VENTILATOR ASSOCIATED PNEUMONIA AMONG PATIENTS ON MECHANICAL VENTILATION AT TERTIARY CARE CENTRES

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ABSTRACT

Objective: To determine the frequency of ventilator associated pneumonia (VAP) among patients on mechanical ventilation, and to identify the causative bacterial pathogens and antibiotic susceptibility pattern of isolated microorganisms in intensive care units of tertiary care settings.

Study Design: Descriptive cross sectional.

Place and Duration of Study: This study was conducted at Microbiology Department, Armed Forces Institute of Pathology (AFIP), Rawalpindi, from Dec 2014 to Aug 2015.

Material and Methods: A total of 176 patients on mechanical ventilation were included in the study; patients having respiratory tract infection before putting on ventilator were excluded. Endotracheal aspirate (ETA) and Bronchoalveolar lavage (BAL) samples were collected aseptically from patients on mechanical ventilation on day zero i.e. the day on which the patient was put on ventilator to rule out any previous respiratory tract infection and then after 48 hours to observe the development of VAP. Samples were processed in the laboratory by standard culture techniques, pathogens were identified and their antibiotic susceptibility was performed as per CLSI guidelines.

Results: Out of 176 patients on mechanical ventilation, 59 (33.5%) developed VAP. Acinetobacter baumanii being the predominant pathogen isolated from 32 (54.2%) patients followed by MRSA 11 (18.6%), Klebsiella pneumoniae 9 (15.2%), Pseudomonas aeruginosa 5 (8.47%) and Stenotrophomonas maltophila from 2 (3.38%) patients.

Conclusion: Frequency of VAP is quite high in our setup, identification of causative bacterial pathogens and their antibiotic susceptibility pattern will not only help in providing effective treatment to the patients but will also help in the formulation of antibiogram according to local resistance patterns for empirical therapy and to reduce the morbidity and mortality.

Keywords: Bronchoalveolar lavage, Intensive care unit, Mechanical ventilation, Multidrug resistant, Ventilator-associated pneumonia (VAP).

INTRODUCTION

Ventilator-associated pneumonia (VAP) is the type of pneumonia which develops after 48 hours or more in patients receiving mechanical ventilation (MV)[1]. VAP is considered as one of the most common infections of Intensive care units (ICUs). Frequency of VAP varies between 8 to 28% in patients receiving mechanical ventilation[2,3]. VAP brings about increased mortality and morbidity, along with extra financial burdens on patients and hospitals[4,5]. Mortality of VAP varies between 24 to 50%, it is much higher as compared with other healthcare associated infections (HAIs). In settings, where infection is caused by multidrug resistant (MDR) pathogens mortality is high up to 76%. It has also been established that the frequency of VAP is higher in countries with limited resources[6,7].

Pathogens commonly associated with VAP include gram negative bacilli such as, pseudomonas aeruginosa, escherichia coli, klebsiella pneumoniae, acinetobacter. And Gram positive cocci, such as staphylococcus

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aureus especially methicillin-resistant Staphylococcus aureus (MRSA). Most of the isolates responsible for VAP are MDR pathogens with very few treatment options available which makes it even more difficult to treat such cases[8].

VAP is a serious health care concern. It is associated with increased duration of hospital stay, increased morbidity, mortality and extra financial burden on patients and institutes. Detection of causative organisms and their antibiotic susceptibility is very important not only for diagnosis but also required to provide accurate treatment to the patients; furthermore, it also helps in the formulation of empirical therapy as per local resistance patterns. Empirical therapy needs diagnosis of VAP in order to initiate the right antibiotic treatment and to reduce the morbidity and mortality[9].

MATERIAL AND METHODS

This descriptive cross sectional study was conducted at the Department of Microbiology, Armed Forces Institute of Pathology, Rawalpindi Pakistan. Specimens were received from ICU of Combined Military Hospital (CMH) and medical ICU of Military Hospital (MH). Study was completed in period of nine months, Sample size was calculated using WHO sample size calculator with confidence level of 95% with anticipated population proportion at 8% with a precision of 0.04. Total of 176 patients were consecutively recruited, Descriptive cross sectional study was conducted. Endotracheal aspirate and Bronchoalveolar lavage samples were collected in sterile containers aseptically; Samples were taken on the day zero i.e. the day when patient is put on ventilator to rule out previous chest infection, after 48 hours in suspected cases with development of symptoms like fever with raised TLC and cavitations on chest X-ray. Samples were processed in the laboratory by using standard culture techniques, pathogens were identified and their antibiotic susceptibility was performed as per CLSI guidelines[10]. The data were entered in SPSS (version 17) software. Descriptive statistics were calculated for both qualitative and quantitative variables. For quantitative variables, mean ± SD were calculated. For qualitative variables like gender, frequency of VAP, frequency and percentages were calculated. Qualitative variables were presented as tables and charts. Chi square test was used to ascertain the association between qualitative variables and *p*-value less than 0.05 was considered significant.

RESULTS

Out of 176 patients 123 were male and 53 were female, the mean age of the patients was 63 years ± 13.3 (table-I). Out of 176 patients on mechanical ventilation, 59 (33.5%) developed VAP during the study period. Thirty nine (66.1%) were males and 20 (33.9%) were females showing that males were the predominant gender suffering from VAP in our study the majority of the VAP cases (81.3%) were caused by gram negative organisms (p=0.001) such as Acinetobacter baumanii, Klebsiella pneumoniae, Pseudomonas aeruginosa and Stenotrophomonas maltophila while the remaining percentage of 18.6 was of gram-positive organism like methicillin-resistant staphylococcus aureus (MRSA). Acinetobacter baumanii being the predominant pathogen was isolated from 32 (54.2%) patients (p=0.000) followed by MRSA 11 (18.6%), Klebsiella pneumoniae 9 (15.2%), Pseudomonas aeruginosa 5 (8.4%) and Stenotrophomonas maltophila from 2 (3.3%) patients.

Majority of the isolates were MDR with limited treatment options available. All isolates of acinetobacter baumannii (n=32) were resistant to ampicillin, ceftriaxone and ceftazidime but sensitive to polymyxin B. Resistance for other antibiotics such as sulbactam ampicillin 22 (68.8%), Doxycycline 14 (43.8%), cefipime 31 (96.9%), minocycline 11 (34.4%), tazobactam piperacillin 26 (81.3%), ciprofloxacin 31 (96.1%), gentamicin 20 (62.5%), amikacin 16 (50%), trimethoprim-sulfamethoxazole 28 (87.5%), Meropenem 23 (71.9%) and Imepenem 25 (78.1%) was found.

Among the isolates of staphylococcus aureus (n=11) all the isolates were methicillin resistant. Resistance to clindamycin and cotrimoxazole was 8 (72.7%), doxycycline 7 (63.6%), gentamycin 7 (63%), erythromycin and ciprofloxacin 6 (54.5%) tigecycline 5 (45.5%), amikacin 2 (18.2%), chloramphenicol 2 (18%). While all these 11 isolates were found sensitive to vancomycin and linezolid.

Multi drug resistance pattern of Klebsiella pneumoniae (n=9) showed 9 (100%) resistance to Ampicillin, 7 (77.8%) to Ciprofloxacin, 6 (66.7%) to Cotrimoxazole, Clavulanic acid–Amoxicillin, Gentamycin and Tigecycline, 5 (55.6%) to Ceftriaxone and Sulbactam-piperacillin (Combicin), 4 (44.4%) to Tazobactum-piperacillin (Tazocin), 3 (33.3%) Amikacin, Imepenim and Doxycycline. While all 9 isolates were senstitive to Polymyxin B.

All the isolates of Psuedomonas aeruginosa (n=5) were resistant to Ciprofloxacin but sensitive to Polymyxin B. Four (80%) of isolates showed resistance for Chloramphenicol, 3 (60%) for Ceftazidime, Aztreonam, Cefipime, Meropenem and Cefoperazone. Resistance to Gentamycin, Sulbactam-piperacillin, and Moxifloxacin was 2 (40%) and Amikacin and Tazobactum-piperacillin 1 (20%).

Stenotrophomonas maltophila (n=2) were found resistant to Ciprofloxacin, Chloramphenicol, Levofloxacin, Cefipime, Sulbactam-piperacillin, Imipenem and Meropenem. Resistance to Minocycline, Ceftazidime and Tazobactum-piperacillin was 1 (50%). While both isolates were sensitive to Cotrimoxazole and Polymyxin B.

Stratification of data with respect to age, gender and ventilator was done and chi square was applied which revealed the *p*-values of 0.067, 0.272 and 0.270 respectively, which showed that there is no relationship of age, gender and duration on ventilator (table-II, III & IV).

Table-I: Mean and SD of age of the patients.

Total Male Patients	Total Female Patients	Males Positive for VAP	Females Positive for VAP	Mean Age	Standard Deviation
123 (69.8)	53 (30.2)	39	20	63	13.36

Table-II: Stratification with respect to age.

Age Group (Years)	VAP		Total
	Yes	No	
30- 50	10	27	37
51-70	30	53	83
71-90	16	37	53
more than 90	3	0	3
Total	59	117	176

Table-III: Stratification with respect to gender.

Total Male Patients	Total Female Patients	Males Positive for VAP	Females Positive for VAP
123	53	39	20

Table-IV: Stratification with respect to duration on ventilator.

Duration on Ventilator	VAP After		Total
	Yes	No	
48 hours	49	91	140
More than 96	10	26	36
Total	59	117	176

DISCUSSION

Patients receiving MV are at the increased risk to develop VAP secondary to damages in host's first line defenses associated with endotracheal intubation[11]. Ventilator is a very useful device as it provides support the critically ill patients who are not able to breathe spontaneously because of severity of the disease, however its association with the disease like pneumonia is a matter of serious concern for the health care providers and patients aswell.

Thirty nine (66.1%) males developed VAP and 20 (33.9%) developed VAP in our study, this finding is similar to the study conducted at Korea and India which also showed male predominance[12]. The explanation of this finding in our set up could be the reason that this study was conducted in intensive care units of military hospital where most of the retired troops of old age entitled for medical treatment are males and their families are not entitled for treatment after retirement from military service.

Our study revealed high VAP rates (33.5%) among patients who were mechanically ventilated in the intensive care unit. The average VAP rates reported in other Indian studies range from 8.9 to 46%. The INICC data from studies of nosocomial infections in developing countries over 4 years, revealed that VAP infections, with an overall incidence of 41.5%, pose the greatest challenge for treatment among all HCAIs[13].

Results of one study conducted at Korea in 2012 showed the frequency of VAP was 22% with the predominant pathogen Staphylococcus aureus in 44% of cases[12]. This is different from our set up in which gram negative organisms predominated the list. This difference could be due to the difference in the set up and as discussed earlier the pathogens can vary in different set ups, therefore it becomes really important to know the pathogens of own settings and make antibiogram as per the pathogens.

Chinese study in 2013 showed the frequency of VAP 21% with predominant pathogen Klebsiella pneumoniae in 51% of cases[14]. This is similar to our study as far as Gram negative pathogens being the main causative pathogens are concerned, however frequency is much less then our study, probably it could be due to better infection control practices and better resources are then our setup.

Gram negative organisms caused a large majority of the VAP infections in our set up and Acinetobacter spp were the most frequently isolated pathogens in our study and this finding is similar to those of other Asian studies. A recent report presented by a panel of experts from Thailand shows that the Acinetobacter baumannii calcoaceticus complex is emerging as a major pathogen in the majority of their ICUs[15].

Infection by Acinetobacter baumanii specifically occurs in patients on mechanical ventilation in the ICU who have been previously treated with broad spectrum antibiotics such as third generation cephalosporins and carbapenams[16]. It is difficult to treat acinetobacter baumannii as it can survive in the environment for long periods of time and develops multiple drug resistance[17]. Reason for the development of resistance in these isolates is related to their nosocomial origin and repeated exposure to antibiotics which results in selection of genes leading to mutation in genome of bacteria making them more resistant to routinely used antibiotics making the treatment more difficult[18].

Carbepenems are usually the treatment of choice for Acinetobacter baumanii. However, if treatment fails due to the development of resistance, these can be substituted with polymyxins (colistin and polymyxin B), sulbactam and tigeycycline[19]. Our results support the above described statement in relation to Polymyxin B as all isolates were sensitive to Polymyxin B drug while for other drugs isolated pathogens have resistance. Thus, polymyxin B is better therapeutic options in our setup.

Among our patients, the high frequency of MDR organisms causing VAP probably contributed to the prolonged stay in intensive

care units because these infections took longer to treat and generally resulted in poor outcomes in the ICU

CONCLUSION

Frequency of VAP is high in our set up with Acinetobacter baumanii being the predominant pathogen, most of the isolates were MDR with very few treatment options available, this study has identified the pathogens for causing VAP in our set up and their latest susceptibility patterns, which will help in the formulation of antibiogram as per local resistance patterns and is expected in reducing the morbidity and mortality of the patients suffering from VAP in intensive care units.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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