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Original Research Article

Assessing Clinico-Etiological Pattern and Their Drug Sensitivity and Resistance Pattern of Antimicrobial Drug Use in Ventilator Associated Pneumonia (VAP)

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Conflict of interest: Nil

Abstract:

Aim: The aim of the present study was to assess the pattern of antimicrobial drug use in VAP and to assess the etiological organisms and their drug sensitivity and resistance pattern.

Material & Methods: Study participants admitted to Department of Pharmacology, who developed VAP were included in this prospective observational study. Bronchial secretions were subjected to microbiological analysis. The etiological organisms, their drug sensitivity and resistance pattern, and the outcome of drug therapy were recorded. The clinical course of the study participants was monitored till either the resolution of pneumonia or the demise of the participant. Qualitative data were analyzed using the Chi-square test or Fischer's exact test and quantitative data using the independent t-test.

Results: In the present study, 68% were male and 32% were females. 58% patients belonged to 18-60 years of age and 67% were unemployed. 96% were living in rural area and 66% had education of primary school. 905 belonged to lower middle class. Majority of the patients admitted to ICU due to acute respiratory failure (34%), followed by shock (21%). Majority of the patients had systemic hypertension followed by diabetes. Out of 42 patients >60 years, 34 had early LAP and out of 68 male, 60 had early LAP. 74% had VC-AC ventilator mode followed by VC-SIMV 20% and SIMV 6%. Most of the antibiotics used were Piperacillin + tazobactam, Meropenem, Macrolides, Cephalosporins. Comparison of mean duration of intubation, mean period of stay in the intensive care unit and mean period of hospital stay after extubation in early versus late ventilator-associated pneumonia showed significant result.

Conclusion: VAP is a serious problem in ICU leading to prolonged hospitalization and its associated financial implications, and mortality. Effective sepsis practice like hand washing is widely considered as an important but underutilized measured to prevent nosocomial infections like VAP.

Keywords: Antimicrobial Drug Resistance, Clinical Pulmonary Infection Score, Intensive Care, Ventilator-Associated Pneumonia.

Introduction

Pneumonia is the second most common nosocomial infection among critically ill patients, affecting 27% of all critically ill patients. [1] It is one among the leading cause of morbidity and mortality among the hospital acquired infections. [2] Ventilator associated pneumonia (VAP) refers to hospital acquired pneumonia that occurs within 48 hours or longer after mechanical ventilation (MV). It is characterized by the presence of new or progressive infiltrate, sign of systemic infection (fever, altered white cell count), changes in sputum characteristics. [3] Ventilator-associated pneumonia (VAP) is the most commonly seen nosocomial infection among mechanically ventilated patients accounting for 25% of all types of an intensive care unit (ICU)-acquired infections [4] and is the biggest concern for critical care specialists despite advancements in prevention, antimicrobial therapy, and supportive care. VAP imposes a significant economic burden on healthcare systems, and more than half of prescriptions in intensive care units (ICU) are found to be administered for VAP cases. [5,6,7]

Increasing drug resistance rates among Gram-negative pathogens that frequently cause VAP may compromise treatment and result in prolongation of hospital stays, inflation of inpatient health care costs and further increase in hospital mortality. [8,9] The infecting pathogens can be resistant to the chosen antibiotic at the start of its administration or acquire resistance during therapy, particularly with a single-agent treatment. [9]

The appropriateness for initial empiric antimicrobial therapy for VAP is greatly reliant on the type of causative pathogen and its resistance pattern. [9] The resistance against commonly used antimicrobials for VAP-associated pathogens, such as Pseudomonas aeruginosa and Acinetobacter baumannii, has been shown to be higher in the ICUs of developing countries than ICUs in the US. [10,11] The most common pathogens causing VAP are bacteria including multidrug-resistant pathogens. [12]

Hence, the objectives of this study were to assess the pattern of antimicrobial drug use in VAP, the etiological organisms involved, and their antimicrobial susceptibility.

Material & Methods

A prospective observational study was conducted in Department of Pharmacology, DMCH, Laheriasarai, Darbhanga, Bihar, India with 100 patients admitted for mechanical ventilation and developed VAP for the duration of 12 months. All study participants meeting the inclusion and exclusion criteria were included in the study after the study participants signed the written informed consent.

Inclusion Criteria

- Subjects of either gender, aged ≥18 years admitted as inpatients in Dmch, Darbhanga, who received mechanical ventilation and developed VAP.
- Subjects willing to give a written informed consent.

Exclusion Criteria

- Subjects in whom adequate sputum samples cannot be obtained.
- Subjects with viral, fungal, or aspiration pneumonia
- Subjects with tubercular (TB) pneumonia
- Subjects who are seropositive for HIV infection
- Subjects with diagnosed malignancy
- Subjects with pre-existing VAP
- Subjects and/or legal representative(s) not willing to give written informed consent.

Methodology

A diagnosis of pneumonia was made based on clinical examination as well as assessment by diagnostic tests. Diagnostic tests as a part of diagnosis and management included chest X-ray, computed tomography scan (if required), bronchial secretions (microscopy, culture, and drug sensitivity), and blood tests including complete blood counts, erythrocyte sedimentation rate and blood culture and sensitivity (if required) Laboratory investigations including serum urea and creatinine, serum electrolytes, arterial blood gas analysis, and serum procalcitonin (in sepsis patients) were carried out as required for the management of pneumonia. The specimen (bronchial secretions) obtained from all study subjects were subjected to microbiological analysis the various microbiological analysis performed in the bronchial secretions obtained such as by gram staining, 5% sheep blood agar , chocolate agar, MacConkey agar and Brain-heart infusion broth. Drug therapy for VAP was initiated empirically and was further adjusted according to the drug sensitivity and resistance pattern The demographic details, comorbid conditions, duration of hospital stay, and the drug therapy during the hospital stay, including antimicrobial drugs used were recorded The pattern of antimicrobial use including the class of antimicrobial agent(s), formulation, dose, route, frequency, duration of administration, and any change in antimicrobial therapy (and reasons for the change) were recorded. The etiological organisms, their drug sensitivity and resistance pattern, and the outcome of drug therapy were documented. Improvement/worsening of the condition was clinically assessed also using repeat chest X-rays, total blood counts (TC, DC), and other laboratory parameters. The clinical course of the study subject was monitored till either the pneumonia was resolved or the patient was discharged from the hospital or for 30 days, whichever was later. The diagnosis of VAP was made using the clinical pulmonary infection score (CPIS).

The data collected from all the study subjects was entered into a case record form and was subjected to statistical analysis.

Statistical Analysis

Microsoft Excel data sheet was used for data entry and SPSS software, version 22, was used for data analysis. Frequencies and proportions were used for representing categorical data. The test of significance for qualitative data was either Chi-square test or Fischer's exact test. Mean and standard deviation was used to represent continuous data. To identify the mean difference between two quantitative variables, the test of significance was independent t-test MS Excel and MS Word were used for graphical representation of data and to obtain various types of graphs. After

assuming all the rules of statistical tests, $P < 0.05$ was considered statistically significant.MS Excel and SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) were the statistical software used to analyze data.

Results

Table 1: Demographic characteristics

Characteristics	N%
Male	68 (68)
Female	32 (32)
Age in years	
18–60	58 (58)
	42 (42)
Occupation (according to Revised Kuppuswamy's Socioeconomic Status Scale)	
Skilled	6 (6)
Semi-skilled	2 (2)
Unskilled	25 (25)
Unemployed	67 (67)
Living status	
Rural	96 (96)
Urban	4 (4
Education level	
High school	14 (14)
Middle school	7 (7)
Primary school	66 (66)
Illiterate	13 (13)
Socioeconomic background	
Upper middle	2 (2)
Lower middle	90 (90)
Upper lower	8 (8)

In the present study, 68% were male and 32% were females. 58% patients belonged to 18-60 years of age and 67% were unemployed. 96% were living in rural area and 66% had education of primary school. 905 belonged to lower middle class.

Table 2: Reasons for intensive care unit admission

Reasons for ICU admission	N (%)
Acute respiratory failure	34 (34)
Drug/insecticide poisoning	6 (6)
RTA	3 (3)
Cardiac arrest	10 (10)
Congestive cardiac failure	5 (5)
Fulminant hepatic failure	5 (5)
Postsurgical complication	2 (2)
Cerebrovascular accident	7 (7)
Bacterial meningitis	2 (2)
Status epilepticus	3 (3)
Partial hanging	2 (2)
Shock	21 (21)
Total	100 (100)

Majority of the patients admitted to ICU due to acute respiratory failure (34%), followed by shock (21%).

Table 3: Co-morbid conditions

Co-morbidities	N%
Type 2 DM	48 (48)
Systemic essential HTN	58 (58)
Liver dysfunction	10 (10)
Renal dysfunction	40 (40)
IHD	7 (7)
COPD	15 (15)
Hypothyroidism	3 (3)
Seizure disorder	2 (2)

Majority of the patients had systemic hypertension followed by diabetes.

Table 4: Risk factors for ventilator-associated pneumonia

Multiple risk factors	Early VAP (n)	Late VAP (n)	Total (n)
Age >60 years	34	8	42
Male, gender	60	8	68
Coma	0	0	0
ARDS	34	0	34
Reintubation	9	1	10
Neurosurgery	5	0	5
COPD	6	0	6
Thoracic surgery	0	1	1

Out of 42 patients >60 years, 34 had early LAP and out of 68 male, 60 had early LAP.

Table 5: Mode of mechanical ventilation

Ventilator modes	Early VAP (n)	Late VAP (n)	Total (n) %)
VC-AC	68	6	74 (74)
VC-SIMV	18	2	20 (20)
SIMV	4	2	6 (6)
Total	90	10	100 (100)

74% had VC-AC ventilator mode followed by VC-SIMV 20% and SIMV 6%.

Table 6: Antimicrobials used at the time of intensive care unit admission

Antimicrobials used in the ICU	N
Cephalosporins	34
Macrolides	36
Meropenem	40
Piperacillin + tazobactam	70
Linezolid	15
Vancomycin	12
Metronidazole	32
Levofloxacin	12
Clindamycin	4
Amikacin	4

Most of the antibiotics used were Piperacillin + tazobactam, Meropenem, Macrolides, Cephalosporins.

Table 7: Comparison of mean duration of intubation, mean period of stay in the intensive care unit and mean period of hospital stay after extubation in early versus late ventilator-associated pneumonia

Parameters	Group	Days, mean±SD	P
Duration of intubation	Early LAP	6.58±2.6	0.012
	Late LAP	9.6±2.6	
Duration of stay in the ICU	Early LAP	7.11±2.6	0.025
	Late LAP	10±3.3	
Hospital stay after extubation	Early LAP	3.32±2.3	0.144
	Late LAP	2.75±0.5	

Comparison of mean duration of intubation, mean period of stay in the intensive care unit and mean period of hospital stay after extubation in early versus late ventilator-associated pneumonia showed significant result.

Discussion

Pneumonia refers to infection of the pulmonary parenchyma [12] which accounts for 55.4% of deaths due to lower respiratory tract infections and 103 million loss of disability-adjusted life-year. [13] Tracheal intubation and mechanical ventilation used to support the critically ill patients puts them at a greater risk of developing nosocomial infections (NIs). [14] NIs are infections that patients acquire either in the hospital or such facilities such as nursing homes, outpatient clinics, or diagnostic laboratories. [15] NIs are seen in 5%–10% of hospitalized patients. More than 60% of these infections are due to pneumonia, urinary tract infection, and bloodstream infection. [16] Microorganisms are resistant to one or more antimicrobials in 70% of these infections. [17]

In the present study, 68% were male and 32% were females. 58% patients belonged to 18-60 years of age and 67% were unemployed. 96% were living in rural area and 66% had education of primary school. 905 belonged to lower middle class. Majority of the patients admitted to ICU due to acute respiratory failure (34%), followed by shock (21%). Majority of the patients had systemic hypertension followed by diabetes. The common

comorbidities seen in the study participants were type 2 diabetes mellitus, hypertension, liver dysfunction, renal dysfunction, ischemic heart disease and COPD. None of the WHO priority pathogens were encountered in this study. [18] The risk factors for VAP, the reasons for ICU admission and mechanical ventilation and the comorbidities seen in the present study participants were akin to other reports by Karakuzu et al., [19] Chittawatanarat et al [20] and Ali et al. [21]

Out of 42 patients >60 years, 34 had early LAP and out of 68 male, 60 had early LAP. 74% had VC-AC ventilator mode followed by VC-SIMV 20% and SIMV 6%. Most of the antibiotics used were Piperacillin + tazobactam, Meropenem, Macrolides, Cephalosporins. The antimicrobial agents that were used empirically in the study participants upon admission to the ICU included cefotaxime, ceftriaxone, fixed drug combination (FDC) of cefoperazone and sulbactum, azithromycin, clarithromycin, meropenem, FDC of Piperacillin and tazobactam, linezolid, vancomycin, metronidazole, levofloxacin, clindamycin, and amikacin. This was also in consonance with a study by Tran et al. [22] In a study conducted by Akram et al. in South India, 30% of patients had quinolone prescriptions followed by cephalosporins and other antibiotics. Cephalosporins are generally widely used medicine due to their high potent action, available in various formulations in the market, their extended indications and the activity against both the bacteria gram-negative as well as gram-positive means having broad-spectrum activity from the first generation to the third generation of cephalosporins. [23] Comparison of mean duration of intubation, mean period of stay in the intensive care unit and mean period of hospital stay after extubation in early versus late ventilator-associated pneumonia showed significant result.

Conclusion

VAP is a serious problem in ICU leading to prolonged hospitalization and its associated financial implications, and mortality. Effective sepsis practice like hand washing is widely considered as an important but underutilized measured to prevent nosocomial infections like VAP. Main causative organism is pseudomonas in endotracheal aspirate, which needs to be diagnosed and treated as early as possible. Hence, better knowledge of local patterns of pathogens causing VAP can help the clinicians facilitate treatment options. Further studies are needed to under the condition of ICU in detail.

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