Research Article

Bacterial colonization of endotracheal tubes in intubated patients

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Abstract

Background: Ventilator associated pneumonia (VAP) is one of the most important form of hospital acquired infections which is associated with increased mortality and morbidity. VAP occurs in about 9 to 27% of all intubated patients. Intubation is associated with 3 to 10 fold increase in the incidence of VAP among all patients receiving mechanical ventilation. In contrast to other nosocomial infections, the crude mortality rate occurring due to VAP ranges from 24% to 76%. ICU patients with VAP have a 2 to 10-fold higher risk of death when compared with patients without pneumonia. **Aim:** The present study is undertaken to find out the frequency of occurrence of VAP in clinically suspected patients who are mechanically ventilated for more than 48 hours and the major pathogens causing VAP and their antibiotic sensitivity pattern. **Methods:** A total of 392 patients who are mechanically ventilated for more than 48 hours with clinical suspicion of VAP were included in the study. Endotracheal aspirate was collected and subjected to Grams stain and culture. Culture was performed by quantitative culture technique. Growth on the culture plate was identified by standard microbiological techniques and subjected to antibiotic sensitivity testing by Kirby Bauer disc diffusion method and CLSI guidelines. **Results:** Among the 392 clinically suspected VAP patients enrolled in the study 52.8% patients were diagnosed with VAP as per the CPIS score. The most common age group affected was 28- 40 years with male preponderance. 18% of the infections were categorized as early onset VAP while 72% as late onset VAP. *Pseudomonas aeruginosa, Staphylococcus aureus* and *Acinetobacter baumannii* were the most common isolates.78.5% of Gram negative bacteria were β lactamase producers.89.6% of the *Pseudomonas aeruginosa* and 96.2 % of *Acinetobacter baumannii* were meropenem and 84.6% of *Staphylococcus aureus* strains were methicillin resistant. **Conclusion:** *Staphylococcus aureus* was the most common organism causing early onset and *Pseudomonas aeruginosa* in late onset VAP.
Keywords: Ventilator associated pneumonia, MRSA, MβL

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Received Date: 13/11/2020 Revised Date: 18/12/2020 Accepted Date: 20/01/2021

Access this article online

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Website: www.statperson.com

Volume 11
Issue 1

INTRODUCTION

Ventilator associated pneumonia (VAP) is the most frequent and severe health care associated infection. It is being the second most common nosocomial infection in critically ill patients, affecting 27% of all critically ill patients. Eighty-six percent of nosocomial pneumonias are associated with mechanical ventilation and are termed ventilator-associated pneumonia. The mortality attributable to VAP has been reported to range between 0 and 50%. Beyond mortality, the economics of VAP include increased intensive care units (ICU) lengths of stays (from 4 to 13 days) [1] Tracheal intubation thwarts the cough reflex, compromises mucocilliary clearance, injures the tracheal epithelial surface, provides a direct conduit for rapid access of bacteria from upper into the lower respiratory tract, and allows the formation of biofilm on the endotracheal tube surface. The combination of these factors puts the mechanically ventilated patient at great risk of developing ventilator-associated pneumonia. [2,3]

The purpose of this study was to determine the prevalence of bacterial species present in tracheal tubes in patients

How to cite this article: Mayuri K S, VinodKumar C S, Arun Kumar A, Jayasimha V L, Basavarajappa K G. Bacterial colonization of endotracheal tubes in intubated patients. *International Journal of Recent Trends in Science and Technology* January to March 2021; 11(1): 88-92 http://www.statperson.com

admitted to S. S. Hospital ICU and its correlation with demographic variables.

MATERIALS AND METHODS

Study type

A descriptive analytical study, with 392 patients admitted to ICU's of the hospital between January 2013 and December 2013.

Inclusion criteria

Clinically suspected patients according to CDC[1]criteria scored by the Chronic Pulmonary infection Score (CPIS) [4,5]were included in the study

Exclusion criteria

Patients with pneumonia prior to mechanical ventilation or within 48 hours of mechanical ventilation, patients with Adult Respiratory Distress Syndrome (ARDS), cavitary lung disease based on chest X-ray findings, primary lung cancer or another malignancy metastatic to the lungs and cystic fibrosis. Tuberculosis patients and patients with acquired, induced or congenital immunodeficiency, leukopenia <1000 cells/mm3, neutropenia <500 PN/mm3 were excluded from the study[3,4].

Specimen collection

Endotracheal aspirate (ETA) was collected from clinically diagnosed cases. ETA was collected using two catheters where-in a Ramson's 8F suction catheter was guided through a Ramson's 14f suction catheter and gently introduced through the endotracheal tube for approximately 24 cm. The sample was gently aspirated without installing saline and the suction catheters were withdrawn. The sample was transferred into a clean labelled container. The sample was immediately transported to the laboratory for microbiological processing. On Microbiological processing, Gram's stain was performed on all samples before dilutions for estimation of colony count[6].

Dilution and culture of Endotracheal aspirate

ETA were homogenized by vortexing for 1 min followed by centrifugation at 3000 rpm for 10 min. 1 ml of sample was diluted in 9 ml of 0.9%sterile saline(1 in 10) . The specimen were plated on sheep blood agar and Mac-Conkey agar by using Nichrome wire loop with internal diameter of 4 mm, which holds 0.01 ml of homogenized ETA secretions. Both plates were incubated at 37° C for 16-18 hours. Threshold of bacterial counts $\geq 10^6$ CFU/ml for quantitative cultures from ETA secretions was considered for diagnosis of VAP[7]. Bacterial were identified by standard microbial techniques.The antimicrobial susceptibility testing was performed by Kirby Bauer disc diffusion method[8] according to the criteria put forward by the Clinical Laboratory Standards Institute (CLSI)[9].Suspected extended spectrum beta lactamases (ESBLs) producing organisms were confirmed by double disk synergy test as described previously[10].Detection of plasmid-mediated AmpC was done by the AmpC disk test and the isolates showing reduced susceptibility to carbapenems (imipenem and meropenem) were selected for detection of metallo-beta lactamases (MBLs) enzymes by imipenem-EDTA disk method[11]. MRSA was detected by using Cephoxitin discs by disc diffusion method[12]. For quality control of disc diffusion tests ATCC control strains of *Escerichia.coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923 and *Pseudomonas.aeruginosa* ATCC 27853 strains were used.

STATISTICAL ANALYSIS

The results were expressed as percentages for the analysis of various data. Microsoft excel was used for the interpretation of these results.

RESULTS

Table 1: Underlying cause for admission to intensive care units

Primary Diagnosis	N	%
Poisoning	120	30.6
Closed head injury	65	16.6
Central Nervous System infections	43	11.0
Birth asphyxia	26	6.6
Cerebrovascular accidents	36	9.2
Diabetic Ketoacidosis	40	10.2
Haemorrhages	26	6.6
Snake bite	12	3.1
Miscellaneous	24	6.1
Total	**392**	**100.0**

Table 2: Prevalence of bacteria among early and late onset ventilator associated pneumoniae

ORGANISMS	EARLY ONSET	LATE ONSET	Total
Pseudomonas aeruginosa	3	74	77
Klebsiella pneumoniae	3	57	60
Acinetobacter baumannii	3	23	26
Citrobacterfreundii	2	17	19
E.coli	2	3	5
Proteus mirabilis	2	1	3
Staphylococcus aureus	20	6	26
CONS	3	2	5
Enterococcus fecalis	1	1	2
Total	**39(18%)**	**184(82%)**	

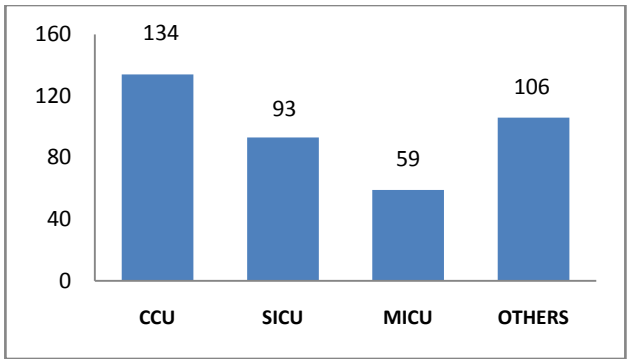

Figure 1: Distribution of cases according to intensive care units

A total number of 392 patients who were on mechanical ventilation for more than 48hrs were included in the study out of which 207 patients were confirmed as VAP according to the CPIS. Among which 71% were males and 29% were females with a mean age of 28.88±2.46 years. Out of 392 patients 34% were admitted in CCU, 24% in SICU, 15% in MICU and 27% in other ICU's (Fig 1).The most frequent cause of ICU admission were suicidal poisoning mainly with organo-phosphorous poisoning the next being closed head injury as a result of road traffic accident (Table 1)**.**

Patients who developed VAP within 96 hrs were categorized as early onset VAP and after 96 hrs were categorized as late onset VAP. Incidence of early onset of VAP was 18% and late onset VAP was 82%. Gram positive bacteria were mainly responsible for early onset of VAP and Gram negative bacteria were responsible for late onset VAP (Table 2). Except *E.coli*, the colony count of all the bacteria isolated was greater than 10^6 CFU/ml. All the bacteria isolated in early onset VAP were associated with respiratory cause and bacteria isolated in late onset VAP were associated with head injuries, trauma, poisoning and snake bite. 3.9% of VAP cases had polymicrobial infection and 96.1% had infection by one bacteria. Antimicrobial susceptibility pattern of Gram negative bacteria revealed that more than 90% of the isolates were resistant for 3 different groups of antibiotics. 94.8% *Pseudomonas aeruginosa* were resistant to Cefixime and Ceftazidime, 92.2% to Cefotaxime, 89.6% to Meropenem and Ceftazidime and Tazobactum. The most effective drug of choice for the treatment of VAP in *Pseudomonas aeruginosa* was Amikacin, Cefipime+Sulbactum and Pipperacillin+Tazobactum (Table 3). Among *Klebsiella pneumoniae* 98.3% of isolates were resistant to Ofloxacin, 95% to Meropenem and Ceftazidime+Tazobactum, 96.6% to Ciprofloxacin and Cefixime and 90% to Imipenem. The drug of choice to the VAP caused by *Klebsiella pneumoniae* was Amikacin and Cefipime and sulbactum. Among *Acinetobacter baumannii* 96.2% of isolates were resistant Ceftazidime, Ceftriaxone, Meropenem and Ceftazidime+Tazobactum, 92.3% of isolates were resistant to Ciprofloxacin, Cefixime and Piperacillin +Tazobactum. The drug of choice for treatment of MDR *Acinetobacter baumannii* in present study is Amikacin, Cefotaxime, Cefaperazone. Antimicrobial susceptibility pattern of Gram positive cocci is depicted in the table. Among 26 *Staphylococcus aureus* isolated 84.6% of the strains were resistant to Methicillin. The drug which was most effective against MRSA was Clindamycin, Linezolid and Vancomycin (Table 4). *Enterococcus feacalis* was resistant to Penicillin, Erythromycin, Cotrimoxazole and sensitive to Clindamycin, Linezolid, Imipenem, Meropenem and Vancomycin. Among 191 gram negative bacteria 78.5% (150) were β lactamase producers out of which 70 were extended spectrum βeta lactamase (ESβL) producers, 18 were AmpC, 62 were metalloβeta lactamase producers (MβL). *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were predominant ESβL producers and *Klebsiella pneumoniae* was predominant AmpC producers while *Acinetobacter baumannii* and *Pseudomonas aeruginosa* produced MβL.

DISCUSSION

VAP is an important nosocomial infection among ICU patients receiving mechanical ventilation. The incidence of VAP (52.8%) in our study was high, almost similar other Indian studies[6,13]. It was observed that most of the VAP episodes occurred within the first two weeks of the mechanical ventilation. The interaction of several risk factors during the initial days of mechanical ventilation put the patient at higher risk and also the exhaustion of most vulnerable patients during the first few weeks leads to the decline in the occurrence of VAP in later days. Patients with neurological disorders and CNS infections were significantly predisposed for the development of VAP. These patients had impaired consciousness and inadequate cough reflexes which predisposed them for developing VAP. The administration of accurate and timely initial empirical antibiotic therapy has been shown to have a major impact on mortality from nosocomial pneumonia. Because early-onset nosocomial pneumonia is most often reported as being due to antibiotic-sensitive pathogens, while late-onset nosocomial pneumonia is frequently caused by more-resistant pathogens, guidelines recommend monotherapy with narrow-spectrum antibiotics for early-onset infections and broad-spectrum therapy for late-onset infections[14]. Early-onset VAP is usually due to the underlying pathology. On the other hand, late-onset VAP could be due to prolonged ventilation, evolution of the underlying disease, quality of

nursing care, duration of antibiotic exposure or environmental ecology of the hospital. Studies have shown that previous antibiotic usage decreases early-onset VAP but markedly increases multidrug-resistant (MDR) pathogens[14,15].Out of 207 VAP cases, 18% were categorized under early-onset VAP and 72% under late-onset VAP which was in concordance with studies conducted by Dey *et al*.,[16] and Chastre *et al*.[17]. Rates of polymicrobial infection vary widely. In our study only 3.9% of cultures were polymicrobial. In a study by Singhal *et al*.,12.3% were polymicrobial[18]. Other studies have reported even higher rates[16]. In our study incidence of VAP was more in OP poisoning followed by head injury patients and CNS infections (*P< 0.001*). In our study *Staphylococcus aureus* (51.3%), was isolated in early onset VAP and *Pseudomonas aeruginosa* (40.2%) was isolated in late onset VAP. Our results does not corroborate with the other studies[13,16,17]. In study conducted by Dey *et al*, *Acinetobacter species* and *Pseudomonas aeruginosa* accounted to 48.9% and 25.5% respectively in early and late onset of VAP[16]. In a study by Rello *et al*, *Staphylococcus aureus* (23.7%) and *Pseudomonas species* (19.7%) were the most common organisms causing early and late onset VAP respectively[18]. According to Fagon *et al*, the members of the *Enterobacteriaceae* accounted for 14% of infections which included *Escherichia coli*, *Proteus* species, *Enterobacter* species, and *Klebsiella* species and smaller numbers of *Citrobacter* and *Hafnia*species[19]. In our study 54.5% of the infections were caused by members of the family *Enterobacteriaceae* which included *Klebsiella pneumonia*(28.9%), *Citrobacter freundii*(9.2%) and *E.coli* (2.4%). 78.5% of Gram negative bacteria were β lactamase producers..Dey *et al*., also observed a high prevalence of ESBL producers in their study[16]. Meropenem resistance was high in this study as 89.6% of the *Pseudomonas* and 96.2 % of *Acinetobacter species* showed multi-drug resistance (MDR), even to carbapenems, which is in concordance with other studies[16].Whereas certain studies reported a lower incidence of meropenem resistance[20,21]. 84.6% of *Staphylococcus aureus* strains were MRSA. Among the 24 MRSA strains, 5 were isolated from patients with late onset VAP. The high incidence of MRSA in our study correlates well with studies done by Gupta *et al*.,[22]. The overall picture suggests that number of drug-resistant strains of various organisms is rising and is an important cause of VAP in our setting.Hence timely surveillance of the organisms and their sensitivity pattern will guide the clinician in appropriate and effective management thereby preventing drug abuse and development of MDR strains. Use of appropriate preventive measures and good nursing care can reduce the incidence of VAP. It seems that there is no much difference between our finding and other studies about microorganism isolated from patients with endotracheal tube. We suggest a similar study designed in another hospital to determine the epidemiologic pattern of microorganism frequency and their drug susceptibility pattern.

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Source of Support: None Declared
Conflict of Interest: None Declared

Table 3: Antimicrobial susceptible pattern of Gram negative bacteria isolated from Ventilator associated pneumoniae

Antibiotics	*P. aeruginosa* N=77				*K. pneumoniae* N=60				*A. baumannii* N=26				*E.coli* N=5				*C. freundii* N=19				*P. mirabilis* N=3			
	S		R		S		R		S		R		S		R		S		R		S		R	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Gentamicin	8	10.4	69	89.6	12	20.0	48	80.0	8	30.8	18	69.2	3	60.0	2	40.0	2	10.5	17	89.5	2	66.7	1	33.3
Cefotaxime	6	7.8	71	92.2	6	10.0	54	90.0	9	34.6	17	65.4	1	20.0	4	80.0	14	73.7	5	26.3	1	33.3	2	66.7
Ciprofloxacin	15	19.5	62	80.5	2	3.3	58	96.7	2	7.7	24	92.3	1	20.0	4	80.0	1	5.3	18	94.7	1	33.3	2	66.7
Cefixime	4	5.2	73	94.8	2	3.3	58	96.7	2	7.7	24	92.3	1	20.0	4	80.0	2	10.5	17	89.5	2	66.7	1	33.3
Amikacin	30	39.0	47	61.0	28	46.7	32	53.3	11	42.3	15	57.7	5	100.0	0	0.0	4	21.1	15	78.9	1	33.3	2	66.7
Cefipimesulbactum	29	37.7	48	62.3	14	23.3	46	76.7	5	19.2	21	80.8	4	80.0	1	20.0	10	52.6	9	47.4	2	66.7	1	33.3
Imepenem	10	13.0	67	87.0	6	10.0	54	90.0	3	11.5	23	88.5	3	60.0	2	40.0	3	15.8	16	84.2	1	33.3	2	66.7
Pipperacillintazobactum	16	20.8	61	79.2	10	16.7	50	83.3	2	7.7	24	92.3	2	40.0	3	60.0	13	68.4	6	31.6	2	66.7	1	33.3
Cefipimetazobactum	10	13.0	67	87.0	5	8.3	55	91.7	3	11.5	23	88.5	2	40.0	3	60.0	5	26.3	14	73.7	2	66.7	1	33.3
Ceftazidimetazobactum	8	10.4	69	89.6	3	5.0	57	95.0	1	3.8	25	96.2	3	60.0	2	40.0	2	10.5	17	89.5	2	66.7	1	33.3
Meropenam	8	10.4	69	89.6	3	5.0	57	95.0	1	3.8	25	96.2	2	40.0	3	60.0	2	10.5	17	89.5	1	33.3	2	66.7
Ceftriaxome	5	6.5	72	93.5	5	8.3	55	91.7	1	3.8	25	96.2	1	20.0	4	80.0	14	73.7	5	26.3	1	33.3	2	66.7
Ofloxacin	9	11.7	68	88.3	1	1.7	59	98.3	3	11.5	23	88.5	1	20.0	4	80.0	1	5.3	18	94.7	2	66.7	1	33.3
Ceftazidime	4	5.2	73	94.8	4	6.7	56	93.3	1	3.8	25	96.2	1	20.0	4	80.0	2	10.5	17	89.5	1	33.3	2	66.7
Cefaperazone	18	23.4	59	76.6	3	5.0	57	95.0	4	15.4	22	84.6	1	20.0	4	80.0	3	16	16	84.2	1	33.3	2	66.7

Table 4: Antimicrobial susceptible pattern of Gram positive bacteria isolated from Ventilator associated pneumoniae

Antibiotics	*S. aureus* N=26				*CoNS* N=5				*E. faecalis* N=2			
	S		R		S		R		S		R	
	N	%	N	%	N	%	N	%	N	%	N	%
Penicilin	3	11.5	23	88.5	2	40	3	60	0	0	2	100
Erythromycin	6	23.1	20	76.9	2	40	3	60	1	50	1	50
Linezolid	8	30.8	18	69.2	2	40	3	60	1	50	1	50
Azithromycin	2	7.7	24	92.3	1	20	4	80	1	50	1	50
Cotrimoxazole	7	26.9	19	73.1	2	40	3	60	2	100	0	0
Clindamycin	5	19.2	21	80.8	2	40	3	60	2	100	0	0
Ciprofloxacin	2	7.7	24	92.3	4	80	1	20	1	50	1	50
Levofloxacin	3	11.5	23	88.5	4	80	1	20	2	100	0	0
Oxacillin	4	15.4	22	84.6	3	60	2	40	1	50	1	50
Doxycycline	8	30.8	18	69.2	4	80	1	20	2	100	0	0
Imipenem	3	11.5	23	88.5	4	80	1	20	1	50	1	50
Meropenem	4	15.4	22	84.6	5	100	0	0	1	50	1	50
Piperacillintazobactum	3	11.5	23	88.5	5	100	0	0	2	100	0	0