

Original Article**A Comparative Cross-Sectional Study to compare the Isolated Organism and their Antibiotic Sensitivity Pattern Between Community-Acquired Pneumonia (CAP) and Ventilator-Associated Pneumonia (VAP) in Intensive Care Unit (ICU).**

*Nahian Ahmed Chowdhury¹, Dipak Kumar Mitra², Afrin Ahmed Clara³, Md. Suhail Alam⁴, MD. Zahed Hossain⁵.

Abstract

Background: The most common cause of in-hospital infection is pneumonia. Pneumonia is prevalent within the ICU (Intensive Care Unit) setting and can be deadly. The incidence of pneumonia is approximately 17% in the therapeutic ICU² but can be 6 to 20 times increased in mechanically ventilated patients. The duration of hospital stay and expenditure are both expanded in patients who develop ventilator-associated pneumonia. This study aims to identify the causative microorganism responsible for CAP (Community-Acquired Pneumonia) and VAP (Ventilator-Associated Pneumonia) and their antibiotic sensitivity pattern.

Methods: This was a comparative cross-sectional study that was carried out at two ICUs in Sylhet city. The data was collected from the patient's medical information, the patient's file, and the hospital information system. Culture and sensitivity (C/S) were collected from the electronic medical information system (MIS). All data from January 2019 to December 2020, including patient's information, course of the disease (in terms of death or recovery-if available), clinical features, and investigation reports, was transferred to an electronic data collection sheet (Microsoft Excel). After completion of all data collection, analysis was conducted through a spreadsheet. Comparison between two disease groups was made by independent t-test. Within the group, the analysis was done by the Chi-Square test.

Results: In this thesis study, it was found that the most common organism responsible for CAP was *Streptococcus* spp. (34.70%) and is sensitive to Meropenem (92.21%), Imipenem (88.16%), Amikacin (70.67%), Piperacillin (70.91%), Moxifloxacin (70.96%), Levofloxacin (67.95%), Amoxiclav (67.92%), and Ceftriaxone (63.95%).

The most common causative organism responsible for VAP was *Staphylococcus* spp. (36.51%) and it was sensitive to Imipenem (100%), Moxifloxacin (100%), Meropenem (94.73%), Amikacin (85.71%), Ceftriaxone (60%), Amoxiclav (66.66%), Levofloxacin (57.14%), and Cefuroxime (50%).

Conclusion: Pneumonia is still one of the most common reasons for hospitalization, particularly for those admitted to ICU. It has been observed in several studies that the majority of the cases are community-acquired pneumonia. Many mechanically ventilated patients often develop VAP, which is fatal if timely diagnosis and appropriate antibiotics administration are not made. *Streptococcus* spp. was the most common organism responsible for CAP, and *Staphylococcus* spp. mainly was responsible for VAP.

Keywords: CAP, VAP, ICU

DOI: <https://doi.org/10.47648/jswmc2021v1102-03>

JSWMC 2021[11(02)] P: 26-34

Introduction

Pneumonia is an inflammation of the alveolar airspace, which is most commonly provoked by bacteria and arises from other pathogen classes and less typically by the autoimmune system.

4. Consultant-Cardiology and Critical Care Dept., Al Haramain Hospital Pvt. Ltd.,
5. Consultant and Head- Critical Care Dept., Mount Adora Hospital, Sylhet.

Corresponding author: Nahian Ahmed Chowdhury
Additional Director (Medical Services), Al Haramain Hospital Pvt. Ltd
E-mail: <nahi_chy@yahoo.com>;
nahian.ahmed01@northsouth.edu

Lung function is impaired due to infiltration of the alveolar space by white blood cells (leucocytes) and fibrinous exudate. Sometimes

1. Additional Director (Medical Services), Al Haramain Hospital Pvt. Ltd.
2. Professor & Chair, Department of Public Health, North South University.
3. Senior Lecturer, Department of Public Health, North South University.

admission to an ICU Intensive Care Unit) is required due to severe form.¹

The most common cause of in-hospital infection is pneumonia. Pneumonia is prevalent within the ICU (Intensive Care Unit) setting and can be deadly. The incidence of pneumonia is approximately 17% in the therapeutic ICU² but can be 6 to 20 times increased in mechanically ventilated patients³. The duration of hospital stay and expenditure are both expanded in patients who develop ventilator-associated pneumonia⁴.

Pneumonia is usually categorized into HAP (hospital-acquired pneumonia), CAP (community-acquired pneumonia), HCAP (healthcare-associated pneumonia), and VAP (ventilator-associated pneumonia). The usual foremost pneumonia was CAP (54.3%) and VAP the least (1.6%). Despite its reduced incidence, VAP created the most elevated death rate during hospitalization (21.6%)⁵.

In ICUs, the etiology of pneumonia remains obscure in about 30% of cases in spite of comprehensive microbiological investigations.⁶ Microorganisms habitually distinguished in respiratory samples from ICU-pneumonia patients included Staphylococci, Klebsiella, Enterobacteria, Pseudomonas aeruginosa, Candida albicans, Cytomegalovirus (CMV), Influenza virus, and Herpes simplex virus (HSV)^{8,9,10,11,12}.

Anti-microbials play a major imperative part in the treatment of bacterial pneumonia. The outcome may improve by initiating early administration of antibiotics. The choice of introducing antibiotics is guided by clinical settings, intensity appraisal, community information of anti-microbial resistance patterns, and epidemiological data. A 5-day course is sufficient for most patients with uncomplicated pneumonia, regardless of the fact that treatment is often necessary for patients with Legionella, staphylococcal, or K. pneumoniae who have been sick for a long time. Unless the patient has a severe disease, diminished consciousness, loss of deglutition reflex, or functional or anatomical grounds for malabsorption, oral anti-microbials are usually appropriate.

Methodology

This cross-sectional study comparing the isolated organism and their antibiotic sensitivity pattern

between CAP and VAP in ICU was conducted at two ICU (Al Haramain Hospital and Mount Adora Hospital) of Sylhet City from January 2021 to May 2021. The aim of the study was to determine the isolated organisms responsible for CAP and VAP with their antibiotic sensitivity pattern.

According to standard guidelines, patients diagnosed with CAP and VAP by the treating physician were included in the study. The appearance of acute pulmonary infiltration on a posteroanterior chest x-ray, as well as at least two of the following symptoms: fever, cough, and purulent sputum, was the diagnostic criteria for CAP. Diagnosis of VAP was based on three elements: new or worsening infiltrates seen on the chest radiograph, systemic signs of infection, and bacteriological prove of pneumonic parenchymal infection.¹⁹

Isolation and identification of causative bacteria was carried out by using specific culture media for both gram positive and gram-negative organism. There in this microbiological procedure, culture media were used (e.g., Blood Agar media, MacConkey's agar media). The culture positive samples were identified by colony morphology, microscopy and conventional biochemical test as per the standard protocol followed in microbiology laboratory. For antibiotic sensitivity test we followed CLSI guideline. Antibiotic sensitivity test was carried out by using the Kirby-Bauer disc diffusion method.

After enrollment in the study, informed consent from the hospital authority was taken. The data was collected the patient's medical information, the patient's file, and the hospital information system. Culture and sensitivity (C/S) were collected from the electronic medical information system (MIS). All data from January 2019 to December 2020, including patient's information, course of the disease (in terms of death or recovery-if available), clinical features, and investigation reports, was transferred to an electronic data collection sheet (Microsoft Excel). After completion of all data collection, analysis was conducted through a spreadsheet. Comparison between two disease groups was made by independent t-test. Within

the group, the analysis was done by the Chi-Square test.

Results

This is an analytical cross-sectional study of 'Comparative cross-sectional study to compare the isolated organism and their antibiotic

sensitivity pattern between CAP and VAP in ICU'. All the patients diagnosed as CAP and VAP in two assigned hospital was included in this study. The total number of cases was 394. Among 394 patients 268 were diagnosed as CAP and 126 as VAP.

Table 1: Demographic distribution of patients according to Age and Gender

Gender	CAP N=268		VAP N=126	
	No.	%	No.	%
Male	178	66.42%	46	37.5%
Female	90	33.58%	80	62.5%
Total	268		126	
Age Group	CAP N= 268		VAP N= 126	
	N	%	N	%
Below 30 years	17	6.34%	22	17.46%
30 – 49 years	32	11.94%	28	22.22%
50 - 69 years	118	44.03%	49	38.89%
70 years and above	101	37.69%	27	21.43%
Mean	61.7		51.61	t-value 4.168 p=.00002

Table (1) shows the distribution of patients according to age and gender. It illustrates that in the CAP group, most patients were male (66.42%), and in the VAP group, females were significantly dominant (62.5%). The table also shows the distribution of CAP and VAP patients according to their age group. Among CAP patients' highest number (44.03%) was in the 50-69 years age group. The second highest was 70 years and above age group (37.69%). Patients of 30-49 years and below 30 years age group

were 11.94% and 6.34%, respectively. The mean age of the CAP group was 61.7.

In the VAP group, patients' highest number (38.89%) was in the 50-69 years age group. Seventy (70) years and above age group (21.43%) and 30 -49 years (22.22%) age group were almost similar in number. There were We had 22 patients (17.46%) who were below the 30 years of age group, which is quite significant. The mean age for VAP patients was 51.61.

T-test was conducted, and the t-value was 4.168, while the p-value was <0.005.

Table 2: Distribution of patients according to pre-existing disease factors

Disease	CAP N= 268		VAP N= 126	
	Y	N	Y	N
HTN	162	106	70	56
	60.45%		55.55%	
DM	126	140	56	70
	47.01%		44.44%	
PREVIOUS H/O LUNG DISEASE	47	221	25	101
	17.54%		19.84%	
HTN+DM	57	211	24	102
	21.27%		19.04%	
HTN+ P/H/O LUNG DISEASE	15	253	8	118
	5.59%		6.35%	
DM+ P/H/O LUNG DISEASE	9	259	5	121
	3.36%		3.97%	
HTN+ DM+ PREVIOUS H/O LUNG DISEASE	16	252	12	114
	5.97%		9.52%	

Table (2) illustrates the co-existing disease factors among patients of both CAP and VAP groups. It shows that the prevalence of hypertension was significantly higher in the two groups, 60.45%, and 55.55%, respectively. Diabetes mellitus was the second common comorbid disease among both groups, 47.01% in CAP and 44.44% in the VAP group. The history of preexisting lung disease among the CAP and

VAP groups was 17.54% and 19.84%, which indicates a slightly higher percentage among VAP patients. A significant number (21.27% among CAP and 19.04% among VAP) of patients in both groups had multiple preexisting diseases like Hypertension and Diabetes mellitus. A small number of patients (5.97% in the CAP group and 9.52% in the VAP group) had a history of all three-preexisting diseases.

Table 3: Distribution of isolated microorganisms among CAP and VAP patients

Name of the organism	CAP N= 268		VAP N= 126	
	No Patient	of %	No Patient	of %
Acinetobacter	1	0.37%	2	1.59%
E-Coli	11	4.10%	2	1.59%
H. Influenza	46	17.17%	0	0%
Klebsiella	61	22.76%	32	25.39%
Pseudomonas spp.	25	9.33%	8	6.35%
Staphylococcus spp.	31	11.57%	46	36.51%
Streptococcus spp.	93	34.70%	36	28.57%
Chi-square test done				
Chi-square test done				

Table (3) has tabulated the list of isolated organisms responsible for CAP and VAP cases. Streptococcus spp. was responsible for more than one-third of the CAP (34.70%). Klebsiella was found in 22.76% of patients, and H. Influenza was responsible for 17.17% of cases. Staphylococcus spp., Pseudomonas spp., and E-Coli was responsible for 11.57%, 9.33%,

and 4.10% of cases, respectively, among CAP patients.

Among VAP patients, Staphylococcus spp. was responsible for 36.51% of cases. Streptococcus spp. (28.57%), and Klebsiella (25.39%) were responsible for a significant number of VAP cases. The other three organisms which were present were Pseudomonas spp. (6.35%), E-Coli (1.59%) and Acinetobacter (1.59%).

Table 4: Distribution of antibiotic susceptibility according to microorganism- CAP

Antibiotic Organism	Meropenem	Imipenem	Amikacin	Ceftriaxone	Piperacillin	Levofloxacin	Moxifloxacin	Azithromycin	Amoxiclav	Cefuroxime
Acinetobacter	100%	—	—	—	—	100%	100%	—	—	—
E-Coli	45.45%	60.00%	66.66%	28.57%	25%	81.82%	85.71%	18.18%	18.18%	11.11%
H. Influenza	96.88%	90.24%	74.36%	62.16%	80.76%	70%	70.83%	23.68%	56.25%	41.46%
Klebsiella	89.65%	88.23%	89.80%	41.37%	64.29%	46.43%	55.55%	35.08%	61.70%	13.72%
Pseudomonas spp.	100%	100%	100%	33.33%	95%	95%	100%	80%	12.50%	5.88%
Staphylococcus spp.	92.85%	94.74%	79.17%	59.25%	63.16%	48.15%	25%	22.58%	43.48%	26.31%
Streptococcus spp.	92.21%	88.16%	70.67%	63.95%	70.91%	67.95%	70.96%	38.15%	67.92%	48.39%

Table (4) illustrates the distribution of antibiotic susceptibility of CAP patients according to isolated microorganisms. Here, Acinetobacter was 100% sensitive to Meropenem, Imipenem, and levofloxacin. E-Coli was 85.71% sensitive to Moxifloxacin, 81.82% to levofloxacin, 66.66% to Amikacin, and 60% to Imipenem. H. Influenza shows sensitivity to Meropenem and Imipenem in more than 90% of cases and 80.76% to Piperacillin and around 70% to Levofloxacin Moxifloxacin. Klebsiella was

sensitive to Meropenem, Imipenem, and Amikacin in around 90% of cases. Pseudomonas sp. shows 100% sensitivity to Meropenem, Imipenem, Amikacin, and Moxifloxacin, while 95% to Piperacillin and Levofloxacin. Staphylococcus spp. was sensitive to Imipenem in 94.74% cases, Meropenem in 92.85% cases, and Amikacin in 79.17% cases. Streptococcus spp. was 92.21% sensitive to Meropenem, 88.16% to Imipenem, and around 70.67% to Amikacin, Piperacillin, Levofloxacin.

Table 5: Distribution of antibiotic susceptibility according to microorganism- VAP

Antibiotic Organism	Mero pene m	Imipe nem	Amika cin	Ceftri axone	Piperaci llin	Levofl oxacin	Moxifl oxacin	Azithro mycin	Amo xicla v	Cefu roxi me
Acinetobacter	100% Resistant to all selected antibiotics									
E-Coli	100%	—	100%	—	—	100%	—	—	100%	—
Klebsiella	54.55 %	54.55 %	28.57 %	26.66 %	30%	40%	—	14.28%	15.38 %	8.33 %
Pseudomonas spp.	100%	100%	—	33.33 %	—	66.66 %	—	33.33%	—	33.33 %
Staphylococcus spp.	94.73 %	100%	85.71 %	60%	37.50%	57.14 %	100%	30.43%	66.66 %	50%
Streptococcus spp.	92.85 %	100%	66.66 %	88.23	70%	75.66 %	75%	22.22%	90%	58.33 %

Table (5) illustrates the distribution of antibiotic susceptibility of CAP patients according to isolated microorganisms. Here, Acinetobacter was 100% resistant to all selected antibiotics. E-Coli was 100% sensitive to Meropenem, Amikacin, levofloxacin, and Amoxiclav. Around 55% of Klebsiella cases were sensitive to Meropenem and Imipenem, 40% to levofloxacin. Pseudomonas spp. Shows 100% sensitivity to Meropenem, Imipenem, and 66.66% to levofloxacin. Staphylococcus spp. was sensitive to Imipenem and Moxifloxacin in 100% cases, Meropenem in 94.73% cases, and Amikacin in 85.71% cases. Streptococcus spp. was 100% susceptible to Imipenem, around 90% to Meropenem, Ceftriaxone, and Amoxiclav

while approximately 75% to Levofloxacin and Moxifloxacin.

Discussion

We have performed our study on “A comparative cross-sectional study to compare the isolated organism and their antibiotic sensitivity pattern between Community-Acquired Pneumonia (CAP) and Ventilator-Associated Pneumonia (VAP) in Intensive Care Unit (ICU).” It was a comparative cross-sectional analytic study. Retrospective data of 394 patients were included in this study from hospital medical records. The primary objective of this research was to identify the isolated microorganisms responsible for CAP and VAP in the intensive care unit (ICU). All patients were diagnosed based on their clinical features,

radiological findings, and sputum culture sensitivity (CAP) or tracheal aspirate culture sensitivity (VAP). Age, sex, pre-existing disease factor, isolated organisms, and antibiotic sensitivity pattern were documented as a variable in the data collection sheet. We have tabulated the result after collecting data and compared it with that of other relevant studies.

The study of Haque M. included 378 patients with CAP. CAP was diagnosed with intense pneumonic infiltration in chest radiograph with leastways two of the taking after indications: fever, cough, and purulent sputum. The study noted 36% of CAP was in the winter season. It also demonstrates that the prevalence of CAP was high within the elderly populace, particularly among males, and most of the patients had comorbidity. The utmost common organism of CAP was the ACB(Acinetobacter) complex; gram-negative bacteria were perceptible to ciprofloxacin, aminoglycosides, and polymyxins.¹³ In our study, it was found that the prevalence of CAP is higher among male patients (66.42%) and in the case of VAP number of affected female patients was significantly higher (62.5%). Both CAP and VAP are higher among the 50-69 years age group (CAP: 44.03%, VAP:33.89%).

According to the study of Mousa Elshamly et al., which includes 54 patients with severe CAP, demonstrate that the utmost isolated organism was *S. pneumoniae* for CAP patients, and a significantly higher mortality rate was detected among the patients with comorbidities. In that study, 51.85% of patients admitted with SCAP had comorbidities, hypertension and diabetes mellitus (13%) were the foremost usual comorbidities. Fever, cough, and dyspnea were the most usual symptoms. Lobar consolidation (63%) was the commonest chest radiograph finding in patients with SCAP, followed by pleural effusion (37%)¹⁴. We found in our study that the most common organism responsible for CAP was *Streptococcus* spp. (34.70%) and is sensitive to Meropenem (92.21%), Imipenem (88.16%), Amikacin (70.67%), Piperacillin (70.91%), Moxifloxacin (70.96%), Levofloxacin (67.95%), Amoxiclav (67.92%), and Ceftriaxone (63.95%).

Andrew P Walden et al. conducted a GenOsept cohort study, which incorporates 1166 patients conceded to 102 centers over 17 nations in Europe with CAP, founds that most of the patients (62%) had one or more comorbidities especially cardiac and respiratory diseases. Most of the patients (62%) had one or more comorbidities especially cardiac and respiratory diseases, 76% of patients required mechanical ventilation support on the day of affirmation, with the number expanding to 84% during the primary week of entry. The most frequent chest x-ray finding was lobar consolidation, which was seen in 43.7% of cases. The most commonly detected organism (29%) was *Streptococcus pneumoniae*, and no isolated organism was detected in over a third of patients¹⁵. In this research, it was found that HTN was the most significant pre-existing disease among both CAP (60.45%) and VAP (55.55%) group patients, the second most common comorbid disease was Diabetes Mellitus (47.01% of CAP patients and 44.44% of VAP patients). Patients who were suffering from a pre-existing lung disease like COPD, Bronchial Asthma, ILD, etc. was about 17% among CAP patients and approximately around 20% among VAP patients. Patients with multiple comorbid diseases like HTN and Dm were 5.59% among CAP patients and 6.35% among VAP patients.

Kalanuria AA et al. conducted their study on VAP, including 51 isolated patients in the ICU. The study reveals that 48 patients develop VAP, in which male patients were dominant (66.7%). The study also reveals early-onset VAP affects 19 % of patients, while late-onset VAP affects 81%, and the most common isolate was *Acinetobacter sepsis* (66%), which had 100% resistance to Amikacin, cefotaxime, ampicillin, ciprofloxacin, and cefepime. Just 8.8% of the patients were sensitive to Imipenem. *Pseudomonas* spp. was the most common familiar causative agent with 100% resistance to ceftazidime, gentamicin, and piperacillin¹⁶. Our study found that the most common causative organism responsible for VAP was *Staphylococcus* spp. (36.51%) and it was sensitive to Imipenem (100%), Moxifloxacin (100%), Meropenem (94.73%), Amikacin

(85.71%), Ceftriaxone (60%), Amoxiclav (66.66%), Levofloxacin (57.14%), and Cefuroxime (50%).

The study of Selina F et al. incorporates 79 patients diagnosed with VAP. The study reveals older people are more prone to develop VAP; 71.5% of the sample population were above 61 years of age. In 68.3% of cases, a single organism was isolated, and *Pseudomonas* (35%) was the most common organism responsible for VAP. In this study death rate of VAP was 26.5%¹⁸. In our research, it was found that the mean age for VAP group patients was around 52 years, and the most common microorganism responsible for VAP was *Staphylococcus* spp.

Conclusion

Pneumonia is still one of the most common reasons for hospitalization, particularly for those admitted to ICU. It has been observed in several studies that the majority of the cases are community-acquired pneumonia. Many mechanically ventilated patients often develop VAP, which is fatal if timely diagnosis and appropriate antibiotics administration are not made. *Streptococcus* spp. was the most common organism responsible for CAP, and *Staphylococcus* spp. mainly was responsible for VAP. This study compared with those of international studies similarities found in causative microorganisms and their antibiotic sensitivity pattern.

Conflict of interest: No conflict of interest was declared by any co-author.

Acknowledgement: We would like to express our deep appreciation and indebtedness particularly to the following: Dr. Khandaker Abu Talha (Associate Professor and Head of the department of Neurosurgery, Sylhet Women's Medical College.), Dr. Farhana Selina (Associate Professor of the department of Anesthesiology, Sylhet Women's Medical College), Dr Shantanu Das (Assistant Professor, Department of Microbiology, Sylhet MAG Osmani Medical College) for their endless support, kind and understanding spirit during the entire journey.

References

1. Storms AD, Chen J, Jackson LA, et al. Rates and risk factors associated with hospitalization for pneumonia with ICU admission among adults. *BMC Pulm Med* 2017; 17:208.
2. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in medical intensive care units in the United States: National Nosocomial Infections Surveillance System. *Crit Care Med* 1999; 27:887-892.
3. Torres A, Aznar R, Gately JM, et al. Incidence, risk, and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. *Am Rev Respir Dis* 1990; 142:523-528.
4. Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Trials Group *Am J Respir Crit Care Med*. 1999; 159:1249-56.
5. Corrado RE, Lee D, Lucero DE, Varma JK, Vora NM. Burden of adult community-acquired, health-care-associated, hospital-acquired, and ventilator-associated pneumonia: New York City, 2010-2014. *Chest*. 2017; 152(5):930-942.
6. Esperatti M, Ferrer M, Theessen A, Liapikou A, Valencia M, et al. Nosocomial Pneumonia in the Intensive Care Unit Acquired during Mechanical Ventilation or Not. *Am J Respir Crit Care Med*. 2010;182(12):1533-9. doi: 10.1164/rccm.201001-0094OC.
7. Potgieter PD, Hammond JM, Etiology and diagnosis of pneumonia requiring ICU admission. *Chest* 1992;101(1):199-203. doi: 10.1378/chest.101.1.199.
8. American Thoracic Society; Infectious Diseases Society of America. Guidelines for

- the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med.* 2005;171(4):388-416. doi: 10.1164/rccm.200405-644ST. PMID: 15699079.
9. Chiche L, Forel JM, Roch A et al. Active cytomegalovirus infection is common in mechanically ventilated medical intensive care unit patients. *Crit Care Med.* 2009;37(6):1850-7. doi:10.1097/CCM.0b013e31819ffea6. PMID: 19384219.
 10. Papazian L, Fraisse A, Garbe L, et al. An unexpected cause of ventilator-associated pneumonia. *Anesthesiology.* 1996;84(2):280-7. doi: 10.1097/00000542-199602000-00005. PMID: 8602657.
 11. Luyt CE, Combes A, Nieszkowska A, Trouillet JL, Chastre J. Viral infections in the ICU. *Curr Opin Crit Care.* 2008;14(5):605-8. doi: 10.1097/MCC.0b013e32830f1e12. PMID: 18787457.
 12. Bouza E, Giannella M, Torres MV, Catalán P, Sánchez-Carrillo C, Hernandez RI, Muñoz P; Gregorio Marañón Task Force for Pneumonia. Herpes simplex virus: a marker of severity in bacterial ventilator-associated pneumonia. *J Crit Care.* 2011;26(4): 432.e1-6. doi: 10.1016/j.jcrc.2010.10.008.
 13. Haque MA. Seasonal Incidence of Community-acquired Pneumonia: A Retrospective Study in a Tertiary Care Hospital in Kathmandu, Nepal. *Cureus.* 2019;11(12):e6417. doi: 10.7759/cureus.6417. PMID: 31988818; PMCID: PMC6970104.
 14. Mousa Elshamly, Mohamed O. Nour, Abdelmaaboud M.M. Omar. Clinical presentations and outcome of severe community-acquired pneumonia. *Egyptian Journal of Chest Diseases and Tuberculosis.* 2016;64(4): 831839. doi.org/10.1016/j.ejcdt.2016.06.002
 15. Walden, A.P., Clarke, G.M., McKechnie, S., et al. Patients with community-acquired pneumonia admitted to European intensive care units: an epidemiological survey of the GenOSept cohort. *Crit Care* 18, R58 (2014). <https://doi.org/10.1186/cc13812>
 16. Kalanuria AA, Ziai W, Mirski M. Ventilator-associated pneumonia in the ICU. *Crit Care.* 2014 Mar 18;18(2):208. doi: 10.1186/cc13775. Erratum in: *Crit Care.* 2016; 20:29. Zai, Wendy [corrected to Ziai, Wendy]. PMID: 25029020; PMCID: PMC4056625.
 17. Mishra DR, Shah N, Shah DS. Incidence and Outcome of Ventilator Associated Pneumonia in ICU of a Tertiary Care Hospital in Nepal. *JNMA J Nepal Med Assoc.* 2017;56(207):304-8. PMID: 29255310.
 18. Selina, F., Talha, K. A., Islam, A., Hasan, Z., Hyder, M., & Selvapandian, S. Organisms associated with ventilator associated pneumonia (VAP) in intensive care units (ICU). *Journal of the Bangladesh Society of Anaesthesiologists,* 2009;22(2),72–77.
 19. Andrews CP, Coalson JJ, Smith JD, Johanson WG. Diagnosis of nosocomial bacterial pneumonia in acute, diffuse lung injury. *Chest* 1981; 80: 254-258
 20. Elliott D, Elliott R, Burrell A, et al Incidence of ventilator-associated pneumonia in Australasian intensive care units: use of a consensus-developed clinical surveillance checklist in a multisite prospective audit *BMJ Open* 2015;5: e008924. DOI: 10.1136/BMJ open-2015-008924
 21. John G Bartlett, Scott F Dowell, Lionel A Mandell, Thomas M File, Jr., Daniel M Musher, Michael J Fine, Practice Guidelines for the Management of Community-Acquired Pneumonia in Adults, *Clinical Infectious Diseases,* 2000, 31;347–382, doi.org/10.1086/313954