

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

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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 aeruginosa* (6.3%). The maximum antimicrobial resistance of gram negative bacteria was to Cefazolin (100%) and Ampicillin (84.6%), while antimicrobial resistance to Clindamycin, Azithromycin, Amoxicillin+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, Jafarian Yazdan Panah, & 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 HAP 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 (Biomerieux, 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 HAP (M:F 11:5, that is, men were 2.2 times more likely to suffer from HAP). In general, the incidence of HAP in this ward was 7.5%. The case fatality rate (CFR) of HAP was 25% (4/16) with an attributable mortality rate of 6.45% (4/62). Table 1 shows the clinical features of patients with HAP. The primary and final diagnosis, invasive procedure and underlying diseases of patients with HAP are shown in Table 2.

The frequency of isolated gram positive and gram negative bacteria form HAP was 18.75% (3/16) and 81.25%

(13/16), respectively. The most common isolated microorganisms were gram negative bacilli, primarily *Klebsiella pneumoniae* (50%), other isolated bacteria include *S. aureus* (18.7%), *Acinetobacter baumannii* (12.5%), *Escherichia coli* (12.5%) and *Pseudomonas aeruginosa* (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, Arterial catheterization, urethral catheterization, ventilation
2	Hypertension	Hypertension	No	Tracheostomy, Suction, venous catheterization, urethral catheterization, ventilation, ventricular shunt, intubation
3	Congestive Heart Failure	Bronchitis	Diabetes Hypertension	Tracheostomy, Suction, venous catheterization, urethral catheterization, intubation
4	Head Injury	Intracerebral hematoma	No	Tracheostomy, Suction, venous catheterization, ventilation
5	Organophosphate Poisoning	Organophosphate Poisoning	NO	Suction, venous catheterization, urethral catheterization, intubation, ventilation, CVP line
6	Sepsis	Adult Respiratory Distress Syndrome	Chronic Obstructive Pulmonary Disease	Suction, venous catheterization, urethral catheterization, intubation, ventilation,

7	Adult Respiratory Distress Syndrome	Adult Respiratory Distress Syndrome	No	venous catheterization, urethralcatheterization, intubation, ventilation,
8	Myocardial Infarction	Myocardial Infarction	Chronic Obstructive Pulmonary Disease	Suction, venous catheterization, urethralcatheterization, intubation, ventilation,
9	Sepsis	Sepsis	No	venous catheterization, urethralcatheterization, 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, urethralcatheterization, intubation, ventilation, CVP line
12	Head Injury/Myocardial Injury	Head Injury/Myocardial Injury	No	Suction, venous catheterization, urethralcatheterization, intubation, CVP line ventilation, Tracheostomy,
13	Head Injury	Head Injury	No	Suction, venous catheterization, urethralcatheterization, intubation, ventilation,
14	Head Injury	Head Injury	Diabetes	Suction, venous catheterization, urethral catheterization intubation, ventilation,
15	Chronic Obstructive Pulmonary Disease	Chronic Obstructive Pulmonary Disease	No	Suction, venous catheterization, urethralcatheterization, intubation, ventilation,
16	Myocardial Infarction	Myocardial Infarction	no	venous catheterization, urethral catheterization, intubation, ventilation, CVP line

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

Antibiotic/	Abbreviation	Break point	<i>P.aeruginosa</i> (1)	<i>A.baumannii</i> (2)	<i>E.coli</i> (2)	<i>K.pneumoniae</i> (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%)
Ciprofloxacin	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 HAP 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; Hughes et 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 cephalosporins 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. (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 HAP 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 HAP 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. baumannii*, 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 resistant bacteria, 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.

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Competing Interests Statement

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

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