**Orginal Article**

# Ventilator-associated pneumonia in Coronary Care Unit of a tertiary level hospital in Bangladesh: causative organisms and pattern of antibiotic sensitivity

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**Abstract:**

***Background:*** *Ventilator-Associated Pneumonia (VAP) is a frequent nosocomial infection. The etiology of VAP varies with different patient populations and types of critical care settings.*

***Materials & methods:*** *This prospective observational study was conducted at the Coronary Care Unit (CCU) of Ibrahim Cardiac Hospital & Research Institute from April 2016 to November 2016. Demographic details and incidence of VAP was recorded and analysed by appropriate statistical tests.*

***Results:*** *52 patients required mechanical ventilation, of whom 19 (36.5%) developed VAP. 15 (78.9%) had early VAP, while 4 (21.2%) had late VAP. CPIS, Modified CPIS and APACHE II Score- all were significantly higher among those who developed VAP ($p<0.01$). The most frequent indication for intubation among those who developed VAP was type I respiratory failure (57.9%), type II respiratory failure (15.8%) and post-cardiac arrest (26.3%). Acinetobacter (31.6%) was the commonest organism isolated on tracheal aspirate, followed by Pseudomonas (21.05%), Candida (21.05%) and Klebsiella (10.5%). Acinetobacter, Klebsiella and MRSA were the organisms isolated from tracheal aspirates of those with late onset VAP. Acinetobacter was mostly sensitive to Colistin, 80% of Pseudomonas is also sensitive to same. A number of organisms were resistant to Amikacin and Imipenem.*

***Conclusion****: The commonest organism responsible for VAP in our CCU was Acinetobacter, which was largely sensitive to Colistin. The emergence of antibiotic resistance of microorganisms causing VAP is a matter of serious concern in this study. Regular surveillance of antibiotic susceptibility pattern is very important to prevent multi-resistant bacterial infections.*

***Key words:*** *Ventilator-Associated Pneumonia (VAP), Multi drug resistant (MDR), Coronary Care Unit (CCU), invasive mechanical ventilation (IMV).*

## Introduction:

Invasive mechanical ventilation is an essential life support given to many patients in the coronary care unit (CCU). The majority of patients admitted, suffer from acute coronary syndrome (ACS) and may develop serious multi-organ complications requiring prolonged intensive care including intubation and mechanical ventilation.

The principal indications for invasive mechanical ventilation in CCU are acute respiratory failure due to pulmonary oedema and resuscitated cardio-respiratory arrest. VAP is a nosocomial pneumonia occurring more than 48 hours after endotracheal intubation and initiation of mechanical ventilation, including pneumonia developing even after extubation[1]. VAP is the most frequent intensive care unit (ICU) acquired infection, occurring in 9 to 24% of patients intubated for longer than 48 hours[2,3].

The etiological agents of VAP vary with different patient populations and types of ICUs and CCUs[1,4]. Hence, it is beneficial to study the local microbial flora causing VAP in each setting, and as such guide to more effective and rational utilization of antimicrobial agents.

VAP is defined as nosocomial pneumonia that occurs 48 to 72 hours or thereafter following endotracheal intubation, characterized by the presence of a new or progressive infiltrate, signs of systemic infection, changes in sputum characteristics, and detection of a causative agent[5-7]. Early-onset VAP is defined as occurring within the first 4 days of hospitalization.[4] Late-onset VAP is defined as occurring 5 days or more after hospitalization.[4]

Previous studies from Bangladesh have investigated common pathogens associated with VAP in ICU settings[5]. However, there is no data on the prevalence, causative organisms or antibiotic prescription practices in a CCU setting, where a number of patients are admitted with respiratory failure requiring mechanical ventilation. This study was aimed to investigate the incidence and characteristics of VAP among cardiac patients requiring invasive mechanical ventilation in CCU, and the antibiotic prescription practices which were influenced by the causative organisms and their antibiotic sensitivity.

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## METHODOLOGY:

This prospective observational study was conducted at the CCU of Ibrahim Cardiac Hospital & Research Institute from April 2016 to November 2016. The study included all consecutive patients admitted to the CCU and requiring assisted mechanical ventilation irrespective of indication for intubation. This study was approved by the hospital Ethical Review Committee, and informed consent was obtained from each patient's next of kin.

All patients included in the study were monitored daily for the development of VAP using clinical and microbiological criteria until either discharge or death. The clinical parameters were recorded from their medical records and bedside charts. Demographic variables, co-morbidities, diagnosis on admission, indication for intubation, clinical & biochemical/ laboratory variables and data pertaining to microorganisms isolated on tracheal aspirate and antibiotic prescription practices were recorded in predefined case report form.

The clinical pulmonary infection score (CPIS) was tabulated from the available data (includes temperature, leukocytes, tracheal aspirate volume and the purulence of tracheal secretions, chest X-ray, oxygenation - PaO2/FiO2 and the semi-quantitative culture of the tracheal aspirates). A clinical suspicion of VAP was made in patients with a Modified Clinical Pulmonary Infection Score (CPIS) >6[8]. The diagnosis was confirmed by performing a quantitative culture of the endotracheal aspirate and observing ≥ 105 cfu/ ml. [5,9,10]

The organisms isolated by quantitative culture of the endotracheal aspirate from VAP patients were identified based on standard microbiological techniques[11]. Antibiotic sensitivity was performed by Kirby Bauer's disc diffusion method as per Clinical and Laboratory Standards Institute (CLSI) guidelines 2015[11]. Extended spectrum beta lactamase (ESBL) testing was performed by combination disc method.

Data entry and analysis were done using SPSS for Windows Version SPSS 16.0 (SPSS Inc, Chicago, Illinois). Quantitative data were expressed as mean ± standard deviation and analyzed using Student's t-test for comparison of two groups of normally distributed variables. Qualitative data were expressed as number and percentage and analyzed using Chi-square and Fisher's exact tests. Univariate analysis was used to compare the variables for the outcome groups of interest. P <0.05 was considered statistically significant.

## RESULTS:

A total of 52 patients were on mechanical ventilation, of which 33 (63.5%) were male and 19 (36.5%) were female. Mean age was 64.76 ± 1.06 years. 29(55%) of the patients were subsequently extubated. 19 (36.5%) of intubated patients developed VAP. Demographic characteristics of the study subjects with comparison between VAP and Non-VAP patients are detailed in Table 1.

Patients with VAP were significantly more likely to have developed in patients with acute left ventricular failure (ALVF) (100% vs 81.8% for VAP vs non-VAP respectively, p=0.04) and anaemia (50% vs 29.7% for VAP vs non-VAP respectively, p=0.04). CPIS, Modified CPIS and APACHE II Score, all were significantly higher among those who developed VAP (p<0.01). Overall, 44 (84.6%) were hypertensive, 41 (78.8%) were diabetic, 22 (42.3%) were smokers and 28(53.8%) had chronic kidney disease (CKD). 15 (28.8%) of patients had a pre-existing respiratory disease (i.e.bronchial asthma or COPD, but not pneumonia). 0.6% of patients had concomitant valvular heart disease. 30 (57.7%) of patients were admitted with acute coronary syndrome. 52 (88.4%) had ALVF.

Among the 19 patients who developed VAP, 15 (78.9%) had early VAP, while 4 (21.2%) had late VAP, as diagnosed by microorganism growth on tracheal aspirate.

The most frequent indication for intubation among those who developed VAP was acute hypoxaemic (type I) respiratory failure (57.9%), followed by type II respiratory failure (15.8%) and post-cardiac arrest (26.3%).

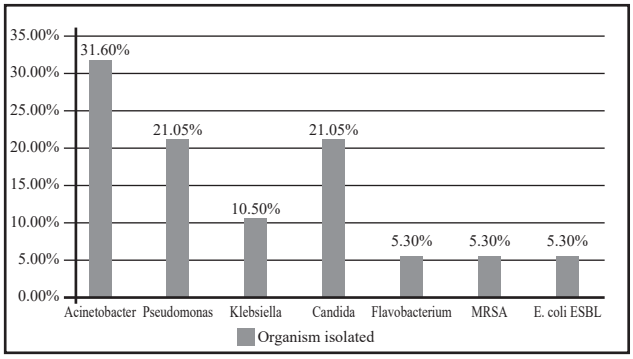


Figure 1

Figure 1 details the micro-organisms responsible for VAP. Acinetobacter (31.6%) was the commonest organism isolated on tracheal aspirate, followed by Pseudomonas (21.05%), Candida (21.05%) and Klebsiella (10.5%). Acinetobacter, Klebsiella and MRSA were the organisms isolated from tracheal aspirates of those with late on set VAP (Table 2).

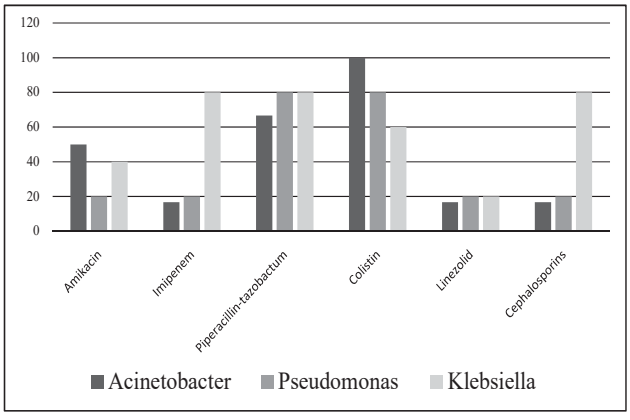


Figure 2 (sensitivity expressed as %)

Figure 2 details the antibiotic sensitivity patterns of Acinetobacter, Pseudomonas and Klebsiella. Acinetobacter was most sensitive to Colistin, to which sensitivity of Pseudomonas is of 80%. Klebsiella was mostly sensitive to Cephalosporins, Imipenem and Piperacillin-Tazobactum.

Figure 3 details the antibiotic resistance patterns of Acinetobacter, Pseudomonas and Klebsiella. 20% of Pseudomonas was resistant to Colistin. Klebsiella was most resistant to Amikacin, Imipenem. And cephalosporins.

In terms of outcomes, all 4 patients with late onset VAP were successfully extubated. However, 4 (26.7%) patients with early onset VAP expired in CCU.

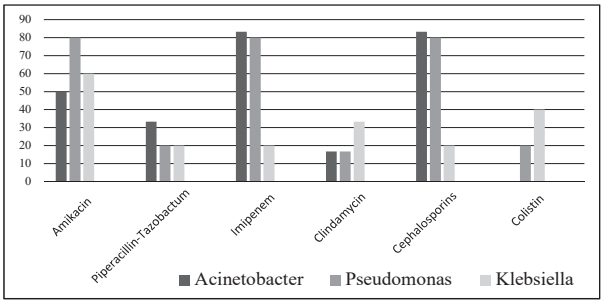


Figure 3 (Resistance expressed as %)

**TABLE 1:**

| Parameter | VAP | Non-VAP | Total *n* (%) | P value |
|---|---|---|---|---|
| n (%) | 19 (36.5) | 33 (63.5) | 52 (100) | |
| Age (years) | 65.31±8.89 | 64.48±11.72 | 64.76±1.06 | 0.17 |
| Hypertension *n* (%) | 17 (89.5) | 27 (81.8) | 44 (84.6) | 0.46 |
| Diabetes *n* (%) | 17 (89.5) | 24 (72.7) | 41 (78.8) | 0.15 |
| Smoking *n* (%) | 8 (42.1) | 14 (42.4) | 22 (42.3) | 0.98 |
| CKD *n* (%) | 12 (62.3) | 16 (48.5) | 28 (53.8) | 0.31 |
| ACS *n* (%) | 11 (59.7) | 19 (57.6) | 30 (57.7) | 0.98 |
| LVF *n* (%) | 19 (100) | 27 (81.8) | 46 (88.5) | 0.04 |
| Shock *n* (%) | 12 (62.3) | 18 (54.5) | 30 (57.7) | 0.54 |
| Pre-existing lung disease *n* (%) | 6 (31.6) | 9 (27.3) | 15 (28.8) | 0.74 |
| Resuscitated cardiac arrest *n* (%) | 9 (42.9) | 12 (57.1) | 21 (40.4) | 0.43 |
| CV catheter present *n* (%) | 18 (94.7) | 27 (81.8) | 45 (86.5) | 0.19 |
| Anaemia *n* (%) | 9 (50) | 6 (29.7) | 15 (31.9) | 0.04 |
| Extubated *n* (%) | 15 (78.9) | 14 (42.4) | 29 (55.8) | 0.01 |
| Expired *n* (%) | 4 (17.4) | 19 (82.6) | 23 (44.2) | 0.01 |
| CPIS | 6.84±1.21 | 5.87±1.51 | 6.23±1.48 | 0.02 |
| Modified CPIS | 8.84±1.21 | 5.87±1.51 | 6.96±2.01 | <0.01 |
| GCS | 7.73±2.74 | 7.94±2.32 | 7.86±2.45 | 0.77 |
| APACHE II Score | 33.11±8.63 | 29.97±7.15 | 31.14±7.8 | 0.16 |

ACS = Acute coronary syndrome; APACHE II= Acute Physiology, Age, Chronic Health Evaluation II; CPIS = Clinical pulmonary infection score; CKD = Chronic Kidney Disease; GCS = Glasgow come scale; LVF= Left ventricular failure

**Table 2:** (n= 19)

| Organism | Early onset VAP | Late-onset VAP | Total n (%) |
|---|---|---|---|
| Acinetobacter | 4 | 2 | 6 (31.6%) |
| Pseudomonas | 4 | 0 | 4 (21.05%) |
| Klebsiella | 1 | 1 | 2 (10.5%) |
| Candida | 4 | 0 | 4 (21.05%) |
| Flavobacterium | 1 | 0 | 1 (5.3%) |
| MRSA | 0 | 1 | 1 (5.3%) |
| E coli ESBL | 1 | 0 | 1 (5.3%) |

MRSA= Methicillin-resistant Staphylococcus aureus; ESBL= Extended spectrum beta (ß) lactamase

## DISCUSSION:

VAP is an important nosocomial infection even among cardiac patients. The pathogenic organisms responsible for VAP in our institute's CCU has striking similarity to that of another Bangladeshi study conducted in ICU setting, where Acinetobacter, Pseudomonas, Klebsiella and Candida were the leading organisms responsible for VAP.[5]

The emergence of antibiotic resistant organisms causing VAP remains a cause for serious concern and highlights the need for treatment of the VAP cases with second-line antibiotics effective against these MDR pathogens. Furthermore, the need for stringent preventive measures for VAP cannot be over-emphasized, especially given that the treatment of an established VAP becomes very expensive.[12]

Although early-onset VAP, is known to be less severe and associated with a better prognosis, in our study, 26.7% of early VAP patients could not be extubated and succumbed, while all 4 patients with late onset VAP were successfully extubated. This finding is in general inconsistent with the literature, [4] and could be confounded by comorbid conditions of heart disease in our patient subset.

Antimicrobial resistance is an increasingly emerging problem worldwide, especially in ICUs and also CCUs´, and as such it is important to be wary of contemporary antibiotic resistance patterns especially when starting empirical antibiotics to treat VAP. Another important observation of our study is the sensitivity of gram-negative organisms to colistin, which has been observed in similar studies in Bangladesh also.

## LIMITATIONS:

The study was conducted in a resource-limited setting. Only a small number of patients with VAP in a single center were studied. This could be considered a limitation of our study. In addition, we recognize that the findings of this study may not necessarily reflect the situation in other similar centers in Bangladesh. Hence, we suggest further multi-centered studies with larger numbers of patients to confirm our findings, in particular the high incidence of MDR pathogens.

## CONCLUSION:

The commonest organism responsible for VAP in our CCU was Acinetobacter, which was largely sensitive to Colistin. The emergence of antibiotic resistance against many microorganisms causing VAP is a matter of serious concern in this study. A knowledge of the antibiotic susceptibility of the organisms isolated in the CCU helps to formulate an antibiotic policy and can guide clinicians in choosing empirical therapy. Adequate attention must also be paid to treatment of co-morbid conditions.

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