ORIGINAL ARTICLE
Clinical and Microbiological Characteristics of Ventilator Associated Pneumonia Patients at Surgical Intensive Care Unit.

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ABSTRACT
Background: Ventilator-associated pneumonia (VAP) is considered one of the most widespread infections present in the intensive care units. It is associated with increase day stay in hospital, ventilation days and mortality. The aim of this study is to determine the incidence, bacteriology, impact and clinical outcome of VAP patients. Methods: Prospective observational non interventional study of VAP cohort, conducted in surgical intensive care unit (ICU), Zagazig University Hospitals over a period of 1 year (June 1, 2016–May 31, 2017). The study was carried on seventeen cases who fulfilled the inclusion criteria and developed VAP after 48 hours of mechanical ventilation. The incidence, microbiological characteristics and the outcome of these cases were observed. This study was approved by the Institutional Review Board, faculty of medicine, Zagazig University. Informed written consents were taken from first degree relatives. Results: incidence of VAP was 9.94%. 76.5% of those patients were male and 23.5% were female. Gram negative bacteria were the main causative organisms in which klebsiella pneumonia was the predominating one. There was significant increase in ventilation days and length of stay (LOS) in ICU. APACHI II score was also significantly higher in VAP patients. VAP cases were associated with higher mortality and lower cure rate. Conclusion: VAP is a serious ICU acquired infection with significant impact and required effective preventive action. Keywords: Ventilator-associated pneumonia; bacteriology; antibiotic resistance; outcome; infection control.

INTRODUCTION
Ventilator-associated pneumonia (VAP) is a pulmonary infection that occurs more than 48 hours after patients have been intubated and received mechanical ventilation". The morbidity and mortality rates of VAP make it one of the biggest challenges for intensivists [1]. According to the National Nosocomial Infections Surveillance (NNIS) system report, the mean incidence of VAP in a medical intensive care unit (ICU) is 7.3 episodes per 1000 ventilator-days, whereas the mean incidence in a surgical or trauma ICU may reach up to 13.2 and 16.2 respectively [2]. There are two types of VAP, early onset and late onset VAP. Early onset VAP is usually less severe, associated with a better prognosis, and is more likely to be caused by antibiotic-sensitive bacteria. Late onset VAP caused by multi-drug resistant (MDR) pathogens and is associated with increased morbidity and mortality [3].
VAP occurs when infectious bacteria obtain direct access to the lower respiratory tract via micro aspiration, development of a biofilm laden with bacteria within the endotracheal tube, pooling and trickling of secretions around the cuff and impairment of mucociliary clearance of secretions with gravity dependence of mucus flow within the airways [4]. Risk factors that plays an important role in VAP development include tracheal intubation, reintubation, duration of mechanical ventilation, endotracheal tube suctioning, position of the patient, enteral nutrition, blood stream infection, prior antibiotic therapy and continuous sedation [5].

Many studies have investigated the causative organisms of VAP. Up to 40% of these infections can be polymicrobial. Pseudomonas species, Acinetobacter species and even Enterobacteriaceae are quite often MDR [6]. Because of the emergence of high percentage of these MDR VAP organisms and the serious impact of VAP in terms of mortality and clinical outcome, early and accurate diagnosis is fundamental in the management of VAP patients.

Diagnosis of suspected VAP cases may be clinical or microbiological. The commonly utilized clinical specimens for microbiological diagnosis are Tracheal Aspiration (TA), Broncho-Alveolar Lavage (BAL), Mini-BAL and Protected Brush Specimens (PBS) [7].

Objectives: To describe the clinical and microbiological characteristics of VAP patients admitted to the surgical ICU, Zagazig University Hospitals.

METHODS

Study Setting: The investigated unit was the surgical ICU at Zagazig University Hospitals. It serves mainly postoperative critically ill patients and some trauma patients.

Study Design: A Prospective observational was conducted over a period of 1 year (June 2016 to May 2017).

Sample size: Seventeen cases were included in the study. The study included all cases admitted to the ICU, mechanically ventilated for more than 48 hours with clinical pulmonary infection score >6.

Ethical consideration: Ethical approval was obtained from the Institutional Review Board, faculty of medicine, Zagazig University. Informed written consents were taken from first degree relatives. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Patients, ≥18 years, who were intubated and mechanically ventilated for more than 48 hours inside the surgical ICU and showed clinical criteria of VAP.

Exclusion criteria: Patients on immunosuppressive drugs, those with chronic lung disease, chronic liver disease and chronic renal disease, immunocompromised patients, patients who were intubated and mechanically ventilated outside the ICU before admission and mechanically ventilated patients with clinically suspected VAP before 48 hours on mechanical ventilation.

Clinical pulmonary infection score (CPIS) is used for VAP diagnosis (table 1). Clinical VAP criteria included the presence of a new or progressive pulmonary infiltrate on chest radiograph, fever greater than 38.3°C, leukocytosis or leucopenia, or purulent tracheobronchial secretions. A clinical suspicion of VAP was made when the clinical pulmonary infection score (CPIS) was >6 with the use of the following criteria: Ventilated for more than 48 h; New and persistent infiltrates shadow developing in the Chest X-ray; presence of fever (temperature >38.5°C); White cell count >11,000/ml or <4000/ml; declining ratio of partial pressure to inspired fraction of oxygen (PaO$_2$/FiO$_2$ ratio) [8].

Cases were enrolled for the study when the diagnosis was confirmed. This confirmation was done by identification of the causative
organism according to standard bacterial protocol followed by antibiotic susceptibility test [9].

Description of Clinical characteristics:
This included recording of VAP incidence and reviewing the impact of VAP on length of stay in ICU, duration of mechanical ventilation and clinical outcome.

A worksheet was used for data collection about the following items: Patients demographic data, clinical data, date and cause of ICU admission, date, indication and duration of mechanical ventilation and length of ICU stay.

VAP incidence or rate was calculated by the following equation:
(Number of cases with VAP/Total number of patients who received MVx100) = VAP rate per 100 patients.

Confirmation by microbiological tests:
Specimens from patients with CPIS >6 were collected by direct catheter aspiration and sent for confirmation by microbiological tests. Tracheal aspirates were the ones used for laboratory testing. The specimens were collected under complete aseptic condition, liquefied, homogenized then centrifuged for about ten minutes [10]. The specimen cultured on MacConkey, blood and chocolate agars then incubated for about two days at 37ºC at 10% Co2. VAP was confirmed when a threshold of more than 1,000,000 colony forming units (cfu)/ml has been reached [11].

Statistical analysis:
Data were analyzed using Microsoft Excel software, then imported into Statistical Package for the Social Sciences (SPSS version 20.0). According to the type of data, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X²), differences between quantitative independent groups by t test or Mann Whitney, paired by paired t or sign. P value was set at <0.05 for significant results &<0.001 for high significant result.

RESULTS

In this study, the number of all ventilated patients admitted to the investigated ICU during the period of the study was 171 patients among them seventeen cases were confirmed to be VAP patients, these cases termed VAP cases and 154 cases didn't show criteria of VAP and termed NON VAP cases (table 2) (figure 1). Nearly all VAP cases included in this study are of late onset VAP as they developed VAP after 5 or more days of mechanical ventilation. Demographic data showing that there was no significant difference between both groups as regard age and sex (table 3) Organisms distribution among of VAP cases showed that out of the seventeen VAP, nineteen bacterial isolates were detected and it was found that klebsiella pneumonia was the most prevalent organism followed by Pseudomonas aeruginosa (figure2).

As regarding ventilation days of VAP cases, there was a significant difference between both groups; the mean days of ventilation in VAP cases group was significantly higher than the NON VAP cases. Not only was the difference in ventilation days but also in the mean length of stay (LOS) in the ICU which was higher in VAP cases group comparing to the other group (table 4).

It was also found that patients with VAP are associated with higher APACHII score than NON VAP cases (table 4).

The outcome distribution between both groups showing significant difference regarding to the survival rate as mortality was higher among VAP group (table 5).
### Table 1. The clinical pulmonary infection score (3)

<table>
<thead>
<tr>
<th></th>
<th>Point 0</th>
<th>Point 1</th>
<th>Point 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Temperature (°C)</strong></td>
<td>36.5 to 38.4</td>
<td>38.5 to 38.9</td>
<td>≥39 or ≤36.4</td>
</tr>
<tr>
<td><strong>Peripheral WBC</strong></td>
<td>4000-11000</td>
<td>&lt;4000 or &gt;11000 or &gt; 50% band: add extra point 1</td>
<td></td>
</tr>
<tr>
<td><strong>Tracheal Secretions</strong></td>
<td>None</td>
<td>Non-purulent</td>
<td>Purulent</td>
</tr>
<tr>
<td><strong>Chest X-ray</strong></td>
<td>No infiltrates</td>
<td>Diffuse or patchy Infiltrates</td>
<td>Localized Infiltrate</td>
</tr>
<tr>
<td><strong>Progression of infiltrate from prior radiographs</strong></td>
<td>None</td>
<td>Heavy growth</td>
<td>Progression (ARDS, CHF thought unlikely)</td>
</tr>
<tr>
<td><strong>Culture of ET Suction</strong></td>
<td>No growth/light Growth</td>
<td>Heavy growth</td>
<td>Same bacteria on gram stain: add 1 extra point</td>
</tr>
<tr>
<td><strong>Oxygenation(PaO2/FiO2)</strong></td>
<td>&gt;240 or ARDS</td>
<td>≤240 or no ARDS</td>
<td></td>
</tr>
</tbody>
</table>

WBC: White Blood Cell  ARDS: Acute Respiratory Distress Syndrome  CHF: Congestive Heart Failure  ET:endotracheal

### Table 2. Incidence of VAP in ICU:

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAP</td>
<td>17</td>
<td>9.94%</td>
</tr>
<tr>
<td>NON VAP</td>
<td>154</td>
<td>90.06%</td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>100%</td>
</tr>
</tbody>
</table>

VAP: ventilator associated pneumonia

### Table 3. Age and sex distribution among studied groups

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Age Group</th>
<th>n (%)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-30</td>
<td>VAP (N=17)</td>
<td>7(41.2%)</td>
<td>65 (42.2%)</td>
</tr>
<tr>
<td>30-50</td>
<td>NON VAP (N=154)</td>
<td>7 (41.2%)</td>
<td>55 (35.7%)</td>
</tr>
<tr>
<td>50-70</td>
<td>3 (17.6%)</td>
<td>34 (22.1%)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>35.11±11.7</td>
<td>38.21±9.65</td>
<td></td>
</tr>
</tbody>
</table>
<
| Gender    |            |       |
| Male      | n (%)      | 13 (76.5%) | 108 (70.2%) |
| Female    | n (%)      | 4 (23.5%) | 46 (29.8%) |
| Total     | n (%)      | 17 (100.0%) | 154 (100.0%) |

VAP: ventilator associated pneumonia
Table 4. Comparison between VAP and NON VAP groups regarding Ventilation days, length of ICU stay and APACHE II

<table>
<thead>
<tr>
<th></th>
<th>VAP (N=17)</th>
<th>NON VAP (N=154)</th>
<th>t/Mann Whitney</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilator days</td>
<td>26.76±10.9</td>
<td>4.39±1.3</td>
<td>8.845</td>
<td>0.00**</td>
</tr>
<tr>
<td>Length of ICU Stay (days)</td>
<td>30.47±13.5</td>
<td>7.56±2.1</td>
<td>6.657</td>
<td>0.00**</td>
</tr>
<tr>
<td>APACHE II</td>
<td>32.51±8.32</td>
<td>12.32±3.54</td>
<td>10.321</td>
<td>0.00**</td>
</tr>
</tbody>
</table>

VAP: ventilator associated pneumonia
APACHE: Acute Physiology and Chronic Health Evaluation
Data expressed as mean ± SD

Table 5. Outcome distribution between VAP and Non VAP

<table>
<thead>
<tr>
<th></th>
<th>VAP</th>
<th>NON VAP</th>
<th>X²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13</td>
<td>146</td>
<td>7.88</td>
<td>0.004*</td>
</tr>
<tr>
<td>(%) (76.5%)</td>
<td>(94.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(%) (23.5%)</td>
<td>(5.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>154</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(%) (100.0%)</td>
<td>(100.0%)</td>
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</tbody>
</table>

VAP: ventilator associated pneumonia

Figure 1. Consort flow chart
DISCUSSION
Ventilator associated pneumonia accounts for one-fourth of the infections occurring in critically ill patients and is the reason for half of antibiotic prescriptions in mechanically ventilated patients. Several countries have reported mortality rates ranging from 24% to 76% [12].

In this study, the incidence of VAP cases was 9.94% while NON VAP cases account for 90.06%. This results coincide with an Indian study where the incidence VAP was 27.71% at tertiary care hospital [13]. Similarly Morehead and Pinto in their study found that the incidence of VAP cases was 15% [14]. This high percentage of VAP incidence could be related to lack of adequate nursing staff which may have adversely affected the quality of care given to patients with elevated VAP incidence.

Demographic characteristic of the studied groups showed that there was no significant difference between both groups regarding to the age and sex. Among VAP cases the incidence of male patients (76.5%) was higher than female patients (23.5%), this coincides with the results of Golia et al., who conducted their study in the intensive care unit of the tertiary care hospital in Bangalore and found that VAP incidence in male patients was higher than female ones [15].

It was found that gram negative organisms was the predominating causative organisms of which klebsiella pneumonia (31.6 %) was the main responsible one followed by pseudomonas aeruginosa (26.3%). This results are similar to the results of Shahrokhi et al., who conducted their study in a respiratory ICU of a University Teaching hospital in Iran and found that 34.37% of isolates from VAP cases were klebsiella pneumonia followed by pseudomonas aeruginosa 33.33% [16]. Also Chawla in his study in 2008 found that 87% of the causative organisms were gram negative organisms [17]. Nosocomial Gram-negative pathogens colonize on healthy skin of ICU people, catheters, instruments, and environments that can be even transmitted through the air. Thus it becomes an important target to face such threatening organisms especially in our ICU as unfortunately similar results were obtained by a study done for VAP patients in emergency ICU, which is a nearby ICU in Zagazig University Hospitals, and revealed that gram negative bacilli are the main causative organisms (73.3%) with klebsiella predominating (43%) [11].

The mean duration on mechanical ventilation showed also significant reduction in NON VAP cases in comparison to VAP cases (26.76 ± 10.90 days in VAP cases while only 4.39 ± 1.3
in NON VAP cases), these results are similar to that reported by Rodrigues et al., who found that time on MV was significantly longer in VAP cases, 23 days while only 9 days in NON VAP cases [18]. Not only the increase in ventilation days but also the length of stay of VAP patients in ICU showed significant increase in duration in comparison with that of NON VAP cases (30 days in VAP cases vs 7 days in NON VAP cases). Tejerina et al., in evaluating more than two thousand patients, concluded that VAP was associated with a significant increase in ICU length of stay [19]. Also Prospective observational study conducted by Heredia et al., on 418 consecutive patients admitted in the ICU, reported that there was a significant increase in ventilation days and LOS among VAP patients [20]. The increase in ventilation days and LOS made VAP patients susceptible to many complications with higher mortality rate.

It was also found that APACHE II score was significantly higher in VAP cases in comparison to NON VAP cases (32.5±8.32 vs 12.32±3.54 respectively). Similarly Pawar et al., in a study made in NewDelhi found that APACHE II score was (10.6±5.33) in VAP cases while it was (7.00 ±2.53) in NON VAP cases [21]. Zhou et al., found that APACHE II score determined at the time of VAP diagnosis has good discriminatory and calibrator power to predict mortality in patients with VAP and it was higher in VAP cases 23.1±4.8 vs. 16.7±4.6 [22]. This indicates that the physiological state of VAP patients deteriorates with infection rather than NON VAP patients.

The mortality rate in our study was found to be 23.5% in the VAP group as compared to 5% in the non-VAP group. This coincides with the results of Mallick et al., who found that mortality rate reached 62.5% among VAP cases [23] and the result of Gadani et al., who found that mortality rate was 54% in VAP cases while 41.2% in NON VAP cases [24]. This indicates that VAP had poor prognosis in terms of mortality.

CONCLUSION

Ventilator associated pneumonia is still a common and serious ICU complication. It is associated with a longer ventilation duration, ICU/hospital stay, and increased in-hospital morbidity and mortality. This may subsequently lead to higher treatment costs. Infection control measures should be revised, antibiotic use should be rationalized to decrease the reported high resistance rates. Effective nursing care and application of VAP bundle should be rigorously applied for VAP prevention.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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