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CLINICAL PROFILE AND PATTERNS OF ANTIMICROBIAL RESISTANCE IN VENTILATOR-ASSOCIATED PNEUMONIA PATIENTS

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ABSTRACT:

Background: Ventilator-associated pneumonia (VAP) is the most common nosocomial infection in people receiving mechanical ventilation. This study aims to detect the etiological agents of VAP and determine their antibiotic susceptibility pattern.

Methodology: This cross-sectional study was conducted among patients admitted to the intensive care unit at a single tertiary care center in south India. All patients who developed VAP in the ICU during the study and qualified for the inclusion criteria were investigated clinically, radiologically, and on a microbiological basis. Clinical history and examination- Relevant clinical history with patient symptoms was noted. Patients suffering from pneumonia on admission or during the first 48 hours of mechanical ventilation were excluded.

Results: The total of 70 patients fulfilling inclusion criteria were included in the present study. The mean age of participants was found to be 49.33±16.46yrs of age, with majority of patients in the age group of 40-60yrs of age. In present study, we have seen male preponderance with 84.3% were male and 15.7% were female patients, with male to female ratio of 6:1. 30% of them had the gram positive infections and 70% had the gram negative infection. Majority were infected with Klebsiella pnemoniae (27.1%), followed with Enterobacter cloacae (14.3%), Acinetobacter baumannii (12.9%), Pseudomonas aeruginosa (10%) and CONS in 8.6%. More than 30% of sensitivity was seen with Tigecycline, followed by more than 20% sensitivity to the gentamycin.

Conclusion: The prevalence of multidrug-resistant microorganisms is at an increasing rate. Among them, gram-negative organisms are more predominant than gram-positive organisms. The resistance pattern of these infections can assist a facility in developing an efficient antimicrobial policy

Keywords: Antibiotics, Ventilator-associated pneumonia, sensitivity pattern, Drug resistance.

1. INTRODUCTION

Pneumonia is frequently categorized based on the site of acquisition. Hospital-acquired (or nosocomial pneumonia) is that which occurs 48 hours or more after admission and does not appear to be incubating at the time of admission. VAP is a type of pneumonia that develops≥ 48 hours after endotracheal intubation.[1] Ventilator-associated pneumonia (VAP) is a type of hospital- acquired pneumonia (HAP) that develops after more than 48 hours of mechanical ventilation.6 In the critical care unit, VAP is a prevalent and dangerous problem that has been related to an increased risk of death.[2] As soon as feasible, the right therapy can begin, while avoiding antibiotic misuse and, consequently, the development of antibiotic resistance.[3] Patients who are mechanically ventilated are at risk for developing ventilator-associated pneumonia. VAP is defined as pneumonia that develops more than 48 hours after endotracheal intubation/mechanical ventilation or pneumonia that continues to develop even after extubation.[4-6] VAP is the most common ICU- acquired infection among mechanically ventilated patients.[7] VAP is a type of hospital-acquired pneumonia. It affects 9-27 percent of mechanically ventilated patients.[8] In ICU patients with ventilator-associated pneumonia in India, the total crude death rate is 67.4 percent, accounting for 40 percent of the mortality.[9-11]
VAP is becoming a global health problem that threatens many medical advances of the last century. Antimicrobial resistance in the intensive care unit (ICU) has been dubbed as the ‘‘epicenter of infections’ in the healthcare industry.[12] In the ICU, ventilator-associated pneumonia (VAP) is a leading cause of death. The most common organisms causing ventilator-associated pneumonia (VAP) are *Pseudomonas aeruginosa*, *Acinetobacter species*, Klebsiella *pneumoniae*, *Enterobacter species,* and *MRSA* (*methicillin-resistant Staphylococcus aureus*). The emergence of ESBL (Extended spectrum beta lactamases), Amp C beta lactamases, and Metallo-beta lactamases by *Pseudomonas* and Acinetobacter species results in multidrug resistance.[13]
Thus, VAP poses serious problems in endotracheally intubated patients in ICUs across the world. It harms clinical outcomes, prolongs hospital stays, and raises healthcare expenses.[14] VAP can be caused by a variety of factors, including the type of critical care unit and the type of patient. Because of this, all clinical environments should be investigated for the presence of VAP- associated microorganisms and their sensitivity patterns to guide the appropriate and effective administration of antimicrobial drugs.[15] Many patients at our tertiary care hospital get mechanical ventilator assistance regularly. Antibiotic susceptibility patterns of the pathogens that cause VAP will be determined in this investigation.[16] This study aims to determine the sensitivity, and resistance pattern of organisms causing VAP and also determines the clinical profile of patients associated with VAP. Hence, the findings can help clinicians determine which antibiotics are most likely to be effective in the presence of VAP-causing microbes.

2. MATERIALS AND METHODS

This cross-sectional study was conducted from Jan 2020 to Dec 2020 in an Intensive care unit at a single tertiary care center in south India. A total of 65 patients were admitted to the intensive care unit (ICU), Patients on Invasive mechanical ventilation developing pneumonia after 48 hours of initiation of mechanical ventilation, and Patients with more than 18 years. Suffering from pneumonia on admission or during the first 48 hours of mechanical ventilation. Intubation was done in another hospital, Aged less than 18 years.
All patients who developed VAP in the ICU during the study and qualified for the inclusion criteria were investigated clinically, radiologically, and on a microbiological basis. Clinical history and examination- Relevant clinical history with patient symptoms was noted. The total count was collected after 48 hours of mechanical ventilation of the patients. A chest X-ray

anteroposterior (AP) view was taken after 48 hours of mechanical ventilation. Endotracheal Tube Aspirate was collected Culture sensitivity was noted. CPIS score was calculated after 48 hours of mechanical ventilation score of more than 6 is indicative of VAP.

Statistical Analysis

Since the study is an observational study the plan of analysis was followed. The mean and standard deviation were determined for the continuous quantitative variables. If the data is separated into two groups based on a certain qualitative trait, the continuous variables were compared using appropriate statistical methods, such as the student's unpaired t-test. Discrete variables were represented by a median. Rates, ratios, and percentages were used to express categorical data. The chi-square test, test of proportion, or Fisher's exact test were used to examine the relationship between the outcome, and clinical and demographic factors. For discrete variables, nonparametric tests were used. ANOVA, correlation, regression, and other appropriate tools were employed in addition to those already mentioned. The contrast was shown through the use of appropriate graphs. *p* less than 5% (0.05) was judged significant in all of the tests. SPSS v21 on Windows 10 was used for statistical analysis.

3. RESULTS

A total of 70 patients were included in the present study, after fulfilling the inclusion criteria. The mean age of participants was found to be 49.33±16.46yrs of age, with the majority of patients in the age group of 40-60 years of age. In the present study, male preponderance is noted with 84.3% male and 15.7% female patients, and male to female ratio of 6:1. All the samples for the study were received from various critical care units, among them majority were from Neurosurgical ICU (NS) (44.3%), followed with 37.1% from Neuro-medicine (NM), 15.7% from medical ICU (MICU) and 2.9% from Surgical ICU (SICU). On the assessment of comorbidities, among the patients, 67.1% showed no comorbidities, 15.8% had hypertension and 12.9% had diabetes mellitus (Table 1 and Table 2).

On the assessment of CPIS scoring, the majority had a score of 7 (42.9%), followed by 34.3% having a score of 8, and 10% had scores of 9 and 10. Among the infections seen due to ventilator- associated pneumonia, 30% of them had gram-positive infections and 70% had gram-negative infections (Table 3) Among the infecting organisms, the majority were infected with *Klebsiella pneumonia* (27.1%), followed by *Enterobacter cloacae* (14.3%), *Acinetobacter baumannii* (12.9%), *Pseudomonas aeruginosa* (10%) and CONS in 8.6%. Other lower percentage infections seen were 4.3% with *Enterococcus faecalis*, *Escherichia coli*, *staphylococcus epidermidis*, 2.9% with *streptococcus bovis*, and *streptococcus pneumonia*. *MRSA* and *Enterococcus gallinarum* in 1.4%. On assessment of the sensitivity profile of the antibiotics among the various patient samples, it was found that more than 30% sensitivity was seen with Tigecycline, followed by more than 20% sensitivity to gentamycin (Table 4). The majority of other drugs in the range of 10-20% sensitivity were openem, colistin, trimethoprim, fosfomycin, teicoplanin. On the assessment of resistance to various antibiotics, more than 90% resistance was shown with oxacillin, penicillin, ampicillin, aztreonam, cefepime, cefotaxim, cefazolin, Cefuroxime, norfloxaxin, ertapenem, rifampicin and daptomycin. Antibiotics showing the least resistance were tigecycline, followed by gentamycin, amikacin, and trimethoprim. The average duration of patients suffering from VAP was 20.31 days (Table 5 and Table 6).

4. DISCUSSION

VAP is responsible for one-fourth of all infections in critically sick patients and is the cause of half of all antibiotic prescriptions in mechanically ventilated patients.[17] Several nations have recorded fatality rates ranging from 24% to 76%. Study participants with ventilator-associated pneumonia were surveyed for their clinical profile and drug sensitivity and resistance patterns. Patients who met the inclusion criteria were enrolled in this trial, which included a total of 70 participants.[18-21] The mean age of participants was found to be 49.33±16.46yrs of age, with the majority of patients in the age group of 40-60 years of age. In our study, we have seen male preponderance with 84.3% being male and 15.7% being female patients, with male to female ratio of 6:1. In similar to the present study, Patil et al., documented that there is male preponderance with male to female ratio of 3:1. The mean age of patients in their study was found to be 49±14yrs.[22]

Fever was found to be the most common presenting symptom in 64.2% of cases, followed by tachycardia (60%) increased tracheal secretions (55.7%), crepitations (51.42%), rhonchi (37.14) hypotension (35.71%) and bronchial breath sounds (28.5).in the remaining cases. 15.7 percent of patients were found to have *Leucocytosis* after further testing. *Leucocytosis* was present in 85.7% of patients with VAP. The average duration of Hospital stays of patients suffering from VAP was 20 Days. 85.7 percent of the patients exhibited improvement, while 14.3 percent died as a result of the disease. Sixty-one percent of those studied were found to have no comorbidities, with 15.8% suffering from hypertension and 12.9% suffering from diabetes mellitus. There were

42.9 percent of CPIS scorers in the 7-score range, followed by 34.3 percent in the 8-score range, and 10 percent in the 9- and 10-score range. Use of corticosteroids, past use of antibiotics, incorrect empirical antimicrobial treatment, and mixed/polymicrobial etiology were all risk factors for VAP in the 40 MDR group.

Among the patients with ventilator-associated pneumonia, 30% of them had gram-positive infections and 70% had gram-negative infections in them. Among the infecting organisms, the majority of the patients were infected with *Klebsiella pneumonia* (27.1%), followed by *Enterobacter cloacae* (14.3%), *Acinetobacter baumannii* (12.9%), *Pseudomonas aeruginosa* (10%) and CONS in 8.6%. Other less percentage infections seen were 4.3% with *Enterococcus faecalis*, *Escherichia coli*, *staphylococcus epidermidis*, 2.9% with *streptococcus bovis*, *streptococcus pneumoniae*. *MRSA* and *Enterococcus gallinarum* were found in 1.4% of the patients.

In a study by Patil et al., showed the presence of gram-positive cocci in 17.46% of patients and the presence of gram-negative bacilli in 70.27% of patients with VAP. The organisms isolated were predominantly GNB Klebsiella 29(23.01587%), Pseudomonas 27(21.42%), Acinetobacter 24(19.04%), and *E. Coli* 19 (15.07%) with high mortality rates.[22] In a study by Ahsan ASM et al., documented Gram-negative organisms (76.13 percent) were the most often isolated species, followed by fungus (17.04 percent) and gram-positive cocci (6.81 percent). [23]

In our study tigecycline was found to be the most sensitive antibiotic, followed by gentamycin, with more than two-thirds of the sample size showing a high degree of sensitivity to these two antibiotics. The majority of the other drugs were in the range of 10% to 20% sensitivity, were Amikacin, Amoxiclav, Cefoxitin, Ceftazidime Ciprofloxacin Levofloxacin, Meropenem, Colistin Trimethoprim, Fosfomycin, Teicoplanin, Oxacillin, Penicillin, Ampicillin, Aztreonam, Cefepime, Cefotaxim, Cefazolin, Norfloxaxin, Ertapenem, Rifampicin, and Daptomycin were all found to be resistant to a wide range of medicines. In a study done by Weiner et al., setfanidis et al., 16 (12.69 percent) isolates were sensitive to meropenem, 19 (15.07 percent) to piperacillin (PI), 20 (15.87 percent) amikacin, 27(21.42 percent) tigecycline and 18(14.28 percent). Several gram-negative isolates are more sensitive to Colistin,

Amikacin, and Meropenem than other antibiotics.[24-25] In a study by Wunderink et al., Staub et al., *Acinetobacter sp*. was the most frequent pathogen, *Klebsiella sp*., *Candida sp*., and *Pseudomonas sp.* were next. Among the gram-negative organisms, Acinetobacter *sp*., *Klebsiella sp*., and *Pseudomonas sp*. were particularly resistant (>80%) to third- generation cephalosporins and fluoroquinolones. Resistance to aminoglycosides (>68%) and imipenem (>60%) was also common. When compared to *Acinetobacter sp*. and *Klebsiella sp*., *Pseudomonas sp*. resistance to piperacillin-tazobactam was lower (18.2 percent).[26,27] Many intensive care units are concerned about the development of therapeutic resistance against the bacteria that causes VAP, according to these findings.[28-35] Antibiotic susceptibility patterns can assist you in avoiding unnecessary antibiotic use and in the effective management of VAP.[36-40]
Gram-negative bacilli were shown to prevail in a study by Chaudhury et al., followed by *Pseudomonas sp*. and *Klebsiella sp*. *Klebsiella sp.* (23.7 percent in 2011 to 19.3 percent in 2013) and *E. coli* decreased slightly in relative frequency over time, although the overall number of these organisms remained stable (14.9-11.5 percent throughout the same period).[31] The most common bacteria causing VAP among the various samples from different ICUs were *Klebsiella Pneumoniae* followed by the presence of *Enterobacter cloacae*. The sensitivity pattern showed that tigecycline has the highest sensitivity followed by Gentamycin among the organisms and more than 90 percent resistance was documented with the oxacillin, penicillin, ampicillin, aztreonam, cefepime, cefotaxim, cefazolin, Cefuroxime, norfloxaxin, ertapenem, rifampicin and daptomycin. VAP prolongs the hospital stay of the patients thus increasing the cost of treatment and also worsening the outcome.

5. CONCLUSION

The prevalence of multidrug-resistant microorganisms is at an increasing rate. Among them, gram-negative organisms are more predominant than gram-positive organisms. The common clinical presenting feature was found to be fever followed by tachycardia and increased tracheal secretions. The common isolates among the various samples from the different critical wards were found to be positive for *Klebsiella Pneumoniae* followed by the presence of Enterobacter cloacae. The sensitivity pattern showed the highest sensitivity to Tigecycline followed by gentamycin among the organism and more than 90 percent resistance was documented with the oxacillin, penicillin, ampicillin, aztreonam, cefepime, cefotaxim, cefazolin, Cefuroxime, norfloxaxin, ertapenem, rifampicin and daptomycin. VAP prolongs the hospital stay of the patients, thus increasing the cost of treatment and worsening the outcome. An understanding of the sensitivity and resistance patterns of organisms causing VAP can help in developing an efficient antimicrobial policy against these infections.

Conflict of Interest: Declared None

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Tables

Table 1. Clinical features of the patient in percentage.

Clinical features	Frequency	Percentage
Fever	45	64.2
Tachycardia	42	60
Tachypnea	38	54.2
Bronchial breath sound	20	28.5
Crepitation	36	51.42
Rhonchi	26	37.14
Increased tracheal secretions	39	55.7
Hypotension	25	35.71

Table 2. Clinical Outcome of the Patients.

		Frequency	Percent
Outcome	Expired	10	14.3
	Improved	60	85.7
	Total	70	100.0

Table 3. Showing the distribution of the type of patients included in the study.

		Frequency	Percent
Type of patient	MICU	11	15.7
	NM	26	37.1
	NS	31	44.3
	SICU	2	2.9
	Total	70	100.0

Table 4. Showing the various organisms isolated from the VAP patients.

		Frequency	Percent
Organism isolated	*Acinetobacter baumannii*	9	12.9
	CONS	6	8.6
	Enterobacter cloacae	10	14.3
	Enterococcus	2	2.9
	Enterococcus faecalis	3	4.3
	Enterococcus gallinarum	1	1.4
	Escherichia coli	3	4.3
	Klebsiella pnemoniae	19	27.1
	MRSA	2	2.9
	Pseudomonas aeruginosa	7	10.0
	Staphylococcus aureus	3	4.3
	Staphylococcus epidermidis	1	1.4
	Streptococcus bovis	2	2.9
	Streptococcus pneumoniae	2	2.9
	Total	**70**	**100.0**

Table 5. Showing the pattern of antibiotic sensitivity and resistance to various drugs.

		Frequency	Percent
Amikacin	Intermediate	5	7.1
	Resistant	55	78.6
	Sensitive	10	14.3
Oxacillin	Resistant	65	92.9
	Sensitive	5	7.1
Penicllin	Resistant	65	92.9
	Sensitive	5	7.1
Ampicillin	Resistant	65	92.9
	Sensitive	5	7.1
Amoxiclav	Resistant	62	88.6
	Sensitive	8	11.4
Aztreonam	Resistant	68	97.1
	Sensitive	2	2.9
Cefoxitin	Resistant	63	90.0
	Sensitive	7	10.0
Cefepime	Resistant	64	91.4
	Sensitive	6	8.6
Cefotaxim	ESBL	2	2.9
	Intermediate	1	1.4
	Resistant	64	91.4
	Sensitive	3	4.3
Ceftazidime	ESBL	1	1.4
	Resistant	62	88.6
	Sensitive	7	10.0
Cefazolin	Resistant	68	97.1
	Sensitive	2	2.9

Cefuroxime	Intermediate	1	1.4
	Resistant	67	95.7
	Sensitive	2	2.9
Ciprofloxacin	Resistant	60	85.7
	Sensitive	10	14.3
Norfloxaxin	Resistant	68	97.1
	Sensitive	2	2.9
Levofloxacin	Intermediate	1	1.4
	Resistant	58	82.9
	Sensitive	11	15.7
Moxifloxacin	Intermediate	2	2.9
	Resistant	62	88.6
	Sensitive	6	8.6
Ertapenem	Resistant	65	92.9
	Sensitive	5	7.1
Imipenem	Resistant	59	84.3
	Sensitive	11	15.7
Meropenem	Resistant	58	82.9

	Sensitive	12	17.1
Piperacillin	Intermediate	2	2.9
	Resistant	63	90.0
	Sensitive	5	7.1
Tigecycline	Intermediate	1	1.4
	Resistant	48	68.6
	Sensitive	21	30.0
Colistin	Intermediate	1	1.4
	Resistant	58	82.9
	Sensitive	11	15.7
Chloremphenic ol	Intermediate	1	1.4
	Resistant	64	91.4
	Sensitive	5	7.1
Tetracycline	Intermediate	2	2.9
	Resistant	58	82.9
	Sensitive	10	14.3
Daptomycin	Resistant	65	92.9
	Sensitive	5	7.1
Gentamycin	Resistant	54	77.1
	Sensitive	16	22.9
Vancomycin	Intermediate	2	2.9
	Resistant	62	88.6
	Sensitive	6	8.6
Clarithromyci n	Intermediate	1	1.4
	Resistant	65	92.9
	Sensitive	4	5.7
Clindamycin	Resistant	62	88.6
	Sensitive	8	11.4
Netilmycin	Intermediate	1	1.4

	Resistant	65	92.9
	Sensitive	4	5.7
Trimethoprim	Resistant	58	82.9
	Sensitive	12	17.1
Linezolid	Intermediate	1	1.4
	Resistant	62	88.6
	Sensitive	7	10.0
Teicoplanin	Resistant	62	88.6
	Sensitive	8	11.4
Fosfomycin	Resistant	63	90.0
	Sensitive	7	10.0
Fusidic acid	Intermediate	2	2.9
	Resistant	64	91.4
	Sensitive	4	5.7
Rifampicin	Resistant	64	91.4
	Sensitive	6	8.6

Table 6. showing WBC counts in patients with VAP

WBC count in patients with VAP	Present in total patients	Percent
Leucocytosis (WBC more then 1100 cells/microL)	60	85.7
Leucopenia (WBC count less then 4400/microL)	1	1.42
Normal WBC count(4400-11000 cells/microL)	9	12.8