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ORIGINAL RESEARCH ARTICLE

BACTERIOLOGY AND ANTIBIOTIC SENSITIVITY PATTERNS IN VENTILATOR-ASSOCIATED PNEUMONIA

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ABSTRACT

Background: Ventilator-Associated Pneumonia is the most common cause of hospital-acquired infections among patients admitted in Intensive Care Unit with mechanical ventilation. Identification of bacteria and their susceptibility to commonly used antibiotics is very essential for the treatment of the patients. The aim of this study was to determine the bacteriological profile and antibiotic sensitivity patterns in the Endotracheal Aspirate cultures that were sent in Microbiology laboratory.

Methods: A hospital-based 3-year retrospective analysis on culture of Endotracheal Aspirate was done. Data from Intensive Care Unit was collected from January 2018 to January 2021, and the laboratory reports were used to determine Ventilator-Associated Pneumonia, pathogen profile and antimicrobial sensitivity patterns. Data entry and analysis was done using Statistical Package for Social Sciences version 16.

Results: Out of 147 ventilated patients in Intensive Care Unit, 115 samples were sent to microbiology laboratory with suspected Ventilator-Associated Pneumonia among which 95 (82.60 %) were positive cultures. The most common etiological agent causing Ventilator-Associated Pneumonia was found to be *Klebsiella pneumoniae* with 24 isolates (25.26%) and multidrug resistance was also mainly found with *Klebsiella pneumoniae* in 17 samples (70.83%). All of the gram-negative isolates were sensitive to colistin and resistant to ampicillin. All gram-positive isolates were sensitive of linezolid and vancomycin and most were resistant to penicillin.

Conclusions: *Klebsiella pneumoniae* is one of the most common organisms that is associated with nosocomial infection like Ventilator-Associated Pneumonia. The emergence of multidrug resistance is still a great threat and hindrance for the treatment of Ventilator-Associated Pneumonia.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a type of nosocomial pneumonia that occurs in patients who receive mechanical ventilation.[1] VAP is usually acquired in the hospital setting approximately 48–72 hours after mechanical ventilation.[1]
VAP contributes to approximately half of all cases of hospital-acquired pneumonia.[2] Approximately 10-28% of critical care patients develop VAP[3], which is still one of the main causes of morbidity and mortality despite the advancements in the antimicrobial regime. Detection of the causative organism is essential for the confirmation of VAP. The American Thoracic society (ATS) guidelines recommend quantitative cultures be performed on Endotracheal Aspirate (EA) or Broncho-alveolar lavage (BAL).[1] Most cases of VAP are caused by bacterial pathogens that normally colonize the oropharynx and gut or that are acquired via transmission by healthcare workers from environmental surfaces or from other patients.[4] Antibiotic resistant pathogens like *Pseudomonas*, *Acinetobacter* species and methicillin resistant strains of *Staphylococcus aureus* are more common after prior antibiotic treatment, prolonged hospitalization or mechanical ventilation.[4,5] Along with high clinical suspicion combined with bedside examination and radiographic examination, diagnosing VAP requires accurate microbiologic analysis of respiratory secretions.[7] This is the most important management decision in the care of these patients, because inadequate initial antibiotic therapy leads to excess mortality, and excessive antibiotic therapy increases treatment related complications and costs and increased prevalence of antibiotic resistance.[3]

The present study has retrospectively assessed the etiology of VAP in Intensive Care Unit (ICU), their antimicrobial patterns and multidrug resistance.

METHODS

TThis was a hospital-based retrospective study review cultures of EA over 3-year period from January 2018 to January 2021 at Dhulikhel Hospital to evaluate the occurrence of VAP. EA culture reports from patients in ICU were collected from the bacteriology unit of Department of Microbiology, Dhulikhel Hospital. Ethical approval was obtained from IRC of Kathmandu University School of Medical

Science (KUSMS).

Within this period, patients who were on mechanical ventilation for more than 48 hours were studied. Clinical and microbiological criteria had been determined for diagnosing VAP. Microbiological criteria included gram stain (>10 polymorphonuclear cells / low power field and ≥1 / oil immersion field). Clinical criteria included modified Clinical Pulmonary Infection Score (CPIS)>6.[6]

The sample of EA sent to microbiological laboratory were processed immediately. The samples were subjected to gram staining and quantitative culture. The samples were plated on Blood Agar (BA), Chocolate Agar (CA) and MacConkey Agar (MA). The plates were then incubated overnight at 37°C, after which they were checked for growth the next day after 24 hours of incubation. The obtained growth was identified by colony characteristics and biochemical tests.[7]The growth that showed 10^5 Colony Forming Unit (CFU) were considered significant for definitive diagnosis of VAP[8] and any growth less than it was considered as contamination. Significant growths were analyzed through colony morphology and gram stain. Antibiotic sensitivity testing was performed on Mueller-Hinton agar using Kirby-Bauer disk diffusion method. Zone-sizes were measured and interpretation was done according to CLSI guidelines.[9] The culture reports were reviewed and entered in a computerized database SPSS 16.0. Inconclusive reports were excluded as incomplete data. Patient demography, bacterial isolates and their antimicrobial susceptibility patterns were included in the data.

RESULTS

During the 3-year time period, there were total of 147 patients who were ventilated. Among them, 115 cultures were sent to Microbiology Laboratory with clinical suspicion of VAP from which 95 isolates were microbiologically confirmed as VAP (Figure1).

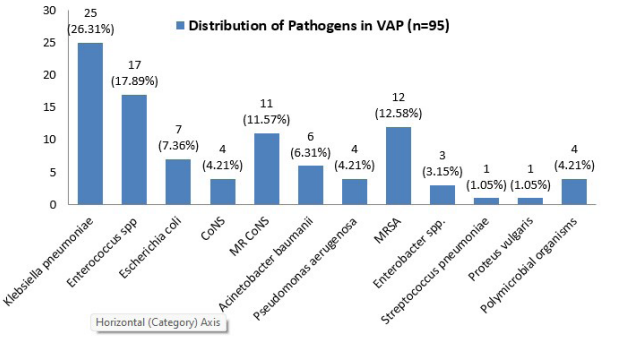

Figure 1: Distribution of pathogens in VAP

VAP was most frequently seen in the age group 46-60 years (Table 1).

Table 1: Distribution among different age-groups

Age (years)	Total patients (n=115)	VAP (n=95)
0-15	28	20 (21.05%)
16-30	14	13 (13.68%)
31-45	11	10 (10.52%)
46-60	36	31 (32.63%)
>60	26	21 (22.10%)

About 40% of the microbiologically confirmed patients were female and 60% were male (Figure 2).

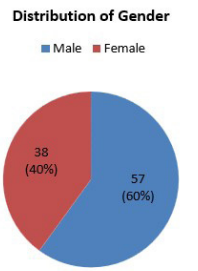

Figure 2: Distribution of gender

Table 2: . Antibacterial sensitivity of gram-negative bacilli (%)

	Klebsiella pneumoniae (n=25)	Acinetobacter baumanii (n=6)	Pseudomonas aeruginosa (n=4)	E coli (n=7)	Enterobacter spp (n=3)	Proteus vulgaris (n=1)
AMP	0	0	0	0	NT	0
AMC	13.04	NT	100	57.14	0	0
CARBEN	NT	100	0	NT	NT	NT
CFP	9.09	NT	50	16.66	50	100
CFS	50	NT	NT	0	NT	NT
CFT	12.5	0	NT	100	0	NT
CAZ	0	0	100	NT	100	NT
CRX	8.33	0	0	16.66	50	0
CIP	17.39	50	100	71.42	66.66	100
COL	100	100	100	100	100	100
CXN	8.33	0	0	16.66	50	100
GEN	25	50	100	71.42	50	100
IMI	38.46	40	50	25	100	0
MRP	35.29	20	0	50	50	100
TZP	29.16	40	100	83.33	33.33	100

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All gram-positive isolates were sensitive of linezolid and vancomycin and most were resistant to penicillin (Table 3).

Table 3: Antibiotic sensitivity of gram-positive bacilli (%)

	CoNS (n=4)	MR Cons (n=11)	Enterococcus spp (n=17)	MRSA (n=12)	S. pneumonae (n=1)
PEN	0	0	57.14	0	0
AK	NT	NT	0	0	100
AMC	100	75.1	35.71	100	NT
CXN	50	NT	11.11	0	100
ERY	50	NT	100	NT	0
CLD	100	67.92	100	0	NT
LZD	100	100	100	100	100
VAN	100	100	100	100	100
CTR	NT	NT	0	0	100
CLOX	100	0	66.66	0	NT

AMP= Ampicillin, A= Amoxiclav, AK= Amikacin, CAR- Carbanpenicillin, CFP- Cefepime, CFS- Cefoperazone-Salbactam, CFT- Cefotaxime, CAZ- Ceftazidime, CRX- Cefuroxime, CIP- Ciprofloxacin, CLD-Clindamycin, CLOX-Cloxacillin, COL- Colistin, CXN, GEN-Gentamicin, IMI-Imipenem, MRP-Meropenem, TZP- Piperacillin-tazobactam, PEN-Penicillin, ERY-Erythromycin, LZD- Linezolid, VAN- Vancomycin, CTR-Ceftriaxone, NT- Not Tested

The most common etiological agent causing VAP was found to be *Klebsiella pneumoniae* with 25 isolates (26.31%) (Figure 1) and Multidrug Resistance (MDR) was also mainly found in *Klebsiella pneumoniae* with 17 (70.83%) (Table 4).

Table 4: Multidrug-resistant organisms that occurred in the isolates

Organism	Isolates (n)	MDR n (%)
Klebsiella pneumoniae	24	17 (70.83%)
Enterococcus spp	17	10 (58.82%)
MR CoNS	10	1 (10.00%)
MRSA	12	1(33.33%)
Escherichia coli	7	1 (14.28%)

DISCUSSION

There were total of 147 patients who were mechanically ventilated out of which 115 were clinically suspected of VAP and their EA were sent to Microbiology Laboratory for culture. The incidence of VAP in our study was 95/147 (64%). Our study is similar to study done in Hyderabad, India where such high prevalence has been reported.[12] However, there are studies showing lower incidence rates.[10,13,14] Incidence of VAP seems to vary depending on hospital settings and sterilization practices during procedures. Majority of patients were male with male: female ratio 60:40. Male dominance is also seen in many other studies[10,11,25,26]; but female dominance has also been reported in a study done in Nepal few years back.[24]

VAP was most frequently seen in the age-group 46-60. Microbiologically confirmed VAP was also found in highest frequency (32.63%) in this age group and was found similar to other studies.[10,11] Many other studies have reported age-group of >60 to be most affected by VAP.[25,26] The incidence of microbiologically confirmed VAP in pediatric age group was found to be quite high (21.05 %) compared to other similar studies[16]; although higher incidence (more than 30% of prevalence) of VAP has been observed in many studies.[15,17-19] VAP has found to be common in ventilated neonates with 6.8% to 57% of all the HAIs.[20-23] Higher incidence pediatric patient in our study may be due to the fact that the testing for EA of adults in the microbiology laboratory was largely hampered by the overwhelming number of samples for COVID test during last 18 months and most of the ICUs for adults was converted to COVID ICUs during that period of time.

The most common organism found in our study was *Klebsiella pneumoniae* followed by *Enterococcus* species. Similar study conducted in our hospital few years ago revealed the most common organism to be *Acinetobacter baumannii*, followed by *Klebsiella pneumoniae*.[24] A study done in VAP cases of Banglore, India showed the most common organism isolated was *Pseudomonas aeruginosa* followed by *E.coli* and *Acinetobacter baumannii*.[9] Another study in France has reported *Enterobacteriaceae* being the most frequently isolated organism, in VAP cases, followed by *Pseudomonas aeruginosa*.[25]

Occurrence of polymicrobial infection vary widely. Incidence of polymicrobial organisms is found to be associated with increased resistance to antibacterials due to interactions between causative microbes causing enhanced pathogenesis.[30] The rate of polymicrobial infection in our study was 4.21%, in which pediatric and adult patient are in equal number. Association between polymicrobial organisms and MDR was not observed in our study. Hence needs to be accessed further.

MDR is defined as resistance to three or more classes of antimicrobial agents: penicillin, cephalosporins, carbapenems, fluoroquinolones and aminoglycosides.[7] Our study has shown large number of *Klebsiella pneumoniae* to be MDR followed by *Enterococcus* species. Out of 95 positive tracheal samples, 30 (31.5%) cases were MDR. Similar study by Hosamirusari H and Shrestha DK also found *Klebsiella pneumoniae* to be the most common organism showing MDR but showed higher rates of MDR which was 72.7% and 57.1% respectively.[28,29] *Acinetobacter baumannii* followed by *Klebsiella pneumoniae* were MDR in a study done by Azzab MM and Salehi M.[26,27]

This study was conducted in one hospital setting; it would have been more informative if it covered other areas of the country as well. Also, a more detailed study in multidrug resistance could not be performed because this was a retrospective study and samples had already been discarded.

CONCLUSION

Gram-negative bacilli like *Klebsiella pneumoniae*,

Acinetobacter baumanii and *Pseudomonas aeruginosa* are the common etiologies of HAPs like VAP. The treatment for nosocomial infection is affected greatly by the administration of empirical antibiotic therapy. MDR is still prevalent in significant isolates. Prevention and control of rising number of MDR in intensive care unit has become very urgent to halt the risk of pan-drug resistance. Efficient antimicrobial stewardship programs involving personnel responsible for distribution and administration of the antimicrobials should be conducted for better clinical outcome of the patients. Bacteriological approach in treatment of VAP is crucial to avoid unnecessary use of antibiotics by separating colonizers from infecting organisms.

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CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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