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Original Article

Microbial Pattern and Their Sensitivity of Ventilator Associated Pneumonia in an Intensive Care Unit of a Tertiary Care Hospital in Dhaka

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ABSTRACT:

Background: *ICU admission imposes great risk of nosocomial infections on the patients due to various invasive interventions. Patients treated in these units receive invasive procedures such as endotracheal intubation and mechanical ventilation which predispose to a nosocomial pneumonia of a special entity named as 'Ventilator Associated Pneumonia'. Almost half of all the cases of hospital acquired pneumonia are due to VAP and about half of all antibiotics administration in ICU are for treatment of Ventilator Associated Pneumonia.*

Objectives: *objective of the current study was to study the local microbiological profile of ventilator associated pneumonia and their sensitivity pattern in the Critical Care department of BIRDEM general hospital.*

Design: *Cross-sectional study.*

Setting: *ICU of an academic tertiary care hospital in the period of July 2017 to June 2018.*

Methods: *All consecutive patients who were intubated and mechanically ventilated for a period of at least 48 hours within the study period were evaluated for the selection criteria of the study. The included study participants were followed up daily for signs of development of VAP. Once VAP was suspected pertinent investigations were sent to confirm the diagnosis. Tracheal aspirate was collected using conventional specimen trap and aseptic endotracheal suctioning technique and sent for Gram staining and culture and sensitivity testing.*

Results: *In this study total 92 patients out of 625 intubated patients during the study period after fulfilling the inclusion criteria were selected as study participants. 35 participants out of 92developed VAP. Only 1 (2.9 %) patient did not yield any microbial growth in the tracheal aspirate sample and 34 (97.2 %) participants had growth of organisms in their tracheal aspirate samples. Total growths of 45 organisms were found in respiratory secretions of 34 VAP patients. The commonest organism was Acinetobacter which was grown in 21 (46.7%) samples followed by Pseudomonas in 10 (22.2%) samples; Klebsiella in 8 (17.8%) samples; Staphylococcus aureus in 3 (6.7%) samples; Candida in 2 (4.4%) and Enterococcus in 1 sample (2.2%). Most of the bacteria grown in the tracheal aspirates of VAP positive participants were sensitive to less than three antibiotic classes.*

Conclusion: *Multidrug resistant organisms are mostly responsible for both early and late onset VAP in ICU.*

Keywords: *VAP, MDR, CPIS.*

Introduction

Ventilator-associated pneumonia (VAP) is the most common nosocomial infection among patients admitted in intensive care units (ICUs) despite advances in preventive strategies, diagnostic techniques, and treatment modalities. It results in high morbidity and mortality, prolonged lengths and increased cost of hospitalization .[1]

Almost half of all the cases of hospital acquired pneumonia are due to VAP and about half of all antibiotic administrations in ICU are for treatment of VAP.[2] American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) guidelines, 2005 on management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia suggested that a diagnosis of VAP may be considered when pneumonia develop in patients who have been receiving mechanical ventilation for at least 48 hours, characterized by the presence of a new or progressive infiltrate in CXR, signs of systemic infection (fever, altered white blood cell count), changes in sputum characteristics, and detection of a causative agent in respiratory secretion.[3] VAP may be further categorized into early-onset VAP (within 4 days) and late-onset VAP (beyond 4 days) (ATS/IDSA) [guidelines 2016].[4]

VAP results in high morbidity and mortality, prolonged lengths and increased cost of hospitalization. This excess morbidity results in estimated costs per case of nearly US$15,000 .[5] VAP rates range from 1.2 to 8.5 per 1,000 ventilator days and are reliant on the definition used for diagnosis. [6]

The causative organisms differ according to the patients' characteristics, the duration of ICU stay, and the antibiotic policy of the institution.[1] Moreover, the microorganisms responsible and their sensitivity pattern change from time to time within an ICU. Organisms responsible usually depend on

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pre-existing lung pathology, the duration of mechanical ventilation and organisms prevailing in the ICU environment. It has been suggested that bacteria causing early-onset VAP are usually antibiotic sensitive including Streptococcus pneumoniae (as well as other streptococcus species), Haemophilus influenzae, Methicillin-sensitive Staphylococcus aureus (MSSA), antibiotic-sensitive enteric Gram-negative bacilli such as Escherichia coli, Klebsiella pneumonia, Enterobacter species, Proteus species and Serratia marcescens. Causatives of late-onset VAP are typically MDR bacteria, such as methicillin-resistant S. aureus (MRSA), Acinetobacter, Pseudomonas aeruginosa, and extended-spectrum beta-lactamase producing bacteria (ESBL).[2]

Combes et al (2002) has shown in his study high rate of polymicrobial infection in VAP without any significant outcome difference.[5]

Therefore, the associated microbial flora needs to be studied in a local setting as a part of infection control surveillance program and also to allow more effective and rational utilization of antimicrobial agents.

Material and Methods

This cross-sectional study was carried out in the Intensive Care Unit of Department of Critical Care Medicine (ICU) of BIRDEM General Hospital, Dhaka, over a period of 12 months in 2017-18. All intubated and mechanically ventilated patients aged above 18 years who were kept intubated for a duration of more than 48 hours were included as study participants by consecutive sampling. Those who were suspected or confirmed as having community-acquired pneumonia, nosocomial pneumonia or ARDS on admission were excluded. Patients intubated in other ICUs prior to admission, patients intubated for less than 48 hours and patients developing pneumonia within 48 hours of intubation were also excluded from the study.

The indication for intubation and MV (Mechanical Ventilation) were respiratory failure, cardiac arrest, airway protection. The endotracheal tube used in the ICU were not antibiotic coated and two types of tubes were used (conventional and tube with subglottic suction lumen). Informed written consent was taken from participants' first degree relatives as the participants were unable to communicate properly due to presence of endotracheal tubes and sedations provided during mechanical ventilation. Study participants were observed regularly to identify signs of pulmonary infection. Once VAP was suspected clinically, complete blood count, portable CXR was advised and tracheal aspirate was collected using conventional specimen trap and aseptic endotracheal suctioning technique and sent for Gram staining, AFB staining, culture and sensitivity testing. Quantitative culture was done (expressed as CFU/ml) and antibiotic sensitivity was done by standard disc diffusion method. A cutoff value of 10^5 CFU/ml was taken as a positive culture. CPIS (Clinical Pulmonary Infection Score) was calculated to diagnose VAP.[7] Participants who were readmitted to the ICU after initial improvement, only the first admission was included in the study.

Appropriate data was collected by using a preformed data sheet. Necessary data including patients' particulars, age, gender, primary diagnosis on admission, comorbidities, indication for intubation and ventilation, date of intubation, physical examination findings and laboratory investigations on admission and on diagnosis of VAP was documented from history sheet and investigation papers.

Collected data was processed and analyzed by using Statistical Package for Social Sciences (SPSS) software version 22. All the descriptive data were expressed by frequency and percentage (%). All the quantitative data were expressed in mean ± SD. Unpaired t test and chi-square tests were performed to assess significance of association between the variables. The level of significance was accepted as <0.05 P value.

Ethical approval from the Institutional Review Board of BIRDEM was obtained prior to the commencement of the study. Informed written consent was taken from the participants family members after explaining all the facts. As the procedure involved in the study were of minimal risk, no further potential ethical issue was to be raised. The participants were assured of confidentiality.

Results

During the study period a total of 1563 patients were admitted into the ICU and 625 patients were intubated. 92 patients had fulfilled the inclusion criteria and were selected as study participants.

Table I shows frequency of Early and Late VAP (n=35)

Table III

Type of VAP	Frequency (n)	Percentage (%)
Early VAP	18	51.4
Late VAP	17	48.6
Total	**35**	**100.0**

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Table II shows microbial growthin tracheal aspirates of the study participants developing VAP (n=35)

Table IV

	Frequency (n)	Percentage (%)
VAP	35	
No growth	1	2.9
Growth	34	97.1
Monomicrobial	25	73.5
Polymicrobial	9	26.5
2 organisms	7	77.8
3 organisms	2	22.2

VAP: ventilator associated pneumonia

Data are expressed as frequency and percentage.

Table III shows pattern of microbial growth in the VAP positive participants

Table V

Microbial growth pattern	VAP	
	Early (n=21)	Late (n=24)
Pseudomonas	6 (28.6)	4 (16.7)
Staph aureus	1 (4.8)	2 (8.3)
Klebsiella	5 (23.8)	3 (12.5)
Acinetobacter	6 (28.6)	15 (62.5)
Enterococcus	1 (4.8)	0
Candida	2 (9.4)	0

Figure 1 shows Pie chart of micro-organism detected in the respiratory secretions of the study participants developing VAP

Figure 1

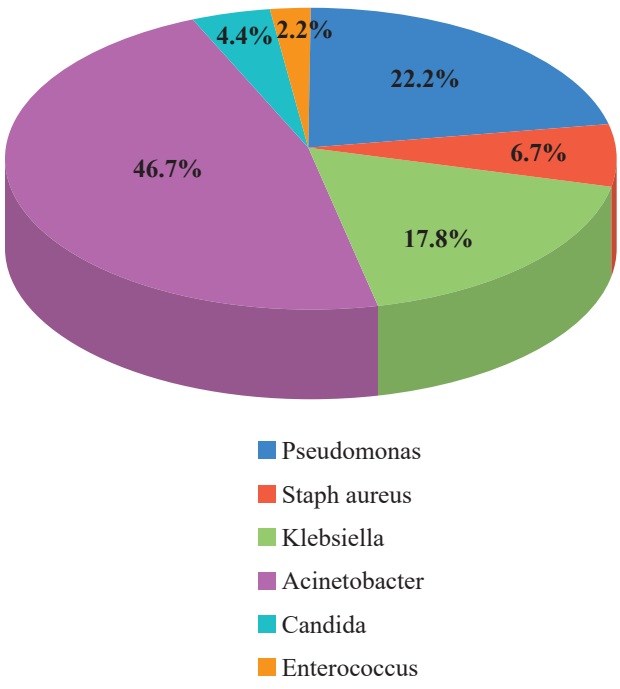

Table IV shows antibiotic sensitivity pattern of the bacterial isolates

Table IV

	Pseudomonas (n=10)	Staph aureus (n=3)	Klebsiella (n=8)	Acinetobacter (n=21)	Enterococci (n=1)
Amikacin	2 (20.0)	2 (66.7)	1 (12.5)	0 (0.0)	0 (0.0)
Colistin	7 (70.0)	0 (0.0)	8 (100.0)	21 (100.0)	0 (0.0)
Piperacillin	4 (40.0)	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)
Vancomycin	0 (0.0)	3(100.0)	0 (0.0)	0 (0.0)	1 (100.0)
Rifampicin	0 (0.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
Cotrimoxazole	2 (20.0)	1 (33.3)	1 12.5)	2 (9.5)	0 (0.0)
Netilmicin	0 (0.0)	1 (33.3)	1 12.5)	2 (9.5)	0 (0.0)
Imipenem	4 (40.0)	0 (0.0)	2 (25.0)	0 (0.0)	0 (0.0)
Tigecycline*	1(10.0)	0 (0.0)	5 (62.5)	17 (81)	0 (0.0)
Ceftazidime	2 (20.0)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)

Data were expressed as frequency and percentage

Multiple responses

*Although Pseudomonas is considered intrinsically resistant to Tigecycline we found in vitro sensitivity for 1 pseudomonas isolate. The clinical significance can't be evaluated.

Discussion

A significant number of studies has been conducted in an attempt to establish a definite diagnostic criteria. Nevertheless, there remains debate regarding the diagnosis. CDC adopted a diagnostic strategy combining clinical, radiological and microbiological criteria. Pugin et al. introduced a scoring system called CPIS (Clinical Pulmonary Infection Score) based on 6 criteria. Score ranges from 0 to 12 with a score of ≥ 6 showing good correlation with the presence of VAP.[7] The Clinical Pulmonary Infection Score (CPIS) includes clinical, physiological, microbiological and radiographic evidence to calculate a numerical value to predict the presence or absence of VAP. One meta-analysis of 13 studies evaluating the accuracy of CPIS in diagnosing VAP reported sensitivity and specificity for CPIS as 65 % and 64% respectively.[8]

Microbiological growth and their sensitivity pattern varies between different ICUs depending on the patient population studied, local microorganism prevalence pattern. [6,9,10]

In this study, among the 35 VAP positive participants, 34 (97.1%) had growth of organisms in their tracheal aspirate samples and 1(2.9%) patient had no growth. Among the 34 participants with positive culture 25 (73.5%) participants had monomicrobial growth and 9 (26.5%) participants had polymicrobial growth. 7 participants out of 9 (77.8%) participants with polymicrobial growth had growth of two organisms and 2 participants out of 9 (22.2%) participants had growth of three organisms. Participants with polymicrobial growth had prolonged M/V duration prior to developing VAP. There was no difference in mortality among the participants with monomicrobial and polymicrobial VAP (72% vs 55.6%).

This finding was in accordance to a study done by Combes et al (2002) where no significant difference could be established for outcome parameters in monomicrobial and polymicrobial VAP.[5] Patil et al(2017) found 55.4% polymicrobial VAP and 44.59% monomicrobial VAP in an ICU of India. [11]

Ali et al (2016) found in a study done in Qatar that, single organism was isolated from respiratory specimen of 49% patients and ≥2 organisms isolated from 49% patients and cultures were negative in 2% patients. This finding is similar to our study.[1]

In this study, growth of 45 organisms were found in respiratory secretions of 34 VAP patients. The commonest organism was Acinetobacter which was grown in 21 (46.7%) samples followed by Pseudomonas in 10 (22.2%) samples; Klebsiella in 8 (17.8%) samples; Staphylococcus aureus in 3 (6.7%) samples; Candida in 2 (4.4%), Enterococcus in 1 sample (2.2%). Pseudomonas and Acinetobacter were equally responsible for early onset VAP and Acinetobacter was the main causative organism for late onset VAP. This finding was consistent with findings of Mallick et al.(2015) who found that in late-onset VAP, Acinetobacter was the commonest causative organism while in early-onset VAP, Pseudomonas was the commonest causative organism. Similar pattern was noticed in Indian ICUs.[12] Kant et al (2015) conducted a study in indian ICU where Acinetobacter (25.37%) was the most common isolate followed by pseudomonas (17.91%), Staphylococcus aureus (17.91%), Klebsiella (10.44%), and Enterobacter (8.9%).[13]

But this finding ,where both early and late VAP are caused by similar organisms was in contrary to the usual belief that organisms responsible for early onset VAP are similar to community acquired pneumonia like Streptococcus, MSSA, drug sensitive Gram negative bacteria. The reason behind this is probably the fact that almost all the participants in the study received antibiotic prior to admission to ICU or on admission to ICU as prophylaxis or pre-emptive therapy. And use of antibiotic increase colonization by resistant pathogens.[6]

In the current study, among the 21 Acinetobacter isolates, 100% were sensitive to Colistin followed by 17(81%) to Tigecycline. Sensitivity to other anti -Gram negative antibiotics were poor, 0% to Imipenen; 2(9.5%) to Netilmicin and cotrimoxazole. Among the 10 Pseudomonas isolates 7(70%) were sensitive to Colistin; 4(40%) to Piperacillin-Tazobactam, 4(40%) to Imipenem, 2(20%) to Amikacin, 2(20%) to Ceftazidime, 1(10%) to Tigecycline. Growth of Staphylococcus aureus was found in only three samples. 2 out of 3 isolates (66.7%) were MRSA with 100% sensitivity to Vancomycin, 2(66.7%) were sensitive to Amikacin,1(33.3%) was sensitive to Rifampicin, Cotrimoxazole, Netilmicin and ceftazidime. Growth of MRSA was found in late onset VAP. 100% (n=8) of Klebsiella were sensitive to Colistin, 5(62.5%) to Tigecycline, 2(25%) to Piperacillin plus Tazobactam, 2(25%) to Imipenem, 1 (12.5%) to Amikacin,Netilmicin and Cotrimixazole. Only one sample had growth of Enterococcus which was sensitive only to Vancomycin. Candida was present in 2 samples. In one sample it was the only grown organism and in one sample it was present along with Klebsiella. 41 out of 43(95.3%) bacteria grown in both early and late VAP were resistant to more than three antibiotic classes. This may be due to the fact that the patients with early onset VAP who were hospitalized for a few days before intubation and received empirical antibiotics were colonized with MDR pathogens prior to developing VAP with these MDR pathogens.

Emergence of antibiotic resistance in critically ill patients imposes a great challenge for the intensivists worldwide. My study shows high rate of MDR pathogens responsible for VAP. Hundred percent Acinetobacter isolates were MDR. Three (14.3%) out of 21 Acinetobacter isolates were sensitive to Colistin only and 14(66.7%) were sensitive to Colistin and Tigecycline only. Two out of 10 Pseudomonas (80%) were MDR with 2(20%) Pseudomonas isolates being sensitive only to Colistin and 2(20%) being sensitive only to Colistin and Piperacillin-Tazobactam combination. One isolate was resistant to all antibiotics. Two out of 3 (66.7%) Staphylococcus aureus were MRSA and all Klebsiella were ESBL positive with 2(25%) being sensitive only to Colistin, 3(37.5%) to Colistin and Tigecycline only. This is in accordance to several studies, which concludes that MDR VAP is on the rise.[6] Kollef (2005) stated that MRSA strains are becoming an important cause of VAP.[14] Several studies implicated that, the use of empirical antibiotic on hospital

admission selects the resistant pathogens and increase the risk of infection with MDR pathogens with an higher mortality.[12,14,15]

Conclusion

This study showed majority of bacteria responsible for VAP were MDR irrespective of whether it was early or late onset in contrary to the common belief that bacterial pattern of early onset VAP is similar to community acquired pneumonia.

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