonia at admission to the ICUs were followed in our study. The mean age which the patient followed in our study was

56.8 ± 19.70. Among them, seventy (52.2%) female, fifty eight (43.3%) of 134 have hypertension, thirty three (24.6%) have DM, sixty nine (51.5%) have cardiac disease and nineteen (14.2%) have cancer. Table 1 shows the characteristic of the ventilated patients.

Among these patients, 29 developed VAP. Giving an incidence rate of (21.6%), about 83.3% of VAP cases occurred in the first 8 days of ventilation.

Table 2 shows the characteristics of VAP compared to non-VAP patients. No significant difference between the VAP and non-VAP patients in relation to age, enteral feeding days or H2 blocker use days was found. However, number of ventilation days were significantly higher in patients with VAP (P value=0.04).

Characteristics	Frequency (%)
Mean age of patients	56.1 ± 19.7
Patients with HTN	58(43.3)
Patients with DM	33(24.6)
Patients with CD	69(51.5)
Patients with cancer	19(14.2)
HTN: Hypertension DM: Diabetes Mellitus CD: Cardiac disease	

**Table 1:** Characteristic of Patients included in the study (n=134).

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Variable	VAP cases (n=29)	Non-VAP cases (n=105)	Difference	P value*	CI**
	Mean (SD)				
Age (Y)	56.57 (18.32)	55.95 (20.15)	- 0.62	0.88	(-8.83 - 7.58)
Ventilation days	10.93 (5.25)	8.87 (4.74)	-2.06	0.04	(-4.08 - -0.04)
Enteral feeding days	2.41 (3.07)	1.16 (5.05)	-1.25	0.09	(-2.74 - 0.23)
H2 blocker days	7.45 (6.39)	6.46 (6.06)	-0.99	0.44	(-3.53 - 1.55)

\*Independent T-test  
\*\*CI: confidence interval 95%

Table 2: Comparison of VAP versus Non-VAP cases.

Factor		VAP Cases	Non-VAP cases	Univariate analysis		Multivariate Analysis	
				Odds ratio (CI95*)	P value**	Odds ratio (CI)	P value
Gender	Female	15	55	1	0.95	1	0.76
	Male	14	50	1.02 (0.45-2.33)		1.15 (0.45-2.97)	
COPD	No	22	97	1	0.01	1	0.01
	yes	7	8	3.85 (1.26-11.76)		4.50 (1.29-15.67)	
Sepsis	No	22	101	1	<0.001	1	0.001
	yes	7	4	8.03 (2.16-29.84)		12.57 (2.99-52.78)	
Neuromu- scular disorder	No	26	104	1	0.009***	1	0.01
	yes	3	1	12.00 (1.19-120.12)		19.3 (1.65-225.95)	
Previous antibiotic use	No	16	49	1	0.41	1	0.13
	yes	13	56	0.71 (0.31-1.62)		0.46 (0.17-1.26)	
H2 blocker use	No	8	32	1	0.76	1	0.63
	yes	21	73	1.15 (0.46-2.87)		1.30 (0.43-3.88)	
Enteral feeding	No	22	88	1	0.32	1	0.27
	yes	7	17	1.64 (0.60-4.46)		1.89 (0.59-602)	

\*CI: confidence interval 95%  
\*\*Chi squared test  
\*\*\*Fisher's exact test

Table 3: Univariate and Multivariate analysis for VAP risk factors.

Table 3 shows the univariate and Multivariate analysis of different variables used in our study.

Different rate of VAP was found between Sepsis and non-sepsis patient; 63% of sepsis patients developed VAP compared to about 18% of non-sepsis patients. This difference is found to be statistically significant (P value<0.001).

There were four cases of neuromuscular disorders three of them developed VAP, (P value=0.009).

For patients who have COPD; about 47% of them developed VAP, compared to 19% of patients who don't have. This difference is found to be statistically significant (P value=0.01).

Those three risk factors (Sepsis, neuromuscular disorders and COPD) remained statistically significant after multivariate analysis with P values of: 0.001, 0.01, and 0.01, respectively. Gender, previous antibiotic use, H2 blocker use and enteral feeding days did not have significant relation with VAP.

## Discussion

We examined the incidence and risk factors for VAP in seven ICU units in Palestine in a prospective cohort study. The incidence rate was (21.6%). This is close to the results of a similar study in King Fahad National Guard Hospital in Riyadh which reported the incidence of VAP to be 25.2% [5].

However, the incidence of VAP in the literature is widely variable and ranges from 6% to 52% [2]. This variability is mainly due to different diagnostic criteria and differences on the patient population included in these studies. This is mainly due to the lack of clinical and radiographic criteria that have high sensitivity and specificity values for the diagnoses of pneumonia in this patient population.

The mean ventilation days for patients who developed VAP were 10.93 compared to 8.87 of non VAP patients. This is found to be statistically significant (P value=0.04). This positive relation between duration of mechanical ventilation and VAP has long been established [6,7], but there is controversy as to whether it is the occurrence of VAP that leads to long stay on ventilator or vice versa. However, since most cases of VAP occur early during ventilation (more than 83% of cases occurred within 8 days in our study), a prolonged stay on ventilator therefore could be a result of VAP, rather than being a risk factor of VAP.

Of the other risk factors we studied, only three had significant effect on VAP: sepsis, neuromuscular disorders and COPD (P value: <0.001, 0.009 and 0.01), respectively.

Of the 134 patients we studied, 15 have COPD and 7 of them developed VAP (P value=0.01) which was statistically significant. These results correspond to the results of retrospective analysis of a database from a prospective, multicenter, international cohort of 5183 adult patients who received mechanical ventilation which found that COPD is a risk factor VAP (P value of 0.003) [8]. These results could be explained by the fact that patients with COPD have underlying structural and functional lung diseases which make them more susceptible to infections.

Four patients in our study were having neuromuscular disorders. Three of them developed VAP (P value of 0.009). Another cohort study of 439 patients who had VAP showed that patients with neuromuscular disorders are not at increased risk of developing VAP; this study showed that the P value for patients of neuromuscular disorders in a univariate analysis is 0.05 [8].

Our results could be explained by the fact that these patients are at increased risk of aspiration due to their neuromuscular disorders.

Sepsis is found to be the 3rd significant risk factor for VAP. As 63% of patients with sepsis developed VAP (P Value less than 0.001). This is consistent with the results of another study which showed that 55% of patients with sepsis developed VAP with a P Value of <0.001 [8]. Sepsis patients have circulating bacteria in their blood which put them at increased risk for developing VAP.

Male gender was not associated with significant increase risk on VAP as suggested by a multi-institutional prospective cohort study of adult surgical and trauma patients [9].

We didn't find any relation between enteral feeding and the developing of VAP (P Value 0.32). A similar study in King Fahad National Guard Hospital in Riyadh studied 202 patients, who were mechanically ventilated and found that enteral feeding is a significant risk factor for VAP (P value of <0.001). They explain their results by that enteral feeding increases the risk of gastric distention, colonization, aspiration, and pneumonia [5]. In our study, only 24 patients received enteral feeding (17.9%). So the lack of significance in our study might be due to the small sample size.

H2 Blocker use was not associated with significant change in VAP rates (P value=0.76). Another cohort study of 202 patients used a multivariate analysis and found that the use of H2 blockers is statistically not significant for the developing of VAP (P value=0.067). This matches with our results [5]. This means that it is neither a risk factor nor protective for the development of VAP. However, H2 blockers are recommended to be used in critically ill patients to prevent stress ulcers [10].

The relation between previous use of antibiotics and VAP is complex. In our study, we didn't find that previous use of antibiotics is protective against VAP. Other study showed that antibiotics were associated with an increased risk for ventilator-associated pneumonia in a cohort study of 320 patients [11]. Another study showed that antibiotics administration were associated with lower rates of VAP [12].

A possible limitation of our study is the criteria used to diagnose pneumonia. In our study, we defined VAP based on the clinical criteria proposed by the Centers for Disease Control. Thus, we believe that in our study, we were able to identify most of the patients who developed this complication. The other limitation is that in some ventilated patients, the CBC was not done and body temperature was not measured. So, we don't know if these patients developed VAP or not.

To avoid misclassification, we excluded those patients with incomplete data from the study.

In summary, our study showed that VAP represents a common problem in our country and should not be neglected. Its epidemiologic profile in terms of incidence, length of stay and clinical course resembles the general pattern described everywhere. Many factors were studied in relation to VAP and among them, sepsis, neuromuscular disorders and COPD were found to be associated with an increased risk of VAP.

A comprehensive multicenter study is warranted, as it should provide deep insight about the specific microbiological, genetic and clinic features of VAP in our setting.

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