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ANALYSIS OF EMPIRICAL THERAPY IN VENTILATOR ASSOCIATED PNEUMONIA IN ICU IN PAKISTAN

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Abstract:
Introduction: Ventilator Associated Pneumonia is one of the common and fatal among Nosocomial infections that requires in time, appropriate and adequate antibiotic therapy. Mortality rates are greater in patients with ventilator associated pneumonia; the chances of mortality are maximum in bed ridden immune compromised patients in ICU.
Objective: The objective of this study was the evaluation of Empirical therapy in suspected VAP cases in ICU patients.
Methods: This prospective study was conducted in Bahawalpur Victoria Hospital during January 2019 to July 2019. The method involved pathogen identification, Antibiotic Sensitivity testing, hepatic, renal and hematological profiles and monitoring of Arterial blood gases of the patient. Pathogens from tracheal aspirates of the patients were subjected to commonly used antibiotics for their antibiograms. The prescribed antibiotics were evaluated by routine culture/sensitivity testing of tracheal aspirates and each patient was followed up to be assessed for the treatment progress. Effect of Antibiotic was evaluated for seven days by maintaining the record of the vital parameters of patients such as Temperature of the patient, PaO2, effect on leukocyte count, and from evaluation of LFTs and RFTs of the patient and chest radiograph obtained at the seventh day and keeping in view the overall disease status of the patient. Other outcomes were the mortality in these patients and the impact of inadequate empirical therapy on patient mortality. Also, to study the contribution of various risk factors upon VAP prognosis.
Results: The microbial flora and their resistance pattern is a matter of great concern for adopting the strict infection control measures, hospital wise antibiotic policy formulation to reduce morbidity, mortality and to prevent the emergence of resistant pathogens.
Conclusions: In this study, there was a high incidence of infection with resistant bacteria and inappropriate initial antibiotic therapy. Treatment failure due to inadequate antibiotics caused most mortality. Organ deterioration was also found to contribute to overall mortality in mechanically ventilated patients.

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INTRODUCTION:

Ventilator associated pneumonia is a nosocomial infection occurring with high frequency in bedridden patients upon mechanical ventilation. It is not present at the time of admission but develops after 48hrs of intubation. There is no golden standard yet for its diagnosis but any patient upon mechanical ventilation greater than 48hrs could be suspected for VAP [1]. Most of the antibiotics prescribed in the intensive care settings are mostly for nosocomial lower respiratory tract infections. Antibiotic selection widely depends upon the pathogen identified and culture sensitivity reports. At this point there is a need for larger, well designed clinical studies. Usually in early onset VAP most of the bacteria are sensitive to most antibiotics but delay in treatment or inadequate treatment increases the chances of emergence of MDR pathogens and thus complicates the treatment [2].

Further the emergence of MDR pathogens is more in ICU patients which are immunocomprimised. Late onset VAP mostly involves MDR pathogens which are difficult to treat and increases the mortality rate. Identification of Pathogen helps to choose more effective antibiotic and sensitivity testing helps to choose the targeted antibiotic thus allowing efficient management [3]. Risk factors involved are the duration of mechanical ventilation, handling of the patient by nurses and health care personnels, history of frequent antibiotic usage – all of these are independent risk factors associated with VAP. Usually increased mortality is observed in severely ill patients [4]. The Ventilator associated pneumonia has been poorly studied in Pakistan, but is likely to be significant problem, with resulting increased morbidity and mortality in the intensive care unit population. Less work has been done in our country to assess the frequency and etiology of nosocomial lower respiratory tract infections in patients admitted to intensive care unit as the causes are many and may vary by hospital, patient population, and type of ICU, thus emphasizing the need for timely, local surveillance data [5].

Objectives:

The study was designed to fulfill the following objectives:
1. To isolate and identify the bacterial pathogens from ventilator-associated infections in Surgical ICU patients.
2. To determine the antibiotic susceptibilities of bacterial isolates invitro and the trends in antibiotic resistance developed by pathogens from ventilator-associated infections.

METHOD:

This prospective study was conducted in Bahawalpur Victoria Hospital during January 2019 to July 2019. The method involved pathogen identification, Antibiotic Sensitivity testing, hepatic, renal and hematological profiles and monitoring of Arterial blood gases of the patient and frequent culturing of tracheal aspirates to evaluate the response for antibiotic therapy provided. Pathogens from tracheal aspirates of the patients were subjected to commonly used antibiotics for their antibiograms. Effect of antibiotic was evaluated for seven days by recording the parameters of patients such as Temperature of the patient, PaO2/FiO2 ratio, effect on leukocyte count, and monitoring of LFTs and RFTs of the patient for the possible organ deterioration. Other outcomes were the mortality in these patients and risk factors that result in overall high mortality among VAP patients.

A total of 90 morbid samples of tracheal aspirates were collected with the help of a trained physician. This process was performed on the day-one of the insertion of endotracheal tube. These specimens were collected with sterilized disposable Nelton catheters attached to the aspirator. The specimens were immediately transferred to the microbiological laboratory and subjected to bacteriological examination. The collected samples were cultured to check the evidence of any previous bacterial infection. The patients having negative results on the basis of their initial cultures were further included for the study and the cases with positive cultures were excluded from the study. A second sample was collected after 48 hours of mechanical ventilation for suspected VAP cases. After seven days of the second sample a third sample was taken to further assess the response of antibiotic therapy and there outcome. Isolation of microbes was achieved by agar plate inoculation method. Identification and confirmation of respiratory tract isolates were performed following the standard protocols as per Bergey's Manual of Determinative Bacteriology, basic parameters for identification of bacteria were based on morphological colonial characteristics, microscopic features and biochemical profiles.

Analysis:

To assess the safety of empirical medication provided the liver and renal functional tests were performed for each patient on the day of admission in ICU and on the last day of the treatment follow-up to access the possible liver and renal damage or change in the liver and renal functional status of these immunosuppressed patients.

RESULTS:

From a total of 90 samples, 58 were found positive for the isolation of bacterial pathogens of VAP. The incidence density of VAP among the patients admitted to ICU was found to be 64%. Patients were suspected for nosocomial lower respiratory tract infection considering Clinical Pulmonary infectious score chart. Out of 58 patients, 5(8.6%) had CPIS 6, 41(70.7%) had CPIS 6-8 and 12(20.7%) had CPIS 9-10 which were found consistent for the diagnosis of pneumonia.

Microbiological analysis of endotracheal samples from the patients suffering from ventilator-associated pneumonia revealed the presence of various types of bacteria. Of the 90 endotracheal samples, 58 (65%) samples were culture positive and remaining 32 (35%) samples were culture negative. A total of 58 bacterial pathogens were recovered from these culture positive samples. On bacteriological examination 18(31%) isolates of Methicillin Sensitive Staphylococcus aureus, 3(5.2%) isolates of Methicillin Resistant Staphylococcus aureus, 2(3.4%) isolates of Streptococcus, 9(15.5%) isolates of Pseudomonas, 5(8.6%) isolates of Acinetobacter, 5(8.6%) isolates of Klebsiella, 12(20.7%) isolates of Escherichia, 2(3.4%) isolates of Enterobacter and 2(3.4%) isolates of Proteus were characterized.

Table 1: Pathogens Isolates of VAP
No. of culture positive cases =58

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	MSSA	18	31.0	31.0	31.0
	MRSA	3	5.2	5.2	36.2
	E.Coli	12	20.7	20.7	56.9
	Pseudomonas Spp.	9	15.5	15.5	72.4
	Klebsiella Spp.	5	8.6	8.6	81.0
	Acinetobacter spp.	5	8.6	8.6	89.7
	Streptococci spp.	2	3.4	3.4	93.1
	Enterobacter spp.	2	3.4	3.4	96.6
	Proteus spp.				
	9.00	2	3.4	3.4	100.0
	Total	58	100.0	100.0	

Frequency of VAP In-relation to Gender
Among selected patients 69% were males and 31% were females. (Fig.2)
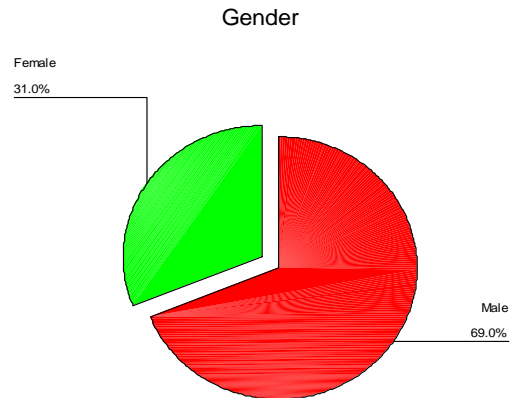

Fig 1: Frequency of Patients in Relation to Gender

Previous Exposure to Antibiotics Regarding previous exposure to antibiotics (within 3 months) it was inferred that the previous exposure to these antibiotics was found to be the most important contributing factor for the emergence of most resistant bacteria as causative agents of life-threatening VAP. Of the 58 patients, 30 (51.7%) had received Augmentin and 12 (20.7%) Clarithromycin, 8 (13.8%) Cephalexin, 5 (8.6%) Ceftazidime and 3 (5.2%) patients had received Flagyl. (Fig. 3)
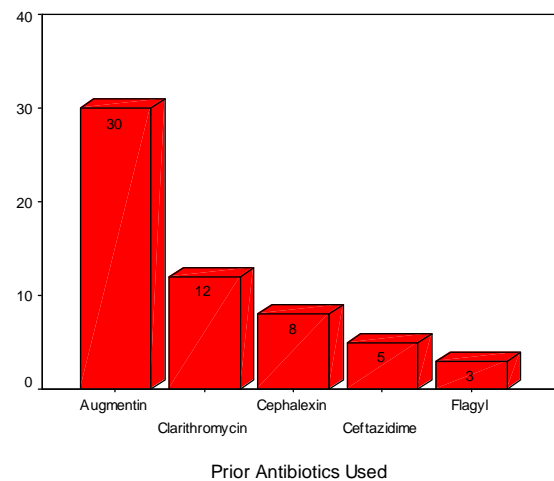

Fig 2: Frequency of Patients in Relation to Prior Exposure to Antibiotics

DISCUSSION:
The pathogenic bacteria most frequently isolated from the patients were MSSA (Methicillin Sensitive Staphylococcus aureus) (18; 31%), E.coli (12; 20.7%), Pseudomonas isolates (9; 15.5%), Acinetobacter (5; 8.6%) and Streptococci (5; 8.6%). Other organisms isolated were MRSA (Methicillin Resistant Staphylococcus aureus) (3, 5.2%), Streptococci (2, 3.4%), Enterobacter (2, 3.4%) and Proteus (2, 3.4%) [6]. MRSA was isolated from comatose patients with multiple neuronal damage. MSSA was the most dominant pathogen isolated. A comprehensive study conducted and revealed Pseudomonas aeruginosa as the most dominant pathogen isolated in VAP patients which in our study is the third most common pathogen

isolated [7]. Another study on Pathogens isolated from nosocomial infections reported Staphylococcus aureus as the leading pathogen isolated which is consistent with our study. Increased E.coli isolation has been reported by various studies in VAP patients as oropharyngeal aspiration is the most frequent route of entrance of these organisms into the lower respiratory tract which in our study is the second leading bacteria isolated [8]. All the isolated bacteria in our study are consistent with those reported in different studies on microbiology of ventilator associated pneumonia [9,10].

CONCLUSION:

The present study documents declining in vitro antibiotic susceptibility and development of resistance among virulent bacterial pathogens of ventilator-associated pneumonia (VAP). These bacteria developed increased resistance against commonly used antibiotics including Augmentin, Tetracycline, Ceftazidime, Ceftriaxone, Gentamicin, Erythromycin and Ciprofloxacin.

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