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MICROBIAL PROFILE AND RESISTANCE PATTERN OF PATHOGENS CAUSING VENTILATOR ASSOCIATED PNEUMONIA IN MECHANICALLY VENTILATED PATIENTS IN THE MEDICAL ICU OF A TERTIARY CARE HOSPITAL IN PUNJAB

Medical Microbiology

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ABSTRACT

Introduction: Ventilator-associated pneumonia (VAP) is a serious health care-associated infection. It prolongs hospital stay and drives up hospital costs reporting high morbidity and mortality. VAP is defined as pneumonia that occurs 48h or more after endotracheal intubation or tracheostomy, caused by infectious agents not present or incubating at the time mechanical ventilation. VAP requires rapid diagnosis and initiation of the appropriate antibiotics. **Materials and Methods:** The present study was done in the department of Microbiology, Christian Medical College & Hospital, Ludhiana. All the clinically suspected cases of VAP from intensive care units over a period of one and a half year were included in the study. Endotracheal aspirate (ETA) and bronchoalveolar lavage (BAL) samples were collected from all patients and processed. Identification was carried out according to standard biochemical tests. Sensitivity pattern was determined using Kirby-Bauer disc diffusion according to latest CLSI guidelines. **Results:** Out of 125 patients, who were on mechanical ventilation, 36 were culture positive. We report an incidence of 27.2% VAP in patients admitted at ICU. The major organisms isolated in the VAP patients were Acinetobacter spp. (58.82%), Klebsiella spp. (17.65%), Enterobacter spp. (14.71%), Pseudomonas spp. (8.82%), E. coli and non albicans Candida spp. (2.94%) each. Majority of the isolates were multi-drug resistant. All isolates combined; Metallo Beta Lactamase (MBL) producers were most common (60%). **Discussion and Conclusion:** Even in the era of advanced medical care VAP remains a major challenge. The risk of developing VAP can be reduced by VAP prevention care bundles. Timely diagnosis is a major step to initiate appropriate antibiotics for better outcomes. Both patients and units are at risk of developing multidrug–resistant organisms and therefore appropriate antibiotic stewardship is essential. Better knowledge of local patterns of pathogens causing VAP can help facilitate treatment choice, in turn reducing the ventilator days and hospital stay.

KEYWORDS

Ventilator-associated pneumonia (VAP), Intensive care units (ICU), Multi-drug resistant (MDR)pathogens, Acinetobacter spp.,

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a significant type of hospital-acquired infection; VAP is defined as pneumonia that occurs 48-72 hours or there after following endotracheal intubation, characterized by the presence of a new or progressive infiltrate, signs of systemic infection (fever, altered white blood cell count), changes in sputum characteristics and detection of a causative agent.[1] Nearly 50% of total cases of hospital-acquired pneumonia are caused by VAP.[2]

Even with heightened vigilance and advances in diagnostic methods, the identification of VAP in ventilated patients is riddled with hurdles due to the lack of a 'gold standard' for diagnosis and also due to incomplete data on etiologic agents and epidemiology.[3] VAP is typically bacterial and from a single organism. But, polymicrobial infections are on an increase.[4]

The etiology of VAP depends on multiple factors such as time of ventilation, prior administration of antibiotics, and the presence of chronic obstructive pulmonary disease, coma and local factors.[5] Gram-negative bacteria such as Pseudomonas spp., Escherichia coli, Klebsiella spp., Acinetobacter spp., and Gram-positive bacteria such as Staphylococcus aureus are the common causative pathogens of VAP. The prevalence of multidrug-resistant (MDR) organisms as a cause of VAP is also becoming a major health concern. [6]

Local microbial flora causing VAP needs to be studied in each setting to guide more effective and rational utilization of antimicrobial agents. So far there is scanty literature about incidence, bacteriology, and antibiotic susceptibility pattern about VAP in India. The initial empirical therapy of VAP is modified based on the knowledge of local microbiological data. Delay in starting appropriate antibiotic therapy can increase the mortality associated with VAP, and thus, therapy should be started immediately.[7] Although mechanical ventilation (MV) is a life-saving intervention, it has its own potential complications. Newer antibiotics in the past decade have not brought down the mortality in the critical care facilities across the world, associated with VAP.[8]

We conducted this study to provide an insight on the incidence, etiological agents and antibiotic susceptibility pattern of isolates causing VAP and to help establish guidelines for treatment of VAP in our ICU.

MATERIALS AND METHODS

This prospective observational cohort study was conducted in the Department of Microbiology at Christian Medical College and Hospital, a tertiary care teaching hospital in Ludhiana, for a duration of 1 and a half year from 1st Dec 2020 to 31st May 2022. The study population included were intubated patients in medical ICU who were > 18 years of age after clearance from Institutional Research Committee and Ethical Committee. The relevant clinical date of each patient was recorded. During the study period, 125 patients who were on mechanical ventilation were analyzed and diagnosis of VAP was made using modified clinical pulmonary infection score (CPIS) > 6. The endotracheal aspirates (ETA) and Mini bronchoalveolar lavage (MINIBAL) samples were collected using proper aseptic precautions and transported to the clinical microbiology laboratory without delay.

Direct microscopy was performed for each sample and organisms were identified on the basis of morphology, arrangement and Gram's reaction. The specimens showing >25 pus cells and <10 epithelial cells per low power field microscope and plenty of organisms under oil immersion were further processed.[9]

For this,10 µL of the specimens were inoculated on blood agar, MacConkey agar, nutrient agar and chocolate agar using 4 mm diameter inoculation loop which holds 0.01 ml of specimen. The culture plates were incubated at 37°C in an aerobic incubator. All plates were checked for growth overnight and then after 24 and 48 hours of incubation. The specimens showing growth of 10^5 CFU/ml of pathogenic organisms were considered significant.[10] Cultures with lower colony count were considered as colonization or contamination. The organisms isolated were identified based on their Gram staining properties, cultural characteristics and standard biochemical reactions.[11]

Antibiotic sensitivity tests testing (AST) was done by Kirby-Bauer disc diffusion method. The following antibiotics were used for

susceptibility testing: ampicillin, amoxyclav, cefuroxime, ceftazidime, cefepime, ciprofloxacin, gentamicin, amikacin, piperacillin, piperacillin+tazobactam, meropenem, imipenem, aztreonam, netilmycin, tigecycline, colistin, and co-trimoxazole. All the discs were procured from [Hi-media laboratories limited]. The diameter of the zone of inhibition was measured and interpreted according to the current Clinical and Laboratory Standards Institute (CLSI) guidelines.[12]

If the isolate was suspected to be an extended-spectrum beta lactamases (ESBL) producer, they were confirmed by double disk synergy test using Ceftriaxone (30 µg) and Ceftriaxone-Clavulanic acid (30 µg + 10 µg) as described in earlier studies. A zone diameter difference of more than 5 mm with the double discs confirmed that the isolates were ESBL producers.

Isolates showing reduced susceptibility to carbapenems (imipenem/ meropenem) were selected for detection of metallo-beta lactamases (MBLs) enzymes by imipenem-EDTA disk method. This was performed by Imipenem & EDTA combined disc test. Two (10 µg) imipenem discs were placed on a plate inoculated with the test isolate, and 10 µl of 0.5 M EDTA solution was added to one of the two discs. An increase in zone diameter of ≥ 7mm around imipenem + EDTA disk in comparison to imipenem disk alone indicated production of MBL.[12]

For quality control of disc diffusion tests ATCC control strains of Escherichia coli ATCC 25922, Staphylococcus aureus ATCC 25923 and Pseudomonas aeruginosa ATCC 27853 strains were used.

RESULTS

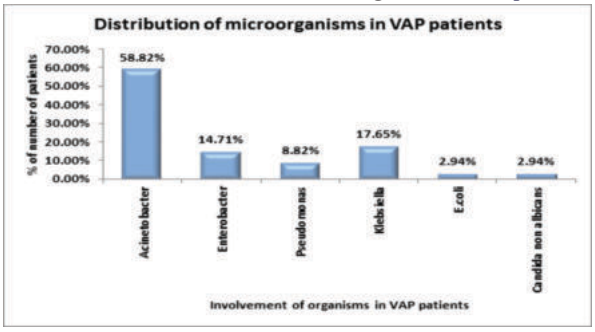
A total of 125 intubated patients >18 years of age admitted in medical ICU at CMC Hospital, Ludhiana were included in the study. Their clinical profile data, time and date of intubation was noted. After 48 hours of intubation any evidence of VAP was looked by based on CPIS score more than 6 and results are as follows.

The prevalence of ventilator associated pneumonia was 9% and we reported an incidence of 27.2% VAP in patients admitted at ICU. There majority of patients were in the age group of 61-70 years (24.80%). Mean value of age(years) of study subjects was 52.93 ± 16.9 with median (25th-75th percentile) of 56(43-65).

In our study, VAP was seen predominantly among male 74(59.20%) patients as compared to female 51(40.80%) patients.

Among the 36 confirmed cases of VAP, Acinetobacter spp. was isolated from 20(58.82%) patients followed by Klebsiella spp. 6(17.65%), Enterobacter spp. 5(14.71%) and Pseudomonas spp. 3(8.82%). E.coli and Candida non albicans infections were seen in only 1 patient (2.94%) each.(Table 1).

Table 1:-Distribution of involvement of organisms in VAP patients.



The antimicrobial resistance pattern seen in Acinetobacter spp. was predominantly MBL producers (65%) followed by ESBL producers (25%) whereas only (10%) were pan sensitive. Majority (60%) of Enterobacter isolates were also MBL producers. Among Klebsiella spp. and Pseudomonas spp. the percentage distribution of MBL producers and pan sensitive strains was equal.

For all organisms combined together, MBL resistance (60%) was the most common pattern that emerged. (Table 2, Figure 1).

Table 2:-Distribution of antibiotic sensitivity pattern in various organism.

Antibiotic sensitivity pattern	Acinetobacter (n=20)	E.coli (n=1)	Enterobacter (n=5)	Klebsiella (n=6)	Pseudomonas (n=3)	Total
Pan sensitive	2 (10%)	0 (0%)	1 (20%)	3 (50%)	0 (0%)	6 (17.14%)
Extended spectrum beta lactamase	5 (25%)	0 (0%)	1 (20%)	0 (0%)	1 (33.33%)	7(20%)
MetalloBeta Lactamase	13 (65%)	1 (100%	3 (60%)	3 (50%)	1 (33.33%)	21 (60%)
AMP-C	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (33.33%)	1 (2.86%)

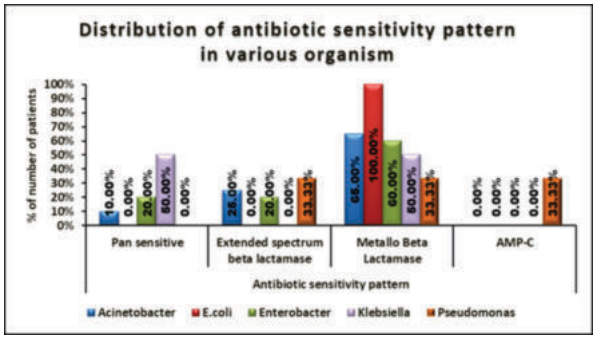


Figure 1: -Distribution of antibiotic sensitivity pattern in various organism

DISCUSSION

Even with the implementation of strict hospital infection control practices VAP remain as an enduring hitch in the critical care units. 28% of patients who receive mechanical ventilation in the critical care units are at risk of developing VAP. Knowledge on local pathogens and their sensitivity patterns causing VAP is a preliminary requisite to facilitate treatment choice, thus reducing the ventilator days and hospital stay.[13]

We report an incidence of 27.2% VAP in patients admitted at ICU. This is in concordance with findings from other similar studies by Patil et al (27.71%,) and Rit K et al (20%) on the other hand Ranjan et al reported a higher incidence (57.14%).[14,15,16] There may be variation in the incidence of VAP that depends on the condition of the patient, diagnosis as well as the duration of use of ventilator. Also, our lower VAP incidence could be because of strict vigilance on infection control practices, adequate nursing staff and stern convenance of VAP prevention care bundles.

We observed the mean age of the patients with VAP was 52.93 ± 16.9 years with a male preponderance. Bhattacharjee S et al and John et al. also reported that VAP was highest among this demographic.[17,18]

In our study, organisms causing VAP included Acinetobacter baumannii 20(16%), Klebsiella pneumoniae 6(4.80%), Enterobacter 5(4%), Pseudomonas 3(2.40%), and single case each of E. coli and Candida non albicans. This is in correlation with the bacteriological profile reported by Bhattacharjee S et al where were Acinetobacter baumannii was isolated in majority of the patients.[17] Joseph et al, from JIPMER, Pondicherry also reported Gram-negative bacteria (80.90%) accounting for majority of the cases of VAP.[19] International studies have also reported that majority of isolates were gram-negative bacteria among VAP group patients.[18,20]

VAP by multi-drug resistance organisms is an emerging global health concern. We observed that almost all the isolates were multidrug resistant pathogens. Majority of the isolates of E. coli (100%), Acinetobacter spp.(65%), Enterobacter spp.(60%) and Klebsiella spp.(50%) were MBL producers. The second most common resistance pattern was ESBL producers see in Pseudomonas (33.33%), Acinetobacter spp. (25%) and Enterobacter spp. (20%). Very few isolates were pan-sensitive. Other studies by Bhattacharjee S et al, and Maebed AZ et al found that the *Acinetobacter* isolates showed significant resistance with majority of antibiotics demonstrating pan and extensively drug resistance patterns.[17,21]

There is enough evidence to indicate that VAP is preventable and that

hospitals can decrease VAP rates, a factor that the new Centers for Disease Control and Prevention (CDC) VAP definitions are poised to demonstrate more objectively. The diagnostic challenge of VAP has multiple implications for therapy. Microbiological data should be used for tailoring antibiotic therapy and not be restricted only to diagnosis. The pitfall in using empirical antibiotics for suspicion of VAP is the potential for antibiotic overuse, emergence of multi drug resistance, unnecessary adverse effects and potential toxicity. The major goals of VAP management are early, appropriate antibiotics in adequate doses followed by de-escalation based on microbiological culture results and the clinical response of the patient.

Stringent Antimicrobial stewardship programs and time proven pprevention strategies like necessary barrier precautions, contact isolation of the patients with VAP and maintaining recommended nurse to patient ratio are to be emphasized in ICUs to reduce the burden of transmission of colonized MDR organisms in the hospitalized patients will impact the incidence of VAP in a positive manner and allow the best clinical outcome.

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Conflicts of interest
There are no conflicts of interest.

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