

ORIGINAL ARTICLE

Microbial Profile of Pneumonia in Patients with Late Onset Ventilator Associated Pneumonia

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ABSTRACT

Key words:

Ventilator-associated pneumonia, Late-onset

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Background: Ventilator-associated pneumonia (VAP) is pneumonia occurring 48-72 hours or later following endotracheal intubation. It is characterized by the presence of an infiltrate, whether new or progressive, signs of systemic infection (fever, leukocytosis), change in sputum, and detection of an agent. VAP is mainly acquired through either major or micro aspiration of oropharyngeal organisms into the distal bronchi, directly or via reflux from the stomach into the oropharynx. **Objectives:** This study aimed to measure VAP rates, identify the causative organisms and demonstrate whether an association exists between bacterial pathogens causing late onset VAP and bacteria isolated from gastric aspirate in mechanically ventilated patients admitted to the Respiratory Intensive Care Unit of Ain Shams University Hospital, Cairo, Egypt. **Methodology:** This cross-sectional study was carried out over a period of 6 months from September 2015 to February 2016 and included 100 mechanically ventilated patients. Gastric aspirate from naso-gastric lavage and bronchoalveolar lavage (BAL) were obtained after establishment of diagnosis of late onset ventilator associated pneumonia. **Results:** *Candida* species and *P. aeruginosa* were the most predominant microorganisms found in BAL, each being isolated in 23.1% of cases. *Klebsiella pneumoniae* was the second commonest isolated organism from BAL and the most common in Ryle tube. **Conclusion:** Agreement between BAL and Ryle organisms occurred in 8 of 100 mechanically ventilated patients only. We concluded that a clear association can not be reached by the limited number of specimens. We recommend tight adherence to infection control preventive measures for mechanically ventilated patients in ICU to reduce the VAP rates.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is pneumonia occurring 48-72 hours or later following endotracheal intubation. It is characterized by the presence of an infiltrate, whether new or progressive, signs of systemic infection (fever, leukocytosis), change in sputum, and detection of an agent¹. VAP is acquired through either major or micro aspiration of oropharyngeal organisms into the distal bronchi, directly or via reflux from the stomach into the oropharynx.

VAP contributes immensely to cases of hospital-acquired pneumonia², with its risks being highest early in hospitalization³. It is a major threat in the intensive care unit (ICU)⁴. VAP is a significant contributor to hospital morbidity and mortality in ICU patients, in spite of advances in diagnosis and management.

VAP develops through aspiration of oropharyngeal organisms into the distal bronchi, either directly or via gastric reflux. Other potential routes are less common, such as haematogenous spread (e.g. from catheter-

related bloodstream infections) or through the environment, via the hands of healthcare workers, or through contaminated respiratory equipment as bronchoscopes⁵.

Early-onset VAP, developing within the first 4 days of hospitalization, carries a better prognosis, as it is usually caused by antibiotic-sensitive bacteria. Late-onset VAP (5 days or more) is usually caused by multidrug-resistant (MDR) pathogens and carries higher risks of mortality and morbidity⁶.

Tracheobronchial aspiration is defined as inhalation of oropharyngeal or gastric contents into the respiratory tract. Aspiration from both sources is important, however, tracheobronchial aspiration of gastric contents in tube-fed patients is of greater concern⁷.

Early initiation of enteral feeding is advised in critically ill patients, but this may increase the risk of gastric colonization, gastroesophageal reflux, aspiration and pneumonia⁸.

Common causative organisms of VAP include *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter* species, and *Staphylococcus*

*aureus*⁴. The prevalence of causative pathogens and their patterns of drug resistance vary widely, depending on hospitals and regions. Thus, surveillance data is essential.

This study aimed to measure VAP rates, identify the causative organisms and demonstrate whether an association exists between bacterial pathogens causing late onset VAP and bacteria isolated from gastric aspirate in mechanically ventilated patients admitted to the respiratory Intensive Care Unit of Ain Shams University Hospital, Cairo, Egypt.

PATIENTS AND METHODS

Ethical issues.

This work was accepted by the Ethical Committee of Ain Shams University after explaining the whole steps, aim and beneficial goals of the study.

Study design:

This cross-sectional study was carried out over a period of 6 months, from September 2015 to February 2016 and included 100 mechanically ventilated patients.

The data was collected from the case records of the patients who were admitted to the Respiratory Intensive Care Unit of Ain Shams University Hospital, (RICU), Cairo, Egypt.

Study population:

A total 150 patients were admitted to the RICU during the above-mentioned period. One hundred patients on mechanical ventilation (MV) and nasogastric tube (NGT) insertion for feeding were selected, 40 of them fulfilled the criteria of late-onset VAP.

Population definitions:

Patients fulfilling both the clinical and microbiological criteria of VAP were diagnosed as VAP cases and the remaining were categorized as non-VAP cases. Microbiological criteria included positive Gram stain and quantitative endotracheal aspirate culture showing $\geq 10^5$ CFU/ml⁹. Clinical criteria included modified Clinical Pulmonary Infection Score (CPIS) of more than or equal to 7¹⁰ (table 1). Patients on mechanical ventilation for 5 days or more were included in the late onset VAP.

Table 1: Modified Clinical Pulmonary Infection Score (CPIS):

CPIS points	0	1	2
Tracheal secretions	Rare	Abundant	Purulent
Leukocyte count(mm ³)	>4,000 and <11,000	<4,000 and >11,000	<4,000 or >11,000 + band forms
Temperature (°C)	>36.5 and < 38.4	>38.5 and < 38.9	>39 or <36
PaO ₂ /FiO ₂ ratio(mmHg)	>240 or ARDS	-	≤240 and no ARDS
Chest radiograph	No infiltrate	Diffuse infiltrate	Localized infiltrate
Culture of tracheal aspirate	Negative	-	Positive

When VAP was suspected, samples were obtained prior to any changes in the antibiotic therapy.

Exclusion criteria:

Patients with pneumonia prior to mechanical ventilation or within less than 48 hours of mechanical ventilation, patients with Adult Respiratory Distress Syndrome (ARDS), cavitary lung disease, primary lung cancer or metastatic disease, cystic fibrosis, tuberculosis patients, patients with acquired, induced or congenital immunodeficiency, leukopenia <1000 cells/mm³, and neutropenia <500 PMN/mm³ were excluded from the study.

Data collection:

The clinical parameters that were assessed included full medical history, the ventilator days, the timing of sample collection, and clinical examination of the patient.

Relevant investigations : These included blood counts and chest X-rays and any other relevant investigations

Microbiological Specimens

Nasogastric Tube Lavage:

Following overnight fasting (fasting ≥ 8 hrs), 10 ml of sterile saline were injected through the nasogastric tube and aspirated after 2-3 minutes.

BAL sample:

Using a flexible bronchoscope (Olympus CLE-10, USA), BAL was performed by 0.9% NaCl to a total volume of 120–150 ml.

Samples Processing:

Both nasogastric tube lavage and BAL were processed immediately. The samples were first subjected to Gram staining and then quantitative cultures were performed. A quantitative bacteriological culture threshold of 10^4 CFU/ml was considered significant for BAL¹¹. All plates were checked for growth overnight and then after 24 and 48 hours of incubation.

Statistical analysis

Analysis of data was done by IBM computer using SPSS (statistical program for social science version 12) and include; description of quantitative variables as mean, standard deviation (SD) and range, description of qualitative variables as number and percentage. Chi-square test was used to compare qualitative variables between groups. A probability value (p value) of less than or equal to 0.05 was considered as statistically significant.

RESULTS

VAP incidence:

Baseline surveillance was done to determine the incidence of VAP per 1000 bed days. Of 150 patients admitted to RICU, 100 patients were mechanically ventilated, 40 patients developed LOP VAP. LOP represented 41.2 per 1000 ventilator days.

Patient demographic data :

The mean age of the participants was 58.9 ± 13.0 and their ages ranged from 24-85 years. More than half of the participants (57.5%) were 50-70 years; while (22.5%) were younger than 50 years and only 20.0% were older than 70 years. In addition (67.5%) of the study participants were males while (32.5%) were females. The demographic data of all cases are summarized in table 2.

Table 2: The demographic data:

Age of the Participants	No.	%	χ^2 test	P-value
Less than 50 yrs	9	22.5	10.550	0.005**
50-70 years	23	57.5		
More than 70 yrs	8	20.0		
$\bar{x} \pm SD$	58.9 ± 13.0			
Range (years)	(24-85)			
Gender	No.	%	4.900	0.027*
Male	27	67.5		
Female	13	32.5		

(*) Statistically Significant at $P < 0.05$

Causative organisms in Clinical samples:

Three samples of 40 late-onset VAP patients (7.5%) showed no growth in gastric aspirate from NGT samples while 37/40 samples (92.5%) showed uncountable growth. *Klebsiella pneumoniae* was the most frequent microorganism found in the gastric aspirate (27.0%), followed by *Pseudomonas aeruginosa* & *E. coli* (16.2% & 13.5%), respectively. Co-infection with more than one etiologic agent was found in six patients (16.2%) (table 3).

Table 3: Types of microorganisms that isolated from gastric aspirate from NGT.

Type of Organism in gastric aspirate from NGT	No.	%
<i>Staph aureus</i>	3	8.1
<i>Candida species</i>	4	10.8
Gm +ve Bacilli	2	5.4
<i>Klebsiella pneumoniae</i>	10	27.0
<i>E. coli</i>	5	13.5
<i>Pseudomonas aeruginosa</i>	6	16.2
Anthracoids	1	2.7
<i>Candida species</i> + <i>Klebsiella pneumoniae</i>	1	2.7
<i>Candida species</i> + <i>Pseudomonas aeruginosa</i>	1	2.7
<i>Klebsiella pneumoniae</i> + <i>Viridans Streptococci</i>	2	5.4
<i>E. coli</i> + <i>Viridans Streptococci</i>	2	5.4
Total	37	100.0

As regards BAL-isolated organisms; 14/40 samples (35.0%) showed no growth in BAL while 26/40 samples (65.0%) showed uncountable growth. *Candida species* and *Pseudomonas aeruginosa* were the most frequent organisms isolated from BAL, (23.1%) each. Co-infection was found in 5 cases 19.1% (table 4).

Table 4: Types and percentages of microorganisms that isolated BAL:

Type of Organism in BAL	No.	%
<i>Staph aureus</i>	1	3.8
<i>Candida species</i>	6	23.1
Gm +ve Bacilli	1	3.8
<i>Klebsiella pneumoniae</i>	2	7.7
<i>Viridans Streptococci</i>	2	7.7
<i>Pseudomonas aeruginosa</i>	6	23.1
Gram Negative Cocci	2	7.7
<i>Acinetobacter baumannii</i>	1	3.8
<i>Candida species</i> + <i>Klebsiella pneumoniae</i>	1	3.8
<i>Candida species</i> + <i>Viridans Streptococci</i>	1	3.8
<i>Candida species</i> + <i>Pseudomonas aeruginosa</i>	2	7.7
<i>Viridans Streptococci</i>	1	3.8
Total	26	100.0

Overall prevalence of organisms that occurred in both gastric aspirate in NGT and BAL in the same patient was $(8/40 * 100 = 20.0\%)$; *Pseudomonas aeruginosa* was the most frequent organism that occurred in both gastric aspirate in NGT and BAL in the same patient followed by *Candida species* (25.0%) and *Streptococci*, *Klebsiella pneumoniae* and *Staph aureus*, (12.5%) each (Table 5)

Table 5: Types of organism isolated from both gastric aspirate from NGT and BAL in the same patient (n=8)

Type of Organism	Gastric aspirate NGT + BAL	
	No.	%
<i>Pseudomonas aeruginosa</i>	3	37.5
<i>Candida species</i>	2	25.0
<i>Viridans Streptococcus</i>	1	12.5
<i>Klebsiella pneumoniae</i>	1	12.5
<i>Staph aureus</i>	1	12.5
Total	8	100.0

DISCUSSION

VAP is the most common complication after mechanical ventilation with the incidence estimated to be 3% per day during first 5 days of ventilation, 2% per day between days 5 and 10 of ventilation and 1% per day thereafter¹.

In the present study, VAP rates were 41.2 per 1000 ventilator days; this result agrees with Injac et al.¹² and Azzab et al.¹³ who found the incidence rate of VAP ranged from 13.2 to 51 per 1,000 ventilator days.

Lower VAP rates were reported by Ergul et al.¹⁴, Edwards et al.¹⁵ and Magill et al.¹⁶ (8.6, 0.4-10.7 and 6.89-8.79 patients per 1,000 ventilator days), respectively. The variation in VAP prevalence is due to the differences in infection control practices and compliance to VAP preventive measures.

This study showed that patients in the age group of 50-70 years were more prone to develop VAP and this result was similar to Mallick et al.¹⁷ and Chi et al.¹⁸. The incidence of VAP was more in males (67.5%) compared to females (32.5%) which was similar to studies conducted by Mallick et al.¹⁷, Chi et al.¹⁸, Sharma et al.¹⁹ and Aly et al.²⁰.

Candida species and *P. aeruginosa* were the most predominant microorganisms found in BAL represented by 23.1% for each. Similar results were reported by Rocha et al.²¹ and Mehta et al.²² while higher prevalence of *P. aeruginosa* was detected by Prospero et al. (31%)²³, Rosenthal et al. (30.4-66.9%)²⁴ and Awny et al. (33%)²⁵.

Klebsiella pneumoniae was the second commonest isolated organism from BAL (7.7%) and the most common (27%) in Ryle tube, and this result agrees with Madani et al. (15.4%)²⁶, Rosenthal et al. (10.8-27%)²⁴ and Awny et al. (33%)²⁵. Azzab et al.¹³ found *Klebsiella pneumoniae* to be most common isolated pathogen (37.2-43%).

In this study, *S. aureus* prevalence was 3.8%. This result disagrees with Chi et al.¹⁸, who found *S. aureus* to be the most common causative organism in his study. Moreno et al.²⁷, Madani et al.²⁶ and Rosenthal et al.²⁴,

reported higher prevalence rates of methicillin-resistant *S. aureus* (MRSA) in VAP (40% and 78% and 84%, respectively).

Acinetobacter baumannii was isolated from one BAL specimen only and represented 3.8% and this disagrees with Werarak et al.²⁸, who found *Acinetobacter baumannii* to be the most common isolated pathogen (92.3%) in his study. Mathai et al.²⁹ found *Acinetobacter baumannii* in 53% of cases, and stated that they didn't perform quantitative cultures which may have led to an over-estimation of infection rates.

CONCLUSION

VAP incidence in RICU was relatively high, with *Pseudomonas aeruginosa* and *Candida species* being the most frequent organisms isolated from BAL. *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *E. coli* were frequent organisms isolated from Ryle. Agreement between BAL and Ryle organisms occurred in 8 patients only. A clear association can't be reached by the limited number of specimens.

Recommendation:

Application of VAP infection control preventive measures for mechanically ventilated patients in ICU to reduce the VAP rates is highly recommended, as VAP rates are high compared to international rates. Further larger-scale studies are needed to clarify the role of gastric aspiration in occurrence of late-onset VAP.

Declaration: The authors hereby declare no conflicts of interest with any persons or parties.

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