Research Paper

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Nosocomial Pneumonia in Critically Ill Patients in India-A Clinical Study

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ABSTRACT

Background and aim: Nosocomial pneumonia (NP) and ventilator-associated pneumonia (VAP) remains the commonest cause of morbidity and mortality in spite of latest diagnostic and management modalities. This project aims to study the bacterial pattern and their associated risk indicators in patients admitted to different intensive care units (ICUs) Study design: This Prospective study was done at KLEs, Jawaharlal Nehru Institute of Medical sciences and Research centre, a tertiary care centre with a total bed capacity of 1600 in Belgaum, Karnataka, India. Study included critically ill patients admitted at different ICUs, {MICU (medical ICU) with 45 beds, CICU (Coronary ICU) 25 beds} who developed NP and VAP. Materials and Methods: Total of 100 patients were studied for 10 months between 20-80 yrs. Signs and symptoms, bacterial pattern and risk indicators were noted. Statistical analysis used: Observational study. Results: Among total 100 patients (in different ICUs set ups), 60 patients developed NP but were not mechanically ventilated whereas 40 patients developed VAP after MV for 4-8 days. Majority of the patients were males. Pneumonia developed in patients with diabetes mellitus 21(21%) then least among Ischemic heart diseases (IHDs) and bronchial asthma patients 5(5%). The predominantly organisms among NP were Klebsiella pneumonia 7(70%), Streptococcus pneumoniae and Pseudomonas aeruginosa, whereas in VAP were Pseudomonas aeruginosa 6 (37.5%) and Streptococcus pneumoniae. The prognosis with late onset NP was better than VAP. Conclusion: Knowledge about risk indicators may be useful in implementing simple and effective preventive measures in order to minimize the occurrence of Nosocomial infections.

INTRODUCTION

Infections acquired during hospital stay are generally called nosocomial infections.[1] NP is the second most frequent hospital acquired infection and the most frequently acquired infection in the ICUs (Intensive Care Units). [2] The incidence of NP in the intensive care unit ranges from 9–24%. [3] NP develops in 0.5 to 1 patient per 100 hospital admissions and is associated with high morbidity and mortality. [4, 5] Mechanically ventilated patients have a high risk for developing NP; indeed, VAP has a cumulative incidence ranging from 18% to 60%, and it was found in more than 70% of patients who died of acute lung injury. [6, 7, 8, .9]

National health care safety network (NHSN) [2] USA system defines a nosocomial infection as a localized or systemic condition that results from adverse reaction to the presence of an infectious agent(s) or its toxin(s) that was not present or incubating at the time of admission to the hospital. As incubation period varies with the type of pathogen and patient's underlying condition, each infection must be assessed individually. [1, 10]

The American Thoracic Society (ATS) statement [6] suggests the categorization of NP as early-onset NP which occurs within 4 days after hospital admission and late-onset NP which occurs after 5 days of hospital admission. Most cases of NP in the ICU occur in patients who are tracheally intubated and are receiving MV. VAP which occurs after MV categorized as early-onset VAP which occurs within 48hrs, where as late-onset VAP occurs after 4 days of endotracheal intubation and initiation of mechanical ventilation (MV). [12]

Microbiological surveillance for bacterial growth of the high risk areas is in our hospital done monthly. Whenever a surveillance culture shows growth the area is washed down, the operating room is cleaned thoroughly, and a repeat surveillance is done. The operating room is made operational only after the next swab culture is shown to be sterile.

To date, very few information is available regarding these hospital acquired infections in India. We performed a prospective study to determine the clinical presentation of NP and VAP, to study the bacterial pattern and the risk indicators (patients who have high risk to develop these infections) in critically ill patients admitted in different ICUs of the Jawaharlal Nehru Medical College and Research centre, a tertiary care hospital in Belgaum, India.

METHODS AND MATERIAL

Nearly 100 ICU beds {which included SICU (surgical ICU) with 30 beds, MICU (medical ICU) with 45 beds, CICU (Coronary ICU) 25 beds} where all critically ill patients would be treated. Every year nearly 36,000 patients are admitted into these ICUs. The patients who were referred from different fraternity to the department of Respiratory medicine, where they were asked to take care of the lung infection. The study was approved by the JNMC Ethical Committee (KLE University Ethical Committee) and Informed consent was obtained from the nearest relatives of every patient. The 100 critically ill patients (both NP and VAP) were studied for the duration of 10 months. All the patients developed pneumonia after they are admitted to ICUs. Inclusion of those patients' done following, according to American thoracic society (ATS) guidelines. Exclusion of those cases with other causes of radiological infiltrates like pulmonary haemorrhage, pulmonary embolism, atelectasis, congestive cardiac failure and acute respiratory distress syndrome were done.

The patients were diagnosed for NP clinically, based on radiological findings and bacteriological investigations by isolation of causative microorganism. Patients with the presence of conditions like diabetes mellitus, chronic obstructive lung disease, and chronic renal failure etc were also included in this study.

Following investigations were performed, which included Complete hemogram, sputum examination for Gram stain, Acid Fast Bacillus, culture and sensitivity, blood culture, fasting blood sugar (FBS), Post pranadial blood sugar (PPBS), Human Immunodeficiency Virus, blood urea, serum creatinine, serum electrolytes and Echo cardio Gram, Chest x-ray, endotracheal aspirate for Culture and sensitivity in deserving candidates, Bronchoscopy with Bronchial alveolar lavage (BAL) & endobronchial brush, Arterial blood gas analysis was done in deserving candidates. Diagnostic bronchoscopy was not used routinely in the present study as it was not considered safe in critically ill patients. Bronchoscopy was done in those patients whose sputum and endotracheal aspirate reports were inconclusive.

Development of NP depends on following factors like age, sex, habits-smoking, alcoholism, clinical signs and symptoms, comorbid illness, organism isolated, use of medical devices like Ryles tube, intubation, ventilator, duration of hospital stay etc. All data were entered into a standard proforma and analyzed.

RESULTS

A total of 100 Patients in which 60 Males and 40 Females were present, with the age ranging between 20-80 years (mean age ±50yrs). Among these 100 patients 60 patients had developed

NP and 40 developed VAP on MV. All patients developed pneumonia at ICUs.

The American Thoracic Society (ATS) statement6 suggests the categorization of NP as early-onset which occurs within 4 days after hospital admission and late-onset which occurs after 5 days of hospital admission. VAP which occurs after mechanical ventilation12. VAP categorized as early-onset which occurs within 48hrs, where as late-onset occurs after 4 days of endotracheal intubation and initiation of mechanical ventilation (MV).

Table 1 shows among total of 60 NP patients 22 (36.66%) patients were in early onset stage and 38 (63.33%) were in late stages of NP. Whereas among total of 40 VAP cases 15 (37.5%) were in early onset stage and rest 25 (62.5%) were in late onset stage. Table 2 shows that older patients above 60 yrs developed more pneumonia (27%) than others.

Those above 61yrs of age were 30% and those below 61 yrs were 70%. Table 2 describes that maximum number of patients with diabetes mellitus developed, Pneumonia 21 (21%) with least number being in patients with ischemic heart disease and Bronchial asthma 5 (5%). Table 3 shows Majority of organisms isolated in early onset NP were K. pneumonia 7(70%) with least being S. pneumoniae and P. aeruginosa. Whereas in late onset NP majority of organisms isolated were K. pneumonia 6 (30%) with least being S. pneumoniae 3 (15%). In early onset VAP majority of organisms isolated were S. aureus 3 (50%) with least being others, whereas in late onset VAP Majority of organisms isolated were P. aeruginosa 6 (37.5%) with least S. pneumoniae were found. Table 4 shows that major risk indicator found was Diabetes mellitus 13 (21.66%) in NP and 9 (22.5%) in VAP with least risk being use of steroids 1 (1.66%) in NP with least being altered sensorium in VAP. Table 5 describes the prognosis of both the group of patients. The prognosis with late onset NP 32 (84.21%) was better than VAP 15 (60%).

Table 1 Pneumonia Categorization (n=100)

Nosocomial pneumonia (Non-ventilated Patients)	
Total No.Of patients	
Early onset	22 (36.6%)
Late onset	38 (63.3%)
Total	60
Ventilator Associated Pneumonia (VAP)	
Early onset	15 (37.5%)
Late onset	25 (62.5%)
Total	40

Table 2 List of patients who Developed Pneumonia

Primary Diagnosis	Number of patients (%)
Stroke	12 (12%)
Gullain Barre Syndrome	4 (4%)
Organophosphorous poisoning	8 (8%)
Chronic Renal Failure	7 (7%)
Burns	8 (8%)
COPD	8 (8%)
Ischemic heart disease	10 (10%)
IHD	8 (8%)
Diabetes Mellitus	21 (21%)
Bronchial Asthma	5 (5%)
RTA	9 (9%)
Total	100

* RTA with head injury=7, *COPD-Chronic Obstructive pulmonary disease, * IHD

Table 3 Bacterial patterns among pneumonia patients

Organisms	Early onset (n) (%)	Late onset (n) (%)
Nosocomial pneumonia (NP)		
i. Klebsiella pneumonia	7(70%)	6 (30%)
ii*S. aureus	3(30%)	6 (30%)
iii Pseudomonas aeruginosa	0	5 (20.5%)
iv Streptococcus pneumoniae	0	3 (15%)
Total	10	20
VAP		
i. Klebsiella pneumonia	2 (33.3%)	2 (12.5%)
ii. S aureus	3 (50%)	3 (18.7%)
i.Pseudomonas aeruginosa	0	6 (37.5%)
iv. Streptococcus pneumoniae	1(16.6%)	0
v.*Klebsiella pneumonia+Candidia albicans	0	2 (12.5%)
vi.*Klebsiella pneumonia + Pseudomonas	0	3 (18.7%)
Total	6	16

*S.aureus- Streptococcus aureus*Mixed infections- Klebsiella pneumonia+Candidia albicans

Table 4 Risk indicators in NP and VAP

Risk factor	NP	VAP_
Advanced Age	2 (3.33%)	4 (10%)
Diabetes Mellitus	13 (21.66%)	9 (22.5%)
* COPD	5 (8.33%)	3 (7.5%)
* CRF	6 (10%)	1 (2.5%)
Head trauma	7 (11.66%)	2 (5%)
Altered sensorium	9 (15%)	0 (0%)
Use of H2 blockers	4 (6.66%)	6 (15%)
Nasogastric tube	5 (8.33%)	3 (7.5%)
Steroids	1 (1.66%)	4(10%)
Enteral feeding	3 (5%)	5 (12.5%)
Surgical intervention	5(8.33%)	3(7.5%)
Total	60	40

* COPD-Chronic obstructive pulmonary disease * CRF-Chronic renal failure

Table 5 Prognosis

Nosocomial pneumonia	Early	Late
Recovered	20 (90%)	32 (84.2%)
Expired	2 (10%)	6 (12%)
Total	22	38
VAPneumonia		
Recovered	13 (86.66%)	15 (60%)
Expired	2 (13.33%)	10 (40%)
Total	15	25

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DISCUSSION

The widespread use of tracheal intubation and mechanical ventilation to support the critically ill patients who are at particularly high risk for development of NP. Despite advances in the diagnosis and treatment, our understanding of the NP remains subject to important limitations.

Fagon and collegues documented that the risk of infection increases with duration of hospital stay. [13] A prevalence survey conducted under the auspices of WHO in 55 hospitals of 14 countries representing 4 WHO Regions (Europe, Eastern Mediterranean, South-East Asia and Western Pacific) showed an average of 8.7% of hospital patients had nosocomial infections. At any time, over 1.4 million people worldwide suffer from infectious complications acquired in hospital. [14] The highest frequencies of nosocomial infections were reported from hospitals in the Eastern Mediterranean and South-East Asia Regions (11.8 and 10.0% respectively), with a prevalence of 7.7 and 9.0% respectively in the European and Western Pacific Regions. [15]

The National health care safety network (NHSN) [10] USA, formulated a standardized reporting system to monitor hospital acquired infections to prevent and minimize the occurrence of such infections. Factors which influence immunocompetence are changes in nonadaptive immunity, chronic diseases, medications, malnutrition and functional impairments. Chronic diseases such as cancer, malnutrition, atherosclerosis, diabetes mellitus, and dementia predispose to certain types of infections. Medications such as sedatives, narcotics, anticholinergics, and gastric acid suppressants may further decrease inner defences. Malnutrition reduces cell-mediated immunity and is common in the Indian population. [10]

The development of VAP also dependent on age, the presence of chronic lung disease or acute respiratory distress syndrome, and admission for other medical or neurological reasons. [5, 16-19] Multiple hospital-associated factors have been identified, to include: increased duration of intubation, ventilation, and tube feeding; manipulation of airway/ventilator circuits; reintubation; tracheostomy; frequent ventilation circuit changes; low intracuff pressure of the endotracheal tube; failed subglottic suction; patient transport; supine position; pH altering agents; enteral feeding; and multiple central venous line insertions have been found to both decrease and increase the risk of VAP. [20] In addition to patient and hospital-associated risk factors, colonization of the trachea and/or oral cavity are important precursor factors in the development of VAP .[18, 21, 22]

In the present study, 38% of cases were late-onset NP, 62.5% were late onset VAP cases the findings were higher than other studies. [23-25] It was observed that majority of the VAP episodes occurred within the first weeks of MV. The interaction of several risk factors during the initial days of MV put the patient at higher risk and also the exhaustion of most vulnerable patients during the first few weeks leads to the decline in the occurrence of VAP in later days. [26]

Our study has shown that those above 61yrs of age were 30% and those below 61yrs were 70%. The incidence is age dependent, with about 5/1000 cases in hospitalized patients aged under 35 and up to 15/1000 in those over 65 years of age. [13, 27, 28]

The bacterial pattern & organisms depend upon the host microbial flora. NP is frequently caused by gram negative bacilli and usually results from aspiration of bacteria from the colonized oropharynx. [29-31] Colonization of the pharynx by gram-negative bacilli [31-34] is associated with chronic illness and previous use of antibiotic agents and endotracheal intubation; in the pathogenesis of VAP, the relation between chronic aspiration of colonized secretions through a tracheal cuff and the development of pneumonia is well established. [35, 36]

In the present study, most common bacterial pathogens in ICU acquired infections in early onset NP were K. pneumonia 7(70%) with least being S. pneumoniae and P. aeruginosa. Whereas in late onset NP majority of organisms isolated were K. pneumonia 6 (30%) with least being S. pneumoniae 3 (15%). In early onset VAP majority of organisms isolated were S. aureus 3 (50%) with least being others, whereas in late onset VAP Majority of organisms isolated were P. aeruginosa 6 (37.5%) with least S. pneumoniae were found.

Streptococcus pneumoniae was the most common organism isolated in early onset nosocomial pneumonia and Klebsiella pneumoniae was the most common organisms isolated in the patients not on ventilator. [37, 38]

In our study one elderly 1(16.66%) patient with a history of COPD was isolated with Streptococcus pneumoniae similar to other study. [38]

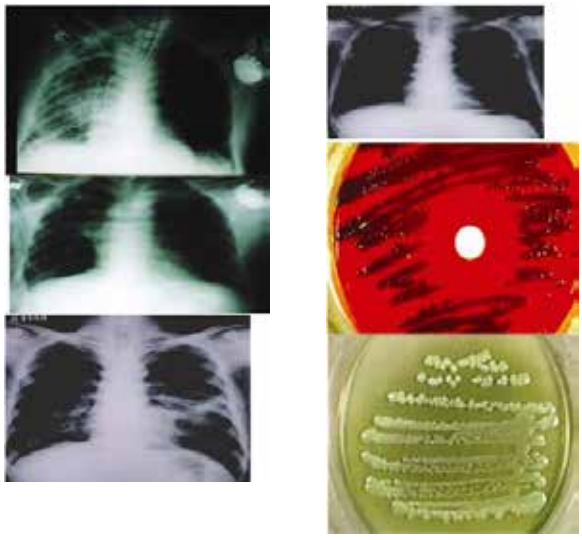
In another study where those infected with pseudomonas, [23, 24, 39, 40] mixed infections staphylococcus aureus (23%) and Klebsiella (30%) showed poor prognosis. [21, 41- 44]

In a study by Singh et al, most frequent isolates causing RTIs were Klebsiella (24.48%), followed by Proteus (18.33%) and E. coli (12.24%).[45]

Death from NP in ventilated patients reaches 30–50%, with an estimated attributable mortality of 10–50%. [28, 37, 40, 47, 48] Whereas death rate ranged between 2-6% in our study group. Total mortality among patients who developed nosocomial pneumonia in was 8 (22%) in this study and high risk indicators for mortality were presence of comorbid conditions, and chronic obstructive pulmonary disease 3(15%), Chronic renal failure 2(10%), Diabetes Mellitus 1(5%). In previous studies the mortality due to nosocomial pneumonia has been between 55% to 75%. [37]

Conclusion

Nosocomial infections occur worldwide and affect both developed and poor countries. Infections acquired in health care settings are among the major causes of death and increased morbidity among hospitalized patients. Diagnostic delays should be shortened at ICUs in order to reduce these infections. There should be a concerted effort on the part of all treating physicians to restrict risk factors like use of mechanical ventilation, total parenteral nutrition, and long stay in the hospital especially in intensive care.



REFERENCE

1. CDC definitions for Nosocomial infections In: Olmsted RN ed: APIC Infection control and Applied Epidemiology St Louis; Mosby 1996, pp A1-A20. | 2. Jarvis WR, Edward JR, Culver DH Nosocomial Infection rates in ICUs in the United States. National Nosocomial Infection Surveillance System. Am J Med 1991;91:1855-1915. | 3. Vincent JL. Nosocomial Pneumonia. IJCCM 2001;5:148-156. | 4. Wenzel RP. Hospital-acquired pneumonia: overview of the current state of the art for prevention and control. Eur J Clin Microbiol Infect Dis 1989;8:56-60. | 5. Gross PA, Neu HC, Aswapokee P, Van Antwerpen C, Aswapokee N. Deaths from nosocomial infections: experience in a university hospital and community hospital. Am J Med 1980; 68:219-23. | 6. Andrews CP, Coalson JJ, Smith JD, Johanson WG Jr. Diagnosis of nosocomial bacterial pneumonia in acute, diffuse lung injury.Chest. 1981;80:254-8. | 7. Jiménez P, Torres A, Rodríguez-Roisin R, de la Bellacasa JP, Aznar R, Gatell JM, Agustí-Vidal A.Incidence and etiology of pneumonia acquired during mechanical ventilation.Crit Care Med. 1989;17:882-5. | 8. Meduri GU. Ventilator-associated pneumonia in patients with respiratory failure. A diagnostic approach. Chest.1990;97:1208-19. | 9. Rello J, Quintana E, Ausina V, Castella J, Luquin M, Net A, Prats G.Incidence, etiology, and outcome of nosocomial pneumonia in mechanically ventilated patients.Chest. 1991;100:439-44. | 10. Larry James Strausbaugh. Emerging Health Care-Associated Infections in the Geriatric Population. Emerging Infectious Diseases 2001;7:268-271. | 11. Andrews CP, Coalson JJ, Smith DJ, Johanson WG Jr. Diagnosis of nosocomial bacterial pneumonia in acute, diffuse lung injury. Chest 1981;80:254-58 | 12. Catherine A, Fleming MD, Balaguera H, Craven DE. Risk factors for nosocomial pneumonia. Niederman. Medical Clinics of North America. 2001;85:1545-1563. | 13. Fagon JY, Chastre J, Domart Y, et al. Nosocomial pneumonia in patients receiving continuous mechanical ventilation. Prospective analysis of 52 episodes with use of a protected specimen brush and quantitative culture technique. Am Rev Respir Dis 1989;139:877–84. | 14. Tikhomirov E. WHO Programme for the Control of Hospital Infections. Chemiotherapia, 1987;3:148– 151. | 15. Mayon-White RT, Ducel G, Kereselidze T, Tikomirov E.An international survey of the prevalence of hospital-acquired infection. J Hosp Infect. 1988;11:43-8. | 16. Byers JF, Sole ML. Analysis of factors related to the development of ventilator-associated pneumonia: use of existing databases. Am J Crit Care 2000;9:344-9. | 17. Cook DJ, Kollef MH. Risk factors for ICU-acquired pneumonia. JAMA 1998;279:1605-6. | 18. Bonten MJ, Bergmans DC, Ambergen AW, et al. Risk factors for pneumonia and colonization of respiratory tract and stomach in mechanically ventilated ICU patients. Am J Respir Crit Care Med 1996;154:1339-46. | 19. Torres A, Serra-Batlles J, Ros E, et al. Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. Ann Intern Med 1992;116:540-3. | 20. Ibrahim EH, Tracy L, Hill C, Fraser VJ, Kollef MH. The occurrence of ventilator-associated pneumonia in a community hospital: risk factors and clinical outcomes. Chest 2001;120:555-61. | 21. Garrouste-Orgeas M, Chevret S, Arlet G, et al. Oropharyngeal or gastric colonization and nosocomial pneumonia in adult intensive care unit patients. A prospective study based on genomic DNAanalysis. Am J Respir Crit Care Med 1997;156:1647-55. | 22. Fourrier F, Duvivier B, Boutigny H, Roussel-Delvallez M,Chopin C. Colonization of dental plaque: a source of nosocomial infections in intensive care unit patients. Crit Care Med 1998;26:301-8. | 23. Noyal Mariya Joseph, Sujatha Sistla, Tarun Kumar Dutta, Ashok Shankar Badhe, Subhash Chandra Parija .Ventilator-associated pneumonia in a tertiary care hospital in India: incidence and risk factors . J Infect Dev Ctries 2009;3:771-777. | 24. Chastre J, Fagon J. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165:867-903. | 25. Kollef MH What is ventilator-associated pneumonia and why is it important? Respir Care 2005;50:714-721. | 26. Apostolopoulou E, Bakakos P, Katostaras T, Gregorakos L Incidence and risk factors for ventilator-associated pneumonia in 4 multidisciplinary intensive care units in Athens, Greece. Respir Care 2003;48:681-688. | 27. Torres A, Aznar R, Gatell JM, et al. Incidence, risk, and prognostic factors of nosocomial pneumonia in mechanically ventilated patients. Am Rev Respir Dis 1990;142:523–8. | 28. Fagon JY, Chastre J, Vuagnat A, et al. Nosocomial pneumonia and mortality among patients in intensive care units. JAMA 1996;275:866–9. | 29. Cross AS, Roup B. Role of respiratory assistance devices in endemic nosocomial pneumonia. Am J Med.1981;70:681-5. | 30. Craven DE, Driks MR. Nosocomial pneumonia in the intubated patient. Semin Respir Infect. 1987;2:20-33. | 31. Johanson WG Jr, Pierce AK, Sanford JP, Thomas GD. Nosocomial respiratory infections with gram-negative bacilli.The significance of colonization of the respiratory tract. Ann Intern Med. 1972;77:701-6. | 32. Johanson WG, Pierce AK, Sanford JP. Changing pharyngeal flora of hospitalized patients. Emergence of gramnegative bacilli. N Engl J Med 1969;281:1137-40. | 33. Higuchi JH, Johanson WG Jr. The relationship between adherence of Pseudomonas aeruginosa to upper respiratory Ovid: Valles: Ann Intern Med, 1995;122:179-186. | 34. Louria DB, Kaminski T. The effects of four antimicrobial drug regimens on sputum superinfection in hospitalized patients. Am Rev Respir Dis 1962;85:649-65. | 35. Craven DE, Steger KA, Barber TW. Preventing nosocomial pneumonia: state of the art and perspectives for the 1990s. Am J Med 1991;91:44S-54S. | 36. Tobin MJ, Grenvik A. Nosocomial lung infection and its diagnosis. Crit Care Med. 1984;12:191-9. | 37. Leu HS, Kaiser DL, Mori M, et al. Hospital-acquired pneumonia attributable mortality and morbidity. Am J Epidemiol 1989;129:1258–67. | 38. Seaton A, Seaton D. Crofton and Douglas's Respiratory diseases. chap13. Pneumonia. Blackwell science. 5th edition, United Kingdom.vol-1 pp356-444. | 39. Fagon JY, Chastre J, Hance AJ, et al. Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. Am J Med 1993;94:281–8. | 40. Fagon JY, Chastre J, Domart Y, Trouillet JL, Gibert C. Mortality due to ventilator-associated pneumonia or colonization with Pseudomonas or Acinetobacter species: assessment by quantitative culture of samples obtained by a protected specimen brush. Clin Infect Dis 1996;23:538-42. | 41. Jordi R, Daniel AO. Gerry O, Montserrat VL,Lisa B , Rebecca R ,Kollef, M H. Epidemiology and Outcomes of Ventilator-Associated Pneumonia in a Large US Database Chest 2002;122:2115-2121. | 42. Ibrahim, Emad H, Suzanne RN; Sherman, et al Nosocomial Pneumonia in the ICU Setting [Clinical Investigations In Critical Care] Chest 2000;117:1434-1442. | 43. Jean-Louis Vincent, David J. Bihari, Peter M. Suter, Hajo A, Jane White, Marie-Helene Nicolas-Chanoin, et al.The Prevalence of Nosocomial Infection in Intensive Care Units in Europe: Results of the European Prevalence of Infection In Intensive Care (EPIC) Study [Concepts in Emergency and Critical Care] JAMA 1995;274:639-644. | 44. Patwardhan R.B,. Dhakephalkar P.K, Niphadkar K.B, Chopade B.A. A study on nosocomial pathogens in ICU with special reference to multiresistant Acinetobacter baumannii harbouring multiple plasmids. Indian J Med Res 2008;128:178-187. | 45. Singh AK, Sen MR, Anupurba S, Bhattacharya P. Antibiotic sensitivity pattern of bacteria isolated from nosocomial infections in ICU. J Commun Dis 2002;34:257-63. | 46. Kollef MH. Ventilator-associated pneumonia. A multivariate analysis. JAMA 1993;270:1965–70. | 47. Papazian L, Bregeon F, Thirion X, et al. Effect of ventilator-associated pneumonia on mortality and morbidity. Am J Respir Crit Care Med 1996;54:91–7. | 48. Kollef MH, Silver P, Murphy DM, Trovillion E. The effect of late-onset ventilator-associated pneumonia in determining patient mortality. Chest. 1995;108:1655-62. |