A Study on Bacterial Etiology of Ventilator Associated Pneumonia and its Antimicrobial Pattern

N Chidambaram[1], Reena Rajan[2], G Sasikala[3], V Anandi[4]

ABSTRACT

Introduction: Ventilator Associated Pneumonia(VAP) remains a major cause of mortality and morbidity among critical ill patients. An imbalance between normal host defenses and the ability of microorganisms to colonize and invade the lower respiratory tract results in hospital acquired pneumonia. Aims and objectives were to isolate and identify bacterial pathogens from VAP and to determine their antibiogram.

Material and Methods: A total of 66 Endotracheal aspirates were included in this study. 0.01 ml of sample was inoculated onto Blood agar,Chocolate agar and MacConkey agar and plates were incubated overnight at 37°C for 24 and 48 hours. Bacterial isolates were identified by standard biochemical tests. Antimicrobial sensitivity testing was performed on Muller Hinton Agar by Kirby Bauer disk diffusion and interpreted as per the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: The occurrence of VAP was more common in the age group of 18-30 years (46.51%). Of the total cases 59.09% showed monomicrobial growth and 6.06% showed polymicrobial growth. The predominant gram negative isolate obtained was Klebsiella sp (68.89%) followed by Acinetobacter sp(15.56%) and Pseudomonas aeruginosa (13.33%). Among the Gram negative bacilli, 24.44% were resistant to Piperacillin Tazobactam and 35.56% to Cefoperazone sulbactam and 31.11% isolates were resistant to meropenem.All gram negative isolates were sensitive to Imipenem.

Conclusion: Knowledge on incidence of VAP, its etiology and susceptibility patterns is essential to initiate the empirical antibacterial therapy for patients on mechanical ventilation

Key words: Ventilator Associated Pneumonia, Endotracheal Aspirate, Quantitative Culture, Gram Negative Bacilli, Multidrug Resistant Klebsiella

INTRODUCTION

Ventilator Associated Pneumonia(VAP) is the most common nosocomial infection in patients on mechanical ventilation. VAP is defined as pneumonia occurring ≥ 48 hrs of intubation and the start of mechanical ventilation.[1] The principal risk factors for the development of VAP is endotracheal tube,which predispose to microaspiration of contaminated oropharyngeal secretions. Duration of mechanical ventilation,supine patient positioning,enteral feeding,modifiable factors associated with prolonged intubation such as oversedation or lack of protocol driven weaning increases the risk of developing pneumonia.[2]

Ventilator associated Pneumonia is categorised as early onset, if the infection occurs within first four days of mechanical ventilation and late onset if it occurs from 5 th day onwards.Early onset is commonly caused by antibiotic sensitive,community acquired organisms, where as late onset is caused by multiple drug resistant nosocomial strains.Early onset pneumonia is likely to be caused by Staphylococcus aureus,Streptococcus pneumoniae or Hemophilus influenzae, where as late onset is caused by multidrug resistant strains of Pseudomonas aeruginosa, Acinetobacter or Methicillin resistant Staphylococcus aureus(MRSA).[1,2]

The incidence of VAP occurs in 9-27% of mechanically ventilated patients with about 5 cases per 1000 ventilator. The etiologic agents of VAP include common nosocomial pathogens such as Pseudomonas spp, Acinetobacter and other non fermenters, members of Enterobacteriaceae family, Staphylococcus and Candida sps.[3,4]

Accurate diagnosis of VAP remains a challenge, with no consensus on a reference "gold standard" definition.Clinical diagnosis is established based on new or persistent infiltrates on chest radiography plus two or more of the following: (a). Purulent tracheal secretions

(b) Blood leucocytosis (>12×109 white blood cells/L) or leucopenia (<4×109 white blood cells/L), (c) Temperature greater than 38.3°C.[1,4]

Detection of the etiologic agents is crucial for the diagnosis of VAP which is done by collecting the lower respiratory tract sample either by invasive methods like protected specimen brush (PSB) and broncho-alveolar lavage (BAL) or non-invasive techniques endotracheal aspirate (ETA). For diagnosis of VAP, quantitative/semi-quantitative culture of endotracheal aspirate or bronchoscopic aspirates from the infected lungs segments are recommended for the optimization of antibiotic use.[4] Hence the present study was undertaken to determine the bacteriological profile and

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antimicrobial pattern of the isolates obtained from clinically suspected patients of VAP.

MATERIAL AND METHODS

This was a retrospective, cross sectionl study conducted at a tertiary care hospital over a period of 8 months from January 2018 to September 2018. All critically ill adult patients above the age of 18 years who were on mechanical ventilation for more than 48 hours were included in this study. 0.01 ml of endotracheal sample was inoculated on Blood agar,Chocolate agar and Mac Conkey agar and plates were incubated overnight at 37°C for 24 and 48 hours. Plates with growth were subjected to analysis for bacterial counts and were expressed as colony forming units per mL (CFU/mL). For definite diagnosis of VAP, along with clinical criteria a bacterial count of 10^5 CFU/mL of endotracheal aspirate was considered significant.[5] Cultures with lower colony count were considered as colonization or contamination. Identification of the bacterial isolates was done by standard biochemical tests.[5]

Antimicrobial sensitivity testing was performed on Muller Hinton Agar and interpreted as per the Clinical and Laboratory Standards Institute (CLSI) guidelines.[6] The antibiotics used for Gram negative organisms were Meropenem (10µg), Piperacillin-Tazobactam (100/10µg), Ceftriaxone (30µg), Ceftazidime (30µg), Cefepime (30µg), Cefotaxime(30µg), Imipenem (10µg), Cefoperazone/ sulbactam (75/30µg), Gentamicin (10 µg), Amikacin (30 µg) and Ciprofloxacin (5µg), Levofloxacin (5µg) and Tigecycline (15µg). For Gram positive organisms, Erythromycin (15µg), Penicillin (10U), Ampicillin (30µg), Clindamycin (2µg), Cotrimoxazole (25µg), Cefoxitin(30µg), Linezolid (30 µg), Teicoplanin (30µg) and Vancomycin (30µg) were tested. Colistin (10µg) and Polymyxin B (300units) were tested for carbapenem resistant Gram negative organisms. *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853 were used as quality controls.

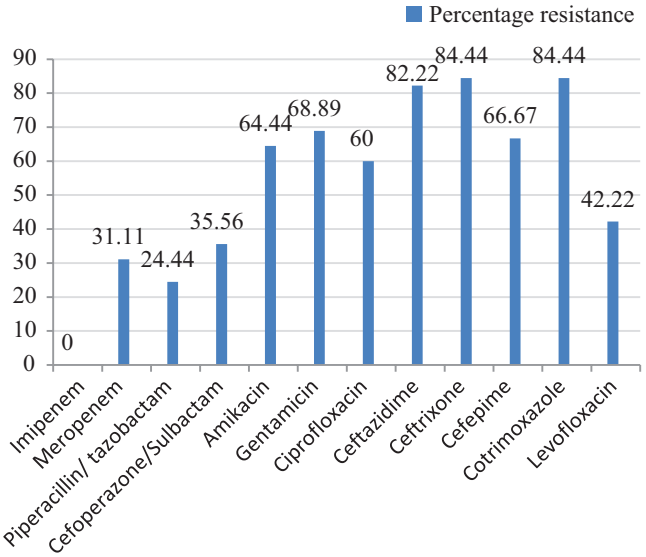

Table-1: Overall resistance pattern of Gram negative bacilli

RESULTS

Out of 66 endotracheal samples studied, 43(65.15%) showed significant growth. This consists of 37 male patients and 6 female patients. Out of which 39/43 (90.70%) showed monomicrobial growth and 4/43 (9.30%) showed polymicrobial growth.The isolation rate of Gram negative bacilli in this study was 45/66(68.18%) and Gram positive cocci isolated were 1/66(1.51%).[Fig:1]

Out of 45 gram negative bacilli, the predominant organism were Klebsiella sp 31/45 (68.89%) followed by Acinetobacter sp 7/45(15.56%) and Pseudomonas aeruginosa 6/45 (13.33%) and E.coli 1/45(2.22%). One staphylococcus aureus and 2 candida sp were isolated.

The incidence of VAP was more common in the age group of 18-30 years 20/43(46.51%)

followed by 31-45 years 8/43(18.60%) and 46-60 years 8/43(18.60%) respectively. 16.28%(7/43) were in the age group of 61-85 years.

Antibiotics Isolates	Klebsiella sp n=31	Pseudomonas aeruginosa n=6	Acinetobacter sp n=7	E.coli n=1
Imipenem	0(0.00%)	0(0.00%)	0(0.00%)	0(0.00%)
Meropenem	8(25.81%)	3(50.00%)	2(28.57%)	1(100%)
Piperacillin Tazobactam	9(29.03%)	1(16.67%)	0(0.00%)	1(100%)
Cefoperazone Sulbactam	16(51.61%)	0(0.00%)	0(0.00%)	0(0.00%)
Colistin	0(0.00%)	0(0.00%)	0(0.00%)	0(0.00%)
Polymyxin B	0(0.00%)	0(0.00%)	1(14.29%)	0(0.00%)
Tigecycline	7(22.58%)	NT	3(42.86%)	0(0.00%)
Amikacin	20(64.52%)	3(50.00%)	6(85.71%)	0(0.00%)
Gentamicin	21(67.74%)	4(66.67%)	6(85.71%)	0(0.00%)
Ciprofloxacin	19(61.29%)	2(33.33%)	5(71.43%)	1(100%)
Levofloxacin	13(41.94%)	2(33.33%)	3(42.86%)	1(100%)
Cefotaxime	28(90.32%)	NT	7(100%)	1(100%)
Ceftazidime	26(83.87%)	3(50.00%)	7(100%)	1(100%)
Ceftrioxime	27(87.09%)	3(50.00%)	7(100%)	1(100%)
Cefepime	23(74.19%)	3(50.00%)	4(57.14%)	0(0.00%)
Cotrimoxazole	26(83.87%)	5(83.33%)	7(100%)	0(0.00%)

Table-2: Resistance pattern of Gram negative bacilli

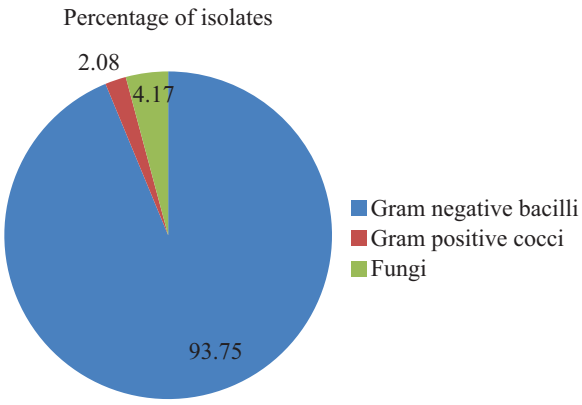

Figure-1: Percentage distributiom of isolates from VAP

All gram negative isolates showed 100% sensitivity to Imipenem, 11/45, 24.44% were resistant to Piperacillin Tazobactam and 16/45, 35.56% to Cefoperazone sulbactam, 10/45, 22.22% to tigecycline. Among the aminoglycosides studied, 29/45 (64.44%) were resistant to amikacin and 31/45, (68.89%) were resistant to gentamicin. 27/45 (60%) isolates were resistant to ciprofloxacin and 30/45, (66.67%) were resistant to cefepime [Table:1].

About 84% isolates of Klebsiella were resistant to Cephalosporins.64.52% klebsiella isolates were resistant to amikacin, 51.61% to cefoperazone sulbactam, 67.74% to gentamicin and 61.29% to ciprofloxacin.

One isolate of Acinetobacter sp was resistant to Polymyxin and three isolates were resistant to tigecycline.All isolates of Acinetobacter were resistant to third generation cephalosporins.

DISCUSSION

VAP remains a major cause of morbidity and mortality in Intensive care units.The incidence of VAP, its etiology and susceptibility patterns may not only vary from hospital to hospital but also within the same hospital or ICU over time. Changes in pathogen distribution and antimicrobial resistance pattern complicate antibiotic treatment and care of the patients.[7]

In this present study from South India, 65.15% samples showed significant growth. The isolation rate of Gram negative bacilli in our study was 45/66(68.18%). The incidence of VAP was found to be more common in the age group of 18-30 years 20/43(46.51%).An Indian study by John et al have reported the overall incidence of VAP as 14.85% with 23.2 VAP episodes per 1000 ventilator days.[8] In a North Indian study, Gupta et al have reported, higher incidence of Gram negative bacilli from VAP cases and maximum number of VAP patients were in the age group of 16-30 years.[9] The incidence of VAP was more in males (75.29%) as compared to females (24.70%) in a study reported by Garg N.[10]

In the present study 39/43 (90.70%) showed monomicrobial growth and 4/43 (9.30%) cultures were polymicrobial. The commonest gram negative bacilli isolated in our study were Klebsiella sp 31/45 (68.89%) followed by Acinetobacter sp 7/45(15.56%) and Pseudomonas aeruginosa 6/45 (13.33%). One Staphylococcus aureus is isolated from surgical ICU patient. About 67.9% VAP cultures were monomicrobial and 32.1% showed polymicrobial growth in a study reported by Vamsi. C.K et al.[11] In a North Indian study by Ankita patel et al, Klebsiella pneumoniae (16%), Acinetobacter sps. (16%) and Pseudomonas sps. (9%) were the commonest isolates obtained in both early and late onset VAP cases.[12] In a study by Kant et al among elderly patients,Acinetobacter (25.37%) was the most common isolate, followed by Pseudomonas (17.91%) and Staphylococcus aureus (17.91%).[13] In a south Indian study,Pseudomonas, E.coli, Klebsiella, Acinetobacter and Staphylococcus were reported as commonest isolates from VAP cases.[11] In a similar study by Garg N, Staphylococcus aureus (80%) was the most common gram positive isolate obtained from VAP followed by Enterococcus species (20%).[10]

In critical ill patients, the longer period of mechanical ventilation and hospital stay increases colonization rate and the incidence of resistant bacteria.[14] In this study all gram negative isolates were sensitive to Imipenem. 24.44% isolates were resistant to Piperacillin Tazobactam and 35.56% to Cefoperazone sulbactam. One isolate of Acinetobacter sp was resistant to Polymyxin. 64.52% klebsiella isolates were resistant to amikacin, 51.61% to cefoperazone sulbactam, 67.74% to gentamicin and 61.29% to ciprofloxacin.

A study by Chaudhury et al from South India have shown an increasing resistance to Imepenem,Cefoperazone sulbactam and Piperacillin Tazobactam among gram negative bacterial isolates from VAP patients.Among the carbapenem resistant strains, polymyxin B resistance rates were 1.6-2.4% for non-fermenters and 5.3-8.2% for Pseudomonas spp.[15] In a study from North India, Mehndiratta, et al have reported isolates of Pseudomonas, Klebsiella and E. coli with 100% sensitivity to imipenem and all the gram-positive isolates studied were sensitive to linezolid.[16]

In this study,the most effective antibiotic against gram negative bacilli was found to be Imipenem followed by Piperacillin tazobactam. An Indian study by Patil have reported Piperacillin Tazobactam, amikacin, and meropenem as good antibiotic options for VAP to start with till culture reports are available.[17] In a South Indian by Jakribettu and Boloor, Levofloxacin, amikacin, and carbapenemes have found as reasonable alternatives to cephalosporins for the treatment of VAP.[18] In a similar study by Rit et al,colistin was found to be most effective antibiotic followed by piperacillin/tazobactum combination and the imipenem.[19]

Early administration of broad-spectrum antibiotics, in patients with clinical suspicion of hospital acquired pneumonia, decreases their bacterial load, minimizes potential risks and devastating consequences of delays in therapy.

CONCLUSION

The outcome of VAP depends on rapid identification of the causative microorganism. Empirical therapy based on knowledge of the most prevalent microorganisms and their resistance pattern has an impact on lowering morbidity and mortality, shortening the length of hospital stay, lowering of treatment expenses, and prevents the development of MDR

bacteria in patients with VAP.

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