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RESEARCH ARTICLE

BACTERIOLOGICAL PROFILE AND ITS ANTIMICROBIAL RESISTANCE PATTERN AMONG PATIENTS OF VENTILATOR ASSOCIATED PNEUMONIA

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ABSTRACT

Background and Objectives: Ventilator-associated pneumonia (VAP) is an important cause of healthcare-associated infections, resulting in prolonged hospitalization with increased morbidity and mortality. Early diagnosis with appropriate antibiotics can reduce the emergence of resistant pathogens. The objective of this study is to find the bacteriological profile and antimicrobial resistance patterns among patients diagnosed with VAP. **Materials and methods:** This is a cross-sectional observational study carried out at a tertiary care hospital. All endotracheal specimens from mechanically ventilated patients with a clinical suspicion of VAP sent to the department of microbiology. All isolates were processed as per standard laboratory procedures and antibiogram was determined. **Results and Interpretation:** The study comprised 100samples, in which 40 bacterial isolates were obtained, most of them were gram-negative organisms (90 %) and only 10 % were gram-positive organisms of which Klebsiella pneumoniae (30 %) Acinetobacter baumannii (22.5 %) and Pseudomonas aeruginosa (20%) were the commonest. High rates of resistance to cephalosporins were noted. Among gram-negative bacilli, multidrug-resistant organisms constituted 27.50%. **Conclusions:** Due to high rate of multidrug resistant organisms in ICU, early and correct diagnosis of VAP is an urgent challenge for an optimal antibiotic treatment and cure. Hence, knowing the local microbial flora causing VAP and effective infection control practices are essential to improve clinical outcomes.

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INTRODUCTION

Nosocomial infections, also known as hospital acquired infections (HAIs), are a major contributor to morbidity and mortality in patients receiving intensive care unit (ICU) treatment in healthcare settings. Ventilator-associated pneumonia (VAP) refers to pneumonia that occurs 48-72 hrs or thereafter, following endotracheal intubation or mechanical ventilation whereas Hospital acquired pneumonia (HAP) is pneumonia occurring in patient after 48 hrs or more, which was not incubating at the time of admission[1]. Despite medical advances, HAP and VAP continue to be frequent complications of hospital care. The risk of VAP is highest early in the course of hospital stay and it is estimated to be 3%/day during the first five days of ventilation, 2%/day during the next five to ten days, and 1%/day beyond that[2,3]. Research indicates VAP occurs in 9 - 27% of all intubated individuals[3].

The occurrence of VAP in Asian countries is significantly higher, ranging from 3.5 to 46 infections per 1000 MV days[4]. Several studies found that mortality of VAP can range from 24 to 80%[5,6,7]. Time of onset of pneumonia is an important epidemiologic factor for specific pathogens and outcomes in patients with VAP and it can be categorized into - Early-onset and late-onset VAP. Early-onset VAP generally manifests within the first four days of mechanical ventilation and also carry a better prognosis, as they are more likely to be caused by antibiotic-susceptible bacteria such as Streptococcus pneumoniae, Haemophilus influenzae and Methicillin-sensitive Staphylococcus aureus whereas Late-onset ventilator-associated pneumonia (VAP) predominantly impacts individuals who have been on a ventilator for five or more days and also it more commonly due to drug resistant pathogens like Pseudomonas, Acinetobacter and Methicillin-resistant Staphylococcus aureus and hence more frequently has chances of high mortality and morbidity[8,9].

The Endotracheal tube (ETT) can itself serve as a reservoir for microorganisms and can have a substantial risk for the development of VAP by compromising mucociliary clearance of secretions, pooling of secretions around the cuff and also sometimes development of a biofilm within the ETT. All these factors can further enhance lung infections or pneumonia. Endotracheal aspiration is a best suitable non-invasive approach of collecting samples in patients with ventilator-associated pneumonia (VAP). In hospital settings, intubation and mechanical ventilation are linked to a much higher chance of contracting pneumonia, with an increased risk ranging from 7 to 21 times[11]. But only the presence of pathogens in tracheal secretions in the absence of clinical findings doesn't suggest VAP. Traditionally, the clinical diagnosis of VAP has included a combination of the following: clinical symptoms/signs, chest radiography and microbiological findings. Clinical symptoms and signs include changes in sputum characteristics or tracheal secretions, temperature $\geq$38 ^{0}C or $\leq$35^{0}C and worsening oxygenation. Laboratory findings include WBC >12000/mm^3/< 4000mm^3 and radiological signs (Chest Xray) such as progression of new or worsening infiltrates[8].

Similarly, Pugin and his co-workers has developed Clinical Pulmonary Infection Scoring system (CPIS)[11] for diagnosis and management of VAP based on parameters (clinical, radiological and microbiological) with each one given a score scale ranging from 0 to 2. The maximum score that can be obtained is 12 and scoring > 6 is diagnostic of VAP. It has a good sensitivity (65%) and specificity (64%)[12]. Beyond that, now a days antibiotic-resistant strains of bacteria are the major problem globally, especially where considerable resources are not available. Also, the impact of antimicrobial-resistant organisms is particularly severe in low and medium-income countries. Highly resistant strains of Gram-negative bacilli (GNB) are spreading rapidly in hospitals, leading to therapeutic challenges in many regions worldwide. This issue is especially prominent in developing countries where there is a lack of adequate facilities to isolate these patients. So, this study aims to find out the bacteriological profile and antimicrobial resistance patterns among patients with VAP.

METHODOLOGY

The present study was conducted in the Department of Microbiology from June 2016 to August 2017 at SRM Hospital, Trichy and approved by Institutional Ethical Committee. During this period, patients over 20 years of age, who were intubated and mechanically ventilated for more than 48hrs were included in the study and patients diagnosed as pneumonia at the time of admission were excluded. Based on the Modified Clinical Pulmonary Infection Score (CPIS), patients have been classified as VAP or non-VAP cases. It has been organised in a tabular format in Table1.

Processing of sample: Endotracheal aspirate (ETA) samples were collected from ICU patients with a clinical suspicion of VAP. A minimum of 2 ml of aspirate was collected and immediately transported to the laboratory. The samples were first stirred and homogenized. Direct Gram stain was done to determine the presence of pus cell and bacteria. Simultaneously semi-quantitative cultures performed by using a calibrated nichrome wire loop holding 0.01 mL of aspirate were done on the following media - blood agar, Mac Conkey agar, and chocolate agar using standard techniques. The plates were incubated at 37^{o}C. The plates were checked after 24 and 48 hr of incubation for any growth. For endotracheal aspirate, colony count 10^5CFU/mL were taken as threshold value (cut off). Plates with growth less than threshold was assumed to be a contaminant or colonizer and plates without growth after 48h were discarded. After observation of the colony morphology, Gram staining was done from isolated colonies. A detailed biochemical testing done in isolates with significant growth followed by antibiotic sensitivity testing performed on Mueller–Hinton agar plates by Kirby–-Bauer disc diffusion method. Zone diameter was measured and interpreted as per the Clinical and Laboratory Standards Institute (CLSI) guidelines[2016][13]. Suspected extended-spectrum beta lactamases (ESBLs) producing organisms were confirmed by double disk synergy test and also plasmid-mediated AmpC producers were detected by the AmpC disk test. For quality control of disc diffusion tests, ATCC control strains of Escherichia coli ATCC 25922, Staphylococcus aureus ATCC 25923 and Pseudomonas aeruginosa ATCC 27853 strains were used.

RESULTS

A total of 100 endotracheal samples were received by the Department of Microbiology for over 1.5 years. Out of the total, 67 individuals were male and 33 were female, as seen in Figure 1. In a sample of 100 patients, 30% were between the ages of 51 and 60, 22% were between the ages of 41 and 50, and 17% were over the age of 71, as indicated in Table-2. The calculated median age is found to be 57 years. Out of a total of 100 samples, 60 samples that either showed insignificant or no bacterial growth ($\leq 10^5$cfu/mL) were excluded from the study. Only 40 samples exhibiting considerable bacterial growth ($\geq 10^5$cfu/mL) are taken for the study (considering along with clinical criteria). Table 3 exhibits the distribution of genders among cases of VAP and non-VAP. Our study found that males were the predominant gender, accounting for 67% of the participants. However, this difference was not considered statistically significant, as indicated by p-value of 0.2206. The prevalence observed in our study was found to be 40%. Of the 40 VAP cases, 17 (42.50%) were classified as early onset VAP and 23 (57.50%) as late onset VAP.

Out of the 40 bacterial isolates obtained from VAP, the majority were Gram negative bacilli, accounting for 90% of the total. Klebsiella pneumoniae was the most common GNB isolated accounting for 30% of the cases while Acinetobacter spp. were 22.5% and Pseudomonas aeruginosa reported 20%. Escherichia coli, Elizabethkingia meningoseptica, and Enterobacter spp. each accounted for 5% of the cases, while Proteus mirabilis was isolated in only 2.5% of the cases. Among Gram positive bacteria, only 4 (10%) Staphylococcus aureus were isolated. All members of the Enterobacterales group exhibited complete resistance to ampicillin. All of the E.coli and the majority (83%) of Klebsiella pneumoniae isolates were extended-spectrum beta-lactamase (ESBL) producers. A significant degree of resistance is observed in Klebsiella isolates, with rates reaching 42% for Carbapenems and 83% for fourth generation Cephalosporins, Ciprofloxacin, and Amoxy clavulunate. Fortunately, no resistance was detected in the isolates of Enterobacter and Proteus mirabilis. Table 4 displays the resistance pattern of Enterobacterales.

Table 1. Modified Clinical Pulmonary Infection Score (CPIS)

CPIS points	0	1	2
Temperature(ºC)	≥ 36.5 and ≤ 38.4ºC	≥38.5 and ≤ 38.9ºC	≥ 39 or ≤ 36ºC
Leukocyte count (mm3)	4,000 – 11,000	<4,000 or>11,000	<4,000 and >11000 + band forms ≥ 50%
Tracheal secretions	Rare	Non-purulent	Abundant and Purulent
Oxygenation PaO2/FiO2 mmHg	>240 or ARDS	-	≤ 240 and on ARDS
Chest radiograph	No infiltrate	Diffuse or patchy infiltrate	Localized infiltrate
Culture of tracheal aspirate	Pathogenic bacteria cultured ≤1 or no growth	Pathogenic bacteria cultured >1+	Pathogenic bacteria cultured >1+ plus same pathogenic bacteria on gram stain >1+

Table 2. Age wise distribution of VAP cases

Age group	Males	Females	Total
21-30 years	5	1	6
31-40 years	7	4	11
41-50 years	15	7	22
51-60 years	19	11	30
61-70 years	10	4	14
> 71 years	11	6	17
Total	67	33	100

Table 3. Gender distribution of VAP and non-VAP cases

	Total no. of cases	No. of VAP cases	Percentage of VAP cases
Males	67	31	46.2 %
Females	33	9	27.2 %
Total	100	40	40%

Table 4. Antimicrobial resistance pattern of Enterobacterales

Organism	No. of isolates	Amp	Amox	CZ	CFU	CTX	CPM	CIP	LFX	COT	AMC	CFS	PTZ	IPM	MRP
K.pneumoniae	12	IR	12	12	12	12	10	10	12	12	10	12	12	5	5
E.coli	2	2	2	2	2	2	2	2	2	2	2	2	0	0	0
Enterobacter spp.	2	IR	0	0	IR	0	0	0	0	0	0	0	0	0	0
Proteus mirabilis	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table 5. Antimicrobial resistance pattern of Non-fermenters

Organisms	No. of isolates	CTX	CAZ	CPM	CIP	LFX	COT	AZT	CFS	PTZ	IPM	MRP
Acinetobacter spp.	9	9	9	9	9	9	9	IR	9	9	9	9
Pseudomonas aeruginosa	8	IR	2	0	0	0	IR	0	0	0	0	0
Elizabethkingiameningoseptica	2	IR	2	2	2	2	2	IR	2	IR	IR	IR

Table 6. Antimicrobial resistance pattern of Gram positiveorganism

Organism	No. of isolates	PEN	CX	ERY	CD	CIP	COT	TE	LZ
Staphylococcus aureus	4	4	1	0	0	3	0	0	1

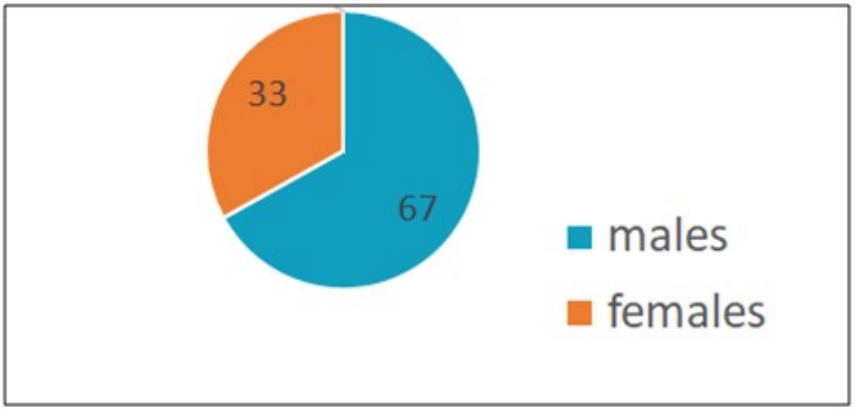

Fig 1. Overall Gender distribution

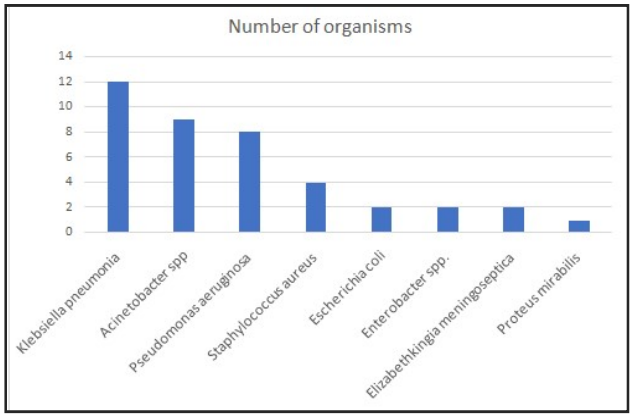

Fig. 2. Total organisms isolated in VAP

Among the Non-fermenters isolated, Acinetobacter spp. and Elizabethkingia meningoseptica exhibited complete resistance to all antibiotics, while Pseudomonas aeruginosa only showed 25% resistance to ceftazidime. Table 5 illustrates the resistance pattern of Non-fermenters. Among gram positive organisms, only 4 strains of Staphylococcus aureus were isolated, among which 1 was found to be methicillin resistant. The resistance pattern of Gram positive organism is shown in Table 6.

DISCUSSION

The prevalence of antimicrobial resistance among VAP pathogens is steadily increasing and detecting the cases at the earliest is important to avoid drug resistant pathogens, as most of these are responsible for late-onset VAP. The occurence of VAP in our study is 40%, which correlates with the findings of study by Jakribettu R P et al[14] where the rate is 44.2% and also one of the studies of International Nosocomial Infection Control Consortium for the surveillance of VAP proved that VAP infections accounted for 46% of all device-associated healthcare-associated infections[15]. The national nosocomial infection surveillance of the Centres for Disease Control, USA reported 60% of nosocomial pneumonia is due to aerobic Gram-negative bacilli[16]. Our study shows patients in the age group of 41-60 years were more prone to VAP as the number of patients exposed to mechanical ventilation (>48hours) were also more in this age group and this was found in accordance with the study by Golia S[17] and Jakribettu R.P et al [14] in which 39.13% and 22% were in age group of 46-60 yrs and 45–55years respectively. Similar to our study, Sharma et al[18] also reported that males were more affected with VAP than females. But its discordant with a study by Rabab Ganju et al[19] in which females (57%) were more affected than males (43%). In our study, Klebsiella pneumonia (30%) was the predominant isolate followed by Acinetobacter spp (22.5%), Pseudomonas aeruginosa (20%). The prevalence of organisms is similar to the study done by Ankita Patel et al[20] where Klebsiella pneumoniae (20%) is predominantly seen followed by Acinetobacter spp. (16%) and Pseudomonas aeruginosa (14%) whereas it is conflicting to the study of Golia S et al[17] were Pseudomonas aeruginosa (33.9%) was frequently isolated organism. Among Enterobacterales, all of the isolates of E.coli were ESBL producers and Carbapenems susceptible which is in concurrence to the study by Jakribettu et al[14] where except one isolate all were susceptible to Carbapenems. All Klebsiella isolates showed 83% of resistance to cefepime, ciprofloxacin and amoxy-clavulunate while they were only 42% resistant to Imipenem whereas in Chaudhury A et al[21], similar kind of resistance is seen only in amoxy-clavulunate, however resistance to cefepime and ciprofloxacin are only 30.3% and 52.5% respectively. Moreover, in our study all Enterobacter and Proteus mirabilis were 100% susceptible to all antibiotics. Among all Nonfermenting Gram-Negative Bacilli (NFGNB) isolated in VAP, Acinetobacter spp. and Elizabethkingia meningoseptica showed maximum resistance, whereas Pseudomonas aeruginosa exhibited only 25% resistance to Ceftazidime while all others were susceptible. This study shows similarity with Quereshi S et al[22] were most of the non-fermenters were resistant to majority of antibiotics. Among gram positive organisms, 4 Staphylococcus aureus were isolated and all were resistant to Penicillin whereas 2 among the 4 were resistant to Ciprofloxacin and only one isolate was found to be resistant to Cefoxitin (MRSA) and Linezolid. This study is similar to the study done by Ranjan et al[23] where among the 2 isolates of S.aureus only one was resistant to Cefoxitin (MRSA). In the study, 27.50 % MDR Gram negative pathogens are isolated. Among that, 72% were resistant to 2nd and 3rdgeneration cephalosporins while 63.8% resistance to 4th generation cephalosporins. Carbapenems are the least resistant drug that are seen in ICU. As Gram positive isolates are less in number, it is difficult to comment on it. The strengths of our study were that it was prospectively conducted and it also adds information to the growing problem of healthcare associated infections in the country.

LIMITATIONS

The limitation of our study is that endotracheal samples were blindly obtained and quantitative cultures could not be done on tracheobronchial microbiological aspirates, due to limitation of resources. These may have led to an overestimation of the percentage of infection.

CONCLUSION

Ventilator-associated pneumonia (VAP) is the prevailing nosocomial infection among patients who are mechanically ventilated. It poses a significant challenge in the intensive care unit (ICU) resulting in extended hospitalisation, high treatment expenses and increased rates of morbidity and mortality. It is also a huge challenge for critical care physicians. This study showed that semi- quantitative culture of ETA is a useful test for early diagnosis of VAP. This knowledge is crucial for determining the appropriate initial preventive measures and treatment strategies for patients on mechanical ventilation. The resistance pattern of these pathogens along with their antimicrobial profile can help an institution to formulate effective antimicrobial policy for VAP based on evidence of the local scenario along with the necessary infection control measures. Furthermore, to gain a comprehensive understanding of the entire nation, it is imperative to carry out multicentric research study involving a substantial number of patients as the resistance patterns vary depending on the patient group and hospital setting. Proper hospital infection control and adequate provision of health personnel with continued education of the staff on importance of hand hygiene may reduce the rates of VAP.

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