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Ventilator associated pneumonia (VAP) in an intensive care unit of a tertiary care hospital: incidence, their microbial etiology, risk factors and role of multidrug resistant pathogens

KEYWORDS: VAP, Microbial suscepiiity, Multidrug reasistance

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ABSTRACT

Background

VAP is serious nosocomial infection and is associated with multi-drug resistant organisms studied. The aim of study is to find the incidence, microbial causes, antibiotic susceptibility pattern and the incidence of multidrug resistant organisms associated of VAP in mechanically ventilated patients in intensive care units of a tertiary care hospital. **Patients and Methods:** In this study, a prospective study of 50 patients with VAP between January 2016 and December 2016 was performed based on age, gender, underlying illness, duration of hospitalization and mechanical ventilation, prior antibiotic treatment were obtained . **Result: 6** (12%) were diagnosed to have VAP of which, 2(33.3%) patients developed early onset and 4(66.6%) have late onset VAP. VAP was polymicrobial in 2 (33.3%) patients and monobacterial in 4(66.6%) cases. , *Klebsiella pneumoniae* was the most common organism associated with VAP. Out of 7 gram negative organisms, 6(85.7%) were multidrug resistant and ESBL producers. Mortality rate in VAP patients 50% and in neonates 100%. Risk factor found in VAP cases were increased duration mechanical ventilation, prior antibiotic therapy in adults and in neonates was low birth weight. **Conclusions:** VAP is increasingly found to be associated with multi-drug resistant organisms that explain the high rate of colonization due to these pathogens. Etiological agents also vary based on type of ICU and patient studied. Therefore knowing the susceptibility pattern of local microbial isolates guide the clinician to choose the appropriate empirical therapy followed by de-escalation strategy focused on narrow spectrum antibiotics after the culture and sensitivity report.

Introduction

Pneumonia is the second most common hospital acquired infection in the intensive care unit patients and 86% of which are VAP. Ventilator associated pneumonia (VAP) is defined as Pneumonia that occurs 48hrs or more after the initiation of endotracheal intubation and mechanical ventilation. (1)

During the period of prolonged intubation, the oropharynx , nasopharynx and dentition of patient becomes colonized with microorganisms. These micro-organisms enter the lower respiratory tract via micro- leak in the endotracheal tube cuff and lead to Pneumonia.(2) Contaminated nebulizers , ventilation circuits and humidifiers can act as the source of micro-organisms for VAP.(3)

VAP is classified as Early onset and Late onset. Early onset VAP, which develops within first four days of mechanical ventilation, is usually less severe, caused by antibiotic sensitive organisms and associated with better prognosis. Late onset VAP developing at the day of 5 or more after the initiation of mechanical ventilation, more likely to be caused by multidrug resistant organisms and lead to increased morbidity and mortality.(1) Early onset VAP are largely due to *Staphylococcus aureus, Streptococcus pneumoniae and Haemophilus influenzae* while organisms responsible for the late onset VAP are drug resistant nosocomial pathogens such as *Pseudomonas aeruginosa,* methicillin resistant *Staphylococcus aureus, Klebsiella* species and *Acinetobacter baumannii*. (3)

Incidence of Ventilator associated pneumonia ranging from 8%-28% in patients receiving mechanical ventilation. (4)The cumulative risk of developing VAP is estimated 1%-3% per day of mechanical ventilation.(2,5)Incidence of VAP varies depending on the definition, the type of ICU or hospital, the study group, hospital resources or level of exposure to antibiotics.(2,6) The etiologic agents also differ based on duration of hospital stay, prior antimicrobial therapy, underlying conditions and intubation of patients in ICU. (7) Independent risk factors for VAP are re-intubation, multiple invasive lines, immunosupression , enteral feeding via nasogastric tube, histamine blockers, antacids, supine head position, paralytic agents and sedations.(2)

The American thoracic society (ATS) guidelines recommended the quantitative culture of lower respiratory secretions ETA (endotracheal aspirate), BAL(Broncho-alveolar lavage) or PSB (Protected Specimen Brush) collected with or without a broncho-scope) as the bacteriologic

strategy to define the presence of pneumonia and the causative agent. Number of trials have shown that there is no advantage of brochoscopic cultures over ETA culture. So being a noninvasive technique endotracheal aspirate culture is a reliable alternative to invasive techniques. Detection of causative agent of VAP and antibiotic sensitivity pattern of that agent is important in order to start the appropriate antibiotic and for better patient prognosis. (4) Although microbiology helps in diagnosis but the clinical pulmonary infection scoring system helps in diagnosis with better sensitivity (72%) and specificity (80%).(8)

Treatment of VAP which consist of inappropriate antimicrobial coverage or delay in therapy associated with higher hospital mortality rate. (7)Treatment of colonizing microorganisms result in exposure to broad spectrum antibiotics and risk to infection with multidrug resistant pathogens.(9)The mortality rate is considerably high in VAP and varies from 20-50% and can be as high as 70% when infection is caused by multidrug resistant pathogens. (10)

VAP is preventable and the institute of Healthcare improvement developed the 'Ventilator Bundle' to improve the outcome of patients receiving mechanical ventilation that consist of elevation of the head of the bed to 30 -45 C, daily sedation vacation and daily assessment of readiness to extubate , prophylaxis of peptic ulcer disease, and deep venous thrombosis .The use of chlorhexidine gluconate antiseptic solution is effective in control of ventilator circuit colonization, oropharyngeal decontamination, and pneumonia caused by multidrug resistant bacteria. Continuous aspiration of

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subglottic secretions also found to be effective in VAP Prevention strategy. (11)

Inspite of the advances in the techniques of the diagnosis, treatment and prevention, it remain the major cause of mortality and morbidity. Early and appropriate antimicrobial therapy is the only way to alter the outcome once the diagnosis of VAP is established. Therefore, the incidence of VAP, local microbial flora causing VAP, its antibiotic susceptibility pattern and risk factors need to be studied for the development of more effective preventive measures and rational utilization of antimicrobial agents.

Objectives

1) To find the incidence of VAP in mechanically ventilated patients in intensive care units of a tertiary care hospital.
2) To find out the microbial causes and antibiotic susceptibility pattern associated with VAP.
3) To find the incidence of multidrug resistant organisms associated with VAP.
4) To determine the risk factor associated with the VAP.

Materials and methods

Study design: To determine the incidence, microbial etiology, risk factors and role of multidrug resistant pathogens in VAP at this center.
Type of study: Prospective observational study
Duration: 12 months period from January 2016 - December 2016

Inclusion criteria: Patients (both adults and paediatrics) on ventilator support due to various reasons in intensive care units for more than 48 hr of Dr. D.Y Patil Hospital will be included in the study.

Exclusion criteria: Patients suggestive of pneumonia prior to or within 48 hr of mechanical ventilation will be excluded from the study. **Clinical sample:** Endotracheal aspirate will be obtained every third day from the patients admitted in intensive care units for more than 48 hr after endotracheal intubation and mechanical ventilation. Patients will be monitored using clinical and microbiological criteria until discharge or death. **Sample processing:** Endotracheal aspirate (≥1ml) will be collected from patients under aseptic precaution and sent to the laboratory immediately. The sample will be first bacteria/oil immersion field on Gram stain, quantitative EA culture showing ≥105 CFU/ml and clinically chronic pulmonary infection score (CPIS) > 6 will be considered to diagnose the VAP. (4, 6,7 ,9 ,19)

Clinical pulmonary Infection score CPIS (6, 10) CPIS points	0	1	2
Temperature(°C)	36.5-38.4	38.5-38.9	<36 or >39
Leucocyte count(per mm3)	4000-11000	<4000 or >11000	<4000 or >11000+ band forms≥500
Tracheal secretions	Rare	Abundant	Abundant+Purulent
Pao2/Fio2 mm Hg	>240 or ARDS	-	≤240 and no ARDS
Chest radiograph	No infiltrate	Diffuse infiltrate	Localized infiltrate
Culture of tracheal aspirate	Light growth or no growth	Moderate or heavy growth of pathogenic bacteria	Moderate or heavy growth of pathogenic bacteria and presence of the same bacteria in Gram stain

For culture all samples will be inoculated on blood agar, MacConkey agar and Saboraud's dextrose agar (SDA) plates using standard sterilized 4mm nichrome wireloop which holds 0.01ml of ETA. Blood and MacConkey agar plates will be incubated at 37°C and SDA plate at room temperature. Growth on blood and MacConkey agar plates will be checked after 24 hrs of incubation and for SDA up to one week. (7)

The organisms isolated from the samples will be identified by standard methods and the susceptibility of antibiotics will be checked by the Kirby-Bauer disk diffusion method according to the CLSI guidelines.

The following information will be collected from the patient included in the study: age, gender, underlying illness, duration of hospitalization and mechanical ventilation, prior antibiotic treatment.

Results

Total 50 patients on ventilator who fulfilled the study's predefined inclusion criteria were enrolled in the study. Among them 6 (12%) were diagnosed to have VAP by microbiological and clinical criteria during their ICU stay and 1(2%) patient have a discrepancy between CPIS and microbiological criteria. Total 8 patients were enrolled from NICU and 2 (25%) were diagnosed as VAP, 13 from PICU and 1 (7.69%) identified as VAP, 22 from MICU and 7 from SICU and 2 (9.09%) and 1 (14.2%) cases respectively diagnosed as VAP .Out of 6 patients of VAP, 2(33.3%) patients developed early onset VAP and 4(66.6%) late onset VAP.

VAP was *polymicrobial* in 2 (33.3%) patients and monobacterial in 4(66.6%). Among the 8 isolates, *Klebsiella pneumoniae* 4 (50%) was the most common organism associated with VAP followed by *Acinetobacter sps.* 3(37.5%) and *MRSA* 1(12.5%). None of the VAP case was due to fungal organism. Out of 2 poly microbial cases, one was due to *Klebsiella pneumoniae* and *Acinetobacter sps,* and the other one due to *Acinetobacter sps.and MRSA.* Out of 7 gram negative organisms, 6 (85.7%) were multidrug resistant and ESBL producers, resistance percentage of antibiotics of gram negative organisms had shown in Table2. Both cases of VAP in neonates were caused by *K.pneumoniae* and sensitivity pattern of both isolates were same except discrepancy in amikacin where first isolate is sensitive and second is resistant.

Among 6 VAP patients, 4 (66.6%) were in the pediatric category and 2 (33.3%) were in the adult category. Neonates accounted for 2 (33.3%) among all VAP cases and 2 (50%) among pediatric age group of VAP. Mortality rate in VAP patients was found to be 50% as compared to (36.3%) in the non-VAP group. Mortality is 100% in the neonatal group. Among 6 patients of VAP, 1 is still in ICU with bad prognosis. The onset of VAP was more likely to appear during the period of first two weeks of mechanical ventilation. The mean duration of mechanical ventilation was found to be 14 days for VAP patients. Out of these 50 patients, 23 patients were male and 27 were female. In VAP patients 4(66.6%) were male and 2(33%) were female showing predominance of male patients. Risk factors associated with VAP found in this study were low birth weight of neonates, increased duration of mechanical ventilation and prior antibiotic treatment in 2 adult patients.

Table1 Causative organisms of VAP Bacterial isolates	No. of isolates from early onset	No. of isolates from Late onset
K.pneumoniae	**2**	**2**
Acinetobacter sp.	**1**	**2**
MRSA	**0**	**1**

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Table 2 Antibiotic resistant pattern in gram negatives Pathogens (no. of isolates)	Antibiotics	Resistance no.(%)
K.pneumoniae(4)	Amikacin	2(50%)
	Gentamicin	4(100%)
	Imipenem	0(0%)
	Ampicillin	4(100%)
	Chloramphenicol	1(25%)
	Cotrimoxazole	4(100%)
	Ceftazidime	4(100%)
	Ceftazidime-clavulanic acid	0(0%)
	Ceftazidime-tazobactum	2(50%)
	Cefoxitin	4(100%)
Acinetobacter sps.(3)	Amikacin	2(66.6%)
	Gentamicin	1(33.3%)
	Imipenem	1(33.3%)
	Ampicillin	3(100%)
	Ceftazidime	2(66.6%)
	Ceftazidime-clavulanic acid	0(0%)
	Ceftazidime-tazobactum	0(0%)
	Cefoxitin	3(100%)

Discussion

VAP is an important nosocomial infection in ICU patients receiving mechanical ventilation. The incidence of VAP in our study was 12%. VAP frequency in different reports varied from 8% and 28 %.(15) Joseph NM et al. in their study found the incidence of VAP 18%. (14) In a study of Rit K et al, the incidence rate was 20%. (1) In a study of Gupta A et al. incidence of VAP was high 28.4 %.(20) In this study incidence of early onset VAP was 2(33.3%) and late onset VAP was 4(66.6%) . Study done by Qureshi S et al showed the percentage of 47.37% for early onset VAP and 52.63% for late onset VAP.(21) In a study of Goel V et al. incidence of early onset VAP was 39.62% and for late onset VAP was 60.38% . (4) Increase no. of late onset in this VAP associated with the prolonged duration of mechanical ventilation which first lead to colonization with organisms and then infection.

In the present study, Polymicrobial VAP infection was found in 2 (33.3%) patients and infection due to single bacteria in 4(66.6%). Patel A et al. in their study found 53.57% of poly microbial growth and 46.4% of monomicrobial from total 28 VAP cases. (7) In this study, most common organism associated with VAP cases was *Klebsiella pneumoniae* 4 cases (66.66%) followed by Acinetobacter sps.3 cases (33.33%) and MRSA 1 case (16.66%). In a study of Patel A et al. *Klebsiella pneumoniae ,Acinetobacter* spps. and *Pseudomonas spps.* were the commonest isolates found in both early and late onset VAP cases.(7) Qureshi S et al.found that S.aureus and Enterobacteriaceae members were more common in early onset VAP and nonfermenter gram negative organisms associated with late onset VAP. [21]

In the present study, most of the gram negative isolates 6/7 (85.71%) were multidrug resistant (MDR) and ESBL producers. In a study of Saldana Dominic et al. 52.7% isolates were MDR pathogens and Joseph NM et al.found in their study, 78.7% MDR pathogens.(19,14) In this study imipenem is the most effective antibiotic against *K.pneumoniae and for Acinetobacter species* susceptibility to imipenem and gentamicin is more. From β-Lactam/β-Lactam inhibitor combination clavulanic acid is more effective than tazobactum for *K.pneumoniae* and for *Acinetobacter* species both inhibitors are equally effective. Joseph et al. found colistin is highly active against *Acinetobacter sps.* (14) In this study incidence of MDR isolates was found high that indicates the need of appropriate empirical treatment effective against MDR organisms. Limitation of this study was that numbers of isolates were less and need to be further confirmed by larger studies.

Mortality rate in VAP patients was found to be 50% (3/6). Kumar A et al found 60% mortality rate associated with VAP while in study of Gadhani H et al. mortality rate was 54 %.(5,8). In this study, 8 patients were included from NICU and 2(25%) were diagnosed with VAP with100% mortality. In the NICU, VAP is also common and found in proportions between 6.8%

and 57.0%. In a Taiwan NICU, out of 528 neonates 11.4% had suffered one or more HAIs, with VAP leading in 18.6 %.(16) Risk factor associated with both the neonates found in this study was their low birth weight. The main risk factors in neonates are low birth weight (hazard ratio [HR], 1.37; CI, 1.0-1.9]) and mechanical ventilation (HR, 9.7; CI, 4.6-20.4) (16) .The immunity mechanisms are also not well developed in case of neonates and lead to high risk to infection.

In VAP patients 4(66.6%) were male and 2(33%) were female showing predominance of male patients like other studies. In a study of Goel V et al. they found 30.9% of female patients and 69.81% were male. (4)

Conclusion

VAP is increasingly found to be associated with multi-drug resistant organisms that explain the high rate of colonization due to these pathogens. Hence the susceptibility pattern of local microbial isolates guides the clinician to choose the appropriate empirical therapy. It reduces the colonization and also leading to better outcome of patient with less morbidity and mortality. To reduce the incidence, more efforts also required to increase the knowledge in medical and paramedical staff regarding its prevention like nursing care and judicious use of broad spectrum antibiotics with good infection control practices.

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