Global Journal of Health Science;Vol. 9, No. 3; 2017
ISSN 1916-9736 E-ISSN 1916-9744
Published by Canadian Center of Science and Education

Incidence of Hospital-Acquired Bacterial Pneumonia and Its Resistance Profiles in Patients Admitted to Intensive Care Unit

Vahid Boostani[1], Farzaneh Dehghan[1,2], Afsaneh Karmostaji[3], Nader Zolghadri[4] & Afsaneh Shafii[2]

[1] Molecular Medicine Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

[2] Hormozgan Social Security Management, Khalij Fars Hospital of Social Security, Bandar Abbas, Iran

[3] Infectious & Tropical Diseases Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

[4]Department of Mathematics, Islamic Azad University, Sama College, Bandar Abbas, Iran

Correspondience: FarzanehDehghan,Molecular Medicine Research Center, Shahid Mohammadi Hospital, Jomhouri Blvd & Hormozgan Social Security management,Khalij Fars Hospital of Social Security, Bandar Abbas, Iran. Tel: 98-917-168-5935; Fax: 98-763-335-4939. E-mail: dehghanfarzaneh@ymail.com

Received: January 2, 2016 Accepted: May 18, 2016 Online Published: July 11, 2016

doi:10.5539/gjhs.v9n3p73 URL: http://dx.doi.org/10.5539/gjhs.v9n3p73

Abstract

Hospital-acquired bacterial pneumonia (HABP) is one of the most important causes of morbidity, mortality and economic problems especially for patients admitted in the intensive care unit (ICU) ward. The aim of this study was to determine the incidence of nosocomial pneumonia in ICU, identify the causative bacteria and their resistance profiles. This cross sectional study was performed on 214 patients who were admitted in the ICU ward of a general hospital requiring mechanical ventilation for at least 48 h. Identification of HABP was based on the clinical signs manifested 48 h or more after admission, new chest X-ray infiltrates and microbiologic examination of endo tracheal secretion. Data were analyzed using SPSS 21 to perform the descriptive statistics. The isolated gram negative bacteria were *Klebsiella pneumoniae* (50%), *Staphylococcus aureus* (18.7%), *Acinetobacter baumannii* (12.5%), *Escherichia coli* (12.5%) and *Pseudomonas aeroginosa* (6.3%). The maximum antimicrobial resistance of gram negative bacteria was to Cefazolin (100%) and Ampicillin (84.6%), while antimicrobial resistance to Clindamycin, Azithromycin, Amoxycillin+clavulanate, Trimethoprim+sulfamethoxazole and Ciprofloxacin was 33.3%. No resistance was seen towards carbapenems.The most frequent gram negative isolated bacterium was *K. pneumoniae,* and maximum antimicrobial resistance rate was observed for Cefazolin and Ampicillin, which is due to betalactamase production.

Keywords: hospital infection, gram-negative bacterial infections, pneumonia, Antimicrobial Drug Resistance

1. Introduction

Hospital-acquired bacterial pneumonia (HABP) is one of the most important acute complications that affects hospitalized patients in the Intensive Care Unit (ICU) (Uvizl, Hanulik, Husickova, Sedlakova,&Adamus,2011; Ghazvini, Ghanaat, JafarianYazdanPanah, &Irani,2005).

It develops mainly in patients who have received mechanical ventilation for more than 48 h (Pileggi, Bianco, Flotta, Nobile, & Pavia, 2011; Dandagi, 2010).

The incidence of HABP among patients has been reported to be between 9-27% (Rea-Neto et al., 2008; Katherason et al., 2009; Koenig & Truwit, 2006). The relatively high incidence of nosocomial infection observed among patients hospitalized in the intensive care unit as compared with patients admitted to other wards of the hospital (Kaoutar, Joly, Heriteau, &Barbut, 2004; Defez et al., 2004) may be due to the severity of the underlying problems or aggressive procedures such as tracheal intubation, urinary tract catheterization, as well as peripheral and central venous catheterization (Kawagoe et al., 2001). HABP is commonly caused by species of the Enterobacteriaceae family, non-fermentative gram–negative bacilli and *Staphylococcus aureus* (Chung et al., 2011; Ronald, 2010; Fica, Cifuentes, & Hervé, 2011; Sadeghi, Asghazadeh, Baratlu, & Montazeri, 2009). But its incidence, microbial aetiology and resistance patterns differ from country to country and also from hospital to hospital (Dandagi, 2010; Rello, 2007; Kuti, Shore, Palter, & Nicolau, 2009; Song & Chung, 2010). The

antimicrobial control of HABP can be changed by determining the causative pathogens(Masterton,2008), but antibiotic resistance in particular, multi drug resistance, are major problems of microbial agents isolated from ICU patients (Ilić & Marković-Denić, 2009)

.It seems that the prevalence of antibiotic-resistant pathogens is under development, in which these conditions in turn constitute a serious threat to this group of patients (Grundmann, Aires-De-Sousa Ai, Boyce,&Tiemersma, 2006). The identification of HAP causative bacteria and antimicrobial resistance patterns is necessary for the improvement of hospital infection control system and application of effective methods for the prevention and control of HAP (Afkhamzadeh, Lahoorpour, Delpisheh, &Janmardi, 2011). The aim of this study therefore, was to determine HABP incidence and detect the causative bacterial agents and their resistance profiles in ICU patients. Access to such information is clinically beneficial in selecting appropriate empirical antibiotic therapy by physicians, reducing the length of ICU admission, decreasing the costs of hospitalization, and finally to reduce the mortality and morbidity rates in these patients.

2. Methods and Materials

2.1 Patient Studied

In this cross sectional study from Jan 2013 to Jan 2014, ICU patients requiring mechanical ventilation for at least 48 h in a general hospital in the south of Iran were included. Patients with signs of infection during ICU admission were excluded. For each patient, a form was filled according to the National Guideline of Controlling hospital acquired infections (HAI). Since this study is focused on nosocomial bacterial pneumonia, only patients with chest x-rays with new infiltrations and endotracheal tube secretions and with clinical signs of pneumonia were included in this study. New chest X-ray infiltrates were observed and endotracheal secretions were examined for the identification of bacterial agents and antimicrobial susceptibility pattern of isolates.

2.2 Culture Methods

Homogenized samples were cultured on blood agar and Eosin methylene blue (EMB) agar. The samples with colony counts of more than 10^4 cfu/ml were considered positive (Medell, Hart, Duquesne, Espinosa, & Valdés, 2013). Diagnostic tests were performed using API-20E commercial kit for gram negative bacilli and API-20NE for gram negative non-fermentative bacilli (Biomerieus, Spain). *Staphylococci* were identified based on gram stain, morphology, catalase, bacitracin sensitivity with Rosco antibiotic disc, coagulase test with fresh plasma from Darvash® Company, DNase activity and fermentation of manitol using a commercial media (Condo, Spain). The susceptibility test of all isolates to different antibiotics was performed using the Kirby-Bauer disk diffusion method on Muller-Hinton agar plates (Condo, Spain) as recommended by the clinical laboratory standards institute (CLSI) with commercial antimicrobial disks (Rosco, England). The antibiotic disks used in this study were Amoxicillin+Clavulanate (20+10μg), Trimethoprim+Sulfamethoxazole (1.25+23.75 μg), Cefotaxime (30 μg), Ceftazidime (30 μg), Ceftriaxone (30 μg), Ciprofloxacin (5 μg), Cefazolin (30 μg), Ampicillin (10 μg), Amikacin (30 μg), Penicillin (5 μg), Vancomycin (30 μg), Clindamycin (2 μg) and Azithromycin (15 μg). The antibiogram pattern of microorganisms was determined using the Kirby Bauer method on Mueller Hinton agar medium (Baily & Scott, 1990). The results were recorded according to the standards provided by the Clinical and Laboratory Standards Institute (CLSI, 2013).

In the study, the frequency of the extended spectrum beta-lactamase (ESBL) producing isolates was determined by double disk synergy test (DDST) using a disk of cetazidime placed 12-15 mm from a ceftazidime-clavulnic acid disk (30+10 μg), and cefoxitin disk (30 μg) diffusion method was used for the detection of Methicillin-resistant *Staphylococcus aureus* (MRSA).

The study protocol was approved by the research ethics committee of Khalij Fars Hospital and informed consent was obtained from each patient's family (as the patient was admitted to the ICU) before entering the study.

2.3 Data Analysis

The data were analyzed using Statistical package for Social Sciences SPSS 21, using descriptive statistics.

3. Results

In this study, of the 148 men and 66 women admitted to the ICU, 11(3.03%) male and 5(1.8%) female patients were diagnosed with HABP (M:F 11:5, that is, men were 2.2 times more likely to suffer from HABP). In general, the incidence of HABP in this ward was 7.5%. The case fatality rate (CFR) of HABP was 25% (4/16) with an attributable mortality rate of 6.45% (4/62). Table 1 shows the clinical features of patients with HABP. The primary and final diagnosis, invasive procedure and underlying diseases of patients with HABP are shown in Table 2.

The frequency of isolated gram positive and gram negative bacteria form HABP was18.75% (3/16) and 81.25% (13/16), respectively.The most common isolated microorganisms were gram negative bacilli, primarily *Klebsiella pneumoniae* (50%), other isolated bacteriainclude *S. aureus* (18.7%), *Acinetobacter baumannii* (12.5%), *Escherichia coli* (12.5%) and *Pseudomonas aeroginosa* (6.3%). The maximum antimicrobial resistance of gram negative organisms was observed for Cefazolin (100%) and Ampicillin (84.6%). Gram positive bacteria were resistant to Penicillin while gram negative organisms were resistant to Cefazolin (66%) and Ampicillin (66%), but the resistance rate to Clindamycin, Azithromycin, Amoxycillin+Clavulanate, Trimethoprim+Sulfamethoxazole and Ciprofloxacin was 33.3%. Table 3 shows the antibiotic resistance of gram negative bacteria. Of the 13 gram negative isolates, 23.1% were found to produce ESBL. Among the isolated bacteria, two *K. pneumoniae* isolates and one *A. baumannii* (23.07%) produced ESBL. In addition, one third of the isolated *S. aureus* (33.3%) were methicillin resistant (MRSA).

Table 1. Demographics & Clinical Signs of Patients with HABP (n=16)

Demographics and Clinical Signs		Case, No. (%)
Age		57.63 ± 20.54
Number of Days In ICU		16.4 ± 9
Clinical Sign		
	Underlying Disease	2 (12.5%)
	Dullness	2 (12.5%)
	Tachypnea	7 (43.7%)
	Tachycardia	6 (37.5%)
	Coarse Crackles (Rvnkay)	2 (12.5%)
	Wheezing	8 (50%)
	Purulent Sputum	16 (100%)
	Cough	3 (18.8%)
Rales		14 (87.5%)
Increased Respiratory Secretion		10 (62.5%)

Table 2. Primary and Final Diagnosis, underlying disease and invasive procedure of patients with HAI

No	Primary Diagnosis	Final Diagnosis	Chronic Underlying disease	Invasive procedures
1	Myocardial Infarction	Myocardial Infarction	Congestive Heart Failure	Tracheostomy,Suction,Arteialcatherterization, uretheral catheterization, ventilaton
2	Hypertension	Hypertension	No	Tracheostomy, Suction, venous catheterization, uretheral catheterization, ventilaton, ventricular shunt, intubation
3	Congestive Heart Failure	Bronchitis	Diabetes Hypertension	Tracheostomy, Suction, venous catheterization, uretheralcatheterization,intubation
4	Head Injury	Intracerebral hematoma	No	Tracheostomy, Suction, venous catheterization, ventilation
5	Organophosphate Poisoning	Organophosphate Poisoning	NO	Suction, venous catheterization, uretheral catheterization, intubation, ventilation, CVP line
6	Sepsis	Adult Respiratory Distress Syndrome	Chronic Obstructive Pulmonary Disease	Suction, venous catheterization, uretheral catheterization, intubation, ventilation,

7	Adult Respiratory Distress Syndrome	Adult Respiratory Distress Syndrome	No	venous catheterization, uretheralcatheterization,intubation, ventilation,
8	Myocardial Infarction	Myocardial Infarction	Chronic Obstructive Pulmonary Disease	Suction, venous catheterization, uretheralcatheterization,intubation, ventilation,
9	Sepsis	Sepsis	No	venous catheterization, uretheralcatheterization,intubation, ventilation,
10	Cerebrovascular accident (hemorrhagic)	Cerebrovascular accident	Diabetes	Tracheostomy venous catheterization,, ventilation,
11	Ventricular Tachycardia	Congestive Heart Failure	Chronic Obstructive Pulmonary Disease	Suction, venous catheterization, uretheralcatheterization,intubation, ventilation, CVP line
12	Head Injury/Myocardial Injury	Head Injury/Myocardial Injury	No	Suction, venous catheterization, uretheralcatheterization,intubation, CVP line ventilation,Tracheostomy,
13	Head Injury	Head Injury	No	Suction, venous catheterization, uretheralcatheterization,intubation, ventilation,
14	Head Injury	Head Injury	Diabetes	Suction, venous catheterization, uretheral catheterization intubation, ventilation,
15	Chronic Obstructive Pulmonary Disease	Chronic Obstructive Pulmonary Disease	No	Suction, venous catheterization, uretheralcatheterization,intubation, ventilation,
16	Myocardial Infarction	Myocardial Infarction	no	venous catheterization, uretheral catheterization, intubation, ventilation, CVP line

Table 3. Frequency of antibiotic resistance among gram negative bacterial isolates in the study

Antibiotic/	Abbreviation	Break point	*P.aeroginosa* (1)	*A.baumannii* (2)	*E.coli* (2)	*K.pneumoniae* (8)
Amoxicillin+clavulanate	AMC	≤13	1(100%)	2(100%)	1(50%)	6(75%)
Trimethoprim+sulfamethoxazole	SXT	≤10	1(100%)	2(100%)	2(100%)	5(62.5%)
Cefotaxime	CTX	≤22	0(0%)	2(100%)	2(100%)	4(50%)
Ceftazidime	CAZ	≤14	0(0%)	2(100%)	1(50%)	4(50%)
Ceftriaxone	CTR	≤19	0(0%)	1(50%)	2(100%)	4(50%)
Ciprofloxacine	CIP	≤15	0(0%)	2(100%)	1(50%)	4(50%)
Cefazolin	CFZ	≤19	1(100%)	2(100%)	2(100%)	8(100%)
Ampicillin	AMP	≤13	1(100%)	1(50%)	1(50%)	8(100%)
Amikacin	AMI	≤14	0(0%)	2(100%)	1(50%)	1(12.5%)
Imipenem	IMI	≤19	0(0%)	2(100%)	0(0%)	2(25%)

4. Discussion

Hospital -acquired pneumonia is one of the main concerns of the intensive care unit of hospitals in Asian countries with record of high mortality rate. In the present study, the prevalence of HABP was 7.5%, which is less than those obtained in previous studies in India (9.4%), Spain (10.5%) and Bangladesh (50%) (Trivedi, Shejale, & Yeolekar, 2000; Alvarez-Lerma et al., 2007; Diouf et al., 2005). The low prevalence reported in this study could be due to differences in risk factors, medical experience and the characteristics of patients mentioned in Table 3 (Ilić & Marković-Denić, 2009; Hugheset al., 2005).

The present study also provides insight into the impact of bacterial Pneumonia on outcomes of Patients Admitted

to Intensive Care Units. In this study, it was shown that the leading bacterial pathogen in patient with Hospital-Acquired Bacterial Pneumonia were mainly Enterobacteriaceae (62.5%), nonfermenting bacilli (18.7%) and *S. aureus* (18.7%). In comparison with studies in other Asian countries on the most frequent bacteria in HAP, the present study showed an increasing incidence of *K. pneumoniae* in HAP infections (50% versus 25% in Philippine and 30.6% in Indonesia). In a study conducted in Korea, the isolation of *S. aureus* (30.7%) was more than that in the present study. However, a study conducted in China reported that *Acinetobacter* spp. isolation was lower as compared with the present study (16.2%). In Malaysia and Taiwan, the prevalence of *P. aeruginosa* have been determined as 21.9 and 10%, respectively which is higher than that obtained in the present study (6.3%) (Chung et al., 2011). However, these differences in results in the different geographical places is not so unexpected, but the emergence of antibiotic resistant bacteria, such as *K. pneumoniae* and *Acinetobacter*, point to the fact that it should be considered as a serious challenge.

The investigation of antibiotic resistance of nosocomial bacteria in this study showed that only *Pseudomonas* was susceptible to cephalosporins and carbapenems. *Acinetobacter* and *Klebsiella* were the resistant strains both to caphalosporins and carbapenems, indicating the presence of betalactamase and carbapenemase. These findings showed that *Acinetobacter*could emerge as an extremely drug resistant organism (XDR-AB), but these findings should be confirmed with molecular studies to determine the presence of metallo-β-lactamase (MBL) and OXA genes. Park et al. (Park et al., 2010) studied the *OXA* gene and found that the resistance was due to the upregulation of *OX* type carbapenemases. *K. pneumoniae* (Kp) producing carbapenemase (KPC) is also a big clinical challenge because treatment of their infections is difficult, and their blood stream infection is associated with high mortality. Clinicians are advised to control *K. pneumoniae* infections with caution and in combination with a carbapenem, tigecycline, and colistin (Tumbarello et al., 2012). An overview of these results is necessary for managing HAI, as improper control could result in increased mortality rate, treatment costs and reduction of life span.

Also, similar to the result obtained in this study, the highest rates of infection have been observed in individuals of 50 years and above, and this could be ascribed to weak immune system, which makes them more vulnerable to infection by opportunistic microorganisms in the hospital (Zolldann, Haefner, Poetter, &Buzello, 2003).

Furthermore, a lower mortality rate of HABP was observed in this study as compared with previous studies from an Asian country (34.4%) (Chung et al., 2011) and western countries (18.4-30.4%). Yang et al. (Yang et al.,2013) concluded that patients receiving ventilator assistance had lower mortality as a result of better airway protection,the same could be inferred to patients in this study. Only one fourth of patients with HABP had respiratory complications and eventually died, although 14 (87.5%) of them received ventilator assistance. However, it should also be noted that the mortality may be affected by other factors rather than the bacterial pneumonia such as organ failure or severity of illness. Certainly, bacterial infections are important in increasing mortality risk, thus *P. aeruginosa, A. baumanii*, and other multidrug-resistant organisms have been reported as a cause of high mortality and this cannot be attributed to the underlying disease alone(Rello& Torres,1996; Campbell et al.,1996). This study has several limitations. The prevalence of bacterial etiology and the antimicrobial resistance patterns of nosocomial pneumonia in the ICU, as well as the therapeutic protocols considered in this study are probably different in comparison with other hospitals. Beside, the limited patient population considered for this study makes it difficult to conclude based on the obtained results.

5. Conclusion

The results of the present study showed the emergence of multidrug resistantbacteria, such as *K. pneumoniae* and *A. baumannii*, in patients with HAP. Therefore, it is essential to develop new therapeutic approaches to bacterial infections in ICU patients. In addition, further studies on the epidemiology of health care associated infection and the preventive measures of the pathogens should be considered.

Acknowledgements

Authors would like to express their gratitude to Dr. KamyarVosoughi, Director of Medical Management of Social Security Organization in Hormozgan Province for his provision and support, and Dr. Fereshteh Bostan, who diagnosed and confirmed the diagnosis of the patients with HAP and managed them. Authors wish to thank the staff of the ICU in collecting the specimens and the staff of laboratory for helping to carry out the tests.

Financial Disclosure

None.

Competing Interests Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

Afkhamzadeh, A., Lahoorpour, F., Delpisheh, A., & Janmardi, R. (2011). Incidence Of Ventilator- Associated Pneumonia (Vap) And Bacterial Resistance Pattern In Adult Patients Hospitalised At The Intensive Care Unit Of Besat Hospital In Sanandaj. *Sjku, 16*(1), 20-26.

Alvarez-Lerma, F., Palomar, N.I., Olaechea, P., Otal, J.J., Insautti, J., & Cerda, E. (2007). National Study of Control of Nosocomial infection in Intensive Care units.Evaluative report of the years 2003-2005.*medIntensiva, 31*(1), 6-17. http://dx.doi.org/ 10.1016/S0210-5691(07)74764-2.

Campbell, G. D., Niederman, M. S., Broughton, W. A., Cleeson, K., Hornick, D. P., Lynch, J., ... Wunderink, C. R. (1996). Hospital-acquired pneumonia in adults: Diagnosis, assessment of severity, initial antimicrobial therapy and preventative strategies: A consensus statement. *Am J RespirCrit Care Med, 153*, 1711-1725. http://dx.doi.org/ 10.1164/ajrccm.153.5.8630626

Chung, D. R., Song, J.H., Kim, S. H., Thamlikitkul, V., Huang, S.G., Wang, H., … Peck, K. R. (2011). High Prevalence of Multidrug-Resistant Nonfermenters In Hospital-Acquired Pneumonia In Asia. *Am J RespirCrit Care Med, 184*, 1409-141. http://dx.doi.org/ 10.1164/rccm.201102-0349OC.

Dandagi, G. L. (2010). Nosocomial pneumonia in critically ill patients. *Lung India: Official Organ of Indian Chest Society, 27*(3), 149–153. http://doi.org/10.4103/0970-2113.68321

Defez, C. F., Peray, P., Bouziges, N., Gouby, A., Mahamat, A., Daurès, J. P., & Sotto, A. (2004). Risk Factors for Multidrug Resistant Pseudomonas Aeruginosa Nosocomial Infection. *Jhosp Infect, 57*, 209-216. http://dx.doi.org/10.1016/j.jhin.2004.03.022

Diouf, E., Beye, M. D., Diop, N. M., Kane, O., Seydi, A. A., Ndiaye, P. I., ... Sall, K. B. (2005). Nosocomial ventilator-associated pneumonia in a tropical intensive care unit.*Dakar medical, 51*(2), 81-88. [in French].

Fica, C. A., Cifuentes, D. M., &Hervé, E. B. (2011). Actualización Del Consenso "NeumoníaAsociada A VentilaciónMecánica".Primera Parte. AspectosDiagnósticos. *Rev Chilena Infect., 28*(2), 130-151. http://dx.doi.org/10.4067/S0716-10182011000200005

Katherason, G. S., Naing, L., Jaalam, K., I. Musa, K., Mohamad, N. A., Aiyar, S, … Ismail, A. (2009). Ventilator-Associated Nosocomial Pneumonia In Intensive Care Units In Malaysia. *The Journal of Infection In Developing Countries, North America, 3*(9), 704-710. http://dx.doi.org/10.3855/jidc.115

Ghazvini, K., Ghanaat, J., Jafarian, M., YazdanPanah, M., & Irani, N. (2005). Incidence Of Nosocomial Pneumonia And Bacterial Agents Causing This Infection In Intensive Care Unit In Qaem University Hospital In Mashhad. *Journal of Ilam University of Medical Sciences, 13*, 55-61. [In Persian]

Grundmann, H., Aires-De-Sousa Ai. M., Boyce, J., & Tiemersma, E. (2006). Emergence Resurgence of Meticillin-Resistant Staphylococcus AureusAs A Public Health Threat. *Lancet, 368*, 847-85. http://dx.doi.org/10.1016/S0140-6736(06)68853-3

Hughes, A. J., Ariffin, N., Huat, T. L., Molok, A. H., Hashim, S., Sarijo, J., Latif, A. N. H., … Kamarulzaman, A. (2005) .Prevalence of nosocomial infection and antibiotic use at a University Medical Center in Malaysia. *Infection Control Hospital Epidemiology, 26*, 100-104. http://dx.doi.org/10.1086/502494

Ilić, M., & Marković-Denić, L. (2009). Nosocomial infections prevalence study in a Serbian university hospital. *Vojnosanit Pregl, 66*(11), 868-875. http://dx.doi.org/10.2298/VSP0911868I

Ilić, M., & Marković-Denić, L. (2009).Nosocomial Infections Prevalence Study In A Serbian University Hospital .*Vojnosanit Pregl,66*(11), 868-875.http://dx.doi.org/10.2298/VSP0911868I

Kaoutar, B., Joly, C., Heriteau, F. L., & Barbut, F. (2004). Nosocomial Infections and Hospital Mortality: Aulticenter Epidemiological Study. *J Hosp, 58*, 268-275. http://dx.doi.org/10.1016/j.jhin.2004.06.006

Kawagoe, J. Y., Segre, C. A., Pereira, Cr., Cardoso, M. F., Silva, C.V., & Fukushima, J. T. (2001). Risk Factors For Nosocomial Infections In Critically Ill Newborns: A 5-Year Prospective Cohort Study. *Am J Infect Control, 29*,109-114.http://dx.doi.org/10.1067/mic.2001.114162

Koenig, S. M., & Truwit, J. D. (2006). Ventilator-Associated Pneumonia: Diagnosis, Treatment, and Prevention. *Clinical Microbiology Reviews, 19*(4), 637-657. http://dx.doi.org/10.1128/CMR.00051-05

Kuti, J. L., Shore, E., Palter, M., & Nicolau, D. P. (2009). Tackling Empirical Antibiotic Therapy For Ventilator-Associated Pneumonia In Your Icu: Guidance For Implementing The Guidelines. *SeminRespirCrit Care Med, 30*, 102-115. http://dx.doi.org/10.1055/s-0028-1119814

Masterton, R. G., Galloway, A., French, G., Street, M., Armstrong, J., Brown, E., … Wilcox, M. (2008). Guidelines For The Managementof Hospital-Acquired Pneumonia In The Uk: Report Of The Party On Hospital-Acquired Pneumonia Of The British Society For Antimicrobialchemotherapy. *J Antimicrob Chemother., 62*, 5-34. http://dx.doi.org/10.1093/jac/dkn162

Medell, M., Hart, M., Duquesne, A., Espinosa, F., &Valdés, R. (2013). Nosocomial Ventilator-Associated Pneumonia In Cuban Intensive Care Units: Bacterial Species And Antibiotic Resistance. *Medicc Rev., 15*(2), 26-29.

Park, Y. S., Lee, H., Lee, K. S., Hwang, S. S., Cho, Y. K., Kim, H. Y., … Kim, J. M. (2010). Extensively drug-resistant Acinetobacterbaumannii: risk factors for acquisition and prevalent OXA-type carbapenemases—a multicentre study. *International Journal of Antimicrobial Agents, 36*(5), 430-435. http://dx.doi.org/10.1016/j.ijantimicag.2010.06.049

Pileggi, C., Bianco, A., Flotta, D., Nobile, C. G., & Pavia, M. (2011). Prevention of ventilator-associated pneumonia, mortality and all intensive care unit acquired infections by topically applied antimicrobial or antiseptic agents: A meta-analysis of randomized controlled trials in intensive care units. *Critical Care, 15*(3), R155. http://dx.doi.org/10.1186/cc10285

Uvizl, R. V., Hanulik, V., Husickova, M., Sedlakova, H. M., & Adamus, M. O. (2011). Hospital-Acquired Pneumonia InIcu Patients. *Biomedical Papers ofThe Medical Faculty of Palacky University, 15*(4), 373-378. http://dx.doi.org/10.5507/bp.2011.067

Rea-Neto, A.., Youssef, N. C. M., Tuche, F., Brunkhorst, F., Ranieri, V. M., Reinhart, K., &Sakr, Y. (2008). Diagnosis of ventilator-associated pneumonia: a systematic review of the literature. *Critical Care, 12*(2), R56. http://dx.doi.org/10.1186/cc6877

Rello, J. (2007). Importance of Appropriate Initial Antibiotic Therapy and De-Escalation In The Treatment Of Nosocomial Pneumonia. *EurRespir Rev, 16*(103), 33-39. http://dx.doi.org/ 10.1183/09059180.00010302

Rello, J., & Torres, A. (1996). Microbial causes of ventilator-associated pneumonia. Paper presented at the *Seminars in Respiratory Infections, 11*, 24-31. Abstract retrieved from http://europepmc.org/abstract/med/8885060

Ronald, N. J. (2010). Microbial Etiologies Of Hospital-Acquired Bacterialpneumonia And Ventilator-Associated Bacterial pneumonia.*Etiologies of Habp and Vabp, 51*, 81-87. http://dx.doi.org/10.1086/653053

Sadeghi, M., Asghazadeh, S. A., Baratlu, A. R., & Montazeri, M. (2009). Antibiotic Resistance Pattern Of Gram Negative Bacillus Isolated From Respiratory Culture In Intensive Care Unit's Patients Of Yahyanejad Hospital. *Journal of Infectious Diseases And Tropical Medicine, 14*, 39-43.

Song, J. H., & Chung, D. R. (2010). Respiratory Infections Due To Drug-Resistant Bacteria.*Infect Dis Clin North Am, 24*, 639-653. http://dx.doi.org/10.1016/j.idc.2010.04.007

Trivedi, T. H., Shejale, S. B., & Yeolekar, M. E. (2000). Nosocomial pneumonia in medical intensive care unit. *J Assoc Physicians India, 48*(11), 1070-1073.

Tumbarello, M., Viale, P., Viscoli, C., Trecarichi, E. M., Tumietto, F., Marchese, A., … Bassetti, M. (2012). Predictors of Mortality in Bloodstream Infections Caused by KlebsiellapneumoniaeCarbapenemase–Producing K. pneumoniae: Importance of Combination Therapy. *Clinical Infectious Diseases, 55*(7), 943-950. http://dx.doi.org/10.1093/cid/cis588

Yang, Y. S., Lee, Y. T., Huang, T. W., Sun, J. R., Kuo, S. C., Yang, C. H. … Chang, F. Y. (2013). AcinetobacterBaumannii Nosocomial Pneumonia: Is The Outcome More Favorable In Non-Ventilated Than Ventilated Patients? *Bmc Infectious Diseases, 13*, 142. http://dx.doi.org/10.1186/1471-2334-13-142

Zolldann, D., Haefner, H., Poetter, C., & Buzello, S. (2003). Assessment of a selective surveillance method for detecting nosocomial infections in patients in the intensive care department. *Am J Infect Control, 3*, 261-265. http://dx.doi.org/10.1067/mic.2003.72