Original Article

Incidence, bacteriology, and clinical outcome of ventilator-associated pneumonia at tertiary care hospital

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Abstract

Background: Ventilator-associated pneumonia (VAP) is the most frequent Intensive Care Unit acquired infection. **Aims:** The aim is to determine the incidence, bacteriology and factors affecting VAP and to determine the multi-drug resistant (MDR) pathogens. **Settings and Design:** This was a prospective observational study conducted over a period of 1 year from April 1, 2011, to March 31, 2012. **Materials and Methods:** The patients fulfilling criteria of VAP were included in this study. **Statistical Analysis:** This was performed using SPSS trial version 11.0 software (SPSS Inc., Chicago, Illinois, USA) and the values of $P < 0.05$ were considered statistically significant. **Results:** Totally 74 (27.71%) patients were developed VAP. Of total 74 patients with VAP 53 (71.62%) were females and 21 (28.37%) were females ($P < 0.0001$). Total 13 (17.56%) patients had early-onset VAP and 61 (82.43%) had late-onset VAP ($P < 0.0001$). The overall incidence of VAP rate per 1000 ventilator days was 39.59. Total 126 bacterial isolates found in 74 patients with VAP. Predominant isolates were Gram-negative 52 (70.27%). Total 41 (55.40%) patients had polymicrobial VAP, and 33 (44.59%) had single isolate. Total 55 (43.65%) isolates were MDR organisms. Total 22 patients with VAP succumbed during treatment with overall case fatality rate of 29.72%. Of total 55 MDR isolates in VAP, 13 (26.63%) were *Klebsiella* spp., 11(20%) *Pseudomonas aeruginosa,* 14 (25.45%) *Acinetobacter,* 8 (14.54%) *Escherichia coli,* and 9 (16.36%) coagulase positive *Staphylococcus aureus.* Total 12 (21.41%) patients succumbed among MDR isolates. **Conclusions:** There was a high incidence of MDR pathogens in late-onset VAP. The Gram-negative organisms *Klebsiella, Pseudomonas E. coli* and *Acinetobacter* were the most commonly isolated organisms with high mortality rates.

Key words: Bacteriology, Intensive Care Unit, multi-drug resistant organisms, poly-microbial, ventilator-associated pneumonia

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a major cause of hospital morbidity and mortality in Intensive Care Unit (ICU) patients despite recent advances in diagnosis and accuracy of management. VAP is the most frequent ICU acquired infection, occurring in 25% of patients intubated for longer than 48 h. The incidence of VAP ranges from 13 to 51 per 1000 ventilator days.[1] Early-onset VAP is usually less severe, associated with a better prognosis, and is more likely to be caused by antibiotic-sensitive bacteria. Late-onset VAP, is usually caused by multi-drug resistant (MDR) pathogens and is associated with increased morbidity and mortality.[2,3] Many studies from India have investigated the causative organisms of VAP. *Pseudomonas* spp., *Acinetobacter* spp., *Escherichia coli, Klebsiella pneumoniae*, and *Staphylococcus aureus* were identified as the common VAP pathogens, with varying prevalence. Up to 40% of

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these infections can be polymicrobial. *Pseudomonas* spp., *Acinetobacter* spp. and even *Enterobacteriaceae* are quite often MDR.[3,4] Therefore, the local microbial flora causing VAP needs to be studied in each setting to guide more effective and rational utilization of antimicrobial agents. So for there is scanty literature about incidence, bacteriology, and antibiotic susceptibility pattern about VAP in India. The initial empirical therapy of VAP modified based on the knowledge of local microbiological data. Although mechanical ventilation (MV) is a life-saving intervention, it has its own potential complications. Newer antibiotics in the past decade have not brought down the mortality in the critical care facilities across the world, associated with VAP. The increasing incidence, mortality, MDR pathogens of VAP in critical care units we did this study to identify the culture sensitivity pattern of microbial isolates from endotracheal aspirates (EA). The objectives of this study were to determine the incidence, bacteriology, antibiotic susceptibility, and resistance pattern including MDR isolates, risk factors, and outcome of VAP at a tertiary care teaching hospital.

MATERIALS AND METHODS

Study design

This was the prospective observational noninterventional study of VAP cohort, conducted in medical ICUs of a tertiary care teaching hospital over a period of 1 year (April 1, 2011–March 31, 2012). This study was approved by the research and ethical committee. Informed consent was obtained from each patient's next of kin.

Aims and objectives

The objectives of this study were to determine the incidence bacteriology, risk factors, and outcome of VAP patients and to determine their antibiotic susceptibility and resistance pattern including MDR isolates.

Setting

The study was conducted in the medicine ICU of a tertiary care teaching hospital. The Departments of Microbiology and medicine were involved in this study. The ICU is comprised well-spaced beds and patients were either admitted directly to the ICU or transferred from other wards, namely medicine, surgery, obstetrics, and neurosurgery. The nurse-patient ratio was as per standard norms.

Definition of ventilator-associated pneumonia

VAP is defined as pneumonia occurring more than 48 h after endotracheal intubation and initiation of MV.

Early-onset ventilator-associated pneumonia

Developed during the first 4 days of MV.

Late onset ventilator-associated pneumonia

Developed five or more days after initiation of MV.

Subject and sample size

During 12 months study, a total of 673 patients who were intubated and were on MV of them only 267 patients who were ventilated for more than 48 h were eligible for inclusion in the study.

Procedure for data collection

All patients included in the study were monitored at frequent intervals (every 2 days) for the development of VAP using clinical and microbiological criteria until either discharge or death. The clinical parameters were recorded from bedside charts. Details of antibiotic therapy, surgery, use of steroids, duration of hospitalization, presence of neurological disorders, and impairment of consciousness were also noted.

Criteria for diagnosis of ventilator-associated pneumonia

The diagnosis of VAP was based on clinical and microbiological criteria. A clinical suspicion of VAP was made in patients with a modified clinical pulmonary infection score (CPIS) >6; the diagnosis was confirmed by performing a quantitative culture of the EA and observing ≥105 cfu/ml.[4-6] We used the following criteria to diagnose VAP: Ventilated for more than 48 h; New and persistent infiltrates shadow developing in the Chest X-ray; presence of fever (temperature <96.8 or >99°F); White cell count >11,000/ml or <4000/ml; declining ratio of partial pressure to inspired fraction of oxygen (PaO_2/FiO_2 ratio) was found to be the earliest indicator of VAP; Cultures positive from endotracheal secretions.[4] (The CPIS was developed to serve as a surrogate tool to facilitate the diagnosis of VAP. The CPIS is calculated on the basis of points assigned for various signs and symptoms of pneumonia [fever and extent of oxygenation impairment]). Based on these criteria, 74 of 267 enrolled patients were diagnosed with VAP.

Microbiological techniques

The organisms isolated by quantitative culture of the EA from VAP patients were identified based on standard microbiological techniques. The susceptibility of the clinical isolates to some routinely used antibiotics was determined by the Kirby-Bauer disk diffusion method.[7,8]

Multi-drug resistance

MDR pathogens were defined as those resistant to three or more antimicrobial classes.

Exclusion criteria

All patients with clinical and radiological signs suggestive of pneumonia on admission and clinic-radiological evidence

with alternative diagnosis other than VAP were excluded from the study.

Statistical analysis

Data entry and analysis were performed using SPSS for windows version SPSS 11.0 software (Trial version SPSS Inc., Chicago, Illinois, USA). Means and standard deviations were calculated for numerical variables. The Chi-square test was calculated and all $P < 0.05$ were considered statistically significant. Odds ratio and relative risk (RR) was calculated for univariate analysis. The VAP rate per 1000 ventilator days was calculated as total number of VAPs in ICUs/total number of ventilator days in medical ICU × 1000.

RESULTS

Total 267 patients were intubated and were on MV for more than 48 h (fulfilling inclusion and exclusion criteria) for various reasons for respiratory failure during the study period of 1 year (April 1, 2011–March 31, 2012). Of 267 patients on mechanical ventilator, 74(27.71%) patients developed VAP [Figure 1]. The incidence of VAP in present population was 27.71%. Of total 74 patients with VAP, 53(71.62%) were males (mean age 57 ± 17 years) and 21(28.37%) were females (mean age 49 ± 14 years) with male to female ratio of 2.52 (RR: 2.5238 95% confidence interval [CI]: 1.7099–3.7252: χ statistic: 4.660 $P < 0.0001$: Odds ratio: 6.369). Total 13(17.56%) patients had early-onset VAP and 61(82.43%) had late-onset VAP (odds ratio: 0.0454; 95% CI: 0.0195–0.1059; χ statistic: 7.157; $P < 0.0001$; RR: 0.2131). The overall incidence of VAP rate per 1000 ventilator days was 39.59 [Table 1].

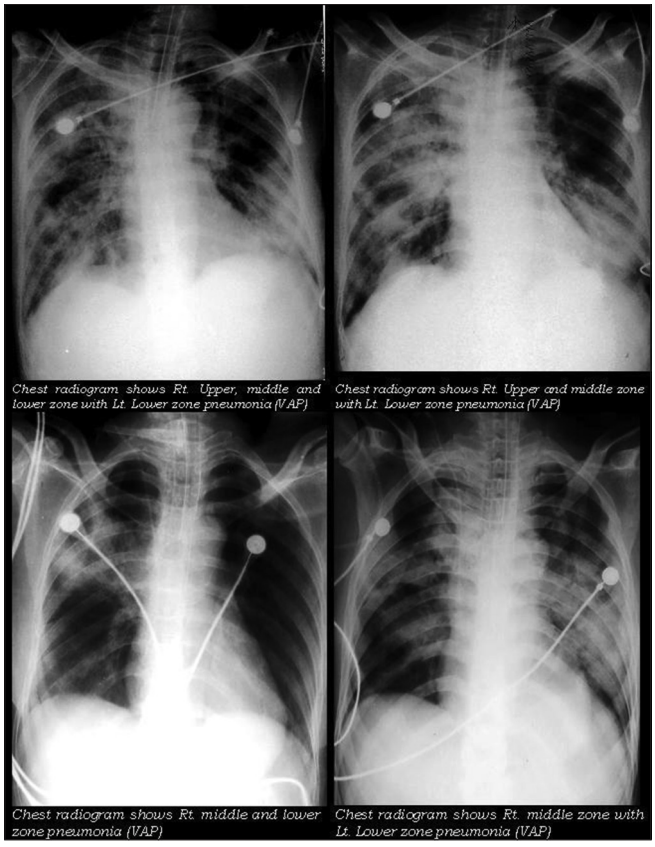


Figure 1: Chest radiogram of patient with ventilator associated pneumonia

Total 126 cultures were positive for pathogenic bacteria among 74 patients with VAP (i.e., more than one organism were present in EA). Total 102(80.95%) isolates were found in male and 24(19.04%) isolates in female population. Total 41(55.40%) patients had polymicrobial VAP and 33(44.59%) had single isolate [Table 2, Figure 2 and Graph 1].

Of total 126 isolates with VAP 55(43.65%) were MDR organisms. Total 39(38.23%) MDR isolates in male patients and 16(66.66%) female patients, predominated by females. Of total 55 patients with MDR isolates 13(23.63%) had early VAP (≤5 days) and 42(76.36%) had late-onset VAP (>5 days) VAP (odds ratio: 0.0958; 95% CI: 0.0397–0.2309; χ statistic: 5.225; $P < 0.0001$; RR: 0.3095; 95% CI: 0.1882–0.5089; χ statistic: 4.622; $P < 0.0001$) [Table 3].

Total Gram-positive cocci (GPC) were 22(17.46%) and 52(70.27%) were Gram-negative *bacilli* (GNB). The organisms isolated were predominantly GNB *Klebsiella* 29(23.01587%), *Pseudomonas* 27(21.42%), *Acinetobacter* 24(19.04%), and *E. coli* 19(15.07%) with high mortality rates. The list of antibiotics and sensitivity pattern with various bacterial isolates is shown in Table 3. Total 16(12.69%) isolates were sensitive to meropenem, 19(15.07%) to piperacillin (PI), 20(15.87%) to amikacin, 27(21.42%) to colistin, and 18(14.28%) to

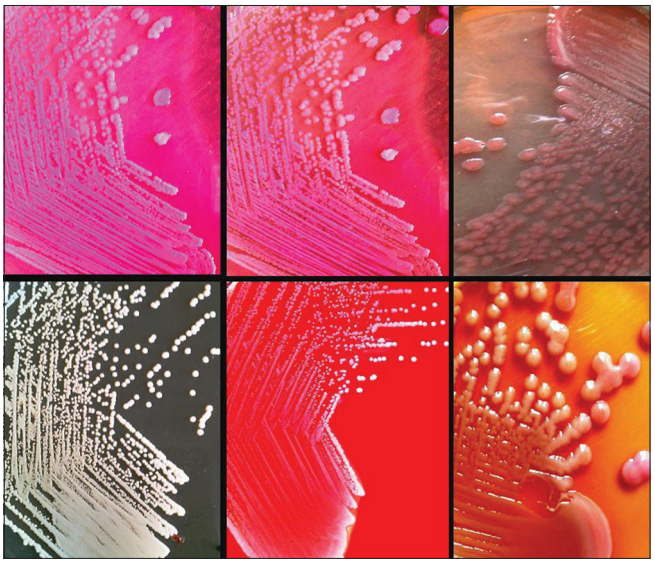


Figure 2: Culture growth of endotracheal aspirate. MacConkey Agar (*Escherichia* coli), MacConkey Agar *Pseudomonas aeruginosa*, Nutrient Agar (*Staphylococcus aureus*), blood Ager (*Staphylococcus aureus*), blood Ager (*Klebsiella* spp.)

tigecycline. Colistin, PI-T, amikacin, and meropenem have found to the better sensitivity to the majority of GNB isolates [Table 4 and Graph 2].

Of total 55 MDR isolates in VAP, 13(26.63%) were *Klebsiella,* 11(20%) *Pseudomonas,* 14(25.45%) *Acinetobacter,* 8(14.54%) *E. coli* and 9(16.36%) coagulase positive *S. aureus* (COPS).

Ceftizoxime was sensitive in 12(9.52%) and cefoxitin 19(15.07%) should be equally considered for treating late-onset VAP, considering their sensitivity pattern [Table 5].

Total 52(70.27%) patients (mean age 58 ± 13) with VAP were discharged after successful treatment (males: 38 [71.69%], females: 14 [66.66%]) (RR: 0.8491; 95% CI: 0.4046–1.7818; odds ratio: 0.7895; 95% CI: 0.2664–2.3398; χ statistic: 0.426; $P = 0.6698$; χ statistic: 0.433; $P = 0.6653$). Total 22 patients with VAP succumbed during treatment with overall case fatality rate of 29.72% (mean age [58 ± 13]). Of total 22 death due to VAP 15(71.62%) were male and 7(28.37%) were female patients. Total 5(22.72%) had early-onset VAP and 17(77.27%) patients had late-onset VAP (odds ratio: 0.0865; 95% CI: 0.0211–0.3544; χ statistic: 3.402; $P = 0.0007$). The mean age of patients with death was significantly more than discharge patients (58 ± 13: 45 ± 15). Total 2(25%) patients died and six discharged with *Klebsiella.* spp. isolates. Total 3(75%) patients died and one discharged with *Klebsiella* + *Acineto* spp. isolates. Total 3(42.85%) patients died and four discharged with *E. coli isolates.* Total 2(28.57%) patients died and five discharged with *Klebsiella* + *pseudomonas isolates.* Total 1(33.33%) patients died and two discharged with *E. coli* + *Pseudomonas aeruginosa* isolates. Total 2(22.22%) patients died and seven discharged with COPS isolates. Total 1(100%) patient died with *Klebsiella* + *P. aeruginosa* + *Acineto* spp. isolates. Total 2(100%) patient died with *P. aeruginosa* + *Acineto* spp. isolates. Total 1(10%) patients died and 9 discharged with *Acineto* spp. isolates. Total 1(50%) patients died and one discharged with COPS + *Acineto* spp. isolates. Total 1(100%) patients died with *Klebsiella* + *E. coli* isolates. Total 2(22.22%) patients died and seven discharged with COPS isolates. Total 1(50%) patients died and one discharged with *Klebsiella* + *P. aeruginosa* + *E. coli* isolates. Total 1(33.33%) patients died with *P. aeruginosa* isolates. Total 1(100%) patients died with *Klebsiella* + COPS isolates. The multiple and GNB isolates had higher mortality rate compared to single isolate ($P < 0.001$). The comparison of mean duration of stay in death and discharged group by ANOVA was $P = 0.657$ (Degree of freedom: 1) [Table 6].

Total 12(21.81%) succumbed among MDR isolates (RR: 1.20; 95% CI: 0.6613–2.1775; χ statistic 0.600; $P = 0.5487$). Total 4(33.33%) isolates of MDR *Klebsiella,* 3(37.5%) *E. coli,* 1(8.33%) *Pseudomonas*, 2(14.28%) *Acinetobacter,* 2(22.22%) COPS succumbed during treatment. The emergency

Table 1: Incidence, demographic and clinical profile of ventilator associated pneumonia

Incidence of VAP	Total (%)
VAP (*n*=267)	74 (27.71)
Males (57±17 years)	53 (71.62)
Females (49±14 years)	21 (28.37)
Early-onset VAP	13 (17.56)
Late-onset VAP	61 (82.43)
VAP/1000 days	39.59

VAP: Ventilator-associated pneumonia

Table 2: Organisms isolated in patients with ventilator-associated pneumonia

Organism	(*n*=126) (%)
COPS	10 (7.93)
COPS + *Klebsiella*	1 (0.79)
COPS + *Klebsiella* + *P. aeruginosa*	2 (1.58)
COPS + *P. aeruginosa*	3 (2.38)
COPS + *P. aeruginosa* + *Acinetobacter* spp.	2 (1.58)
COPS + *Acinetobacter spp.*	2 (1.58)
E. coli	9 (7.14)
E. coli + *P. aeruginosa*	3 (2.38)
E. coli + *P. aeruginosa* + *Klebsiella* spp.	2 (1.58)
E. coli + *Klebsiella*	1 (0.79)
Klebsiella	7 (5.55)
Klebsiella + *COPS*	6 (4.76)
Klebsiella + *Acinetobacter* spp.	4 (3.17)
Klebsiella + *P. aeruginosa*	7 (5.55)
Klebsiella + *P. aeruginosa* + COPS	2 (1.58)
Klebsiella + *P. aeruginosa* + *E. coli*	2 (1.58)
Klebsiella + *E. coli*	1 (0.79)
Klebsiella + *P. aeruginosa* + *Acinetobacter spp*	1 (0.79)
Alpha hemolytic streptococci	1 (0.79)
Total	66 (52.38)
P. aeruginosa	2 (1.58)
P. aeruginosa + *Citrobacter* spp.	3 (2.38)
P. aeruginosa + *Acinetobacter* spp. + COPS	3 (2.38)
P. aeruginosa + COPS	6 (4.76)
P. aeruginosa + *E. coli*	3 (2.38)
P. aeruginosa + *Acinetobacter* spp.	4 (3.17)
P. aeruginosa + *Klebsiella*	7 (5.55)
P. aeruginosa + *Klebsiella* + COPS	2 (1.58)
P. aeruginosa + *E. coli* + *Klebsiella*	2 (1.58)
P. aeruginosa + *Klebsiella* + *Acinetobacter*	1 (0.79)
Acinetobacter spp.	10 (7.93)
Acinetobacter spp. + COPS + *P. aeruginosa*	2 (1.58)
Acinetobacter spp. + *Klebsiella*	1 (0.79)
Acinetobacter spp. + *P. aeruginosa*	4 (3.17)
Acinetobacter spp. + *Klebsiella*	3 (2.38)
Acinetobacter + COPS	2 (1.58)
Acinetobacter spp. + *Klebsiella* + *P. aeruginosa*	1 (0.79)
Nonhemolytic streptococci	3 (2.38)
Diptheroids	1 (0.79)
Total	60 (47.61)

COPS: Coagulase positive *Staphylococcus aureus, P. aeruginosa: Pseudomonas aeruginosa, E. coli: Escherichia coli*

Table 3: Bacteriological isolate profile of ventilator associated pneumonia

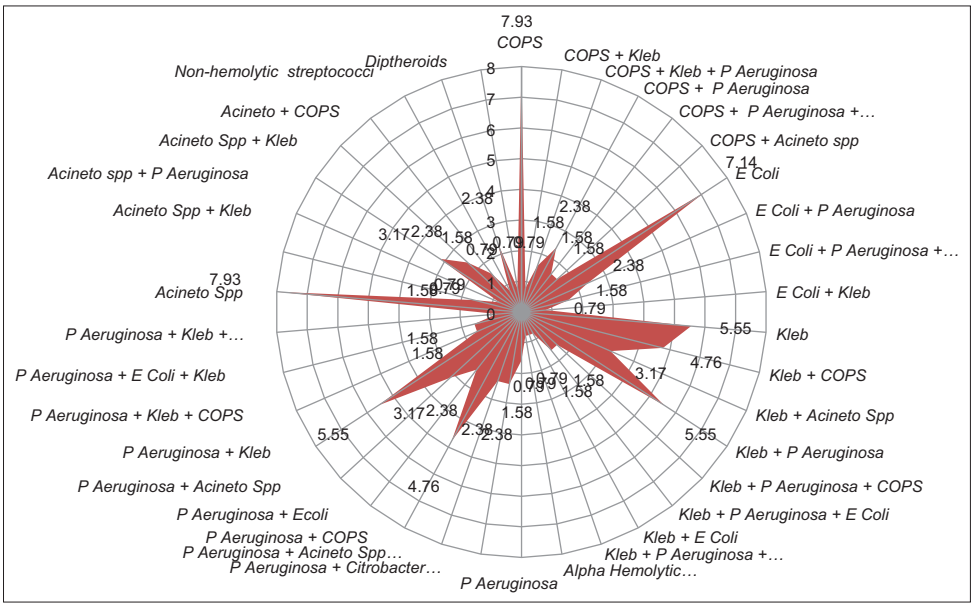
Organism	*n*=126 (%)	Antibiotic sensitivity patterns	MDR (%)
Klebsiella spp.	29 (23.01)	AK, Cs, PI, COT, CIP, Me, Tg, CX, CAZ, CZX, NE	13 (56.48)
P. aeruginosa	27 (21.42)	AK, Cs, PI, COT, CIP, Me, Tg, CX, CAZ, CZX	11 (51.33)
Acinetobacter	24 (19.04)	AK, Cs, PI, Me, Tg, NET, CZX	14 (73.5)
COPS	22 (17.46)	CP, CTR, CZX, CPZ, CAZ, AMC, COT, CIP, AZM	9 (51.54)
E. coli	19 (15.07)	AK, Cs, PI, COT, CIP, Me, Tg	8 (53.05)
Alpha Hemolytic Streptococci	1 (0.79)	CP, COT, COX, CIP, ER, CE, NIT, AZM, CZX, CXM, TE, AMC, CTR, CN, CPZ, CX, AZM, NET, CAZ, AK	0 (0)
Non-Hemolytic Streptococci	3 (2.38)	CP, COT, COX, CIP, ER, CE, NIT, AZM, CZX, CXM, TE, AMC, CTR, CN, CPZ, CX, NET, CAZ, PI	0 (0)
Diptheroids	1 (0.79)	CP, COT, COX, CIP, ER, CE, NIT, AZM, CZX, CXM, TE, AMC, CTR, CN, CPZ, CX, NET, CAZ	0 (0)
Total	126 (100)	Total	55 (43.65)

E. coli: *Escherichia coli*, COPS: Coagulase positive *Staphylococcus aureus, P. aeruginosa: Pseudomonas aeruginosa,* MDR: Multidrug resistant, AK: Amikacin, Cs: Colistin, PI: Piperacillin, COT: Co trimaxazole, CIP: Ciprofloxacin, AZM: Azithromycin, Me: Meropenem, Tg: Tigecycline, CAZ: Ceftazidime, CZX: Ceftizoxime, TE: Tetracyclin, AMC: Amox-Clav, CTR: Ceftriaxone, COX: Cloxacillin, ER: Erythromycin, NIT: Nitrofurontoin, CE: Cephalothin, CXM: Cefuroxime, CPZ: Cefoperazone, CN: Cephalexin, NET: Netilmycin, AX: Azetreonam

Table 4: Classification of drug sensitivity for important bacterial isolates causing ventilator associated pneumonia

Organism	AK (%)	Cs (%)	PI (%)	COT (%)	CIP (%)	AZM (%)	Me (%)	Tg (%)
Klebsiella (29)	6 (33.33)	9 (50)	6 (33.33)	8 (44.44)	5 (27.77)	0 (0)	6 (33.33)	7 (38.88)
Pseudomonas (27)	6 (31.57)	8 (42.10)	7 (36.84)	1 (5.26)	5 (26.31)	0 (0)	4 (21.05)	5 (26.31)
Acinetobacter (24)	3 (20)	5 (33.33)	1 (6.66)	0 (0)	0 (0)	0 (0)	3 (20)	3 (20)
COPS (22)	0 (0)	0 (0)	0 (0)	2 (15.38)	4 (30.76)	4 (30.76)	0 (0)	0 (0)
E. coli (19)	5 (55.55)	5 (55.55)	5 (55.55)	3 (33.33)	2 (22.22)	0 (0)	3 (33.33)	3 (33.33)
Total	16 (21.62)	27 (36.48)	19 (25.67)	14 (18.91)	16 (21.62)	4 (5.40)	16 (21.62)	18 (24.32)

AK: Amikacin, Cs: Colistin, PI: Piperacillin, COT: Co trimaxazole, CIP: Ciprofloxacin, AZM: Azithromycin, Me: Meropenem, Tg: Tigecycline, *E. coli: Escherichia coli*, COPS: Coagulase positive *Staphylococcus aureus*

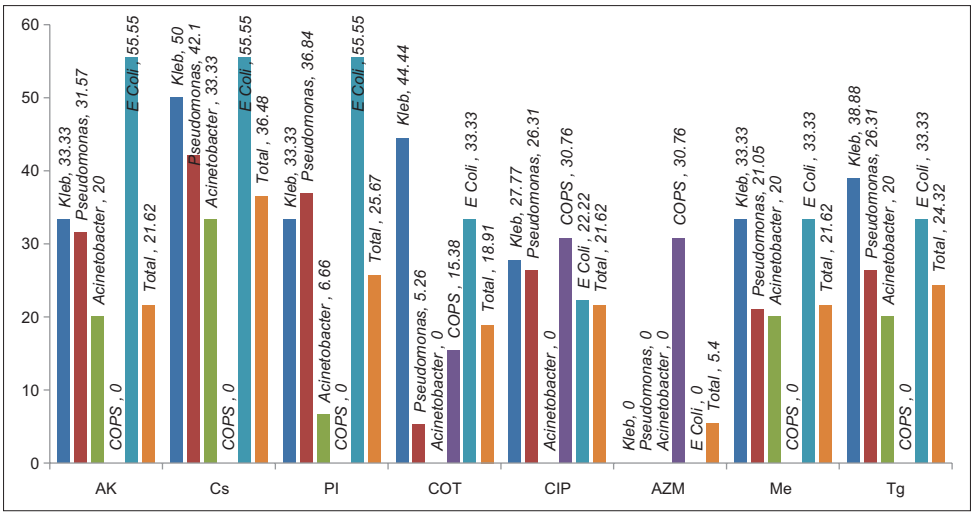


Graph 1: Bacteriological profile of ventilator associated pneumonia isolates

intubation, re-intubation, tracheostomy, cerebrovascular accidents and longer duration of ventilation, advancing age, preexisting comorbidities (chronic obstructive pulmonary disease [COPD], and coronary artery disease), multi-organ dysfunction, prior use of antibiotics and LV systolic dysfunction were the risk factors for developing VAP ($P < 0.02$) [Table 7].

DISCUSSION

VAP accounts for one-fourth of the infections occurring in critically ill patients and is the reason for half of antibiotic prescriptions in mechanically ventilated patients. Several countries have reported mortality rates ranging from 24% to 76%. Total 22 patients were GP and 52 were with GNB.



Graph 2: Culture sensitivity and antibiotic suceptibility pattern of important ventilator associated pneumonia isolates

Table 5: List of antibiotics and sensitivity pattern with various bacterial isolates

Antibiotics	Sensitive (*n*=126), (%)
PG	4 (3.17)
COT	14 (11.11)
COX	4 (3.17)
CIP	16 (12.69)
ER	4 (3.17)
CE	2 (1.58)
NIT	3 (2.38)
AZM	4 (3.17)
OF	13 (10.31)
TI	9 (7.14)
CZX	12 (9.52)
AM	1 (0.79)
CXM	2 (1.58)
TE	13 (10.31)
AMC	5 (3.96)
CTR	5 (3.96)
CN	4 (3.17)
CDN	1 (0.79)
B PB	2 (1.58)
GEN	16 (12.69)
CPZ	5 (3.96)
CX	19 (15.07)
AX	1 (0.79)
NET	6 (4.76)
CAZ	3 (2.38)
Me	16 (12.69)
PI	19 (15.07)
AK	20 (15.87)
Cs	27 (21.42)
Tg	18 (14.28)

TG: Tigecycline, Cs: Colistin, AK: Amikacin, PI: Piperacillin, Me: Meropenem, CAZ: Ceftazidime, NET: Netilmycin, AX: Azetreonam, CX: Cefoxitin, CPZ: Cefoperazone, GEN: Gentamicin, B BP: Polymyxin, CDN: Cefdinir, CN: Cephalexin, CTR: Ceftriaxone, AMC: Amox-Clav, TE: Tetracyclin, CXM: Cefuroxime, AM: Ampicillin, CZX: Ceftizoxime, OF: Ofloxacin, AZM: Azithromycin, NIT: Nitrofurontoin, TI: Ticarcillin, CE: Cephalothin, ER: Erythromycin, CIP: Ciprofloxacin, COX: Cloxacillin, COT: Co trimaxazole, PG: Penicillin

Klebsiella, Pseudomonas, Acinetobacter, COPS and *E. coli* were the most commonly isolated organisms with high mortality rates in this study. The prevalence of MDR organisms were 43.65%. About 55.40% of patients had poly-microbial VAP and 44.59% had single isolate. We compared our results with various studied from India and overseas [Table 8]. Gadani *et al.* reported that the most common organism isolated was *Pseudomonas* with early-onset VAP was found in 27% and late-onset in 73%. Late-onset VAP had poor prognosis regarding mortality (66%) as compared to the early-onset type (20%).[9] These findings are comparable with our study were *Klebsiella* 29(23.01587%), *Pseudomonas* 27(21.42%), *Acinetobacter* 24(19.04%), and *E. coli* 19(15.07%).

Were isolated in patients with VAP with 23.63% had early VAP and 76.36% had late-onset VAP. In this study, the case fatality rate was 29.72% (early-onset VAP: 22.72%, late-onset VAP: 77.27%). Similarly, Rakshit *et al.* reported that half of the cases developed VAP with *P. aeruginosa*.[10] Pawar *et al.* reported that significant risk factors for VAP were COPD, reintubation, coma, steroid treatment, intra-aortic balloon counter pulsation, enteral feedings, and tracheostomy. The most common pathogens isolated were *P. aeruginosa*, *E. coli*, *K. pneumoniae*, *Staphylococcus species*, and *Acinetobacter species* with mortality rate of 16%.[11] Similarly, in our study, most common organisms were *Klebsiella*, *Pseudomonas, Acinetobacter, E. coli and* COPS with overall mortality of 29.72%. In this study, impaired consciousness, re-intubation, emergency intubation, and preexisting co-morbidities were the significant risk factors for developing VAP. Joseph *et al.* reported the incidence of VAP 30.67 and 15.87 per 1000 ventilator days in the two different ICUs.[12] Similarly, in the current study, the incidence of VAP was 27.71% with the rate per 1000 ventilator days was 39.59 predominated by late-onset VAP. Joseph *et al.* and Combes *et al.* reported poly-microbial VAP in 30–70% and 48%, respectively.[3,13] Similarly, in our study, 55.40% patients had poly-microbial VAP. The VAP is significant public health issues all over the world including

Table 6: Single and multiple isolates associated with mortality in ventilator associated pneumonia

Organisms	Deaths (*n*=22)	Mean stay days	Mortality rate %	Discharges (*n*=52)	Mean stay days
Klebsiella spp.	2	14.5	25	6	13.66
Klebsiella + *Acinetobacter* spp.	3	17.66	75	1	24
Klebsiella + *COPS*	1	17	100	0	-
Klebsiella + *Pseudomonas*	2	9	28.57	5	9.2
Klebsiella + *E. coli*	1	7	100	0	-
Klebsiella + *P. aeruginosa* + COPS	0	-	0	2	8
Klebsiella + *P. aeruginosa* + *E. coli*	1	7	50	1	29
Klebsiella + *P. aeruginosa* + *Acinetobacter*	1	19	100	0	-
E. coli	3	7	42.85	4	23
E. coli + *P. aeruginosa*	1	53	33.33	2	19
COPS	2	4	22.22	7	9.85
COPS + *P. aeruginosa*	0		0	3	9
COPS + *Acinetobacter* spp.	1	5	50	1	26
P. aeruginosa	1	9	33.33	2	19
P. aeruginosa + *Acinetobacter* spp.	2	9.5	100	0	-
P. aeruginosa + *Citrobacter* spp.	0	-	0	4	
P. aeruginosa + *Acinetobacter* + COPS	0	-	0	1	
Acinetobacter spp.	1	20	10	9	18.44
Nonhemolytic streptococci	0	-	0	1	
Alpha hemolytic streptococci	0	-	0	2	
Diptheroids	0	-	0	1	

E. coli: Escherichia coli, COPS: Coagulase positive *Staphylococcus aureus*, *P. aeruginosa: Pseudomonas aeruginosa*

Table 7: Risk factors associated with ventilator associated pneumonia

Variables	*n*=74 (%)
Emergency intubation	9 (12.16)
Re-intubation	14 (18.91)
Tracheostomy	3 (4.05)
Cerebrovascular accidents	12 (16.21
Age >60 years	17 (22.97)
COPD	9 (12.16)
CAD	8 (10.81)
LV systolic dysfunction	9 (12.16)
Multi-organ dysfunction	11 (14.86)
Organophosphorus compound poisoning	7 (9.45)
Prior antibiotic treatment	13 (18)

COPD: Chronic obstructive pulmonary disease, CAD: Coronary arterial disease, LV: Left ventricular

Asian countries.[14] Dey and Bairy quoted 45.4% incidence of VAP, (early-onset: 47.7%, late-onset VAP: 52.3%) with *Acinetobacter* spp. and *P. aeruginosa* were the most commonly isolated multiresistant pathogens.[15] These findings are comparable with our results in which 43.65% isolates were MDR predominated by *Pseudomonas, E. coli, Klebsiella* spp., *Acinetobacter* and COPS. Chung *et al.* quoted major bacterial isolates in VAP were *Acinetobacter* spp., *P. aeruginosa, Staphylococcus aureus*, and *K. pneumoniae* with MDR isolates with mortality rate was 38.9%.[16] Rello *et al.* stated that the *Acinetobacter* spp. prevalence >10% in pneumonia episodes requiring carbapenems and colistin.[17] Similarly, in our study, 33.33% were *Acinetobacter* spp. sensitive to colistin. Arabi *et al.* stated that the rates of VAP varied from 10 to 41.7 per 1000 ventilator days. GNB were the most common pathogens (41–92%), followed by GPC (6–58%). VAP was associated with a crude mortality that ranged from 16% to 94%.[18] These findings are comparable with our study with incidence of VAP rate per 1000 ventilator days was 39.59 predominated by GNB (70.27%) with case fatality rate of 29.72%. Werarak *et al.* reported VAP predominated by elderly males with and late onset caused by *A. baumanni* (92.3%) with MDR or pandrug-resistant. The other common isolated pathogens were *K. pneumoniae, P. aeruginosa* and *methicillin-resistant S. aureus* (MRSA) with mortality of 42.5%, these findings are comparable with our results.[19] Combes *et al.* reported mortality of VAP was 18% which is relatively less compared to our results (29.72%).[13] Joseph *et al.* reported that *Enterobacteriaceae*, *Haemophilus influenzae, Staphylococcus aureus,* and *Streptococcus pneumoniae* were more common in early-onset VAP and *Pseudomonas* spp. and *Acinetobacter* spp. were significantly associated with late-onset VAP ($P = 0.0267$) with three fourth of them were MDR. Prior antibiotic therapy and hospitalization of 5 days or more were independent risk factors for VAP by MDR pathogens. These findings are comparable with our results in which 43.65% isolates were MDR and 18% of patients with VAP received prior antibiotics.[20] Werarak *et al.* quoted *A. baumannii* as most common cause of VAP 30.4%, of them 80% had late-onset Niemann-pick with the median duration of 10 days after admission and were resistant to many antibiotics including carbapenems.[21] Similarly, in our study, 19.04% were *A. Baumannii* prevalent in late-onset VAP with MDR isolates of *A. Baumannii were* 73.5%. Panwar *et al.* reported incidence of 47.05% VAP predominantly caused by *P. aeruginosa* with mortality of 37%.[22] Similarly, in our study, the incidence of VAP in present population was 27.71% (VAP rate per 1000 ventilator days was 39.59). Total 55(43.65%) were MDR organisms. *Klebsiella, P. aeruginosa, Acinetobacter* and *E. coli* were the most commonly isolated organisms.

Table 8: Comparison of various studies

Study/incidence	Isolates	MDR (%)	Risk factors	Mortality (%)	Sensitive drugs/ resistance
Werarak *et al*. 30.4%	*K. pneumoniae, P. aeruginosa* and MRSA	*A. baumannii* 92.3 MDR	82.9% late-onset VAP	42.5	Carbapenems (R)
Joseph *et al*. 30.67 and 15.87/1000 ventilator days	Enterobacteriaceae, *H. influenzae, S. aureus, S. pneumonia*	78.7	Prior antibiotic therapy *Pseudomonas* spp. and *Acinetobacter* spp.		Colistin, meropenem piperacillin, vancomycin
Gadani *et al*. Early-onset VAP: 27% Late: 73%	*P. aeruginosa*	Late-onset type VAP	Late-onset VAP had poor prognosis	66 20	
Dey *et al*. 45.4%	*Acinetobacter spp. P. aeruginosa*	*Acinetobacter* spp. and *P. aeruginosa*	47.7% had early-onset VAP and 52.3% had late-onset VAP		
Gupta *et al*. 28.04%	*P. aeruginosa,* MRSA, *K. pneumoniae, Acinetobacter*	*P. aeruginosa,* MRSA, *K. pneumoniae, A. baumannii*	Re-intubation tracheostomy	46.67	Carbapenems MRSA Beta-lactam (R)
Chittawatanarat *et al*.	GNB: 94.7% *S. aureus:* 4.0%	*A. baumannii, K. pneumoniae, P. aeruginosa*	Age, MDR, sepsis, APACHE-II score	41.4, 30.8	Colistin, meropenem cefoperazone, piperacillin-T
George *et al*.	*Acinetobacter, K. pneumoniae, Enterobacteriaceae, Staphylococcus*				Amikacin, piperacillin, meropenem
Panwar *et al*. 47.05%	*P. aeruginosa*	*P. aeruginosa*		37	
Rit *et al*. VAP: 20%	21.87 per 1000 ventilator days	MDR: 69.7, *Pseudomonas* spp. and *Acinetobacter*	Polymicrobial infections	5	
Pieter *et al*.	*MRSA, Enterobacteriaceae, P. aeruginosa*	MRSA, *Enterobacteriaceae, P. aeruginosa*	Prior exposure to more than two antibiotics		
Walkey *et al*. 14.6%	*Acinetobacter* MRSA	Polymicrobial 95	*Acinetobacter* MRSA		
Grgurich *et al*.	MRSA, *P. aeruginosa, Acinetobacter, Enterobacteraciae*		Age, immunosuppression, antibiotic exposure, prolonged ventilation		
Ranjan *et al*. 57.14%. 31.7/1000 ventilator days	*P. aeruginosa, Acinetobacter. Klebsiella, Citrobacter, Enterobacter, E. coli*	65 and 19	Broad spectrum prolonged antibiotic	48.33	
Moreira *et al*. 25.3%	Monomicrobial: 87.7% Polymicrobial: 12.3%	47.3	Stay, corticoids, prior antibiotics, mixed etiology	52.5, 19.5	
Present study VAP: 27.71%	*K. pneumoniae, Acinetobacter, E. coli* COPS, single isolate: 33	43.65 Late-onset VAP Poly-microbial: 41	Re-intubation, prior antibiotic exposure, prolonged ventilation	29.72	Amikacin, colistin, piperacillin, meropenem

K. pneumoniae:Klebsiella pneumoniae, MRSA: Methicillin-resistant *Staphylococcus aureus, E. coli: Escherichia coli,* COPS: Coagulase positive *Staphylococcus aureus, P. aeruginosa: Pseudomonas aeruginosa,* MDR: Multidrug resistant, *S. pneumonia: Streptococcus pneumonia, H. influenza: Hemophilus influenza, A. baumannii: Acinetobacter baumannii, S. aureus: Staphylococcus aureus,* VAP: Ventilator associated pneumonia, GNB: Gram-negative *Bacilli*

The overall case fatality rate was 29.72%. Park reported common pathogens for VAP include *Pseudomonas species,* resistant GNB, *Staphylococci*, *Enterobacteriaceae, streptococci* and *Haemophilus species*.[23] These findings are comparable with our results. Similar to our study, Chittawatanarat *et al.* reported that Gram-negative organisms were the major pathogens (94.7%). The first three most common organisms were *Acinetobacter baumannii*, *K. pneumoniae*, and *P. aeruginosa* with significant case fatality rate. The most common GP organism was *Staphylococcus aureus*. Half of all VAP cases were caused by susceptible organisms. Antibiotic resistance was demonstrated by 49.3% of the GNB and 62.5% of the GPCs.[24] Walkey *et al.* reported VAP rate of 14.6% frequently caused by poly-microbial bacteria including *Acinetobacter* spp., GNB and MRSA (MDR). Patients with VAP were more likely to have a neurological reason for ventilator dependence, (69.6%) with mortality rate of 5%.[25] The rate of VAP was relatively low compared to our study (27.71%), which could be because of different clinical setting, duration of ventilation, organism resistance pattern, antibiotic policy and indication for MV. Ranjit and Bhattarai reported VAP rate of 31.88%, which is comparable with our rate of 27.71%.[26] Gupta *et al.* quoted incidence of 28.04% VAP with mortality of 46.67%, caused

by *P. aeruginosa*, MRSA, *K. pneumoniae and A. baumannii.* About 50% isolates of *Acinetobacter* were resistant to carbapenems. Mortality was highest for infections caused by *A. baumannii* (83.33%) and *K. pneumoniae* (71.42%).[27] Comparable to our study, Rit *et al.* quoted incidence of VAP of 20% with 21.875 per 1000 ventilator days with late-onset VAP in 60.7% caused by *Pseudomonas* spp. and *Acinetobacter* spp. and poly-microbial infections with about three fourth were MDR.[28] George and Sequiera reported *Acinetobacter* were isolated in 37.5% (12), *Pseudomonas* in 21.87% (7), *Klebsiella* in 15.6% (5), *Enterobacter* in 12.5% (4), and *Staphylococcus* in 6.25% (2) in patient with VAP. *Acinetobacter* were sensitive to amikacin (44.66%), meropenem (25%). Pseudomonas was sensitive to amikacin, PI, (85.71%) and meropenem (57.14%). The most common organism isolated was *Acinetobacter*.[29] These findings are comparable with our results. Similarly, Moreira and Gontijo Filho carried out a case–control using patients with VAP by MDR pathogens (case) and non-MDR pathogens (control). They found that 25.3% developed VAP and 47.3% due to MDR pathogens. The risk factors for MDR group for VAP were length of hospital stay, use of corticoids and prior use of antibiotics, inappropriate empirical antimicrobial therapy, and mixed/poly-microbial etiology and were significantly associated mortality.[30] In the present study, 18% of patients with VAP have received prior antibiotics for other source of infection developed VAP. The administration of broad-spectrum antibiotics is a risk factor for developing MDR VAP. Ranjan *et al.* observed that the prior use of antibiotics increases the risk of acquiring drug resistant pathogens (*P. aeruginosa* and *Acinetobacter* spp.).[31] Similarly, Joseph *et al.* stated that prior antibiotic therapy was independent risk factors for VAP by MDR pathogens.[20] Similarly Depuydt *et al.* and Grgurich *et al.* stated that the risk of MDR pathogens causing VAP was mainly determined by prior exposure to antibiotics.[32,33] The organisms isolated in the present study were predominantly Gram-negative. The antibiotics such as PI-T, amikacin, and meropenem have been found to the good antibiotic options for VAP to start with till culture reports are available.

CONCLUSIONS

This study highlights the burden of VAP. The incidence of VAP in present population was 27.71%. VAP is associated with 43.65% MDR pathogens. The overall case fatality rate of VAP was 29.72%. Late-onset VAP was predominated, caused by MDR pathogens (77.27%) and was associated with increased morbidity and mortality. GNB isolates were more prevalent in this study (*Pseudomonas, Klebsiella, E. coli* and *Acinetobacter*) with high mortality rates. The emergency intubation, re-intubation, tracheostomy, and longer duration of ventilators were the risk factors for developing VAP. The present study highlight burden of MDR pathogens in VAP. Knowledge of the susceptibility pattern of the local pathogens will guide for de-escalation strategy (switching from a broad-spectrum empiric antimicrobial therapy to a narrower spectrum) depending on the microbiological data. Colistin and PI-tazobactam along with Amikacin and Meropenem may be used for successful treatment *Acinetobacter* spp. and *Pseudomonas* spp. as they showed good *in vitro* activity against these pathogens. Prior antibiotics have no role in prevention of VAP. Previous use of antibiotic will leads to MDR organisms. Newer therapy like, inhalation antibiotics and infusion should be investigated. An appropriate and judicious use of antibiotic is recommended to treat VAP, empirically. Knowledge of risk factors for VAP may be useful in implementing simple and effective preventive measures. Evidence-based protocol based strategies is suggested to prevent VAP, associated healthcare costs and to reduce the mortality. Future studies should attempt to determine whether specific diagnostic or therapeutic strategies could markedly improve VAP outcomes.

Limitations of study

Our results cannot be applied to other institute, as various factors and bacteriological agents causing VAP may vary from institution to institution. This is single center study and included patients from medical ICU, findings and interpretation of our result cannot be generalized to other institute or other ICU.

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Conflicts of interest

There are no conflicts of interest.

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