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Original Research Article

BACTERIOLOGICAL AGENTS CAUSING VENTILATOR ASSOCIATED PNEUMONIA IN THE ICU AND THEIR ANTIMICROBIAL RESISTANCE PROFILE

Shweta R. Sharma[1], Amit Mishra[2], Imran Ahamad[3], Vasundhara[1], Umar Farooq[4]

[1]Associate Professor, Department of Microbiology, TMMC & RC, Moradabad, Uttar Pradesh, India
[2]Associate Professor, Department of Medicine, TMMC & RC, Moradabad, Uttar Pradesh, India
[3]Assistant Professor, Department of Microbiology, TMMC & RC, Moradabad, Uttar Pradesh, India
[4]Professor & Head, Department of Microbiology, TMMC & RC, Moradabad, Uttar Pradesh, India

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Corresponding Author:
Dr. Shweta R Sharma,
Email: drshwetamicro@gmail.com

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Abstract

Background: Ventilator-associated pneumonia is one of the most important device associated health care related infection having high impact on mortality and morbidity of patients. These infections are difficult to treat as they are multidrug resistant organisms and the options available for their treatment are very limited thereby increasing the toxicity of drugs as well as high cost. This study was aimed to analyse the microbiological profile of VAP in our hospital and determining the antimicrobial susceptibility profile of these organisms. Also it determines ESBL, Amp C, Carbapenemase and MBL production in the isolates thereby helping in implementing effective prevention strategies. **Materials and Methods:** This study was conducted during the period of Jan 2020 to June 2022 in the ICUs setting and all mechanically ventilated patients developing pneumonia after >48 hrs of ventilation were included in our study. **Result:** In our study late onset VAP accounted for 86.2% cases and 50-60 years male were most commonly affected. Most common underlying condition was hypertension (54.23%) followed by diabetes mellitus (23.4%). Acinetobacter spp. was the most common isolate 66 (53.6%) having 100% resistance to ampicillin, gentamicin, ciprofloxacin, doxycycline and 98% resistance against cefotaxime. MRSA were detected in 57.1% of S. aureus while among gram negative bacilli ESBL, Carbapenemase production and MBL production accounted for 24.1%, 62.9% and 46.5% respectively. **Conclusion:** Thus, to conclude, the alarmingly high rates of MDR organisms causing VAP in ICUs along with the ominous presence of ESBL, AmpC, carbapenamase and metallo-beta lactamase in them, suggest that preventive interventions like Staff education, Hand hygiene training, antimicrobial stewardship program, infection control guidelines and antibiotic policy can reduce the incidence of VAP in ICU patients thereby reducing the mortality associated with it.

INTRODUCTION

Ventilator-associated pneumonia (VAP) as per the CDC is defined as pneumonia in patients on mechanical ventilator support for >48 h, with day of ventilator placement being Day 1 and it was neither present nor in incubation at the time of intubation.[1] It is diagnosed commonly in mechanically ventilated patients with an incidence of 20-36% in India.[2-4] VAP is further divided into early onset VAP (≤ 96 hours of intubation) caused by community acquired pathogens such as Streptococcus pneumoniae and S. aureus and late onset VAP (> 96 hours of intubation) caused by hospital acquired pathogens like P. aeruginosa, methicillin resistant S. aureus (MRSA), Acinetobacter spp. and Enterobacter spp.[2,5] The etiological agents widely differ geographically depending on risk factors like duration of Endotracheal intubation, prior antimicrobial therapy, regular enteral feeding, immunosuppressant therapy, gastric aspiration, airway defects and other co-morbid conditions.[6]

Hospital acquired agents are multi-drug resistant and these bacteria are resistant to diverse classes of antimicrobial agents, including carbapenems, colistin thereby challenging the appropriateness of the empirical antibiotic therapy and making the therapeutic options limited.[7] Inadequate antimicrobial therapy, such as inappropriate antimicrobial coverage, or delayed initiation of

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antimicrobials has been associated with higher hospital mortality in subjects with VAP. The mortality with VAP is considerably high, varying from 24 to 76% according to the population of patients in ICU (Intensive care unit), duration of hospital stay, time of onset, causative organisms and prior antimicrobial therapy.[8] Thus, regular analysis of VAP causative organisms and their antimicrobial susceptibility patterns are essential for initiation of the appropriate antimicrobial treatment, thereby reducing the adverse effects on patients' prognosis and preventing emergence of multidrug resistant (MDR) pathogens.

Diagnosis and treatment of VAP is dependent on detection of the causative organism which is done by collecting the lower respiratory tract sample like protected specimen brush (PSB) and broncho-alveolar lavage (BAL) or endotracheal aspirate (ETA). Recent studies suggested that quantitative ETA cultures give results comparable to invasive procedures, thus making quantitative ETA as a diagnostic tool more effective.[9] Therefore the aim of this study was to analyse the microbiological profile of VAP in our hospital and determining the antimicrobial susceptibility profile of these organisms. This study further extends to determine ESBL, Amp C, Carbapenemase and MBL production in the isolates thereby helping in implementing effective prevention strategies.

MATERIALS AND METHODS

This study was conducted during the period of Jan 2020 to June 2022 in the ICUs of a tertiary care hospital in north India. All mechanically ventilated patients above 18 years of age developing pneumonia after >48 hrs of ventilation were included in our study. Patients aged < 18 yrs, having pneumonia at the time of ICU admission or developing pneumonia in the first 48 hours of mechanical ventilation were excluded. For clinical diagnosis, CDC's criteria were used. Patients should have atleast one of the following: fever ≥100.4˚F, leukopenia (4,000 cells/ cu.mm)/ leukocytosis (≥ 12,000 cells/cu.mm) and adult ≥70 yrs with altered state without any other clear cause. Also they must be presenting with two of the following features: 1. Newly purulent sputum or change in character of sputum 2. Excessive airway secretions 3. Need of suctioning increased 4. Cough, tachypnea, or dyspnea 5. abnormal bronchial sounds 6. requiring more oxygen or ventilator use.[10] Only patients exhibiting bacteriologically documented pneumonia were studied; bacteria were isolated using semi-quantitative culture methods on 5% sheep blood agar and MacConkey agar in significant quantity from samples like ETA >105 cfu/ml, PSB >103 cfu/ml and BAL >104 cfu/ml).[11,12] All the bacteria isolated were identified to the species level by standard biochemical tests and their antibiotic susceptibility testing was performed by the Modified Kirby–Bauer disc diffusion method on Muller–Hinton agar as per the Clinical and Laboratory Standards Institute (CLSI) guidelines.[13] Minimum inhibitory concentration (MIC) values were determined by E-test as per CLSI guidelines. VITEK® 2 automated system (bioMérieux, Craponne, France) was used to confirm the identification of both bacterial as well as MIC of antibiotics were determined. Extended Spectrum Beta Lactamase (ESBL) production was determined by double disc synergy testing (DDST) using antibiotic disc of ceftazidime 30µg and ceftazidime-clavulanic acid 30/10µg, also cefotaxime 30µg and cefotaxime-clavulanic acid 30/10µg.[13] Strains resistant to carbapenems were tested for carbapenemase production by Modified Hodge test. Metallo beta lactamase (MBL) production was determined by using Disc Potentiation test by using Imipenem disc 10µg and Imipenem-EDTA disc.[14] Isolates were screened for AmpC β- lactamases by standard disc diffusion breakpoint for cefoxitin. Isolates with zone diameter less than 18mm for cefoxitin were tested for AmpC activity by Disc potentiation test by using Cefotaxime 30 µg disc and cefotaxime-3 amino phenylboronic acid 30 µg/300 µg disc.[15]

ATCC control strains of Escherichia coli (ATCC 25922), Staphylococcus aureus (ATCC 25923) and Pseudomonas aeruginosa (ATCC 27853) strains were used for quality control.

RESULTS

During this duration, 123 patients developed VAP, 83 (67.4%) were male and 40 (32.6%) were female. Most common age group involved was 50-60 years accounting for 35.8%, followed by 40-50 years (22.7%), and 60-70 years (17.1%). 74 patients (60.2%) were admitted to the Medicine ICU (MICU) and 49 (39.8%) were admitted to the Surgical ICU (SICU). 98 patients (79.7%) were having underlying diseases, like hypertension (54.23%), diabetes mellitus (23.4%), cardiovascular disease (19.8%) and renal diseases (8.9%). Early onset VAP was seen in 17 patients (13.8%) while late onset VAP was seen in 106 patients (86.2%).

Most common organism isolated in Early onset VAP is S. aureus (41.2%) followed by A. baumanii (29.4%) while in late onset VAP, gram negative bacilli were more isolated, A. baumanii being most common (57.5%), followed by Pseudomonas spp and Klebsiella spp as shown in [Table 1].

Overall, Acinetobacter spp. was the most common isolate 66 (53.6%) having 100% resistance to ampicillin, gentamycin, ciprofloxacin, doxycycline and 98% resistance against cefotaxime. Only 15.2% isolates were sensitive to carbapenems group (Imipenem and Meropenem) with MIC value ranging from 0.25 to 1.5 mcg/ml and breakpoint MIC (Vitek 2) <4 mcg/ml.

Pseudomonas spp. showed 100% resistance to gentamicin, ciprofloxacin, ceftazidime and

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piperacillin. 25% were sensitive to piperacillin-tazobactam and 45% to imipenem. The MIC were found to be 12 mcg/ml for piperacillin-tazobactam and .38-1.5 mcg/ml for imipenem. The breakpoint MIC were <16 mcg/ml and <4 mcg/ml respectively. The antibiotic resistance pattern of all the causative isolates is shown in table 2. There is no discrepancies in results from MIC E- test and disc diffusion test.

Out of 116 gram negative isolates, 11 isolates (9.5%) were found resistant to Colistin by broth microdilution method i.e. MIC> 4mcg/ml as per CLSI guidelines 2022. Also out of 7 S. aureus isolates, 57.1% were MRSA (Methicillin Resistant S. aureus) while 2 isolates were found resistant to Linezolid and 1 was found resistant to Vancomycin.

ESBL production was detected in 24.1% of the isolates with Klebsiella spp being the most common producer (57.1%). 62.9% isolates were producing carbapenemase. 84.8% of Acinetobacter spp., 55% in Pseudomonas spp, showed carbapenemase production. 46.5% of the isolates showed MBL production, Acinetobacter spp (65.1%) being most common followed by Pseudomonas spp and Klebsiella spp. 25% of the isolates were AmpC producers. Pseudomonas spp (40%) was the most dominant producer followed by Enterobacter spp (33.3%) and Acinetobacter spp. (22.7%). However 7.8% of the isolates were having both ESBL & AmpC production. The details are there in [Table 3].

Table 1: Organisms isolated from Early onset and Late onset VAP cases

Micro-organisms	Early onset VAP (%)	Late-onset VAP (%)	Total (%)
Acinetobacter baumanii	05 (29.4%)	61 (57.5%)	66 (53.6%)
Pseudomonas aeruginosa	02 (11.7%)	15 (14.1%)	17 (13.8%)
Pseudomonas spp.	01 (5.9%)	02 (1.9%)	03 (2.4%)
Klebsiella pneumoniae	01 (5.9%)	13 (12.3%)	14 (11.4%)
Enterobacter aerogenes	0	06 (5.7%)	06 (4.9%)
Escherichia coli	01(5.9%)	06 (5.7%)	07 (5.7%)
Staphylococcus aureus	07 (41.2%)	0	07 (5.7%)
Serratia marcesens	0	02 (1.9%)	02 (1.6%)
Stenotrophomonas maltophila	0	01 (0.9%)	01 (0.8%)
Total	17 (13.8%)	106 (86.2%)	123

Table 2: Antibiotic resistance pattern of isolated micro-organisms

	Acinetobacter (66)	Pseudomonas (20)	Klebsiella (14)	Enterobacter (6)	E. coli (7)	S. aurues (7)	S. marcescens (2)	S. maltophila (1)
A	66(100%)	-	14(100%)	6(100%)	7(100%)		2(100%)	1(100%)
G	66(100%)	20(100%)	14(100%)	6(100%)	7(100%)	6(85.7%)	2(100%)	1(100%)
AK	64(96.9%)	19(95%)	14(100%)	5(83.3%)	6(85.7%)		2(100%)	1(100%)
CF	66(100%)	20(100%)	14(100%)	6(100%)	7(100%)	7(100%)	2(100%)	1(100%)
DO	66(100%)	-	14(100%)	6(100%)	7(100%)			
CE	65(98.5%)	-	14(100%)	5(83.3%)	6(85.7%)		2(100%)	1(100%)
CA	65(98.5%)	20(100%)	-	-	-			
CI	65(98.5%)	-	14(100%)	5(83.3%)	6(85.7%)		2(100%)	1(100%)
CPM	63 (95.4%)	19(95%)	13(92.8%)	5(83.3%)	5(71.4%)		2(100%)	1(100%)
AT	62 (93.9%)	18 (90%)	13(92.8%)	5(83.3%)	5(71.4%)		2(100%)	1(100%)
PC	-	20(100%)	-	-	-			
PT	60(90.9%)	15(75%)	9(64.3%)	4(66.7%)	4(57.1%)		1(50%)	1(100%)
TCC	61 (92.4%)	15(75%)	9(64.3%)	4(66.7%)	4(57.1%)		1(50%)	1(100%)
IMP	56(84.8%)	11(55%)	3(21.4%)	2(33.3%)	1(14.3%)		0	0
MRP	56(84.8%)	11(55%)	3(21.4%)	2(33.3%)	1(14.3%)		0	0
CL	8 (12.1%)	2 (10%)	1 (7.1%)	0	0		0	0
CN	-	-	-	-	-	4(57.1%)		
T	-	-	-	-	-	7(100%)		
AZM	-	-	-	-	-	7(100%)		
CO	-	-	-	-	-	7(100%)		
VA	-	-	-	-	-	1(14.2%)		
LZ	-	-	-	-	-	2(28.6%)		

Note: A-Ampicillin, G-Gentamycin, AK- Amikacin, CF-Ciprofloxacin, DO-Doxycycline, CE-Cefotaxime, CA-Ceftazidime, CI-Ceftriaxone, CPM-Cefepime, AT-Aztreonam, PC-Piperacillin, PT-Piperacillin-Tazobactam, TCC-Ticarcillin-Clavulanate, IMP-Imipenem, MRP_Meropenem, CL-Colistin, CN-Cefoxitin, T-Tetracycline, AZM-Azithromycin, CO- Cotrimoxazole, VA-Vancomycin, LZ-Linezolid

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Table 3: Determination of ESBL, AmpC, Carbapenemase and MBL producer among isolated micro-organisms

ISOLATES	ESBL Producer (%)	Amp C Producers (%)	Carbapenamase producer by MHT (%)	MBL Producer (%)
Acinetobacter(66)	11 (16.7%)	15 (22.7%)	56 (84.8%)	43 (65.1%)
Pseudomonas(20)	2 (10%)	8 (40%)	11 (55%)	7 (35%)
Klebsiella(14)	8 (57.1%)	2 (14.3%)	3 (21.4%)	2 (14.3%)
Enterobacter(6)	3 (50%)	2 (33.3%)	2 (33.3%)	1 (16.6%)
E.coli(7)	2 (28.6%)	1 (14.3%)	1 (14.3%)	1 (14.3%)
Serratia(2)	1(50%)	1(50%)	0	0
Stenotrophomonas(1)	1(100%)	0	0	0
Total (116)	28(24.1%)	29 (25%)	73(62.9%)	54(46.5%)

DISCUSSION

VAP is considered as the most common health care associated infection in ICU with an incidence ranging from 7 to 36% in intubated mechanically ventilated patients. It is responsible for high morbidity and mortality despite plenty of available antimicrobial therapy, advanced supportive care modalities, and the use of multiple preventive measures.[2,4]

Of the 123 patients diagnosed with VAP as per the CDC's criteria, male female ratio was 2:1. In our ICU set up late onset VAP was seen in 86.2% cases while early onset VAP was seen in 13.8%, proving that the incidence of VAP is directly proportional to the number of days of mechanical ventilation as also shown by Fagon et al.[16] This finding also correlated with other studies.[4,17,18] Early-onset VAP is usually due to the underlying pathology. On the other hand, late-onset VAP could be due to prolonged ventilation, evolution of the underlying disease, quality of nursing care, duration of antibiotic exposure or environmental ecology of the hospital. Studies have shown that empirical antibiotic usage decreases early-onset VAP but markedly increases MDR pathogens.[19] Hence it is very important to have antibiotic policy based on local distribution of pathogens and their resistance pattern.

In our study Acinetobacter species (53.6%), Pseudomonas aeruginosa (12.3%) and Klebsiella pneumoniae (11.4%) were the most common organisms causing VAP, which is similar to study conducted by Arayasukawat et al.,2021 where Acinetobacter species, Klebsiella pneumoniae and Pseudomonas aeruginosa accounted to 52.1%, 15.3% and 8.9% respectively.[4] Gram negative bacilli isolated were found resistant to all 1st line drugs like ampicillin, gentamycin, ciprofloxacin, doxycycline, cefotaxime etc. Resistance for piperacillin-tazobactam were 80-90%, also high level of resistance was observed against Imipenem. However most of the isolates were sensitive to colistin, only 11 isolates were resistant to colistin. These findings were similar to other studies.[20,21] VAP due to MDR organisms is one of the most ominous complication leading to therapeutic failures, prolonged hospital stay, increased cost, morbidity and mortality.

ESBL belonging to groups SHV, TEM, CTX-M have mainly been implicated in the transfer of drug resistance in gram negative organisms of members of Enterobacteriaceae and few other gram negative non fermenting bacilli.[21] In the present study, 24.1% of GNB were identified as ESBL producers, Klebsiella spp being the most common and 25% were AmpC producers. AmpC production is due to plasmid mediated transfer. In the present study 7.8% of gram negative bacteria were seen harbouring both AmpC beta lactamases and ESBL. Dalela G et al. showed ESBL, AmpC β-lactamase and ESBL + AmpC β-lactamase among 66.9%, 21.1% and 3.5% of isolates respectively.[22] The coexistence results in elevated cephalosporin MICs and also false negative detection of ESBLs because AmpC-type beta-lactamases resist inhibition by clavulanate and therefore obscure the synergistic effect of clavulanate and cephalosporins against ESBLs. High detection of AmpC in our study might have obscure ESBL detection in other bacteria[15]

For multi drug resistant organisms and ESBL producers, carbapenems constitute the drug of choice, but alarmingly rising carbapenem resistance in isolates from intensive care units is a serious cause of concern and having very limited treatment options. In our study, 62.9% isolates were producing carbapenemase and 46.5% were MBL producers. The clinical utility of Carbapenems clinical utility is under threat due to acquired carbapenemases, particularly, MBLs which is now spreading worldwide and its early detection is critical. These isolates disseminate rapidly within an institution, leading to poor outcome and hence early detection is of utmost importance.[23]

CONCLUSION

The alarmingly high rates of MDR organisms causing VAP in ICUs along with the ominous presence of ESBL, AmpC, carbapenamase and metallo-beta lactamase in them, suggest that preventive interventions like Staff education, Hand hygiene training, antimicrobial stewardship program and training on proper handling of respiratory secretions of critical ICU patients might reduce the prevalence of VAP in intubated patients.[24] Also intervention of infection control experts, hospital administration and policy planners, introduction of bundle approach, corrective and preventive actions is needed to avoid a situation similar to post antibiotic era where even common infections will no longer have a cure and progress to unabated killings.

REFERENCES

1. National Healthcare Safety Network. Centers for Disease Control and Prevention. Pneumonia (Ventilator-associated

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[VAP] and non-ventilator associated Pneumonia [PNEU]) Event. January 2022: 6: 1-19. https://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.pdf.
2. Papazian L, Klompas M, Luyt CE. Ventilator-associated pneumonia in adults: a narrative review. Intensive Care Med. 2020;46 (5):888–906. doi: 10.1007/s00134-020-05980-0. Epub 2020 Mar 10. PMID: 32157357; PMCID: PMC7095206.
3. Hunter JD. Ventilator associated pneumonia. BMJ (Clin Res Ed). 2012;344:e3325. https://doi.org/10.1136/bmj.e3325
4. Arayasukawat P, So-Ngern A, Reechaipichitkul W, Chumpangern W, Arunsurat I, Ratanawatkul P, Chuennok W. Microorganisms and clinical outcomes of early- and late-onset ventilator-associated pneumonia at Srinagarind Hospital, a tertiary center in Northeastern Thailand. BMC Pulm Med (2021) 21:47. doi: 10.1186/s12890-021-01415-8.PMID: 33516213
5. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Han berger H, et al. Summary of the international clinical guidelines for the management of hospital-acquired and ventilator-acquired pneumonia. ERJ Open Res. 2018. https://doi.org/10.1183/23120541.00028-2018.
6. Villar CC, Pannuti CM, Nery DM, Morillo CMR, Carmona MJC, Romito GA. Effectiveness of Intraoral Chlorhexidine Protocols in the Prevention of Ventilator-Associated Pneumonia: Meta-Analysis and Systematic Review. Respir Care. 2016 Sep; 61(9):1245–59. https://doi.org/10.4187/respcare.04610 PMID: 27507174
7. Farag AM, Tawfick MM, Abozeed MY, Shaban EA, Abo-Shadi MA. Microbiological profile of ventilator-associated pneumonia among intensive care unit patients in tertiary Egyptian hospitals. J Infect Dev Ctries. 2020 Feb 29;14(2):153-161. doi: 10.3855/jidc.12012. PMID: 32146449.
8. Ben Lakhal H, M'Rad A, Naas T, Brahmi N. Antimicrobial Susceptibility among Pathogens Isolated in Early- versus Late-Onset Ventilator-Associated Pneumonia. Infect Dis Rep. 2021 Apr 27;13(2):401-410. doi: 10.3390/idr13020038.PMID: 33925385
9. American Thoracic Society. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am. J. Respir. Crit. Care Med. 2005; 171:388-416. https://doi.org/10.1164/rccm.200405-644ST PubMed: 15699079
10. Aykac K, Ozsurekci, Y and Basaranoglu ST. Future Directions and Molecular Basis of Ventilator Associated Pneumonia. Hindawi Canadian Respiratory Journal Volume 2017, Article ID 2614602, 8 pages https://doi.org/10.1155/2017/261460
11. Kalanuria AA, Zai W, Mirski M. Ventilator-associated pneumonia in the ICU. Critical Care 2014, 18:208. doi: 10.1186/cc13775. PMID: 25029020
12. Wu CL, Yang DIe, Wang NY, Kuo HT, Chen PZ. Quantitative culture of endotracheal aspirates in the diagnosis of ventilator-associated pneumonia in patients with treatment failure. Chest 2002;122:662-8. doi: 10.1378/chest.122.2.662. PMID: 12171848.
13. Clinical and Laboratory standard institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing. 30th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2020.
14. Kali A, Srirangaraj S, Kumar S, Divya HA, Kalyani A, Umadevi S. Detection of metallo-beta-lactamase producing Pseudomonas aeruginosa in intensive care units. The Australasian Medical Journal. 2013;6(12):686- 93. doi: 10.4066/AMJ.2013.1824. PMID: 24391679; PMCID: PMC3877850.
15. Shoorashetty RM, Nagarathnamma T, Prathibha J. Comparison of the boronic acid disk potentiation test and cefepime–clavulanic acid method for the detection of ESBL among AmpC-producing Enterobacteriaceae, Indian Journal of Medical Microbiology, 2011;29(3): 297-301. https://doi.org/10.4103/0255-0857.83917.
16. Fagon JY, Chastre J, Wolff M, Gervais C, Parer-Aubas S, Stéphan F, et al. Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. Ann Intern Med. 2000 Apr 18;132(8):621-30. doi: 10.7326/0003-4819-132-8-200004180-00004. PMID: 10766680.
17. Jakribettu R, Boloor R, Suresh S. Comparison of microbiological profle of pathogens isolated from early-onset and late-onset ventilator associated pneumonia in a tertiary care center. Trop J Med Res. 2016;19(1):14–9. DOI:10.4103/1119-0388.172073
18. Saroj G, Sangeetha KT, Vasudha CL. Microbial profle of early and late onset ventilator associated pneumonia in the intensive care unit of a tertiary care hospital in Bangalore, India. J Clin Diagnost Res. 2013;7(11):2462–6. doi: 10.7860/JCDR/2013/6344.3580. Epub 2013 Nov 10. PMID: 24392373; PMCID: PMC3879896.
19. Rana G, Sharma S, Hans C. Ventilator Associated Pneumonia in the ICU: Microbiological Profile. J Bacteriol Mycol Open Access 2017;4(5): 00109. DOI: 10.15406/jbmoa.2017.04.00109
20. Vamsi CK, Pilli R. Microbiological profile of ventilator-associated pneumonia in the intensive care unit of a tertiary hospital in Visakhapatnam, India. Indian Journal of Microbiology Research, April-June, 2018;5(2):252-257. https://doi.org/10.18231/2394-5478.2018.0053
21. Dey A, Bairy I. Incidence of multi drug resistant organisms causing Ventilator associated pneumonia in a tertiary care hospital: A nine month prospective study. Ann Thorac Med 2007;2:52-57. doi: 10.4103/1817-1737.32230. PMID: 19727346; PMCID: PMC2732076.
22. Dalela G, Gupta S, Jain DK, Mehta P. Antibiotic resistance pattern in uropathogens at a tertiary care hospital at Jhalawar with special reference to ESBL, AmpC β-lactamases and MRSA production. J Clin Diagn Res. 2012;6:645–651.
23. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63(5):e61–111. doi: 10.1093/cid/ciw353. PMID: 27418577; PMCID: PMC4981759.
24. Kharel S, Bist A, Mishra SK. Ventilator-associated pneumonia among ICU patients in WHO Southeast Asian region: A systematic review. PLoS ONE 2021;16(3): e0247832. https://doi.org/10.1371/journal.pone.0247832