
NOSOCOMIAL PNEUMONIA; RADIOLOGIC DIAGNOSIS IN PRANANGKLOA HOSPITAL

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ABSTRACT

Nosocomial Pneumonia is one of the important complications commonly found in the hospital. Early diagnosis and prompt treatment is essential to decrease morbidity and mortality rate of nosocomial pneumonia. This retrospective study was performed in Pranangkloa Hospital to determine the accuracy of chest radiograph. 163 patients diagnosed as nosocomial pneumonia in Pranangkloa Hospital between October 2001 and September 2004 were included in this study. Medical records and chest radiographs of the patients were studied and reviewed. Percentage and Chi-square were used in data analyses.

Finding: Nosocomial pneumonia is commonly occur in male (61.35%) and old aged group (45.39%). The complications were usually found in neurosurgical patients (39.26%) and medical patients (36.20%). The common causative agents are polymicro-organism (56.44%) and gram-negative bacilli (73.23%). Strong association between nosocomial pneumonia and mechanical ventilators was found (93.90%). Chest radiograph was performed in only 65% of the patients, in which positive finding, pulmonary infiltration/consolidation, were 74.53%. Infection in lower lobe, and multifocal or entirely infection were detected in 43.50% and 29.11%, respectively. Chest radiograph is found to be highly accurate in the diagnosis of nosocomial pneumonia ($X^2=76.57$, $p=0.000$, $\alpha<0.05$)

Conclusion: Abnormal chest radiograph is sensitive for early diagnosis of nosocomial pneumonia. Although no specific pattern of abnormal chest radiograph can be identified, strong correlation between abnormal chest radiograph and nosocomial pneumonia was clearly demonstrated, the author suggest that early radiography should be performed in any suspected cases especially in the elderly patients and the group using mechanical ventilators.

INTRODUCTION

Nosocomial pneumonia is one of the top-three problems of nosocomial infection in critically ill patients¹, particularly those in intensive care units (ICU). Nosocomial pneumonia is the second most common problems (27%), while urinary tract infection (31%), and primary blood stream infections (19%) are the first and third most common. The most common form of nosocomial pneumonia, called ventilator

-associated pneumonia (VAP) is highly associated with mechanical ventilation (86%). The incidence of nosocomial pneumonia in mechanically ventilated patients (VAP) ranges from 9% to 68% and the mortality rates ranges from 33% to 71%.^{2,3} VAP is the most common types of infection in ICU patients in Europe and Latin America (45%) and is the second most common in US ICUs.⁴ The diagnosis of VAP is

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complicated, limiting and challenging for the clinicians because the clinical and radiologic presentation vary: fever, leukocytosis, abnormal sputum and abnormal chest radiologic patterns are commonly found. Early institutional diagnostic for empirical antibiotic therapy can decrease morbidity and mortality,⁵ especially in the severely ill patients. Culture of tracheobronchial secretion were used to guide the adjustment of the administration or withdrawal of antibiotic therapy to reduce the consumption of the drugs for lessening of the side effects, resistance, and costs.

Abnormal chest radiograph combined with one of the clinical features (fever, leukocytosis or purulent tracheal secretion) is highly sensitive but poorly specific in the diagnosis of nosocomial pneumonia.⁶ To increase the specificity of clinical diagnosis, all four criterions should be included but this results in an unacceptably low sensitivity (< 50%).

The accuracy of radiographic interpretation has received little research interest,⁷ in postmortem patients and abnormal findings. The focus of radiologic studies of VAP has been an abnormal chest radiograph, the false negative values of chest radiograph were unknown. Several specific radiographic signs have been studied and the range of sensitivity found were 87% to 100% for alveolar infiltration, 58% to 83% for air bronchogram signs, and 50% to 78% for new or worsening infiltrates. The specificity cannot be determined since the total number of cases were unknown and chest radiograph were found to be negative in some VAP patients. The likelihood of VAP is not increased by any specific radiographic sign, so the reliability of chest radiographic interpretation is low.

Despite, lack of sensitivity and specificity of chest radiographs, the daily chest radiographs are indicated on patients with acute cardiopulmonary problems and who receiving mechanical ventilation or new device.⁸

This retrospective study of chest radiographic

interpretation was conducted in the patients who was diagnosed to have nosocomial pneumonia in Pranangkloa Hospital, Thailand between October 2001 to September 2004.

MATERIALS AND METHODS

The ethics committees of my hospital have granted an approval for this study.

Patients

163 patients diagnosed as nosocomial pneumonia in Pranangkloa Hospital were included in this retrospective study, medical admission charts and chest radiographs in the first episode of nosocomial pneumonia were reviewed interpreted and analysed.

Criteria for diagnosis

The patients, admitted in the hospital for at least 48 hours who developed a new or progressive pulmonary infiltration, consolidation, cavity or new pleural effusion on the chest radiograph in association with at least two of the following findings: rales on auscultation or dullness to percussion on chest examination, new onset of purulent sputum or change in sputum character, axillary temperature greater than 38° C or under 36° C (in children under 12 months) in the absence of antipyretic treatment, cough, leucocytes in excess of 12,000/mm³ or under 4000/mm³, positive tracheobronchial aspiration culture (qualitative endobronchial aspiration), or positive blood culture, and the patients who were treated with empirical antibiotic therapy without supporting evidence. For children under 12 months, associated with at least two of the following symptoms e.g., apnea, tachycardia, wheezy sound, or rhonchi.

Chest Radiograph

Plain films, mainly portable chest films, which were done in +/- 2 days from the day that tracheobronchial secretion were collected by doctors or

nurses and sent to the laboratory for culture (qualitative endotracheal aspiration due to limitation of laboratory facilities and the lack of bronchoscopic specialist), and at least 48 hours after admission.

The chest films were evaluated by the author or from the reports of other radiologists in the hospital.

Data collection

Each patient's admission hospital chart was constituted retrospectively and the following data were recorded; age, sex, patient's ward (medical, general-surgical, neuro-surgical and newborn ICU), whether the patient is on endotracheal tube/tracheostomy tube with mechanical ventilator, isolation of microorganisms, mono or polymicroorganism, chest radiograph; positive or negative finding for nosocomial pneumonia, finding patterns, location, sides and pleural effusion.

Statistical Analysis

The data of age, sex, patient's ward (medical, general-surgical, neuro-surgical and newborn ICU), on mechanical ventilator or not, microorganisms isolated, chest radiograph; positive or negative, finding, location, side and pleural effusion, and the relative positive chest radiograph with nosocomial pneumonia diagnosis were analysed using statistical computerized program for research in percentages and chi-square test or Pearson Chi-Square. Statistical significance was defined as $p < 0.05$.

RESULT

A total 163 patients were retrospectively evaluated during October 2001 to September 2004, and divided mainly into two groups, adult and childhood, (newborn).

Table 1. Demographic data of the nosocomial pneumonia patients

Data	Frequency	Percent
1. Sex		
male	100	61.35
female	63	38.65
total	163	100.00
2. Age		
< 1 year	27	16.56
1-14 years	1	0.61
15-29 years	21	12.89
30-44 years	19	11.66
45-59 years	21	12.89
60-74 years	44	26.99
>75 years	30	18.40
total	163	100.00
3. Ward		
medical /ICU med	59	36.20
general-surgical/ ICU surg.	12	7.36
neuro-surgical/ ICU surg.	64	39.26
NICU (newborn)	28	17.18
total	163	100.00

100 of 163 patients were male (61.35%), 63 were female (38.65%), 27 patients (16.56%) were less than 1 year (mostly newborns; mainly were preterms (app.25-36 weeks and birth weight app. 880-3480 grams). Only one boy, 5 year-old was

underlying of cerebral palsy was found. Most of the cases (77 patients, 45.39%) were the old-aged patients, older than 60 years and were admitted in particular neuro-surgical patients 64 (39.26%), 59 cases were medical patients (36.20%).

Table 2. On endotracheal tube/tracheostomy tube with mechanical ventilator of the nosocomial pneumonia patients

Data	Frequency	Percent
On tube	153	93.87
No tube	10	6.31
total	163	100.00

Almost all patients were on endotracheal/tracheostomy tube with mechanical ventilator 153 (93.87%).

Table 3. Microorganisms recovered from respiratory secretion of nosocomial pneumonia patients

Microorganisms	Frequency	Percent
Pseudomonas aeruginosa	58	21.56
Klebsiella species	69	25.65
Staphylococcus aureus	41	15.24
Enterobacter species	18	6.69
Acinetobacter species	52	19.33
Other	31	11.53
total	269	100.00

The most common microorganisms were gram negative bacilli 197 (73.23%), particularly Klebsiella species 69 (25.65%), others are Pseudomonas aeruginosa 58 (21.56%), Acinetobacter species 52 (19.33%) and Enterobacter species 18 (6.69%). The

fourth is Staphylococcus aureus 41 (15.24%), mostly with MRSA (methicillin resistant Staphylococcus aureus). The other were Streptococcus pneumoniae, Serratia species and E.coli.

Table 4. Number of kinds of microorganisms recovered from respiratory secretion of nosocomial pneumonia patients

Microorganisms	Frequency	Percent
None	8	4.91
Monomicroorganism	63	38.65
Polymicroorganism	92	56.44
total	163	100.00

The most common types of microorganisms were mixed infection; 92 (56.44%) and single infection were; 63 (38.65%). Negative culture; 8 (4.91%) were

the cases that had been diagnosed as nosocomial pneumonia and had taken empirical antibiotic therapy without tracheobroncheal secretion cultures support.

Table 5. Chest radiographic diagnosis in nosocomial pneumonia patients

	Microorganisms	Frequency	Percent
1. Chest film			
	Not available	57	35
	Available	106	65
	total	163	100.00
2. Result (pulmonary infiltration/consolidation)			
	Positive	79	74.53
	Negative	27	25.47
	total	106	100.00
3. Distribution:Location of pulmonary infiltration /consolidation.			
	Upper	10	12.66
	Lower	35	44.30
	Entire	23	29.11
	Perihilar	11	13.93
	total	79	100.00
4. Side effected			
	Right	30	37.97
	Left	18	22.79
	Both	31	39.24
	total	79	100.00
5. Pleural effusion			
	None	75	94.94
	Pleural effusion	4	5.06
	total	79	100.00

Chest radiograph were performed in 106 patients (65%), positive finding (pulmonary infiltration/consolidation) found in 79 patients (74.53%), prominently in lower part 35 cases (44.30%), scattered, diffuse, multifocal or entirely both lung fields

23 cases (29.11%). Both sides and Rt. Side are more common. 4 cases (5.06%) show pleural effusion. Air bronchogram signs were not seen in adult but commonly seen in preterm newborns which cannot be excluded from respiratory distress syndrome

(RDS). The relation of positive chest radiograph in nosocomial pneumonia diagnosis by Pearson Chi-Square was 76.574 ($p=0.000$) ($\alpha < 0.05$) and contingency coefficient was 0.565.

DISCUSSION

Nosocomial infections are defined as infections acquired during or as a result of hospitalization after 48 hours⁹ which contribute significantly to morbidity and mortality^{10,11} as well as costs of hospitalized patients. The most common problems are urinary infections, the second and third most common are pneumonia and blood stream infection¹ and showed device-associated infections, nosocomial pneumonias are associated with mechanical ventilator, called ventilation-associated pneumonia (VAP). The majority of nosocomial pneumonias occur in intensive care units or critically ill patients. The incidence of VAP is 9-68%² and mortality rate is 33-71%. *Pseudomonas aeruginosa* was identified as a gram-negative pulmonary pathogen in one report¹² showing uniquely high mortality (70%) as compared to the other gram-negative bacilli. Mortality rate of gram-positive organism (usually *Staphylococcus aureus*) is lower but cannot be neglected. The majority of nosocomial pneumonias are caused by gram-negative bacilli (> 60%).¹³ The common causative agents are listed in order of commonly found: *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Enterobacter* species, *Klebsiella* species, *E. coli*, *Haemophilus influenzae* and *Serratia marcescens*. Order of causative agent varied in each study.¹⁴ Predisposing factors of nosocomial pneumonia are intubation (short/long term),¹⁵⁻¹⁷ intensive care unit (respiratory equipment, contamination of devices),¹⁷⁻²¹ antibiotics,^{22,23} surgery,¹⁶ chronic lung diseases,^{22,24} advanced-ages^{15,16,25,26} and immunosuppression.^{27,28}

The majority of nosocomial pneumonias appear to occur as a result of aspiration of pathogens that colonized at the mucosal surface of the upper airway.^{22,29-30,43} The patients receiving gastric alkalization to prevent stress ulcers and bleeding during

hospitalization can produce extensive bacterial overgrowth in the upper GI tract, that lead to airway colonization, secondary to aspiration of gastric microflora.^{31,32} Patients treated with H₂ blocker (cimetidine) show higher incidence of pneumonias than the group treated with sucralfate.³³

Diagnosis of nosocomial pneumonia is complicated because the classic clinical finding for pneumonia, new fever, new or worse pulmonary infiltration, cough, sputum production, and elevated leukocyte count, may not be seen, while pulmonary infiltration, if found, may cause by diseases other than pneumonia, such as alveolar hemorrhage, atelectasis, pulmonary infarction, ARDS (adult respiratory distress syndrome) or hypersensitivity pneumonitis.³⁴ The isolation of potential gram-negative bacillary or *Staphylococcus aureus* pathogens from the airways cultures may be colonization (isolation of an organism from a patient who has no signs or symptom of infection) or if actual infection is pneumonia or tracheobronchitis. There is no clear clinical manifestation in the diagnosing nosocomial pneumonia.

Microbiologic evaluation of patients with suspected nosocomial pneumonias may or may not be helpful. Sputum or respiratory secretions obtained by endotracheal aspiration are often contaminated with upper airway flora, so the cultured result may not reflect the microbiology of infected lung disease. Blood cultured may help to differentiate between contaminating and infecting bacterial isolated from sputum but the positive rate are in lower than 10% of nosocomial pneumonia patients. Invasive methods, bronchoscopy with quantitative laboratory analysis, such as protected-specimen brush (PSB), bronchoalveolar lavage (BAL) have been described potentially useful for improving diagnostic specific for nosocomial pneumonias.^{34,35} However there are some disadvantages of PSB and BAL in clinical application³⁶ (hypoxemia, sinus tachycardia and minor bronchial hemorrhage) and these techniques require specialists and special equipments, which may delay in sample collection and initiation of empiric antibiotic

therapies,³⁶ there is a high false-negative rate in the culture result. Non-invasive quantitative technique, quantitative endotracheal aspiration (QEA) culture is less complicated, lower costs and relatively sensitive (70%) and specific (72%) method to diagnose VAP but the negative predictive value of QEA cultures were higher (72%) when compared with that obtained using PSB (34%).³⁷ One study showed that the outcome of VAP treatment was not influenced by the technique used for microbial investigation.⁴⁴

Diagnosis of this infection is more complicated in the neonates, for the signs are usually subtle and nonspecific. Definitions of sepsis used in adult and pediatric patients usually cannot be applied to neonates, due to the fact that they rarely get febrile and their vital signs are affected by several factors other than infection such as cold, stress, hypoglycemia, pain and hypoxia. Therefore, sepsis is usually suspected in a newborn just based on poor feeding or a state of not being well, or sometimes just based on major or minor risk factors in the history.^{38,39} On the other hand, neonate prone to be infected by fatal nosocomial microorganisms if they are hospitalized and received invasive procedures such as intubation or catheterization, especially preterm.

In this study, nosocomial pneumonias found prominently in male 100 (61.35%), advanced age patients, more than 60 years, 77 (45.39%), neurosurgical and medical patients (36.20% and 39.26%, respectively) mostly critically ill or impaired conscious patients. Almost all patients of nosocomial pneumonias are found to be associated with mechanical ventilator via endotracheal tube or tracheostomy tube 153 (93.9%). The other risk factors are old patients or the patients who prone to aspiration, such as impaired consciousness or stroke.⁴⁰ Because nosocomial pneumonias are usually associate with aspiration,^{22,29,30,43} so polymicroorganisms are prominent. Polymicroorganisms are two times more common than monoorganism in this study which is correspond with

Rouby et al. study.⁴² Microorganisms (may be oropharyngitis or tracheobronchitis) were gram-negative bacilli 197 (73.23%) as same as other studies^{10,13,14} and mainly in *Klebsiella* species, followed by *Pseudomonas aeruginosa*, *Acinetobacter* species and *Enterobacter* species. Gram positive microorganism is *staphylococcus aureus* and frequent MRSA). Only 106 chest radiographs (65%) could be collected, because some patients received initially empirical therapy without performing chest films. The positive finding, pulmonary infiltration/consolidation, in 79 patients (74.53%), the other signs⁴¹ as air bronchogram sign, silhouette sign, cavities, fissure abutment or atelectasis were not seen. Distribution, prominent in lower part 35 (44.30%), and follow by scattered diffuse, multifocal or entirely both lung fields 23 (29.11%), associated with aspiration. Involving both sides and right side were eminent. A few cases had pleural effusion, 4 (5.06%). Air bronchogram signs were not seen in adult but commonly seen in preterm newborns, but cannot be excluded from respiratory distress syndrome (RDS) pattern, so the radiograph in the preterm newborns suspected of nosocomial pneumonias were very really complicated, history of risk factors may be helpful.^{38,39} The relation of positive chest radiograph in nosocomial pneumonia diagnosis by Pearson Chi-Square was 76.574 ($p=0.000$) ($\alpha<0.05$) and contingency coefficient was 0.565, meaning the positive chest radiographs are useful to diagnose nosocomial pneumonia.

There are some limitations in this study due to retrospective design, chest radiographs were not performed on the day that the tracheobronchial secretion were collected (± 2 days) and some other noninfectious diseases such as alveolar hemorrhage, atelectasis, pulmonary infarction, ARDS (adult respiratory distress syndrome) or hypersensitivity pneumonitis and used qualitative endotracheal aspiration, can depict the same abnormal patterns like pneumonia, causing over estimate of nosocomial pneumonia diagnosis and positive chest radiograph.

CONCLUSION

The nosocomial pneumonia is the most common type of infection in critically ill patients, inadequate or delayed antimicrobial treatment result in high mortality rate. Early diagnosis is important but it is very complicated due to the classic clinical finding for nosocomial pneumonia; (new) recurrent fever, cough, changing sputum production and radiologic pattern and elevated leukocyte count may not be detected. The positive chest radiograph interpretation, pulmonary infiltration/consolidation, is helpful to increase the specificity.

REFERENCES

- 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;27:887-92.
- Bowton DL. Nosocomial pneumonia in the ICU: year 2000 and beyond. *Chest* 1999; 155 (3 suppl):S28-S33.
- Fagon JY, Chastre J, Vuagnat A, Trouillet JL, Novara A, Gibert C. Nosocomial pneumonia and mortality among patients in intensive care units. *JAMA* 1996;275:866-9.
- Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, 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. *JAMA* 1995;274: 639-44.
- Camargo LFA, Marco FVD, Barbas CSV, Hoelz C, Bueno MAS, Rodrigues M, et al. Ventilator associated pneumonia: comparison between quantitative and qualitative cultures of tracheal aspirates. *Critical Care* 2004; 8: R422-R430.
- Wunderrink RG. Clinical Criteria in the Diagnosis of Ventilator-Associated Pneumonia. *Chest* 2000;117:191S-194S.
- Wunderrink RG. Radiologic Diagnosis of Ventilator-Associated Pneumonia. *Chest* 2000; 117:188S-190S.
- Henschke CI, Yankelevitz DF, Wand A, Davis SD, Shiao M. Accuracy and efficacy of the chest radiography in intensive care unit. *Radiol Clin North Am* 1996;34(1):21- 31.
- Dori F, Zaleznik. Hospital-Acquired and Intravascular device-Related infection. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. *Harrison's Principles of Internal Medicine*. 15th ed. New York:McGraw-Hill;2001.857-9.
- Noor A, Hussain SF. Risk factors associated with development of ventilator associated pneumonia. *J Coll Physicians Surg Pak* 2005; 15(2):92-5.
- Apisarnthanarak A, Pazgal GH, Hamvas A, Oisen MA, Fraser VJ. Ventilator-Associated Pneumonia in extremely Preterm Neonates in a Neonatal Intensive Care Unit: Characteristics, Risk Factors, and Outcomes. *PEDIATRICS* 2003;112(6):1283-89.
- Gross PA. Epidemiology of hospital-acquired pneumonia. *Semin Respir Infect* 1989;2: 2-7.
- Centers for Disease Control and Prevention. National Nosocomial Infections Study Report. Annual Summary. 1984. *MMWR* 1986; 35: 17SS-29SS.
- Horan T, Culver D, Jarvis W. Pathogens causing nosocomial infections. *Antimicrob Newslett* 1988;5:65-7.
- Combes A, Figliolini C, Trouillet JT, Kassis N, Wolff M, Gibert C, et al. Incidence and Outcome of Polymicrobial Ventilator-Associated Pneumonia. *Chest* 2002;1918-23.
- Craven DE, Steger KA. Ventilator-associated bacterial pneumonia: Challenges in diagnosis, treatment and prevention. *New Horiz* 1998;6(2 suppl):S30-45.
- Cross AS, Roup B. Role of respiratory assistance devices in endemic nosocomial pneumonia. *Am J Med* 1981;70:681-5.

18. Pierce AK, Sanford JP, Thomas GD, et al. Long-term evaluation of decontamination of inhalation-therapy equipment and the occurrence of necrotizing pneumonia. *N Engl J Med* 1970; 282: 528-31.
19. Craven DE, Lichtenberg DA, Goularte TA. Contaminated medication nebulizers in mechanical ventilator circuits: Source of bacterial aerosols. *Am Rev Respir Dis* 1984; 77: 834-8.
20. Craven DE, Goularte TA, Make BJ. Contaminated condensate in mechanical ventilator circuits: a risk factor for nosocomial pneumonia? *Am Rev Respir Dis* 1984; 129:625-8.
21. Salata RA, Lederman MM, Shlaes DM, Jacobs MR, Eckstein E, Tweardy D, et al. *Am Rev Respir Dis* 1987; 135(2):426-32.
22. Cravan DE, Connolly MG Jr, Lichtenberg DA. Contamination of mechanical ventilators with tubing changes every 28 or 48 hours. *N Engl J Med* 1982; 306: 1505-9.
23. Johanson WG Jr, Pierce AK, Sanford JP. Nosocomial respiratory infection with gram-negative bacilli. *Ann Intern Med* 1972; 77: 701-6.
24. Tillotson JR, Finland M. Bacterial colonization and clinical superinfection of respiratory tract complicating antibiotic treatment of pneumonia. *J Infect Dis* 1969; 119:597-624.
25. Hanson LC, Weber DJ, Rutala WA. Risk factor for nosocomial pneumonia in the elderly. *Am J Med* 1992; 92:161-6.
26. Harkness GA, Bentley DW, Roghmann KJ. Risk factor for nosocomial pneumonia in the elderly. *Am J Med* 1990; 89:457-64.
27. Graybill JR, Marshall LW, Charache p. Nosocomial pneumonia. *AM Rev Respir Dis* 1973; 108:1130-40.
28. Kirby BD, Snyder KM, Meyer RD. Legionnaires' disease: Report of sixty-five nosocomially acquired cases and review of the literature. *Medicine* 1980; 59:188-205.
29. Reynolds HY. Bacterial adherence to respiratory tract mucosa- a dynamic interaction leading to colonization. *Semin Respir Infect.* 1987; 2: 8-19.
30. Parker CM, Heyland DM. Aspiration and The Risk of Ventilator-Associated Pneumonia. *Nutrition in Clinical Practice* 2004; 19(6): 597-9.
31. DuMoulin GC, Paterson DG, Hedley-Whyte J. Aspiration of gastric bacterior in antacid-treated patients: A frequent cause of post operative colonization of the airway. *Lancet* 1982; 1: 242-5.
32. Pingleton SK, Hinthorn DR, Liu C. Enteral nutrition in patients receiving mechanical ventilation. *AM J Med* 1986; 80:827-32.
33. Kappstein I, Schulgen G, Friedrich T. Incidence of pneumonia in mechanically ventilated patients treated with sucralfate or cimetidine as prophylaxis for stress bleeding: Bacterial colonization of the stomach. *Am J Med* 1991; 91(suppl 2A):S125-31.
34. Bouza E, Buisson CB, Chestre J, Fagon JY, Marquette CH, Munoz P, et al. Ventilator-associated pneumonia. *Eur Respir J* 2001; 17: 1034-45.
35. Jourdain B, Novara N, Joly-Guillou ML, Dombert MC, Calvat S, Trouillet JL et al. Role of quantitative cultures of endotracheal aspirates in the diagnosis of nosocomial pneumonia. *Am J Respir Crit Care Med* 1995; 152(1):241-6.
36. Pan Z, Xiaohong W, Kying Y. Diagnostic Value of Quantitative Cultures of Endotracheal Aspirations for Ventilator-Associated Pneumonia. *Chin Med J* 2002; 115(2):1-4.
37. El-Ebiary M, Tones A, Gonzalez J, de la Bellacasa JP, Garcia C, Jimenez de Anta MT, et al. Quantitative cultures of endotracheal aspirates for the diagnosis of ventilator-associated pneumonia. *Am Rev Respir Dis* 1993; 148(6):1552-7.

38. Ergenekon E, Koc E, Atalay Y. Neonatal Infection in Gazi University NICU between 1996-1998. *Gazi Medical Journal*
39. Dear P. Infection in the newborn In: Rennie JM, Robertson NRC (eds): *textbook of Neonatology*, Edinburgh: Churchill Living Stone. 1999;1109-1139.
40. Hilker R, Poetter C, Findeisen N, Sobesly J, Jacobs A, Neveling M, et al. Nosocomial Pneumonia After Acute Stroke Implications for Neurological Intensive Care Medicine. *Stroke* 2003;34(4):975-85.
41. Wunderink RE, Woldenberg LS, Zeiss J, Day CM, Ciemins J, Lecher DK. The radiologic diagnosis of autopsy-proven ventilator-associated pneumonia. *Chest* 1992;101:458-63.
42. Rouby JJ, Martin De Lassal E, Poete P. Nosocomial bronchopneumonia in the critically ill. Histologic and bacteriologic aspects. *Am Rev Respir Dis* 1992;146:1059-66.
43. Parker CM, Heyland DK. Aspiration and the Risk of Ventilator-Associated Pneumonia. *Nutrition on Clinical Practice* 2004; 19(6): 597-609.
44. Ruiz M, Torres A, Ewing S, Marcos MA, Alcon A, Lledo R, et al. Noninvasive Versus Invasive Microbial Investigation in Ventilator-associated Pneumonia. *Am J Respir Crit Care Med* 2000;162:119-125.