ABSTRACT:

Objective: The Study was designed to determine prevalence of Ventilator Associated Pneumonia (VAP) and to identify the commonest pathogens responsible, in a tertiary care hospital located at sub-urb industrial region of Karachi, Pakistan.

Methods: A prospective cross-sectional study was conducted in ICU at JMCH, Korangi Karachi from Jan 2012 to Jan 2013. Patients, who received mechanical ventilation > 48 hours, were prospectively followed for occurrence of VAP. The clinical diagnosis of VAP was made on the basis of CPIS criteria and confirmed by quantitative culture of tracheal secretion.

RESULT: 275 patients meeting inclusion criteria were included in the study, out of which 84 (30.5%) developed VAP. The common pathogens were Pseudomonas aeruginosa (63%), Acinetobacter lwofii (22%) and Staphylococcus aureus (33%). Increased ICU stay and over all mortality (59.5%) was observed in VAP group.

Conclusion: The frequency of VAP in our ICU was comparable to other settings in our region, most common pathogens are gram negative bacilli which showed resistance to many antibiotics. Mortality was high in patients developing VAP when compared to patient on ventilator not developing pneumonia.

Keywords: ventilator-associated pneumonia, nosocomial pneumonia, Gram negative bacilli.

INTRODUCTION:

Ventilator-associated pneumonia (VAP) is defined as pneumonia occurring more than 48 hour, after patients have been intubated and received mechanical ventilation. VAP is most common nosocomial infection in critically ill patients, affecting 27% of all critically ill patients. Frequency of VAP is reported between 15-40%. Prevalence of VAP is higher in countries with limited resources. The risk of developing VAP rises 1-3% each day in ICU patients.

The diagnosis of VAP requires assessment of various clinical criteria which includes; presence of fever, increased WBC, persistent or new X-ray infiltrates, purulent bronchial secretions and impaired oxygenation. A few standardized diagnostic criteria are also used National Nosocomial Surveillance System (NNIS) and Clinical pulmonary infection score (CPIS) having sensitivity of and respectively. The frequency, etiology and antibiotic resistance patterns in VAP vary among different geographical settings. Prevalence of Multi Drug Resistant (MDR) organisms as a cause of VAP is also becoming a major health concern. Gram-negative bacteria such as Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Acinetobacter species, and Gram-positive bacteria such as Staphylococcus aureus are the common causative pathogens of VAP.

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VAP has been widely investigated in most parts of the world. According to the SENTRY antimicrobial surveillance program operated in US, Europe, and South America, the most common causative pathogen taken all regions together is, *Pseudomonas aeruginosa* (27%), followed by *Staphylococcus aureus* (20%), and Acinetobacter species (14%). In the US, S.aureus (32%) is the most common causative pathogen, followed by *P.aeruginosa* (21%), Enterobacter species (9%), and Acinetobacter species (4.4%) ⁶. Meanwhile, according to a recent study on the causative pathogens of nosocomial pneumonia in Asia, S. aureus (27%) was the most common causative pathogen of nosocomial pneumonia in Korea, followed by Acinetobacter species (16%), P. aeruginosa (14%), and K. pneumoniae (9%) ⁷. Noyal et al conducted a study in India showed Enterobacter (25%), Acinetobacter (25%) and S. aureus (25%) ⁸. Demonstration of relationship between death and VAP is a difficult task epidemiologically. Indeed, in ventilator-associated patients, it is very difficult to distinguish between the deaths caused by VAP and deaths occurring while VAP was present at the time of death but not directly the cause. VAP is a frequent complication in these cases and several investigations have demonstrated a direct casual influence on mortality. However some studies also represent no significance in mortality between VAP and non VAP population ¹⁰. Mortality to VAP has been reported to be as high as 40 to 50% ³,⁷. Since the spectrum of VAP varies from hospital to hospital and ward to ward that’s why, the knowledge about local antimicrobial pattern is of paramount importance. The present study was designed to determine prevalence of VAP and to identify the common pathogens responsible, and antimicrobial resistance in a tertiary care hospital located at peripheral industrial region of Karachi, Pakistan.

**MATERIAL & METHODS:**
A prospective cross-sectional study was conducted in Intensive Care Unit (ICU) at Jinnah Medical College Hospital (JMCH), a sub-urban area located in Industrial area in Karachi Pakistan. JMCH is a postgraduate teaching hospital associated with Jinnah Medical and Dental College (JMDC), comprising of 350 beds including 10 bedded ICU. The study was conducted from Jan 2012-Jan 2013. Study population included all the patients > 16 yr of age, who received mechanical ventilator for > 48 hrs. Patients <16 years of age and those having pulmonary infection at the time of admission or shifted from other hospital with Endotracheal Tube (ET) or the patient was known to be HIV positive were excluded from the study. A disposable cuffed endotracheal tube made up of polyvinyl chloride was used for Intubation. The study was approved by our institutional review committee. Informed consent for the study was obtained from legally responsible family member. For all the eligible patients, demographic characters, co-morbidities, daily record of fever, White Blood Count (WBC), sputum characters, requirements of suctioning, chest radiograph findings and Arterial Blood Gases (ABGs) were recorded. The eligible patients were prospectively followed for signs of VAP till weaned from ventilator/discharge or death. The diagnosis of VAP was made on clinical and biological criteria. A clinical diagnosis of VAP was made by using Modified Clinical Pulmonary Infection Score (CPIS) > 6 ⁹. The criteria includes:
- New and persistent infiltrates in X-ray chest.
- Temperature of > 38.5 °C or < 36 °C.
- WBC > 12000/ microlitre or < 4000/ microlitre
- Persistent bronchial secretions.
- Impaired PaO₂/FiO₂ ratio.

Deep Tracheal aspirate samples were obtained for gram stain and quantitative culture. Common bacteria causing pneumonia and their sensitivity were identified. The diagnosis was confirmed by quantitative culture of endotracheal aspirate > 105. We followed the definitions proposed by the European Centre for Disease Prevention and Control for “multidrug-resistant” (MDR), “extensively drug-resistant” (XDR), and “pan drug resistant” (PDR) gram-negative bacilli (10)

- MDR: non-susceptible to ≥1 agent in ≥3 antimicrobial categories.
- XDR: non-susceptible to ≥1 agent in all but ≤2 categories.
- PDR: non-susceptible to all antimicrobial agents listed

The outcome, after VAP was recorded and compared with the outcome of the patients who did not developed pneumonia.

**STATISTICS:**
The data was analyzed using the Statistical Package for the Social Sciences (SPSS) version 17. Qualitative variables were presented as frequencies and proportions while mean and standard deviation was used to assess quantitative measures. The comparison of mean values among different groups was done by using student's t-test. The p value < 0.05 was considered to be significant.

**RESULT:**
275 patients meeting eligibly criteria were enrolled in the study, out of which 84 (30.5%) developed VAP. There were 54 (64%) males and 30(36%) females. Mean age was 48+ 20 years. Twelve (14%) had diabetes, 27 (32%) had COPD and 4 (11%) had hypertension. Mean APACHE score was 22.4. a comparison of demographic characters, APACHE III score, duration of mechanical ventilation and mortality between VAP and non VAP group is shown in table I. Eleven (13%) patients develop VAP within 5 days, while 73 (87%) developed after 5 days. (P VALUE 0.007).

Sixty two (74%) samples showed growth of single organisms while 22 (26%) samples showed group of more than one organism, having mixed bacterial growth mostly comprising of Pseudomonas, Acinetobacter and Staphylococcus. Only 12 (14%) samples all two or three pathogens were >105 colonies. The common microorganism identified was *Pseudomonas aeruginosa* (63.5%) and *Staphylococcus aureus* (33.3 %), Acinetobacter lwoffi (22.6%) followed by Enterobacter (21%). Mortality was high in patients developing ventilator associated pneumonia (60 %)when compared to patient on ventilator not developing pneumonia (10%). (p<0.05) (Table: I)

Result for anti-microbial resistance in major bacterial isolates revealed; In *Pseudomonas aeruginosa* resistance to Tazobactum /piperacillin, Ceftazidime, Ciprofloxacin, Amikacin, Meropenem was 20%, 34%, 48%,31% and 17% respectively. Multi-drug resistance (MDR) was observed in 17% of isolates. No Pan Drug Resistance (PDR) was observed. In Acinetobacter isolates resistance to Tazobactum/piperacillin, Ceftazidime, Ciprofloxacin, Amikacin, Meropenem was 63%, 100%, 73%, 73%, 57% respectively. Fifty two percent of the samples
were MDR. In Enterobacter drug resistance to Tazobactum/piperacillin, Ceftazidime, Ciprofloxacin, Amikacin, Meropenem was 33%, 61%, 50%, 38%, 38% respectively. In *Staphylococcus aureus* resistance to cloxacillin, ciprofloxacin, clindamycin, vancomycin was 25%, 42%, 50%. Methicillin resistant *Staphylococcus aureus* (MRSA) was 25% of all isolates. No Vancomycin resistance was observed.

**TABLE I**: Characteristics of VAP and non VAP

<table>
<thead>
<tr>
<th>CHARACTERS</th>
<th>VAP n (%)</th>
<th>NON VAP</th>
<th>P-VALUES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>47.8 + 17.4</td>
<td>48.2 + 18.7</td>
<td>0.86</td>
</tr>
<tr>
<td>Male</td>
<td>54 (64.2%)</td>
<td>117 (61.2%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Female</td>
<td>30 (35.8)</td>
<td>74 (38.7)</td>
<td></td>
</tr>
<tr>
<td>Mean ICU stay</td>
<td>23.2 + 17.2</td>
<td>7.6 + 54</td>
<td>0.001</td>
</tr>
<tr>
<td>(days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APACHE III Score</td>
<td>22.48+ 9.85</td>
<td>24.92+ 6.53</td>
<td>0.119</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12 (14.2%)</td>
<td>22 (11.5%)</td>
<td>0.65</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (1.1%)</td>
<td>12 (62%)</td>
<td>0.42</td>
</tr>
<tr>
<td>COPD</td>
<td>27 (32.1%)</td>
<td>32 (16.7%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Mortality</td>
<td>50 (59.5%)</td>
<td>20 (10.4%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**TABLE II**: FREQUENCY OF ISOLATED ORGANISMS

<table>
<thead>
<tr>
<th>Micro-organisms</th>
<th>NO (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>29 (63.5%)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>28 (33.3%)</td>
</tr>
<tr>
<td><em>Acinetobacter lwoffii</em></td>
<td>19 (22.6%)</td>
</tr>
<tr>
<td><em>Enterobacteriaceae</em></td>
<td>18 (21.4%)</td>
</tr>
<tr>
<td><em>Streptococcus pneumonia</em></td>
<td>11 (13%)</td>
</tr>
<tr>
<td><em>E.coli</em></td>
<td>2 (2.38%)</td>
</tr>
</tbody>
</table>

**TABLE III**: ANTIBIOTIC RESISTANT PATTERNS IN GRAM – NEGATIVES

<table>
<thead>
<tr>
<th>PATHOGENS</th>
<th>ANTIBIOTICS</th>
<th>RESISTANCE n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>TAZOBACTUM/PIPERACILLIN</td>
<td>6/29 (20%)</td>
</tr>
<tr>
<td></td>
<td>MEROPENEM</td>
<td>5/29 (17%)</td>
</tr>
<tr>
<td></td>
<td>CEFTAZIDIME</td>
<td>10/29 (34.4%)</td>
</tr>
<tr>
<td></td>
<td>CIPROFLOXACIN</td>
<td>14/29 (48.2%)</td>
</tr>
<tr>
<td></td>
<td>AMIKACIN</td>
<td>9/29 (31%)</td>
</tr>
<tr>
<td></td>
<td>POLYMIXIN</td>
<td>0/29 (0%)</td>
</tr>
<tr>
<td></td>
<td>MULTIDRUG RESISTANT(MDR)</td>
<td>5/29 (17%)</td>
</tr>
<tr>
<td><em>Acinetobacter spp</em></td>
<td>TAZOBACTUM/PIPERACILLIN</td>
<td>12/19 (63%)</td>
</tr>
<tr>
<td></td>
<td>MEROPENEM</td>
<td>11/19 (57.8%)</td>
</tr>
<tr>
<td></td>
<td>CEFTAZIDIME</td>
<td>19/19 (100%)</td>
</tr>
</tbody>
</table>
CIPROFLOXACIN 14/19 (73.6%)

AMIKACIN 14/19 (73.6%)

POLYMYXIN 0/19 (0%)

MULTIDRUG RESISTANT(MDR) 10/19 (52%)

Enterobacter spp TAZOBACTUM/PIPERACILLIN 6/18 (33.3%)

MEROPENEM 7/18 (38.8%)

CEFTAZIDIME 11/18 (61.1%)

CIPROFLOXACIN 9/18 (50%)

AMIKACIN 7/18 (38.8%)

MULTIDRUG RESISTANT(MDR) 3/18 (16%)

DISCUSSION:
Nosocomial infection is one of the major health problems, being faced by health care workers. The ventilator associated pneumonias (VAP) are the nosocomial infections associated with high mortality rates and diverse groups of bacteria being involved. These bacteria are usually resistant to many of the routine antibiotics available. Ventilator associated pneumonia not only increases the duration of ICU stay but also increases the burden in the term of cost of treatment. That's why knowledge incidence and identification of causative factors is of utmost importance. It also help to select suitable empirical therapy for early control of infection.

The incidence of VAP is higher in Asian countries as compared to Europe where its around 15-40%. In our study the incidence of VAP was found to be 30.5%, which was comparable to most of the studies in the region. We also observed that increase chances VAP was found in chronic illnesses like Chronic Obstructive Pulmonary Disease (COPD).

The common organisms identified in our study were *Pseudomonas aeruginosa, Staphylococcus aureus*, Acinetobacter and enterococcus, which are similar to other Asian studies. Throughout the world, there is an increase incidence of multi-drug resistance in Gram negative rods especially Pseudomonas and Acinetobacter, especially to fluoroquinolones, ceftazidime and aminoglycosides, which is becoming a major heath problem in treating serious infections like VAP.

Chung et al conducted a surveillance study in 73 hospitals of 10 Asian countries in year 2008 concluded that Acinetobacter, Pseudomonas, *Staphylococcus aureus* and Klebsella were major pathogens. Carbapenem resistance in Acinetobacter and Pseudomonas were 67.3% and 27.2% respectively while MDR and XDR rates were 82% and 42% respectively. While in our study resistance to carbapenems in Acinetobacter and pseudomonas were much less i.e 57% and 17% respectively; MDR rates were also much less in Acinetobacter and pseudomonas 52% and 17% respectively.

Sarauv et al conducted a study in India where major pathogens were Klebsella, Acinetobacter and pseudomonas. MDR infection was observed in 40% of cases especially Acinetobacter and pseudomonas.

Golia et al conducted a study in India found incidence of VAP was 35%. The major pathogens were pseudomonas, E.coli, Acinetobacter baumanii. The incidence of MDR in Acinetobacter and pseudomonas was 37% and 40% respectively.
We observed that VAP not only increased the total ICU stay but also the chances of VAP were also increased with prolonged ventilation, 87% of VAP cases were clinically diagnosed after 5 days of ventilation, this result was also observed in other studies. Similarly VAP also increased the overall mortality. In our study it was found to be 60%. Gadani et al estimated 54% mortality due to VAP while Gupta et al estimated 46% mortality due to VAP.

Even though most of the preventive measures are being taken in our ICU, like hand washing, sterile gloves and gown, isolation, povidone scrubbing of skin before invasive procedures, elevation of head at 30 degrees, sterile ICU procedures especially endotracheal Intubation and oropharyngeal suctioning and proper mouth care, still the prevalence of MDR GNBs and higher mortality rates, suggests more intensive and careful nursing techniques. By the virtue of this study we have aware of higher incidence of VAP and also the percentage of MDR organisms in our ICU. This demands more serious measures to decrease the rate of VAP.

CONCLUSION:
Prevalence of VAP in our hospital is comparable to the other hospitals in the region, with majority due Gram negative bacilli. Occurrence of VAP not only increases the ICU stay but also the overall mortality in ICU population. More efforts are needed to improve the nursing care, judicious use of broad spectrum antibiotics to control the risk of VAP. Organized awareness programs are needed to increase the knowledge in medical and paramedical staff to enhance the knowledge about VAP and its prevention. Further studies are needed to determine various risk factors responsible for VAP in our ICU as well as to assess the efficacy of various preventive measures to minimize the occurrence of VAP.

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REFERENCES:


