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A STUDY OF CLINICAL AND MICROBIOLOGICAL PROFILE OF VENTILATOR-ASSOCIATED PNEUMONIA AND HOSPITAL-ACQUIRED PNEUMONIA IN PATIENTS ADMITTED AT TERTIARY CARE CENTER

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ABSTRACT

Objective: Ventilator-associated pneumonia (VAP) is a serious hospital-acquired infection that has a high death rate. The microbiological features of VAP have been the subject of only a few research conducted on small study populations in India. To evaluate the pathogen profile and identify the trend of antibiotic resistance, this study was conducted in the intensive care units (ICUs) of a tertiary care hospital.

Methods: A prospective investigation of clinically suspected VAP cases was conducted. Our analysis included 247 instances with clinical evidence of VAP who were admitted to ICUs on mechanical ventilation over 1 year. After undergoing a quantitative culture procedure on the endotracheal aspirate samples from these probable cases, a colony count of ≥105 colony-forming units/mL was deemed significant. A test for the isolates' susceptibility to antibiotics was conducted.

Results: The incidence of VAP was more common in the elderly age group (45%) and predominated in males (57.5%) with a statistically insignificant p=0.3130. The majority of the patients were diagnosed with cerebrovascular accidents (41.25%). Poor outcome of VAP was associated with hypertension (51.25%) and diabetes mellitus (48.75%). Around 58 (72.5%) required intubation, and among the intubated, 29 (59.18%) showed improvement, and 29 (93.55%) patients died, with a significant p=0.0010. The majority of patients with VAP have demonstrated growth of Gram-negative organisms. Most of the Cefoperazone sensitive cases showed improvement (87.5%), with death in 12.5% cases, whereas the fatality rate was high in resistance cases (48.48%), which was statistically significant with a p=0.0140.

Conclusion: The mortality incidence was higher in antibiotic-resistant cases than the sensitive cases. The incidence of VAP may be reduced by carefully selecting patients who need ventilator support.

Keywords: Ventilator-associated pneumonia, Antimicrobial resistance, Mortality, Risk factors in ventilator-associated pneumonia.

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INTRODUCTION

One of the most common acquired infections in intensive care units (ICUs) and a major contributor to morbidity and mortality is ventilator-associated pneumonia (VAP) [1]. VAP includes pneumonia that develops after extubation and occurs more than 48 h after endotracheal intubation and the start of mechanical ventilation (MV). Approximately 9–27% of all intubated patients have VAP [2,3]. Early start VAP, which happens within the first 4 days of MV, is more likely to be caused by bacteria that are responsive to antibiotics, is typically less severe, and is linked to a better prognosis [4,5]. Multidrug-resistant bacteria are the source of late-onset VAP, which appears 5 or more days after MV is started and is linked to higher rates of morbidity and mortality [6,7].

The most prevalent VAP pathogens have been determined to be *Pseudomonas* species, *Acinetobacter* species, *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* [8]. Nowadays, conventional antimicrobial agents have failed against many infections due to the emergence of multiple drug-resistant strains [9].

The resistance of pneumococcal bacteria, particularly to penicillin, has increased over the past 10 years. It is also anticipated that rising penicillin resistance would contribute to rising resistance to a number of antibiotic families, including tetracycline, macrolide, cephalosporin, and cotrimoxazole [10].

To direct the more efficient and sensible use of antimicrobial medicines, it is necessary to investigate the local microbial flora producing VAP in each context.

Objectives of the study

To ascertain these VAP pathogens' patterns of antibiotic susceptibility and to study the clinical profile of VAP in SDM Medical College and Hospital's ICU patients in Dharwad.

METHODS

It is a prospective observational study conducted over 2 years on patients on mechanical ventilators admitted to the medical ICU of SDM Medical College and Hospital, Dharwad. A total of 80 patients, on mechanical ventilators, fulfilling the inclusion criteria, were taken as part of the study.

The study was started after approval from the ethical committee of SDM Medical College and Hospital, Dharwad (SDMIEC:81:2020). Informed consent was obtained from the patient or patient's guardian.

Inclusion criteria

Patients admitted in ICU, who are intubated and on MV for more than 48 h and patients in whom VAP is clinically suspected (Centers for Disease Control and Prevention Criteria)>were taken into consideration.

Table 1: Association between the status of outcome with age and gender

Demographic profile	Improved n (%)	Death n (%)	Total n (%)	Chi-square	p-value
Age groups					
20–39 years	8 (16.33)	4 (12.90)	12 (15)	0.2980	0.8610
40–59 years	20 (40.82)	12 (38.71)	32 (40)		
≥60 years	21 (42.86)	15 (48.39)	36 (45)		
Gender					
Male	26 (53.06)	20 (64.52)	46 (57.5)	1.0200	0.3130
Female	23 (46.94)	11 (35.48)	34 (42.5)		
Total	49 (100)	31 (100)	80 (100)		

n=Number of patients (total=80)

Exclusion criteria

Patients who had developed pneumonia within 48 h of MV were excluded.

Among the included patients, the study of isolation of causative organisms and its antibiotic susceptibility were determined along with significant risk factors associated with VAP. Each patient's age, gender, diagnosis at admission, MV indication, clinical examination data, laboratory tests (serum biochemistry and hemogram), and radiographic tests (chest radiograph) were recorded. Whenever feasible, arterial blood gas analysis was performed. The presence of a new and/or progressive infiltrate on chest radiography without any other apparent cause, along with any two of the following: (1) temperature >38°C or <36°C, (2) white blood cell count >11 × 10^9/L or >4 × 10^9/L, and (3) purulent tracheal secretions or a change like tracheal secretions, were considered clinically suspected pneumonia. All patients with clinically suspected pneumonia underwent fiberoptic bronchoscopy to identify VAP. A bronchoalveolar lavage (BAL) culture was deemed positive and added to the study if its threshold value was 10^4 cfu/mL or higher. Of the 80 clinically suspected cases of VAP, 50 (53%) had a positive BAL culture [11,12].

The patients who were recruited were monitored until they either passed away or received effective treatment and were released from the hospital. To start MV, endotracheal intubation was performed; if a patient needed MV for an extended length of time, tracheostomy was performed. Invasive ventilators (SERVO Ventilator 900c [Siemens-Elema, Sweden]) were used to treat the patients. During regular business hours, a qualified physiotherapist provided respiratory therapy. According to established weaning procedures, the patients were weaned off of MV [11].

Analysis of statistics

EPI Info 7.2 and Microsoft Excel 10 were used for data entry and analysis. The Chi-square test and percentage (%) were the analytical tests employed.

RESULTS

A total of 80 patients were analyzed in the present study. Most patients (45%) belonged to the age group of more than 60 years, followed by 40% to 40–59 years and 15% to the 20–39 years.

Out of 80 patients, 46 were males and 34 were females. There was no statistically significant association between age and gender, and the status of outcome (Table 1).

Table 2 shows the diagnosis of the included patients along with their outcome. The majority of the patients were diagnosed with cerebrovascular accidents (CVA) (41.25%), followed by sepsis with shock (31.25%), and decompensated chronic liver disease with portal hypertension (HTN) (11.25%). The rate of improvement was better in patients with CVA. And the death rate was high in patients with sepsis with shock (44%).

Table 2: Association between diagnosis and status of outcome

Diagnosis	Improved n (%)	Death n (%)	Total n (%)
COPD with COR pulmonale	3 (6.12)	1 (3.23)	4 (5)
Cerebrovascular accidents	22 (44.9)	11 (35.48)	33 (41.25)
Decompensated chronic liver disease with portal hypertension	5 (10.2)	4 (12.9)	9 (11.25)
Ischemic heart disease	2 (4.08)	1 (3.23)	3 (3.75)
Poisoning	3 (6.12)	3 (9.68)	6 (7.5)
Sepsis with septic shock	14 (28.57)	11 (44%)	25 (31.25)
Total	49 (100)	31 (100)	80 (100)

COPD: Chronic obstructive pulmonary disease, n=Number of patients (total=80)

Table 3: Association between the status of outcome with risk factors for MDR

Risk factors for MDR	Improved n (%)	Death n (%)	Total n (%)	Chi-square	p-value
Smoker	6 (12.24)	3 (9.68)	9 (11.25)	0.1250	0.7230
Hypertension	23 (46.94)	18 (58.06)	41 (51.25)	0.9410	0.3320
Diabetes mellitus	22 (44.90)	17 (54.84)	39 (48.75)	0.7510	0.3860
Chronic obstructive pulmonary disease	4 (8.16)	2 (6.45)	6 (7.5)	0.0800	0.7770
Ischemic heart disease	7 (14.29)	3 (9.68)	10 (12.5)	0.3690	0.5440
Tracheostomy	8 (16.33)	6 (19.35)	14 (17.5)	0.1210	0.7280

n=Number of patients (total=80), MDR: Multidrug-resistant

An analysis of risk factors shows that a higher number of included patients were suffering from HTN (51.25%) and diabetes mellitus (48.75%). There was no statistically significant association seen between the risk factors and the status of outcome (Table 3).

Among 80 patients, 58 (72.5%) required intubation and among the intubated, 29 (59.18%) showed improvement and 29 (93.55%) patients died. Among the non-intubated patients, 20 (40.82%) showed improvement and 2 (6.45%) patients died. The statistically significant improvement was seen in non-intubated patients with a p=0.0010 (Table 4).

There was no statistically significant association seen between the use of the antibiotic in the past 90 days and the status of the outcome (Table 5).

Table 6 shows the growth of various types of organisms among patients. A high number of patients were affected with *Acinetobacter* 28 (35%)

and among whom 17 (34.69%) were improved and 11 (35.48%) were died. Out of 80 patients, 55 (68.75%) have shown Gram-negative growth.

Table 7 shows the association between the sensitivity of antibiotic and the outcome of the patients.

Most of the Cefoperazone sensitive cases showed improvement (87.5%) with death in 12.5%cases, whereas the fatality rate was high in resistance cases (48.48%), which was statistically significant with p=0.0140. Similarly, Clarithromycin, Meropenem, Imipenem, and Colistin showed high fatality rate in resistant cases (66.67%, 57.69%, 61.9% and 61.36%, respectively).

Table 4: Association between the status of outcome with intubation and the duration of ventilation

Parameter	Improved n (%)	Death n (%)	Total n (%)	Chi-squire	p-value
Intubated					
No	20 (40.82)	2 (6.45)	22 (27.50)	11.2470	0.0010*
Yes	29 (59.18)	29 (93.55)	58 (72.50)		
Duration of ventilation					
1–5 days	11 (22.45)	10 (32.26)	21 (26.25)	0.0950	0.9530
6–10 days	8 (16.33)	8 (25.81)	16 (20.00)		
≥11 days	10 (20.41)	11 (35.48)	21 (26.25)		

*p<0.05. n=Number of patients (total=80)

Table 5: Association between the status of outcome and with use of antibiotics in the past 90 days

Use of antibiotics in past 90 days	Improved n (%)	Death n (%)	Total n (%)	Chi-square	p-value
No	45 (91.84)	26 (83.87)	71 (88.75)	1.2070	0.2720
Yes	4 (8.16)	5 (16.13)	9 (11.25)		
Total	49 (100)	31 (100)	80 (100)		

n=Number of patients (total=80)

DISCUSSION

Patients on MV frequently develop VAP. There is a lot of interest in correctly identifying, treating, and preventing VAP because of the high disease burden, morbidity, and mortality linked to this condition. The protected specimen brush and BAL are two invasive diagnostic procedures that are commonly used and well-standardized for bronchoscopy to determine the etiological pathogen for VAP.

In the present study, most patients belonged to the age group of more than 60 years (45%). Similar findings were found in a study carried out by Kumar and Deepak, where the majority of VAP patients were seen in 50–70 years (28%) [13]. Male patients were predominantly seen in the present study (57.5%) with VAP and similar figures were also observed in a study carried by Borisagar *et al*. [14].

A study was done by Bhattacharjee *et al*. found that there was no significant association of age, gender, and comorbidities with VAP. We also found no statistically significant association between the risk factors and VAP, even though a higher number of included patients were suffering from HTN (51.25%) and diabetes mellitus (48.75%) [15].

In the present study, a high number of patients were affected with *Acinetobacter* 28 (35%) and among whom 17 (34.69%) were improved and 11 (35.48%) were died. Out of 80 patients, 55 (68.75%) have shown Gram-negative growth. A similar organism profile was observed in a study done by Chaudhury *et al*., where the total number of Gram-negative organisms isolated in the 3 years from 2011 to 2013 were 578, 737, and 512, respectively, and Gram-negative bacilli were the predominant organisms, followed by *Pseudomonas* spp. and *Klebsiella* spp. [16]. According to the recent study, the most common etiological agents among Gram-negative bacilli were *Pseudomonas* (23.2%), *Haemophilus influenzae* (10.7%), and *Enterobacter* (8.9%). *Staphylococcus aureus* (25%) was the most common etiological agent among Gram-positive cocci [12].

In a recent study done by Parathsarathy *et al*., in the hospital's bacteriological profile for VAP, Gram-negative organisms accounted for 93.93% of the causal agent in VAP, but Gram-positive organisms were only present in early-onset VAP (6.07%) [17]. Like the present study, *Acinetobacter* was most common among the VAP (35%), in a study carried out by Kanipakam *et al*., *Acinetobacter* was most common (34.73%) [18].

The profile of microorganisms seen in this investigation is similar to that of the present investigation. The present study shows that

Table 6: Association between status of outcome with organisms' growth

Organisms	Improved n (%)	Death n (%)	Total n (%)	Chi-squire	p-value
Escherichia coli	4 (6.16)	1 (3.23)	5 (6.25)	4.9030	0.8430
Pseudomonas+Acenitobcter	0	1 (3.23)	1 (1.25)		
Pseudomonas aeroginosa	6 (12.24)	4 (12.90)	10 (12.50)		
Acenitobacter	17 (34.69)	11 (35.48)	28 (35.00)		
Staphylococcus aureus	3 (6.12)	3 (9.68)	6 (7.50)		
Klebsiella pneumoniae	6 (12.24)	4 (12.9)	10 (12.50)		
MRSA	5 (10.20)	2 (6.45)	7 (8.75)		
Klebshiella+Pseudomonas	0	1 (3.23)	1 (1.25)		
No growth	8 (16.33)	4 (12.90)	12 (15.00)		
Gram N/P					
Gram-negative	33 (67.35)	22 (70.97)	55 (68.75)	0.1850	0.9120
Gram-positive	8 (16.33)	5 (16.13)	13 (16.25)		
No growth	8 (16.33)	4 (12.90)	12 (15.00)		
Positivity of organisms					
Positive	41 (83.67)	27 (87.10)	68 (85)	0.1750	0.6760
Negative	8 (16.33)	4 (12.90)	12 (15)		

n=Number of patients (total=80)

Table 7: Association between status of outcome with sensitivity and resistance with various antibiotics

Antibiotics	Improved n (%)	Death n (%)	Total n (%)	Chi-square	p-value
Amikacin					
Resistance	9 (60)	6 (40)	15 (42.86)	0.3800	0.5370
Sensitive	14 (70)	6 (30)	20 (57.14)		
Cefepime					
Resistance	24 (57.14)	18 (42.86)	42 (84)	0.0790	0.7780
Sensitive	5 (62.50)	3 (37.50)	8 (16)		
Cefoperazone					
Resistance	17 (51.52)	16 (48.48)	33 (67.35)	6.0040	0.0140*
Sensitive	14 (87.50)	2 (12.50)	16 (32.65)		
Ceftazidime					
Resistance	11 (52.38)	10 (47.62)	21 (77.78)	1.8520	0.1740
Sensitive	5 (83.33)	1 (16.67)	6 (22.22)		
Ceftriaxone					
Resistance	9 (52.94)	8 (47.06)	17 (77.27)	0.0780	0.7810
Sensitive	3 (60)	2 (40)	5 (22.73)		
Clindamycin					
Resistance	10 (83.33)	2 (16.67)	12 (85.71)	1.1310	0.2870
Sensitive	1 (50)	1 (50)	2 (14.29)		
Clarithromycin					
Resistance	1 (33.33)	2 (66.67)	3 (25)	3.7040	0.0500*
Sensitive	8 (88.89)	1 (11.11)	9 (75)		
Piperacillin-tazobactam					
Resistance	22 (55)	18 (45)	40 (81.63)	1.5780	0.2090
Sensitive	7 (77.78)	2 (22.22)	9 (18.37)		
Meropenem					
Resistance	11 (42.31)	15 (57.69)	26 (61.90)	4.2730	0.0390*
Sensitive	12 (75)	4 (25)	16 (38.10)		
Imipenem					
Resistance	12 (44.44)	15 (55.56)	27 (61.36)	4.3610	0.0370*
Sensitive	13 (76.47)	4 (23.53)	17 (38.64)		
Colistin					
Resistance	0	3 (100)	3 (5.77)	4.3410	0.0370*
Sensitive	30 (61.22)	19 (38.78)	49 (94.23)		
Levofloxacin					
Resistance	15 (53.57)	13 (46.43)	28 (75.68)	1.6560	0.1980
Sensitive	7 (77.78)	2 (22.22)	9 (24.32)		
Linezolid					
Resistance	4 (100)	0	4 (30.77)	2.5680	0.1090
Sensitive	5 (55.56)	4 (44.44)	9 (69.23)		
Vancomycin				1.7330	0.1880
Resistance	3 (100)	0	3 (23.08)		
Sensitive	6 (60)	4 (40)	10 (76.92)		
Teigecycline					
Resistance	1 (20)	4 (80)	5 (8.77)	3.2290	0.0720
Sensitive	32 (61.54)	20 (38.46)	52 (91.23)		
Teicoplanin					
Resistance	5 (100)	0	5 (35.71)	2.1210	0.1450
Sensitive	6 (66.67)	3 (33.33)	9 (64.29)		

*p<0.05. n=Number of patients (total=80)

a statistically significant mortality was seen in resistant cases of Cefoperazone, Clarithromycin, Meropenem, Imipenem, and Colistin (48.48%, 66.67%, 57.69%, 61.9% and 61.36%, respectively). In a study done by Chaudhury *et al*., an increase in resistance was shown by *Pseudomonas* spp. for CFS, PTZ, AK, and IPM [16].

Limitation of the study: It is single-center study, including a smaller sample size, which raises objections to the generalization of study results.

CONCLUSION

In ICU patients, VAP remains a leading cause of morbidity and mortality. The incidence of VAP was more common in the elderly age group and predominated in males. Poor outcome of VAP was associated with HTN and diabetes. The majority of patients with VAP have shown Gram-negative organism growth. The mortality incidence was higher in antibiotic-resistant cases than the sensitive cases. The incidence of VAP may be reduced by carefully selecting patients who need ventilator support. Reducing the occurrence of VAP may be greatly aided by appropriate monitoring and efforts to remove the patient from the ventilator as soon as possible.

AUTHOR CONTRIBUTIONS

All the authors are equally contributed in designing, collecting the data and analysis of results, and writing the study.

CONFLICT OF INTEREST

None of the authors has conflict of interest.

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