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Ventilator-associated pneumonia – An unwanted terror and a loathsome burden on the health-care cost in the recent era

Sharmila Gupta[1], Debarati Banerjee[2], Rituparna Haldar[3]

[1]Senior Resident, [2]Assistant Professor, [3]Demonstrator, Department of Microbiology, Calcutta National Medical College and Hospital, Kolkata, West Bengal, India

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ABSTRACT

Background: Ventilator-associated pneumonia (VAP) is defined as infection of lung parenchyma in patients exposed to invasive mechanical ventilation for at least 48 h. VAP is the second most common hospital-acquired infection with a mortality rate up to 40%. **Aims and Objectives:** To determine the microbiological profile of VAP-related samples, the demographic profile of patients, and associated risk factors. **Materials and Methods:** VAP-related samples including endotracheal tube tip, tracheal secretions, and bronchoalveolar lavage (BAL) fluid were collected from 73 patients during the study period from January 2023 to November 2023. Their blood samples were also collected for automated blood culture. Samples were processed as per standard protocol. **Results:** Out of the total patients, 60.31% were male and 39.68% were female. 61–80 years was the most commonly affected age group. The most commonly isolated micro-organism was *Acinetobacter baumannii* with the highest sensitivity to polymixin B and tigecycline. Associated blood culture positivity was maximum in patients whose samples of ET tube tip, tracheal secretions, and BAL fluid had isolated *A. baumannii* and *Klebsiella pneumoniae.* Two *Candida albicans* were isolated with sensitivities to voriconazole and amphotericin B. Many patients had associated septicemia. Endotracheal intubation and tracheal suction were the most common risk factors associated. **Conclusion:** As associated septicemia may increase the mortality rate manifold blood samples should also be collected in suspected VAP patients along with VAP-related samples for early detection of sepsis leading to better patient management.

Key words: Ventilator-associated pneumonia; Mechanical ventilation; Hospital-acquired infection; Risk factors; Intensive care unit

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INTRODUCTION

Ventilator-associated pneumonia (VAP) is defined as an infection of lung parenchyma in patients exposed to invasive mechanical ventilation for at least 48 h.[1] Out of all hospital-acquired infections, VAP is the second most common and accounts for 15–20% of all nosocomial infections.[1] It is the most common reason for death in intensive care unit setups with a mortality rate up to 40%.[1] VAP can be classified as early VAP which occurs within 4 days of ventilation and late VAP which occurs in more than or equal to 5 days of ventilation.[2] VAP can be detected by a modified clinical pulmonary infection scoring (CPIS) system which includes – temperature, leukocyte count, tracheal secretions, oxygenation PaO_2/FiO_2, chest radiograph, and tracheal aspirate culture report. A score of >6 is diagnostic of VAP.[2] The more is the CPIS score, the worst is the prognosis and outcome. VAP can cause patients to have difficulty in weaning off the ventilator and may lead to prolonged hospital stays hence increasing the huge financial burden to patients and increasing the need for sophisticated medical equipment or resources.[3] Proper maintenance of bundle care for mechanical ventilation is mandatory to prevent VAP. A better understanding of different risk factors for VAP can predict the occurrence of VAP, improve its prevention and control, and may reduce

Address for Correspondence:
Dr. Sharmila Gupta, Senior Resident, Department of Microbiology, Calcutta National Medical College and Hospital, 32, Gorachand Road, Beniapukur, Kolkata - 700 014, West Bengal, India. **Mobile:**+91-9330420016. **E-mail:** sharmilagupta28091994@gmail.com

the mortality and morbidity risk associated with VAP. Hence, an observational study was undertaken to determine the microbiological profile of VAP-related samples, the demographic profile of patients, and associated risk factors in the Department of Microbiology, Calcutta National Medical College and Hospital.

Aims and objectives

To determine the microbiological profile of VAP-related samples and their blood culture positivity, to determine the demographic profile and associated risk factors for VAP among patients.

MATERIALS AND METHODS

An observational study was conducted for 11 months from January 1st, 2023 to November 30th, 2023 in the Department of Microbiology, Calcutta National Medical College and Hospital, Kolkata, including 73 patients with VAP. VAP-related samples such as endotracheal tube tip, tracheal secretions, and bronchoalveolar lavage (BAL) fluid were collected. Their blood samples were also collected for automated blood culture (BACTEC). Primary Gram stains were done from tracheal secretions and BAL fluid. Then they were inoculated in blood agar and MacConkey agar followed by Gram stain from culture. Rolling plate culture was done directly from ET tube tip and more than or equal to 15 colonies on blood agar and/or MacConkey agar were taken as significant. Gram stain was done from these culture plates. The ET tube tips were also put into brain heart infusion broth followed by subculture from broth on the next day, as there may be low colony count by rolling plate technique in a few cases. Culture-growing *Candida* species on blood agar were reinoculated in Sabouraud's Dextrose agar with chloramphenicol and also germ tube testing was done. Susceptibility testing was done by Kirby Bauer Disk diffusion technique using Mueller Hinton agar (MHA) for bacterial isolates and MHA with 2% glucose and methylene blue for *Candida* isolates as per M100 CLSI and M44 CLSI guidelines, respectively.[4,5] Vitek 2 system was also used for a few highly resistant isolates. The blood samples were put into the BACTEC BD system followed by culture and sensitivity. The demographic profiles as well as the relevant history to assess probable risk factors in patients were collected in a pro forma sheet from patient's relatives. Data were collected and a modified CPIS system which includes – temperature, leukocyte count, tracheal secretions, oxygenation PaO_2/FiO_2, chest radiograph, and tracheal aspirate culture report was calculated.

Inclusion criteria

All patients developing VAP within the study period were included in the study.

Exclusion criteria

Patients with pneumonia due to causes other than mechanical ventilation were excluded from the study.

Ethical clearance

For the present study, the ethical approval was taken from the Institutional Ethics Committee, Calcutta National Medical College and Hospital, Kolkata.

RESULTS

During 11 months from January 2023 to November 2023, an observational study was done and samples were collected from 73 suspected VAP patients. Table 1 shows the age group distribution among VAP patients. Figure 1 pie chart representing the percentage of male and female patients. Table 2 shows the microbiological profile of different samples collected from suspected VAP patients. Figure 2 pie chart showing percentages of VAP patients showing various CPIS scores. Table 3 shows different risk factors associated with VAP patients.

Table 1 shows the age group distribution between 0 and 81 years and above among VAP patients. The most common age group affected was 61–80 years.

Figure 1 shows gender distribution among VAP patients. VAP was more prevalent among male patients.

Table 2 shows the microbiological profile of different VAP-related samples and their rate of blood culture positivity.

Figure 2 shows percentages of VAP patients with various CPIS scores. Out of 73 patients – score 7 in 41%, score 8 in 27%, score 9 in 21% patients, and score 10 in 11% patients.

Table 3 shows different risk factors associated with VAP patients.

Statistical analysis

The data obtained were analyzed with the statistical tool R. The different percentages were calculated.

Table 1: Age group distribution among VAP patients

Age group range (years)	Number of cases	Percentage
0–20	20	27.39
21–40	9	12.32
41–60	18	24.65
61–80	21	28.76
81 and above	5	6.84
Total	73	

VAP: Ventilator-associated pneumonia

Table 2: Microbiological profile of different samples collected from suspected VAP patients

Sample type	Micro-organisms	No. of cases	Sensitive antibiotic (with no. of sensitive cases)	Blood culture positivity* (among no. of cases)
ET tube tip	*Acinetobacter baumannii*	24	TGC (22), CFS (4), GEN (1), DO (1), and PB (23)	14
ET tube tip	*Proteus mirabilis*	2	PTZ (2), IPM (1), CFS (1), and MRP (1)	0
ET tube tip	*Escherichia coli*	6	MRP (3), PB (6), COT (3), AK (1), DO (1), and TGC (1)	2
ET tube tip	CONS and *Enterococcus* spp	1	LZ (1), VA (1), CX (1) LZ (1), and VA (1)	0
ET tube tip	*Pseudomonas aeruginosa*	2	GEN (2), CFS (2), and PB (2)	1
ET tube tip	*Klebsiella pneumoniae*	11	PB (10), CFS (6), TGC (4), MRP (2), PTZ (2), DO (2), LE (1), and CPM (2)	7
ET tube tip	MRCONS	2	VA (2) and LZ (2)	1
ET tube tip	*E. coli* and *Klebsiella pneumoniae*	2	DO (2), TGC (2), MRP (1), AK (2), LE (1), and COT (1) for both isolates	0
ET tube tip	MRSA	1	VA (1) and LZ (1)	1
ET tube tip	*E. coli* and *P.mirabilis*	1	CFS (1), PTZ (1) and MRP (1)	0
ET tube tip	*Enterobacter aerogenes*	1	CFS (1)	0
ET tube tip	*Acinetobacter baumannii* and *Pseudomonas aeruginosa*	1	TGC (1), LE (1) MRP (1), GEN (1), CFS (1), PTZ (1), AK (1), and CPM (1)	0
ET tube tip	*Acinetobacter baumannii* and *Klebsiella pneumoniae*	2	CFS (2), TGC (2), and DO (1) for both isolates	1
ET tube tip	*Candida albicans*	2	VRC (2), AMB (2), and FLU (1)	1
Tracheal secretions	*Acinetobacter baumannii*	7	TGC (5) and CFS (2)	3
Tracheal secretions	*Klebsiella pneumoniae*	2	MRP (1), OF (1), PTZ (1), and DO (1)	1
Tracheal secretions	*E. coli*	2	PB (1), MRP (1), and COT (1)	1
Tracheal secretions	*Proteus mirabilis*	1	CFS (1), MRP (1), and PTZ (1)	1
Tracheal secretions	*Klebsiella pneumoniae* and *Acinetobacter baumannii*	1	CFS (1), DO (1), GEN (1), MRP (1), PTZ (1), and LE (1) CFS (1) and TGC (1)	1
BAL fluid	*Acinetobacter baumannii*	1	CFS (1), TGC (1), and GEN (1)	0
BAL fluid	*Pseudomonas aeruginosa*	1	CFS (1), MRP (1), PTZ (1), LE (1), and AK (1)	0
	Total samples	73	Total blood culture positivity	35

*Associated blood culture positivity suggests sepsis, TGC: Tigecycline, CFS: Cefoperazone-sulbactam, GEN: Gentamicin, DO: Doxycycline, PB: Polymixin B, PTZ: Piperacillin-tazobactam, IPM: Imipenem, MRP: Meropenem, COT: Cotrimoxazole, AK: Amikacin, LE: Levofloxacin, CPM: Cefepime, OF: Ofloxacin, LZ: Linezolid, VA: Vancomycin, VRC: Voriconazole, AMB: Amphotericin B, FLU: Fluconazole

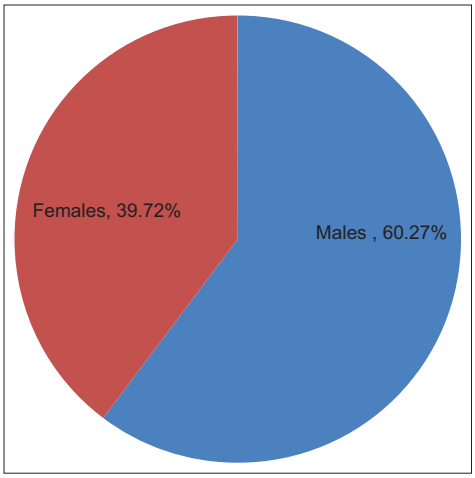

Figure 1: Pie chart represents gender distribution among ventilator-associated pneumonia patients

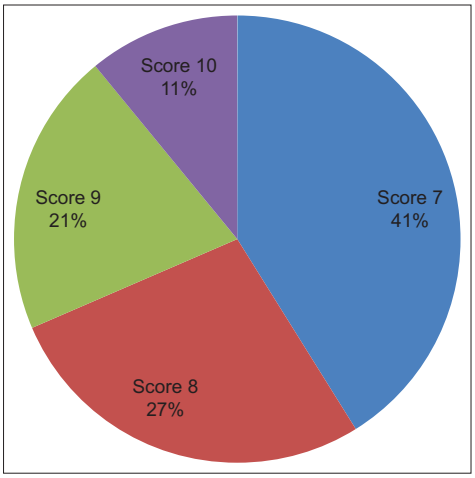

Figure 2: Pie chart showing percentages of ventilator-associated pneumonia patients showing various clinical pulmonary infection scores

Fisher's exact test/one-way Chi-square test was used for comparative analysis. The tests were evaluated at a confidence level of 95% and P<0.05 was considered statistically significant. In the present study, endotracheal intubation and tracheal suction as the risk factors for VAP were found to be statistically significant with P<0.05. Other risk factors were not statistically significant but may be contributory.

Table 3: Different risk factors associated in VAP patients

Risk factors	Number of cases (Out of 73 patients)
Associated COVID-19 infections	3
ET tube intubation and tracheal suction	50
Prolonged duration of ventilation (>5 days)	30
Previous H/O COPD	15
Prior *Staphylococcus* species as a nasal carrier	5
Prior hospital admission in the previous 30 days	25
Corticosteroid intake	20
Prior broad-spectrum antibiotic therapy	35
Tracheostomy	10
Hypercholesterolemia	35
1. Uncontrolled	10
2. On statins	25
Chronic alcoholism	28
Neurological disease affecting levels of consciousness	20
Chronic kidney disease	15
Chronic heart failure	21
Diabetes	25

VAP: Ventilator-associated pneumonia, COPD: Chronic obstructive pulmonary disease

DISCUSSION

The present study was conducted in the Department of Microbiology, Calcutta National Medical College and Hospital, Kolkata, with the objectives of determining the microbiological profile of VAP-related samples, to determine the demographic profile and associated risk factors. The key findings of our study were – out of total patients, 60.31% were male and 39.68% were female. 61–80 years were most commonly affected followed by 0–20 years age group. The most commonly isolated micro-organism was *Acinetobacter baumannii* with the highest sensitivity to polymixin B and tigecycline. Associated blood culture positivity was maximum in patients whose samples of ET tube tip, tracheal secretions, and BAL fluid had isolated *A. baumannii* followed by *Klebsiella pneumoniae*. Two *Candida albicans* were isolated with sensitivities to voriconazole and amphotericin B and one of them was complicated with candidemia. Endotracheal intubation and tracheal suction were the most common risk factors associated.

In our study, male patients (60.31%) were more commonly affected by VAP as compared to female patients (39.68%). In another study by Sharpe et al., showed that although the incidence of VAP was higher in males, mortality was found to be more among females.[6] In our study, 61–80-year age group had the most commonly developed VAP. In another study, Jaimes et al. showed that the median age for VAP was 41 years.[7] These discrepancies may be due to differences in demographic patterns. In the present study, *A. baumannii* was the most common micro-organism isolated from VAP samples followed by *K. pneumoniae*. Similar results were found in another study by Sangale et al.[8] In our study, the most commonly susceptible antibiotic was polymixin B and tigecycline among *A. baumannii* isolates and polymixin B and meropenem in *K. pneumoniae* isolates. In another study by Hassan et al., 100% susceptibility was in polymyxins, but tigecycline was sensitive in only 21% of cases and low susceptibility to meropenem. These discrepancies may be due to differences in antibiogram patterns in different geographical regions.[9] In our study, the different risk factors associated with VAP were ET tube intubation and tracheal suction (50 cases), prior use of broad-spectrum antibiotic therapy (35 cases), hypercholesterolemia (35 cases), prolonged duration of ventilation (>5 days) in 30 cases, prior hospital admission in previous 30 days (25 cases), chronic alcoholism (28 cases), chronic heart failure (21 cases), neurological diseases affecting the level of consciousness (20 cases), chronic kidney disease (15 cases), chronic obstructive pulmonary disease (COPD) (10 cases), diabetes (25 cases), corticosteroids intake (20 cases), tracheostomy (10 cases), prior *Staphylococcus* species as nasal carrier (5 cases), and associated COVID-19 infection (3 cases). Different data show that ET tube intubation is the most common risk factor for VAP.[2] A study by Weinstein et al., shows antibiotics predispose to colonization and infection with antibiotic-resistant pathogens.[10] In a study by Dunham and Chirichella, uncontrolled hypercholesterolemia was shown as a significant risk factor for VAP.[11] Prolonged duration of ventilation for >5 days is associated with higher chances of late VAP with relatively more resistant micro-organisms.[2] Prior hospital admission within the past 30 days may increase the risk for the development of oropharyngeal colonization with highly resistant micro-organisms such as *S. aureus* or other micro-organisms of clinical importance as nasal carriers.[2,10] In studies by Sadigov et al., and Kozka et al., chronic heart failure (26.4%), neurological disease (23.1%), renal disease (2.14%), COPD (34.7%), diabetes mellitus, and chronic alcoholism were found to be important risk factors as they are a high-risk group for VAP.[12,13] In another study by Mesland et al,it has been shown that if high dose systemic corticosteroids are given early to patients with COVID19 disease or other critically ill patients that may increase the risk of developing VAP.[14] In fact, COVID-19 disease patients on mechanical ventilation are itself a risk for VAP which may be due to either corticosteroid intake or immune amnesia during SARS-CoV-2 infection.[2,15] Nseir et al. have identified tracheostomy as an independent risk factor for VAP.[16] Hence, our study results corroborate with all the above studies.

Strengths and limitations

The strength of our study was that it was an extensive study. We studied the gender prevalence, age group distribution, risk factors, and microbiological profile of VAP patients. Furthermore, their clinical pulmonary infection score was also calculated to assess the patients' outcomes. Although the study was extensive, there were a few limitations such

as (1) molecular methods such as biofire film array for rapid detection of micro-organisms could not be performed due to lack of facility and (2) molecular methods for resistance gene detection in micro-organisms were not done due to lack of facility.

CONCLUSION

VAP has become a critical issue in ICU and CCU setups with a high-cost burden associated with emerging multidrug-resistant micro-organisms. Endotracheal intubation and tracheal suction have been found to be the most common risk factor for VAP. Hence, it is required to encourage proper staff training, surveillance programs, maintenance of standard precautions including hand hygiene, adequate bed-to-bed distancing, cohorting of similar infectious patients, etc., and appropriate bundle care approach to prevent or at least reduce the incidence of VAP. As VAP may be complicated with sepsis which increases the mortality manifold, blood samples should also be collected in suspected VAP patients along with VAP-related samples for early detection as well as better management of septicemia, especially helping in the decision of appropriate antimicrobial agents for patients and improve patients' outcome.

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Authors Contribution:
SG- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation, submission of article, concept, design of study, statistical analysis, and interpretation; **DB-** Editing and manuscript revision; **RH-** Editing and manuscript revision.

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Orcid ID:
Sharmila Gupta - https://orcid.org/0009-0005-6982-3907

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