Nosocomial Pneumonia in Patients Admitted to the Intensive Care Unit of a Tertiary Care Center in Mashhad, Northeast of Iran; an Etiologic Survey

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Abstract

Background: Hospital-acquired pneumonia (HAP) prevalence is related to patients' population and diagnostic methods. HAP incidence is reported in different studies from 9% to 46%. The current study aimed at evaluating the etiology of HAP in patients admitted to intensive care units (ICUs).

Methods: The patients admitted to ICU of Imam Reza hospital (a tertiary care and teaching hospital in Mashhad, Northeast of Iran) were evaluated for HAP based on the following criteria: fever, leukocytosis, purulent discharge, new radiologic findings, changes in O_2 saturation, and ventilator setting. Blood and endotracheal aspirates cultures were performed for all patients. Demographic characteristics were recorded in a checklist.

Results: Among the 88 adult patients enrolled in the current study, the most frequent radiologic finding was patchy infiltration in chest X-ray (71.6%). Mean age of the patients was 58 ± 20.1 years; mean hospital stay was 63 ± 40.8 days; mean interval between hospitalization and pneumonia development was 20.9 ± 16.8 days; and 41 patients (46.6%) died. *Acinetobacter* spp. were the most frequent microorganisms in purulent discharge and methicillin-resistant *Staphylococcus aureus* (MRSA) were the main bacteria isolated from blood culture.

Conclusions: Early diagnosis and appropriate antibiotic therapy can decrease HAP mortality and morbidity. The current study findings revealed that *Acinetobacter* app. were the most frequent cause of HAP in ICU patients in the studied center, which should be considered at the time of diagnosis and empirical antibiotics administration. Appropriate infection control and preventive measures should also be taken in ICUs to prevent HAP, especially against those caused by *Acinetobacter* spp.

Keywords: Hospital-Acquired Pneumonia, Ventilator-Associated Pneumonia, Nosocomial Infection, Nosocomial Pneumonia, Intensive Care Unit

1. Background

Hospital-acquired pneumonia (HAP) is an infection that involves patients, minimum 48 hours after admission to hospital. Ventilator-associated pneumonia (VAP) is a condition occurs 48 hours after admission to the intensive care unit (ICU) and endotracheal intubation (1, 2). Despite promotion in infection control strategies and antimicrobial treatments, HAP is still one of the most important causes of mortality and morbidity, and significantly increases the length and cost of hospitalization (3, 4).

It is estimated that HAP affects 1.7 million patients, causes US$28-33 billion financial loss, and leads to 99,000 deaths annually in the United States (5). HAP crude mortality rate is about 10% and increases in intubated patients to 20% - 60%. HAP mortality and morbidity is associated with patients' characteristics, microorganism pathogenicity and virulence, and treatment approach. HAP incidence varies from 5 to 10 episodes in 1000 admitted patients. VAP prevalence is related to patients' population and diagnostic methods. HAP frequency is significantly higher in ICUs and in surgical wards in comparison with internal medicine wards (6, 7), and its mortality rate is much more than those of other hospital-acquired infections. Mortality from HAP (including VAP) ranged 25% to 54% in various studies in Asia (6). HAP mortality rate might be related to underlying diseases and especially higher with resistant pathogens such as *Pseudomonas* spp., methicillin-resistant *Staphylococcus aureus* (MRSA), and *Acinetobacter* spp. (4, 6).

Pneumonia management is difficult in ICU patients due to their clinical and paraclinical features that can be attributed to various conditions and etiologies. Early HAP presents in the first four days of admission and microorganisms such as *Streptococcus pneumonia* and *Haemophilus influenza* are its most frequent causes. *S. aureus*, *Pseudomonas aeruginosa*, *Enterococcus* spp., and *Acinetobacter* spp. are the causes of late HAP onset (5).

Antimicrobial resistance is associated with higher mortality rate in HAP and VAP. On the other hand, complications such as pulmonary abscess, plural effusion, and meningitis occur in 40% of HAP cases that increase the mortality rate. Therefore, microorganism identification and antibiotic determination is very important in such patients and can reduce hospital mortality rate (4). Early diagnosis and appropriate antibiotic treatment decrease HAP mortality and morbidity. Awareness about the most frequent causes of HAP can help with the empiric antibiotic therapy (8, 9).

To the best of authors' knowledge, there is not enough and accurate evidence about demographic, etiologic, and prognostic factors in patients with HAP, especially in Mashhad, Iran, while management of these cases might be much easier with updated information about local epidemiological characteristics. The current study aimed at evaluating the HAP etiology in patients admitted to the ICU of a teaching hospital in Mashhad.

2. Methods

The current cohort study was designed by Mashhad University of Medical Sciences, and approved by the institutional ethical committee. Sample size was set to 88 subjects using NCSS (number cruncher statistical system) and PASS (Power Analysis and Sample Size) software.

2.1. Patient Selection

The current study prospective study was conducted in internal medicine, surgery, cardiac surgery, and infectious diseases ICUs in Imam Reza tertiary referral teaching hospital in Mashhad, Northeast of Iran from 2015 to 16. All patients enrolled in the current study were admitted to ICUs and suspected for HAP. HAP diagnostic criteria were clinical and paraclinical factors including fever, leukocytosis, purulent discharge, changes in radiologic infiltrations, and changes in oxygen demands or ventilator setup. Exclusion criteria were age under 17 years, neutropenia, hematologic malignancies, history of transplantation, and non-HAP complications diagnosis.

2.2. Study Design

Data were gathered using a checklist. The checklist had three parts: demographic information (age and gender), disease related data (admission ward, cause of admission, administered antibiotics, chest X-ray (CXR) report, ventilation duration, and sputum culture results as well as a one-month follow-up. Patients were examined daily for 30 days.

2.3. Statistical Analysis

Data were coded and transferred to SPSS (statistical package for the social sciences) version 16. Frequency of qualitative variables, as well as mean and standard deviation (SD) of quantitative data were reported. The relationship between variables was analyzed by Chi-square, the Fisher exact, and the Mann-Whitney tests.

3. Results

A total of 88 patients with HAP were enrolled in the current study, of which 47 were male and 41 female; Table 1 shows the characteristics of patients. There were no significant differences between expired and survived patients in terms of the studied variables (P < 0.05), except the age (P > 0.05). Thirty-seven (44.6%) patients had no underlying diseases, and the others had diabetes mellitus, ischemic heart diseases (IHD), and renal or liver disease. Eighty-four (95.5%) patients were intubated at the time of diagnosis, and others were intubated later. The most frequent radiologic finding was patchy infiltration in CXR (71.6%) (Table 3).

HAP caused by bacteria (Gram-negative (84.1%) and Gram-positive (15.9%) in all the subjects (P > 0.05). By culturing the respiratory specimens (endotracheal aspirates), the following bacteria were isolated: *Acinetobacter* spp., MRSA, *Klebsiella pneumoniae*, *P. aeruginosa*, methicillin-sensitive *Staphylococcus aureus* (MSSA), and *Enterococcus* spp. Blood culture was negative in 73 patients (83%), while pneumococcus, MRSA, *K. pneumoniae*, *Acinetobacter* spp., and *S. epidermis* were isolated from those of the others (Table 2). The frequency of bacterial isolates in blood and endotracheal aspirates cultures showed no statistically significant difference between expired and survived patients (P > 0.05).

Carbapenems were the most frequently administered antibiotics to the patients (n = 24, 27.9%), since most *Acinetobacter* spp., and other Gram-negative rods were multidrug resistant (MDR) and many were ESBL-producing (extended-spectrum beta-lactamases). Overall mortality rate at the end of the first month (four weeks) was 46.6% (41 patients).

Table 1. Characteristics of Patients with Hospital-Acquired Pneumonia[a]

Characteristic	Incidence
Gender	
Male	47 (53.4)
Female	41 (46.6)
Age, y	58.7 ± 20.1
Underlying diseases	
Diabetes mellitus	9 (10.2)
Ischemic heart diseases	17 (20.4)
Renal and liver diseases	20 (24.1)
Admission location	
Infectious diseases ICU	49 (55.7)
Surgery ICU	10 (11.4)
Internal medicine ICU	19 (21.6)
Cardiac surgery ICU	10 (11.4)
Duration of ICU stay, d	63 ± 40.8
Interval between admission and intubation, d	5.9 ± 1.1
Interval between admission and pneumonia manifestation, d	20.9 ± 16.8
WBC, cell/μL	12820 ± 6958

[a]Values are expressed as mean ± SD or No. (%).

Table 2. Bacteria Isolated from Patients with Hospital-Acquired Pneumonia

Bacteria Isolated from Specimen	%
Sputum	
Acinetobacter spp.	73.9
MRSA	11.4
Klebsiella pneumoniae	5.7
Pseudomonas aeruginosa	4.5
Staphylococcus aureus	3.4
Enterococcus spp.	1.1
Blood	
Pneumococcus	2.3
MRSA	5.7
Klebsiella spp.	3.4
Acinetobacter spp.	1.1
Staphylococcus epidermis	4.5

Abbreviation: MRSA, Methicillin-Resistant *Staphylococcus aureus*.

4. Discussion

Due to the absence of specific and sensitive clinical and laboratory standard tests the exact frequency of nosocomial pneumonia is unknown. Conventional criteria are de-

Table 3. The Chest X-ray Findings in Patients with Hospital-Acquired Pneumonia

Chest X-ray Finding	No. (%)
Patchy infiltration	63 (71.6)
Lobar consolidation	16 (18.2)
Multi-lobar consolidation	9 (10.2)

fined for its diagnosis; therefore, invasive methods such as tracheal lavage and pulmonary biopsy are rarely applied. HAP is one of the deadliest nosocomial infections, which has a great economic burden for patients and health system (10). Mechanical ventilation increases the risk of pneumonia (11). HAP can be diagnosed by finding organisms with bronchoscopy or aspiration. Another definition of HAP is based on clinical criteria including fever, leukocytosis, tracheal purulent discharge, and new and progressive infiltration, especially unilateral, in CXR (12).

Despite recent advances in preventive care and antibiotic therapy, HAP is remained as one of the most important causes of hospital mortality and morbidity with high cost burden. Therefore, determination of microbial etiology of HAP can help with the empirical antibiotic therapy. The current study aimed at evaluating patients admitted to ICUs and developed HAP.

In the current study, the most common microorganisms cultivated from respiratory secretions were *Acinetobacter* spp., MRSA, *K. pneumoniae*, *Pseudomonas* spp., *S. aureus*, and *Enterococcus* spp. In a study in Lebanon, the most frequent organisms in patients with HAP were also *Acinetobacter* and *Pseudomonas* species and 15% of Gram-negative bacilli were resistant to many antibiotics (13). A large multicenter study showed that *Acinetobacter* spp., *Pseudomonas* spp., *S. aureus* and *Klebsiella* spp. were the most common causes of HAP with high resistance to antibiotics (8). Salehifar et al. (14) revealed that *Acinetobacter* spp. and *S. aureus* were the main causes of HAP in Northern Iran. In Thailand, *Acinetobacter* spp. was the most frequent organism in patients with HAP (9). Thus, *Acinetobacter* spp. is the main cause of HAP in patients admitted to ICUs in Iran and many parts of the world.

Another study in Esfahan, Iran showed that coagulasenegative *Staphylococcus* spp., *S. aureus*, *Pseudomonas* spp., and *Klebsiella* spp. were more common in patients with HAP (15). This difference might be due to different local epidemiology, different patient populations and study designs, since the current study evaluated ICU admitted patients with HAP, but Japoni et al. (15) studied patients with VAP.

In the current study, 51 patients (57.9%) had underlying diseases, but Liu et al. (16) showed that 93% of patients with HAP had at least one underlying disease and 91% used at

least one antibiotic in the last three months. This might be due to various causes of ICU admission.

The mean age of the current study patients was 58 years, and the most frequent age group was 60-80 years (35.4%). In the study by Nadi et al. (17) the mean age of the patients was 51 years, while in the study by Shajari et al. (4) it was 61 years. These results showed that the mean age of ICU admitted patients was over 50 in most parts of Iran.

In the current study, the main radiologic finding was patchy infiltration, in comparison with the study by Parsa Yekta et al. (18) in which infiltrations in upper lob of right lung was more common. Radiologic manifestation and infiltration location can be useful to determine the causes of HAP. For instance, infiltration in upper lob of right lung is more frequent in patients lying in supine position for a long period.

In the current study, mean hospital stay was 63 days and mean interval between ICU admission and mechanical ventilation was five days, although the intervals were longer in patients died in the first month, this difference was not significant, while in a study the mean hospitalization was 13 days and was significantly shorter in survived cases (19). It seems that longer ICU stay and ventilator connection might associate with higher mortality rate.

Old age was the only factor related to higher mortality rate in the current study. Some studies confirmed that nasogastric and tracheal tubes could increase the risk of HAP and HAP-associated mortality (8). Nassaji et al. (20) showed that decreased level of consciousness and mechanical ventilation increase the risk of HAP in ICU patients.

Some studies revealed that *Acinetobacter* spp. infections correlated with higher mortality and morbidity rate and poor prognosis, due to antibiotic resistance (20).

In the current study, carbapenem was the most widely used antibiotic while in the study by Japoni et al. (15) carbapenem was the most common form of antibiotic. Salehifar et al. (14) showed that ceftazidime was used more frequently and most effective antibiotic on *Pseudomonas* spp. A study conducted in Hamadan, Iran reported a correlation between cephalosporin administration and hospital-acquired infections (17).

Hospital-acquired infections due to Gram-negative bacteria are of the most serious cases. *Acinetobacter* spp. has a great role in the infections such as pneumonia, bacteremia, urinary tract infections, and meningitis. These bacteria are resistant to various antibiotics and can be transmitted from patient to patient; hence, it is difficult to treat and eradicate it (11, 21).

Appropriate infection control strategies are one of the best methods to reduce *Acinetobacter* spp. and other infections in ICU patients. This goal can be achieved by hand washing strategies before and after nursing each patient or using gloves. Closed-suction of purulent discharge is another method to decrease the risk of infections in ICU patients (12, 22).

The current study did not evaluate the antibiotic resistant patterns in the study population, which was the main limitation of the study. In addition, the current study did not use invasive methods such as bronchoalveolar lavage to obtain respiratory secretions to culture.

4.1. Conclusion

Early diagnosis and appropriate antibiotic administration can decrease HAP mortality and morbidity. Awareness about the most frequent causes of HAP can help with the empiric antibiotic therapy. The current study findings revealed that *Acinetobacter* spp. were the most frequent causes of HAP in patients admitted to ICU; therefore, it should be considered before empirical antibiotic administration, particularly in severe cases and the elderly. Also, appropriate infection control and preventive measures should be taken in ICUs to prevent HAP, especially those caused by *Acinetobacter* spp.

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