

Original Research Article

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## Incidence, Bacterial Profile and Antimicrobial Susceptibility Pattern of Ventilator Associated Pneumonia in Andhra Pradesh, India

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### ABSTRACT

#### Keywords

Bacterial profile, Antimicrobial susceptibility pattern, Ventilator associated pneumonia

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Healthcare associated pneumonia (HAP) that includes ventilator-associated pneumonia (VAP) is the second most common Hospital acquired infection (HAI) only after urinary tract infection accounting for about 15-20% of HAIs. 39% of HAP is VAP. Mortality rate among patients with VAP ranges from 24-50%. Therefore, this study was undertaken with an aim to determine incidence, bacterial profile and antimicrobial susceptibility pattern of VAP in a tertiary care hospital at Andhra Pradesh, India. The patients were suspected of VAP, when Clinical Pulmonary Infection Score (CPIS) was six or greater. Endotracheal aspirate (ETA) from such patients was sent to culture and sensitivity test. Out of 85 patients, 23 patients developed VAP, based on CPIS and culture and sensitivity test. Incidence rate of VAP was found to be 20 per 1000 ventilator days. 22 out of 23 were bacterial pathogens and one was *Candida albicans*. Predominant bacteria was *Acinetobacter* spp (52%) followed by *Pseudomonas aeruginosa* (26%) and members of family Enterobacteriaceae (17%). Gentamicin was found as most effective antimicrobial agent to all gram negative bacteria obtained. Gram negative bacteria are common pathogens of VAP throughout the world. However, antimicrobial susceptibility testing is necessary for determination of antimicrobial therapy as it shows regional variation.

### Introduction

Hospital acquired infections (HAIs) or nosocomial infections, are important cause of morbidity and mortality among intensive care unit (ICU) patients in healthcare settings (Vincent *et al.*, 1995). CDC has reported that the healthcare associated pneumonia (HAP) is the second most common HAI only after urinary tract infection accounting for about

15-20% of HAIs. Among HAP, 39% are ventilator associated pneumonia (VAP) (Magill *et al.*, 2014). A meta-analytic study showed that the incidence of VAP varied from 6.8% to 44% (Peter *et al.*, 2007). Mortality rate among patients with VAP ranged from 24-50% and much higher (76%) with that of multidrug resistant organisms (Chastre and Fagon, 2002). Studies conducted in the past have shown huge variations in the

distributions of pathogens and drug-resistance patterns due to difference in diagnostic criteria of VAP (Campbell *et al.*, 1996). Clinical pulmonary infection score (CPIS) is a better criteria and it takes into consideration certain parameters for evidence based diagnosis of VAP. These parameters are temperature, leukocyte count, ratio of partial pressure of arterial oxygen and percentage of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ), new infiltrates/ cavitation/ consolidation in chest radiograph, culture positivity, purulent secretions/ abundant secretion. A score of zero to two is given to each parameter. Sum total of scores, six or more is considered as significant (Schurink *et al.*, 2004; Pratyusha *et al.*, 2017).

Owing to morbidity and mortality attributed to VAP among seriously ill patients in ICUs, accurate and early diagnosis, timely intervention with appropriate antimicrobial agent apart from tackling underlying condition is crucial for optimal management of VAP. Therefore, this study was undertaken with an aim to determine incidence, bacterial profile and antimicrobial susceptibility pattern of VAP in a tertiary care hospital.

## **Materials and Methods**

A prospective study approved by hospital ethical committee was carried out in a tertiary care hospital at Visakhapatnam, Andhra Pradesh, India for a period of six months (January 2016 to June 2016). 85 patients admitted in ICUs with intubation with EndoTracheal Tube (ETT) and on Mechanical Ventilation (MV), for a period of more than 48 hours were included in the study. Bundle of care was implemented to prevent VAP according to CDC NHSN guidelines. The patients were evaluated for clinical, radiological and laboratory parameters of VAP as and when indicated with reference to CPIS. If CPIS score was greater than six, EndoTracheal Aspirate (ETA) was sent to microbiology laboratory for culture and

sensitivity testing with prompt documentation.

## **Sample collection**

The patient was preoxygenated with 100%  $\text{FiO}_2$ , using bagmask ventilation, if necessary with adequate sedation. A sterile suction catheter with suction trap was applied, instilling 3 to 5 milliliter of saline if an adequate specimen was not obtained. The suction tube was blindly introduced through the ETT wedged into the tracheobronchial tree and ETA was obtained cautiously (Medford *et al.*, 2009). Immediately, the labeled specimens were sent to Microbiology laboratory for processing.

## **Processing of specimens**

The specimens were inoculated on Blood agar and MacConkey agar with a sterile calibrated loop. The media was incubated at 37°C for 24 to 48 hours under aerobic condition. Colony count of equal to more than or  $10^5$  colony forming units per milliliter (CFU/ml) was considered as significant (Liang Wu *et al.*, 2002). Identification of bacterial agents was done based on standard laboratory procedures (Forbes *et al.*, 2007).

Antimicrobial susceptibility test was done according to Kirby Bauer method using antibiotic discs as per CLSI guidelines. The panel of antimicrobial agents was selected based on CLSI, M100 and local utilization.

## **Results and Discussion**

A total of 85 patients were intubated with ETT and were on MV during the study period. Ventilator days were between 2 to 30 days for individual patients. A sum total of 1145 ventilator days were obtained during the study period. 23 out of 85 patients developed VAP based on CPIS, accounting to 27% of VAP cases and incidence rate obtained was 20 per 1000 ventilator days.

Spectrum of causative agents of VAP is depicted in Table 1. All specimens yielded monomicrobial pathogen with significant colony count. Among 23 isolates obtained, 22 (96%) were bacterial pathogens and one (four percent) was fungal agent. All the bacterial pathogens obtained were gram negative bacteria. These included 12 isolates of *Acinetobacter* spp (52%), six isolates of *Pseudomonas aeruginosa* (26%) and four members of family Enterobacteriaceae (17%), namely *Klebsiella pneumoniae*, *Escherichia coli* and *Enterobacter* spp. Single fungal isolate obtained was *Candida albicans* (4%). Three out of four members of family Enterobacteriaceae were of extended spectrum beta lactamase (ESBL) producers. ESBL was detected by combination disc method using both ceftazidime and amoxicillin-clavulanic acid (Thomas *et al.*, 1992).

**Antimicrobial susceptibility pattern of bacterial agents**

Antimicrobial susceptibility pattern of bacterial agents of VAP is depicted in Table 2. Few antimicrobial agents that are not tested are indicated by NT in the table.

All the isolates of *Acinetobacter* spp,

demonstrated 100% sensitivity to ampicillin-sulbactam and gentamicin. 75% of *Acinetobacter* spp. was sensitive to amikacin and imipem, 66.7% for levofloxacin, 33% for cefepime. All were resistant to meropenem, cefotaxime, ceftriaxone and trimethoprim-sulfamethoxazole.

All the isolates of *P. aeruginosa* were susceptible to ciprofloxacin, carbapenems, gentamicin, amikacin and cefepime. 83.3% of isolates were sensitive to ceftazidime, levofloxacin, aztreonam and piperacillin-tazobactam.

All four isolates belonging to family Enterobacteriaceae were susceptible to ampicillin-sulbactam, amoxicillin-clavulanate, levofloxacin, doripenem, imipenem, gentamicin, amikacin, tetracycline and chloramphenicol. The isolates were most resistant to ampicillin, cephalosporin group of drugs followed by meropenem and trimethoprim-sulfamethoxazole.

VAP is defined as pneumonia that occurs after 48 hours after ET intubation and initiation of MV. Incidence of VAP ranges from 6 to 52 cases per 100 patients (Apostolopoulou *et al.*, 2003). In our study it was found to be 27% of VAP cases.

**Table.1** Spectrum of causative agents of VAP

Sl no.	Organism	No. of isolates
1	<i>Acinetobacter</i> spp.	12
2	<i>Pseudomonas aeruginosa</i>	6
3	<i>Klebsiella pneumoniae</i>	2
4	<i>Escherichia coli</i>	1
5	<i>Enterbacter</i> spp.	1
6	<i>Candida albicans</i>	1
	<b>Total</b>	23

**Table.2** Antimicrobial susceptibility pattern of bacterial pathogens

Sl. No.	Antimicrobial Agent	<i>Acinetobacter</i> spp (n=12)	<i>P. aeruginosa</i> (n=6)	Enterobacteriaceae (n=4)
1	Ampicillin	NT	NT	1 (25%)
2	Ampicillin-sulbactam	12 (100%)	NT	4 (100%)
3	Amoxicillin-clavulanate	NT	NT	4 (100%)
4	Ceftazidime	2 (16.7%)	5 (83.3%)	1 (25%)
5	Ciprofloxacin	2 (16.7%)	6 (100%)	3 (75%)
6	Levofloxacin	8 (66.7%)	5 (83.3%)	4 (100%)
7	Doripenem	2 (16.7%)	6 (100%)	4 (100%)
8	Imipenem	9 (75%)	6 (100%)	4 (100%)
9	Meropenem	0	6 (100%)	2 (50%)
10	Gentamicin	12 (100%)	6 (100%)	4 (100%)
11	Amikacin	9 (75%)	6 (100%)	4 (100%)
12	Aztreonam	NT	5 (83.3%)	NT
13	Piperacillin-tazobactam	2 (16.7%)	5 (83.3%)	3 (75%)
14	Cefepime	4 (33.3%)	6 (100%)	1 (25%)
15	Cefotaxime	0	NT	1 (25%)
16	Ceftriaxone	0	NT	1 (25%)
17	Tetracycline	NT	NT	4 (100%)
18	Trimethoprim-sulfamethoxazole	0	NT	2 (50%)
19	Chloramphenicol	NT	NT	4 (100%)

Major risk factors associated with the development of VAP includes aspiration, oropharyngeal and gastric colonization, cross-infection and complications from the use of antibiotics and nasogastric and ETs (Craven and Steger, 1996). The causative agents of VAP may be part of the host's endogenous flora or they may be acquired from health care workers or other patients, devices, or the hospital environment (Craven, 2000). Early-onset VAP is often caused by *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, while late-onset VAP is more frequently caused by multidrug resistant *P. aeruginosa*, *Acinetobacter* or *Enterobacter* spp., or MRSA (Joseph *et al.*, 2010).

Microorganisms responsible for VAP vary from place to place. Though, there was no

defined yard stick for diagnosing VAP in the past, it can now be identified with certainty via CPIS scoring system. Therefore, timely diagnosis of VAP is helpful in curbing its dangerous consequences, such as, increased antibiotic resistance, high mortality rate, prolonged hospital stay and increased cost (Craven, 2000; Chastre and Fagon, 2002; Joseph *et al.*, 2012). Hence, studies on changing trends of etiological agents of VAP are pressing.

In our study, the incidence rate of VAP was 20 per 1,000 ventilator days which is very close to 19.87 per 1000 ventilator days at Madhya Pradesh, India (Tomar *et al.*, 2017). It was found to be 17.5 per 1,000 ventilator days at Kurnool, Andhra Pradesh, India (Pratyusha *et al.*, 2017). One large study conducted in France reported VAP rates of

9.7–26.1 per 1,000 ventilator days (Zahar *et al.*, 2009). The VAP rate was found in a wide range of 10 to 41.7 per 1000 ventilator days in various developing countries other than India (Arabi *et al.*, 2008). In developed countries, the rates are much lower. In the US, the incidence of VAP ranges from 2 to 16 episodes per 1,000 ventilator days (Rosenthal *et al.*, 2012). In Scotland, it is 3.5 per 1,000 ventilator days as reported by Scottish intensive care society audit group, NHS Scotland in 2017. Emphasis on quality improvement and patient safety with initiatives such as the introduction of VAP prevention bundles, together with robust reporting and quality assurance is believed to bring down the VAP rates in any given hospital setting (Daniel *et al.*, 2015; Pugh *et al.*, 2016).

VAP was entirely monomicrobial etiology in this study. A study done at Madhya Pradesh, India showed 94% of VAP cases to be monomicrobial (Tomer *et al.*, 2017). However, at France it was found that 54.8% were polymicrobial (Trouillet *et al.*, 1998) and at Greece, Athens, 27% of VAP cases were of polymicrobial in nature (Apostolopoulou *et al.*, 2003).

Among 23 isolates obtained, 22 (96%) were bacterial pathogens and one (four percent) was fungal agent in our study. *Candida* was found as causative agent in other studies also (Mohanty *et al.*, 2016; Joseph *et al.*, 2010).

All the bacterial isolates obtained were Gram negative bacteria in this study. Gram negative bacteria are nosocomial pathogens which colonize on healthy looking skin of ICU people and they can also harbor on instruments, catheters, and environment (Kuti *et al.*, 2009).

Predominant bacteria in our study was *Acinetobacter* (52%) followed by *P.*

*aeruginosa* (26%). *K. pneumoniae* was 8.6%, whereas *E.coli* and *Enterobacter* spp. 4% each. Similar result was observed with *Acinetobacter* as most frequent candidate pathogen contributing to 58% of cases at Iran (Hashemian *et al.*, 2012). 38.11% of VAP cases at Kurnool, India were caused by *Acinetobacter*, followed by *P. aeruginosa* (26.74%), *K. pneumoniae* (14.85%) and also MRSA (Satputeet *et al.*, 2017). At Chennai, Tamil Nadu, India *Acinetobacter* contributed to 31% of VAP cases (Nanthini Devi *et al.*, 2018). However, at Madhyapradesh, India *P. aeruginosa* (50%) was the leading isolate followed by *Acinetobacter baumannii* (17.64%) and *E. coli* (14.70%) (Tomar *et al.*, 2017). Another study at Visakhapatnam, also found that 81% of pathogens were gram-negative bacilli with predominance of *Pseudomonas* spp (28.4%) followed by *E. coli* (24.3%), *Klebsiella* (12.3%) and *Acinetobacter* spp was only 9.5%. 19% of isolates were found to be gram-positive cocci with *Staphylococcus aureus* as predominant isolate (Kapaganty and Pilli, 2018). The most common organism isolated was *P. aeruginosa*, followed by MRSA, *K. pneumoniae* and *A. baumannii* at Odissa, India (Mohanty *et al.*, 2016). In Pondicherry, India Enterobacteriaceae (25%) and *Acinetobacter* spp. (25%) followed by Methicillin sensitive *S. aureus* (13%) were the most common pathogens causing early-onset VAP and *Pseudomonas* spp. (39%) and *Acinetobacter* spp. (32%) were the most common pathogens causing late-onset VAP (Joseph *et al.*, 2010). In Korea the most commonly identified bacteria was shown to be *S. aureus* (44%), *A. baumannii*, *P. aeruginosa*, *S. maltophilia*, *K. pneumoniae*, and *Serratia marcescens* in that order (Young Chi *et al.*, 2012).

In our study, three of four members of Enterobacteriaceae family were EBSL producers. It was 56% in another study at



Visakhapatnam (Kapaganty and Pilli, 2018), 25% at Nagpur (Satpute *et al.*, 2017). ESBL was produced by 50% of *E. coli* and 67% of *K. pneumonia* at Pondicherry (Joseph *et al.*, 2010). Apart from ESBL, other studies revealed pathogens with AmpC production and MRSA as well (Joseph *et al.*, 2010, 2012; Satpute *et al.*, 2017)

In present study, gentamicin was found as most effective antimicrobial agent with 100% sensitivity to all gram negative bacteria. *Acinetobacter* and Enterobacteriaceae group were 100% sensitive to Ampicillin-sulbactam. In contrast to our study, *P. aeruginosa* exhibited 47.05% resistance to gentamicin at Madhyapradesh (Tomar *et al.*, 2017). At Iran, imipenem showed superior activity over other tested antimicrobial classes against Enterobacteriaceae similar to our study (Hashemian *et al.*, 2012). Gentamicin, amikacin and imipenem appear to be most effective antimicrobial agents which can be considered for empirical therapy for VAP in this region.

In conclusion, gram negative bacteria namely, *Acinetobacter*, *Pseudomonas*, *E. coli*, *Klebsiella* and *Enterobacter* are common pathogens of VAP throughout India and worldwide. However, antimicrobial susceptibility testing is necessary for determination of antimicrobial therapy as it shows regional variation.

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