International Journal of Research and Review
Vol.7; Issue: 12; December 2020
Website: www.ijrrjournal.com
Original Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Microbiological Profile and Clinical Outcome of Ventilator - Associated Pneumonia Patients in an Intensive Care Unit at a Tertiary Care Institute of North India

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ABSTRACT

Introduction: Ventilator associated pneumonia is a serious life threatening condition and a major problem in intensive care units despite advances in diagnostic and treatment modalities. Incidence of this clinical entity varies widely based on agent, host and environment factors. An understanding of these variables in local setting is important so as to allow judicious and more effective use of antimicrobials.

Aims: To determine the incidence of VAP in the surgical intensive care unit (SICU) of the institute, to enumerate the bacterial pathogens causing it and their susceptibility profile.

Material and methods: Data of all the patients diagnosed with VAP for a period of three years (2017-2019) was analysed retrospectively and variables such as age, sex, Clinical Pulmonary Infection Score, diagnosis at the time of SICU admission, duration of ventilation, antibiotics received, sample submitted, type of organism isolated and its susceptibility profile recorded. Statistical analysis was carried out using the MedCalc and NCSS software (trial version).

Results: The incidence of VAP was found to be 33.6%. It was more common in male patients (61.4%) and the mean ± SD age was 43.4 ± 14.7. Most common diagnosis at the time of ICU admission was trauma. Late onset VAP was more common in the study group. A significant portion of patients with VAP were on mechanical ventilation >10 days. Multi-drug resistant *Acinetobacter* spp and *Klebsiella pneumoniae* were the most common Gram negative and *Staphylococcus aureus* and *Enterococcus* spp most common Gram positive organisms recovered from these patients. Cefoxitin resistance among *S. aureus* was 74.6% and vancomycin resistance in *Enterococci* was 24.1%. Mortality in VAP patients was 46.7%.

Conclusion: VAP due to multidrug resistant microorganisms is a serious problem in our hospital with late onset VAP being more common. Emergence of polymyxin B resistance in Gram negative organisms, increasing methicillin resistance in *S. aureus* and vancomycin resistance in *Enterococcus* spp is quite alarming.

Keywords: Antimicrobial resistance, Mechanical ventilation, Methicillin, Polymyxin B, Vancomycin

INTRODUCTION

Pneumonia occurring in a patient 48-72 hrs following endotracheal intubation is referred to as ventilator associated pneumonia (VAP) and is the second most common nosocomial infection in the intensive care units (ICU's). It contributes to nearly half of all cases of hospital

acquired pneumonias [1-3] and is characterised by the presence of new or progressive infiltrate, signs of systemic infection, changes in sputum characteristics and microbiological isolation of an infectious agent [2]. VAP can be categorised into early onset and late onset based on the occurrence within or after 4 days respectively. Early onset VAP is usually caused by pathogens that are sensitive to various antimicrobial agents, whereas late onset VAP is mostly caused by multi-drug resistant (MDR) pathogens [2,3]. The term ventilator-associated event (VAE), was introduced by CDC in 2013. The definition encompasses all conditions that result in a remarkable deterioration in oxygenation and includes both infectious and non-infectious conditions and comprises of three stages; stage 1 is ventilator associated condition (VAC) where the patient develops hypoxemia for >2 days and the cause of hypoxemia is not known. Stage 2 is infection related ventilator associated complication (IVAC) where hypoxemia develops concomitant with infection of inflammation and antibiotics are given for at least 4 days. The last stage is probable or possible VAP which consists of evidence of white blood cells on Gram stain, presence of respiratory pathogens on quantitative cultures, in patients with IVAC. [4]

VAP is a serious problem in critical care patients and its incidence is highly variable amongst health care institutions. What complicates the scenario is the increased recovery of MDR pathogens from these cases which not only contributes to increased length of hospital stay and the costs incurred thereof but also to increased morbidity and mortality [5,6]. VAP is generally caused by bacteria, whereas fungi and viruses are seldom involved [7]. Usually, early-onset VAP is caused by pathogens like *Streptococcus pneumoniae, Haemophilus influenzae,* and methicillin-susceptible *Staphylococcus aureus* (MSSA), antibiotic-sensitive enteric Gram-negative bacilli (e.g. *Escherichia coli, Enterobacter* species, *Proteus* species, *Serratia marcescens* and *Klebsiella pneumoniae*) [3]. On the other hand, late-onset VAP is usually caused by bacteria, such as *Pseudomonas aeruginosa, Acinetobacter* spp., methicillin-resistant *S. aureus* (MRSA), and extended-spectrum β-lactamase (ESBL) producing Enterobacteriaceae [8]. Nonetheless both antibiotic susceptible and resistant microorganisms can be isolated with similar frequencies in early and late-onset VAP. Knowledge about the incidence of VAP, risk factors associated with it, the microbiological milieu causing VAP, can aid the clinicians in developing effective preventive measures that can decrease the mortality and morbidity, duration of treatment and hospital stay associated with it. The present study was undertaken to determine the incidence and outcomes of VAP in the surgical intensive care unit (SICU) of the institute and to determine the etiological bacterial pathogens causing VAP and their susceptibility profile.

MATERIAL AND METHODS

Study design and settings:

This retrospective, cross sectional descriptive study was carried out in the Department of Microbiology Sher-i-Kashmir Institute of Medical Sciences, Soura Srinagar. Data of all the patients diagnosed with VAP, who were admitted in the SICU of the hospital from January 2017 to Dec 2019 was retrieved from the medical records section and analysed. VAP was defined as development of a clinically/radiologically conformed pneumonia in a patient at least 48 hours after having been put on mechanical ventilation. [1] Patients with pneumonia prior to ventilation were excluded from the study.

The following variables were noted on a predesigned proforma for each patient: age, gender, Clinical Pulmonary Infection Score (CPIS) [9], diagnosis at the time of ICU admission, duration of ventilation, antibiotics received, sample submitted for the confirmation of an etiological agent e.g. bronchoalveolar lavage (BAL) or endotracheal aspirate (ETA), type of

organism recovered and its susceptibility profile and the clinical outcome.

Probable VAP was suspected in any patient with a CPIS >6 and positive quantitative cultures of the respiratory samples. The CPIS score was calculated on the parameters shown in table/figure 1. A colony count of $>10^5$ colony forming units (cfu)/ml for ETA and $>10^4$ for BAL was considered significant [10]. A colony count below the cut-off level was considered as colonisation or contamination.

Sample collection and processing:

Respiratory samples like BAL and ETA from the patients admitted in the SICU were subjected to quantitative cultures in the laboratory as per the standard Microbiological procedures [11]. Gram staining and culture on blood agar, chocolate agar and MacConkey agar was done for the recovery of microorganisms. Susceptibility tests were carried out on Muller Hinton agar (MHA) or MHA with 5% sheep blood (for *Streptococcus spp*) or cation adjusted MHA (for *Enterococcus* spp) by disc diffusion method and zone sizes interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines [12]. All the media and discs were procured from HiMedia (Mumbai). In case of confounding results identification and susceptibility was confirmed by Vitek-2.

For members of the family *Enterobacteriaceae* and non-fermentative Gram negative bacilli, antibiotic discs used were: ampicillin (AMP), ampicillin+sulbactam (AS), amoxicillin+ clavulanic acid (AXV), ticarcillin+ clavulanic acid, (TCC), piperacillin+ tazobactam (PIT), amikacin (AK), gentamicin (GEN), co-trimoxazole (COT), ciprofloxacin (CIP), levofloxacin (LE), ceftazidime (CAZ), ceftriaxone (CTR), cefotaxime (CTX), cefoperazone+sulbactam (CFS), cefoxitin (CX), imipenem (IMP), meropenem (MRP), polymyxin B (PB) and tobramycin (TOB). For Gram positive organisms the discs used were: penicillin G (P), vancomycin (VA), linezolid (LZ), erythromycin (E), clindamycin (CD), COT, CIP, CX (as a surrogate marker for methicillin resistance) and AK. Vancomycin resistance in *S. aureus* and *Enterococcus* spp and susceptibility profile of fluconazole (FLC), itraconazole (VRC) and Amphotericin B (AP) for fungal isolates was confirmed by Vitek-2.

Control strains of *Escherichia coli*, ATCC 25922, *Staphylococcus aureus*, ATCC 25923 and *Pseudomonas aeruginosa*, ATCC 27853 were used for antimicrobial susceptibility testing.

Statistical analysis

The data was entered in the Microsoft Excel spreadsheet and analysed using standard tests. Fisher's exact test was applied when two or more set of variables were compared. *P*-value of < 0.05 was considered to be statistically significant. Analysis was done using MedCalc and NCSS software (trial version).

RESULTS

Table/Figure 1: Clinical Pulmonary Infection Scoring CPIS system; parameters included.

CPIS Points	0	1	2
Temperature (OC)	>36.5 and < 38.4	>38.5 and <38.9	>39 or <36
Chest radiograph	No infiltrate	Diffuse infiltrate	Localized infiltrate
Tracheal secretions	Rare	Abundant	Purulent
Leukocyte count (mm3)	>4,000 and <11,000	<4,000 and >11,000	<4000 or >11,000 + band forms
PaO2/FiO2 ratio (mmHg)	>240 or ARDS	-	≤240 and no ARDS
Culture of tracheal secretions	Negative	-	Positive

Of the 2654 patients, who received MV during the study period, 893 (33.6%) had clinical and microbiological evidence of VAP. The patients included 548 males and 345 females, with ages ranging from 18 to 74 years. The mean ± SD age of patients

who developed VAP was 43.4 ± 14.7 years. Table/figure 2 Of the 893 cases, 302 (33.8%) were categorised as early onset and 591 (66.2%) as late onset VAP. The incidence of VAP was more in patients who were on MV for >10 days (n=624, 69.9 %) as compared to those who were ventilated for less than <10 days (n=269, 30.1%). Out of the 893 patients who developed VAP, 542 (60.7%) were on a broad spectrum antibiotics in the preceding 7 days whereas 351 (39.3%) were not. The antibiotics included piperacillin + tazobactam, cefoperazone + sulbactam, levofloxacin, ciprofloxacin, vancomyicn, linezolid, amikacin, meropenem, imipenem, polymyxin B. The A total of 476 (53.3%) patients were discharged from the SICU whereas 417 (46.7%) expired. Comparison between VAP and non-VAP group is given in table/figure 2. Co-morbidities in this subset of patients is given in table/figure 3.

Table/Figure 2: Comparison of various variables among the VAP and non-VAP patients who received MV during the study period

	VAP N (%)	**Non-VAP N (%)**	**Odds ratio**	**95% CI**	***P*-value**
Variable					
Age (mean ± SD)	43.4 ± 14.7	38. 6 ± 16.5	-	-	-
Gender					
Males	548 (61.4%)	918 (52.1%)	1.46	1.2-1.7	<0.0001
Females	345 (38.6%)	843 (47.8%)	1.0		
VAP					
Early onset	302 (33.8%)	-	-	-	-
Late onset	591 (66.2%)	-	-	-	<0.0001
MV					
< 10 days	269 (30.1%)	1368 (77.7%)	1.0	-	-
> 10 days	624 (69.9 %)	393 (22.3%)	8.1	6.7-9.7	<0.0001
Broad spectrum antibiotic intake in the preceding week					
Yes	542 (60.7%)	1039 (59%)	1.1	0.9-1.3	0.4
No	351 (39.3%)	722 (41%)	1.0	-	
Discharged from ICU	476 (53.3%)	1119 (63.5%)	1.0	-	
Mortality	417 (46.7%)	642 (36.5%)	1.5	1.3-1.8	<0.0001
Total no of patients	893 (33.6%)	1761 (66.4%)	-	-	-

Table/Figure 3: Associated co-morbidities in VAP patients

Co-morbidity	**Total no of patients N (%)**
Trauma	209 (23.4%)
respiratory failure	167 (18.7%)
chronic obstructive pulmonary disorder (COPD)	112 (12.5%)
diabetes mellitus	105 (11.8%)
renal failure	99 (11.1%)
neurological disorders	84 (9.4%)
cardiovascular disorders	81 (9.1%)
miscellaneous	36 (4.0%)

Majority of the bacterial isolates recovered (n=728, 81.5%) were Gram-negative bacilli among which *Acinetobacter spp* followed by *Klebsiella pneumoniae* were the most common. This was followed by Gram positive isolates (n=165, 18.5%) and various species of *Candida*. A detailed description of the microorganisms recovered is given in table/figure 4. Among the recovered *Candida spp* most common were *C. albicans* (n=12) followed by *C. glabrata* and *C. krusei* (n=3 each). Table/figure 4. Out of the 893 cases of VAP, 206 (23.1%) were polymicrobial and 687 (76.9%) were monomicrobial. In the polymicrobial infections also, Gram negative bacteria were predominant, with the most common combination being *K. pneumoniae* and *P. aeruginosa*. Antibiotic susceptibility profile of the Gram negative and Gram positive isolates recovered from VAP patients is given in table/figure 5 and 6 respectively. Year wise resistance profile of the micro-organisms recovered in shown in table/figure 7, 8 and 9. All the Gram positive organisms except for Streptococci were resistant to P (100%). CX resistance in S. aureus was 77.0% whereas in CoNS it was 73.3%. Staphylococci continued to be sensitive to VA and LZ however 29.8% Enterococci were resistant to VA with uniform sensitivity to LZ. Among the Enterobacteriacae very high resistance to COT, CTR, CTX and IMP (98%, 98.5%, 98.5% and 94.4% respectively) was seen in K. pneumoniae isolates. In addition, PB resistance was seen in 4.6% of these isolates. All the isolates of E. coli were

resistant to AMP and AS with very high resistance to AXV (100%, 100% and 98.2% respectively). IMP resistance was 94%. Low level resistance among these isolates was seen for AK (41.1%). Isolates of Citrobacter and Enterobacter were also uniformly resistant to AS (100% each) with variable resistance to other antibiotics. Very high resistance to CIP (97%) and COT (96.5%) was seen in isolates of Acinetobacter spp with least resistance to AK and CFS (88.2%). PB resistance was seen in 4.8% isolates. On the other hand 97.8% isolates of P. aeruginosa were found to be resistant to CTR whereas low level resistance was seen for AK and PIT (35.8% and 38.1% respectively) among these isolates.

Table/Figure 4: Most common microorganism isolated from VAP patients

Organism	Total no of isolates N (%)
Gram negative bacteria	**728 (81.5%)**
Acinetobacter spp	228 (31.3%)
Klebsiella pneumoniae	195 (26.8%)
Pseudomonas aeruginosa	134 (18.4%)
Escherichia coli	112 (15.4%)
Citrobacter spp	37 (5.1%)
Enterobacter spp	22 (3.0%)
Gram positive bacteria	**165 (18.5%)**
Staphylococcus aureus	61 (37.0%)
Enteococcus spp	47 (28.4%)
Coagulase negative Staphylococci	30 (18.2%)
Streptococcus spp	9 (5.5%)
Candida spp	18 (10.9%)

Table/Figure 5: Cumulative resistance profile of Gram negative bacteria isolated from patients with VAP.

	Acinetobacter **N (%)**	***Klebsiella*** **N (%)**	***Pseudomonas*** **N (%)**	***Escherichia*** **N (%)**	***Citrobacter*** **N (%)**	***Enterobacter*** **N (%)**
Antibiotics						
AMP	-	-	-	112 (100%)	-	-
AS	-	-	-	112 (100%)	37 (100%)	22 (100%)
AXV	-	-	-	110 (98.2%)	-	-
TCC	210 (92.1%)	-	119 (88.8%)	79 (70.5%)	34 (92%)	19 (86%)
PIT	217 (95.2%)	165 (84.6%)	51 (38.1%)	76 (67.9%)	26 (70.3%)	9 (40.9%)
AK	201 (88.2%)	149 (76.4%)	48 (35.8%)	46 (41.1%)	14 (37.8%)	11 (50%)
GEN	164 (72%)	162 (83.1%)	73 (54.5%)	63 (56.3%)	17 (46%)	11 (50%)
COT	220 (96.5%)	191 (98%)	71 (53%)	90 (80.4%)	28 (75.7%)	16 (72.7%)
CIP	221 (97%)	180 (92.3%)	101 (75.4%)	98 (87.5%)	29 (78.4%)	15 (68.2%)
LE	212 (93%)	186 (95.4%)	111 (82.8%)	96 (85.7%)	22 (59.5%)	14 (63.6%)
CAZ	210 (92.1%)	179 (91.8%)	69 (51.5%)	104 (92.9%)	26 (70.3%)	18 (81.8%)
CTR	214 (93.9%)	192 (98.5%)	131 (97.8%)	98 (87.5%)	26 (70.3%)	18 (81.8%)
CTX	204 (89.5%)	192 (98.5%)	-	100 (89.3%)	29 (78.4%)	19 (86.4%)
CFS	201 (88.2%)	158 (81%)	71 (53%)	84 (75%)	21 (56.8%)	9 (40.9%)
CX	-	-	-	-	-	-
IMP	211 (92.5%)	184 (94.4%)	126 (94%)	87 (77.7%)	26 (70.3%)	19 (86.4%)
MRP	200 (87.7%)	172 (88.2%)	124 (92.5%)	83 (74.1%)	24 (64.9%)	19 (86.4%)
PB	11 (4.8%)	9 (4.6%)	0	0	0	0
TOB	-	-	89 (66.4%)	-	-	-
Total no of isolates	228	195	134	112	37	22

*Note: **AMP**: ampicillin; **AS:** ampicillin+sulbactam; **AXV**: amoxicillin+clavulanic acid; **TCC**: ticarcillin+clavulanic acid; **PIT**: piperacillin+tazaobactam; **AK**: amikacin; **GEN**: gentamicin; **COT:** cotrimoxazole; **CIP**: ciprofloxacin; **LE:** levofloxacin; **CAZ**: ceftazidime; **CTR:** ceftriaxone; **CTX:** cefotaxime; **CFS:** cefoperazone+sulbactam; **CX**: cefoxatin; **IMP:** imipenem; **MRP:** meropenem; **PB:** polymyxin-B; **TOB:** tobramycin.*

Table/Figure 6: Cumulative resistance profile of Gram positive bacteria isolated from patients with VAP.

	Staphylococcus aureus **N (%)**	***CoNS*** **N (%)**	***Enterococcus spp*** **N (%)**	***Streptococcus spp*** **N (%)**	***Candida spp*** **N (%)**
Antibiotics					
PG	61 (100%)	30 (100%)	47 (100%)	0	-
AMP	-	-	38 (80.8%)	-	-
E	57 (80.3%)	27 (90%)	-	2 (22.2%)	-
CD	43 (60.6%)	24 (80%)	-	4 (44.4%)	-
CX	47 (77.0%)	22 (73.3%)	-	-	-
VA	0	0	14 (29.8%)	0	-
LZ	0	0	0	0	-
CIP	55 (77.5%)	25 (83.3%)	-	6 (66.7%)	-
COT	34 (47.9%)	19 (63.3%)	-	4 (44.4%)	-
VRC	-	-	-	-	0
FLC	-	-	-	-	0
AP	-	-	-	-	0
Total no of isolates	61	30	47	9	18

*Note: **PG:** penicillin; **AMP**: ampicillin; **E:** erythromycin; **CD**: clindamycin; **VA:** vancomycin; **LZ:** linezolid; **CIP:** ciprofloxacin; **COT:** cotrimoxazole; **VRC:** voriconazole; **FLC:** fluconazole; **AP:** amphotericin-B.*

Table/figure 7: Year wise breakup of the resistance profile (in no's) of members of Enterobactericae

	Klebsiella (N=195)			***Escherichia (N=112)***			***Citrobacter (N=37)***			***Enterobacter (N=22)***		
	2017	**2018**	**2019**	**2017**	**2018**	**2019**	**2017**	**2018**	**2019**	**2017**	**2018**	**2019**
AMP	-	-	-	30	35	47	-	-	-	-	-	-
AS	-	-	-	36	41	35	11	13	13	6	7	9
AXV	-	-	-	33	41	36	-	-	-	-	-	-
TCC	-	-	-	24	27	28	9	13	12	4	6	9
PIT	48	55	62	21	26	29	8	8	10	0	2	7
AK	44	49	56	12	15	19	1	5	8	4	1	6
GEN	48	50	64	17	22	24	3	6	8	3	4	4
COT	77	61	53	31	26	33	8	9	11	4	7	5
CIP	48	54	78	28	32	38	5	10	14	4	6	5
LE	56	61	69	27	33	36	2	7	13	4	4	6
CAZ	50	68	61	34	32	38	7	8	11	4	6	8
CTR	55	61	76	28	33	37	8	8	10	5	7	6
CTX	64	56	72	31	36	33	9	7	13	5	6	8
CFS	47	50	61	24	29	31	0	9	12	0	2	7
CX	-	-	-	-	-	-	-	-	-	-	-	-
IMP	54	62	68	27	26	34	7	9	10	7	4	8
MRP	42	59	71	21	30	32	5	8	11	3	7	9
PB	0	2	7	0	0	0	0	0	0	0	0	0

Table/figure 8: Year wise breakup of the resistance profile (in no's) of non fermenting Gram negative bacteria

	Acinetobacter (N=228)			***Pseudomonas (N=134)***		
	2017	**2018**	**2019**	**2017**	**2018**	**2019**
AMP	-	-	-	-	-	-
AS	-	-	-	-	-	-
AXV	-	-	-	-	-	-
TCC	56	68	86	31	43	45
PIT	63	74	80	13	17	21
AK	62	70	69	14	15	19
GEN	46	53	65	22	26	25
COT	68	72	80	19	23	29
CIP	70	74	77	32	33	36
LE	51	63	98	24	38	49
CAZ	75	64	71	19	25	25
CTR	72	69	73	40	47	44
CTX	58	70	76	-	-	-
CFS	52	66	83	16	23	32
CX	-	-	-	-	-	-
IMP	68	73	70	36	48	42
MRP	51	68	81	39	40	45
PB	0	3	8	-	-	-
TOB	-	-	-	29	25	35

Table/figure 9: Year wise breakup of the resistance profile (in no's) of Gram positive bacteria

	Staphylococcus aureus (N=61)			***CoNS (N=30)***			***Enterococcus spp (N=47)***			***Streptococcus (N=9)***		
	2017	**2018**	**2019**	**2017**	**2018**	**2019**	**2017**	**2018**	**2019**	**2017**	**2018**	**2019**
PG	18	22	21	6	13	11	11	16	20	0	0	0
AMP	-	-	-	-	-	-	8	13	17	-	-	-
E	16	20	21	7	9	11	-	-	-	0	2	0
CD	11	14	18	8	6	10	-	-	-	1	1	2
CX	14	18	15	6	9	7	-	-	-	-	-	-
VA	0	0	0	0	0	0	1	5	8	0	0	0
LZ	0	0	0	0	0	0	0	0	0	0	0	0
CIP	15	18	22	7	8	10	-	-	-	2	0	4
COT	9	11	14	5	7	7	-	-	-	2	1	1
VRC	-	-	-	-	-	-	-	-	-	-	-	-
FLC	-	-	-	-	-	-	-	-	-	-	-	-
AP	-	-	-	-	-	-	-	-	-	-	-	-

DISCUSSION

The present study is a large compilation of microbiological data of patients diagnosed with VAP for a period of three years in the SICU of one of the largest tertiary care institutes of north India. The prevalence of VAP was found to be 33.6% which was high compared to an earlier study by Maqbool et al. [13] where the authors have reported an incidence of 13.0% only. VAP has been reported in variable frequency among the mechanically

ventilated patients ranging from 13% to 57% [14-16]. The variation in the incidence can be attributed to factors such as the criteria used to define VAP (e.g microbiological, clinical or both), the study population, underlying co-morbidities, the use of preventive strategies, duration of ventilation, pathogen profile etc. In the present study VAP was significantly more common in male patients (61.4%, OR 1.46, *P*<0.0001) and the mean age of the patients was 43.4 ± 14.7. Findings similar to what were seen in this study *viz a viz* gender and age group affected have been reported previously by other authors as well [15-18].

The duration of MV has been reported to be directly associated with the incidence of VAP. In this study patients who had been on MV for >10 days (69.9%) were more likely to develop VAP compared to those with MV for <10 days (OR 8.1, *P*<0.0001). Most of them were categorised as having late onset VAP (66.2%, *P*<0.0001). A longer duration of MV has previously been reported to be associated with a higher incidence of VAP. Ranjan N et al. [15] in their study found that the incidence of VAP increased in patients who were on MV for >15 days whereas Gadani H et al. [16] reported a significantly higher incidence of VAP in patients who require prolonged ventilator support. An exposure to broad spectrum antibiotic intake in the preceding week was almost comparable in the VAP (60.7%) and non-VAP (59%) group in our study (P-0.4). These results were in contrast to other reports of an increased rate of development of VAP caused by *P. aeruginosa* and *Acinetobacter spp*. when patients had a history of prior antimicrobial therapy [19].

A multicenter study from Greece, reported 45% of its VAP cases to have ICU admission due to trauma, [20] which although slightly higher, coincides with our finding of trauma being the most common diagnosis at the time of ICU admission in patients suffering from VAP (23.4%). Ali HS et al. [18] have reported trauma to be the most common diagnosis at the time of ICU admission in VAP patients as have other authors [14,17, 21].

The ESKAPE group of pathogens (*Enterococcus faecium, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa* and *Enterobacter* spp.) are responsible for nearly 80% of the VAP episodes [22]. All these organisms have a very high propensity of forming biofilms on catheters and tubings, which make them the ideal candidates for causing infections in patients requiring intensive care. In the present study also, a similar microbiological profile among VAP cases was seen with *A. baumannii* (31.3%) and *K. pneumonia* (26.8%) being the commonest Gram negative and *S. aureus* (37.0%) and *Enterococcus* spp. (28.4%) being the commonest Gram positive isolates recovered from them. An earlier study conducted in the same institute reported *K. pneumoniae* and *Acinetobacter* spp as the most commonly recovered bacteria from lower respiratory tract specimens of patients admitted in various ICU's [23]. Chawla R et al. [24] in their study reported 87% isolation of Gram negative organisms from VAP cases which is similar to our study where 81.5% isolates were Gram negative and only 18.5% Gram positive. In a study from Tirupati India, *Acinetobacter* spp followed by *P. aeruginosa* and *K. pneumoniae* were reported to be the most common Gram negative bacteria isolated from VAP cases [25].

Very high frequency of resistance was exhibited by Gram negative bacteria for the antibiotics against which they were tested. The two most frequently isolated organisms *Acinetobacter* spp and *K. pneumoniae* in addition to being highly resistant to other classes of antibiotics were resistant to PB as well which is a cause of grave concern as the treatment options for PB resistant, carbapenem resistant isolates are critically limited. Resistance to PB has increased over the years owing to the rising rates of colistin consumption to treat extensively drug-resistant (XDR) organisms [25]. Resistance genes carried on plasmids in

these nosocomial microorganisms confers resistance to a wide variety of antibiotic agents and the inter species transfer of these plasmids helps to spread and maintain MDR pathogens in closed units like ICU's. A study from south India [26] reported PB resistance in most of the Gram negative bacteria isolated from VAP cases along with variable resistance to other antibiotics. Isolates belonging to the family *Enterobacteriaceae* in this study were highly resistant to beta-lactam antibiotics, carbapenems, fluoroquinolones, aminoglycosides and third generation cephalosporins. Isolation of MDR microorganisms from patients suffering from VAP has been reported by various authors previously [14,15,21]. An overall increase in the resistance to various antimicrobial agents was observed in the present study from 2017 to 2019, even though the differences were not statistically significant.

All Gram positive bacteria (100%) except for *Streptococcus* spp were resistant to PG. CX resistance in *S. aureus* was 74.6% which is high compared to an earlier study from the same institute that reported a CX resistance of 52.6% in *S. aureus* isolates [23] but is similar to that reported by Patro S et al. [14] where the authors found 75% CX resistance in *S. aureus* isolates. For CoNS CX resistance was 73.3%. Even though all the *Staphylococcal* isolates were sensitive to VA, 24.1% *Enterococci* were resistant to the antibiotic. Bali N et al. [23] have reported 16.3% VA resistance in *Enterococci* previously from the same institution. High recovery of Vancomycin resistant *Enterococcus* (VRE) as reflected in the present study is alarming as VRE has been linked with the emergence of VA resistant *S. aureus* [27]. No resistance to LZ was seen among Gram positive bacteria. Also all the isolated *Streptococci* spp were sensitive to PG with variable resistance to E, CD, COT, CIP.

In the present study mortality rate in the VAP group was 46.7%, whereas it was 36.5% in the non-VAP group. However, since the two groups were not comparable to each other in all the factors, attributable mortality due to VAP could not be deduced. In a study by Ranjan N et al. [15] the overall mortality associated with VAP was observed to be 48.3% which is comparable to what we saw. Mathai AS et al. [17] in their study found that even though the overall mortality rates were similar between patients with or without VAP infections, elderly patients (>60 years) and those with higher Acute Physiology and Chronic Health Evaluation II scores at admission had significantly greater mortality rates if they acquired a VAP infection. The mortality rate in a study by Gadani H et al. [16] was found to be 54.1% in the VAP group as compared to 41.2% in the non-VAP group.

Limitation

This study is limited by its retrospective design that led to non-availability of all the information about all the variables under study. Further being a single centre study it precludes generalisation of the results, and local ecology of each hospital would be individually important to tailor individual hospital policies.

CONCLUSION

VAP is a serious life threatening problem in the ICU, that continues to a be challenge for the critical care physicians. Multi-centric prospective studies on this clinical entity need to be carried out across the state and country to better understand the dynamic factors associated with it. An updated information about the bacteriological profile and susceptibility patterns of microorganisms can aid the clinicians in making better evidence based treatment choices in patients of VAP.

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How to cite this article: Umara, Bali N, Kour R et.al. Microbiological profile and clinical outcome of ventilator- associated pneumonia patients in an intensive care unit at a tertiary care institute of North India. International Journal of Research and Review. 2020; 7(12): 98-107.

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