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Hospital-acquired pneumonia in nonintensive care unit wards

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Aim: To determine the incidence, risk factors, etiology, and antibiotic susceptibility of hospital-acquired pneumonia (HAP) in nonintensive care units (non-ICU) and nonintubated adult patients.

Materials and methods: A prospective surveillance study was performed from January 2006 through December 2007 in the medical and surgical wards of the İzmir Teaching and Research Hospital.

Results: During the study period, data on 57,133 patients with a total of 413,515 patient-days were analyzed. A total of 106 HAP episodes occurred in 99 patients. The infection rate per 100 patients and per 1000 patient-days was found to be 0.2% and 0.3%, respectively. HAP episodes were detected mostly in medical wards (66%). The mean age of patients was 58.6 ± 15.9 and 73% of the patients were male. The most common intrinsic and extrinsic risk factors observed in patients with HAP, according to the first episode, were cardiovascular disease (47%), central nervous system disease (41%), malignancy (40%), hospitalization longer than 5 days (91%), antibiotic therapy (81%), previous endotracheal intubation (40%), nasogastric tubes (38%), and H2 receptor antagonist/antiacid (37%). Moreover, 109 microorganisms were isolated from 84% of HAP episodes. Overall, the most frequently isolated pathogens from HAP episodes were *Klebsiella pneumoniae* (23%), *Escherichia coli* (21%), and *Staphylococcus aureus* (18%). These were mostly multidrug-resistant. The crude mortality was found to be 25%.

Conclusion: Surveillance of HAP in non-ICU and nonintubated adult patients provides valuable guidance for empirical antimicrobial therapy and infection control measures for some wards.

Key words: Hospital-acquired pneumonia, non-ICU medical and surgical wards, risk factors, etiology, antibiotic susceptibility

Yoğun bakım dışı kliniklerde hastane kaynaklı pnömoni

Amaç: Yoğun bakım dışı kliniklerde entübasyon uygulanmayan erişkin hastalarda gelişen hastane kaynaklı pnömoni insidansının, risk faktörlerinin, etyolojinin ve antibiyotik duyarlılıklarının belirlenmesi.

Yöntem ve gereç: Ocak 2006-Aralık 2007 tarihleri arasında hastanemiz dahili ve cerrahi kliniklerine yatırılan hastalar, aktif prospektif sürveyans yöntemi ile izlendi.

Bulgular: Çalışma süresince, 57.133 hasta ve 413.515 hasta gününde, 99 hastada 106 nozokomiyal pnömoni atağı saptandı. Hastane kaynaklı pnömoni hızı 100 hasta ve 1000 hasta-gününe göre sırasıyla, % 0,2 ve % 0,3 olarak bulundu. Olguların % 66'sı dahili kliniklerinde yatmaktaydı. Hastane kaynaklı pnömoni olgularının yaş ortalaması 58.6 ± 15.9 (17-85) olup, % 73'ü erkekti. En sık saptanan intrensek ve ekstrensek risk faktörleri; kardiyovasküler hastalık (% 47), santral sinir sistemi hastalığı (% 41), malignite (% 40), beş günden fazla hastanede yatış (% 91), antibiyotik tedavisi (% 76), önceden endotrekeal entübasyon (% 40), nazogastrik tüp (% 38) ve H2 reseptör antagonist/antiasit (% 37) olarak saptandı. Atakların % 84'ünde 109 mikroorganizma izole edildi. En sık izole edilen etkenler sırasıyla *Klebsiella pneumonae* (% 23), *Escherichia coli* (% 21) ve *Staphylococcus aureus* (% 18) olarak bulundu. Bu mikroorganizmaların çoğunluğu çok ilaca dirençliydi. Kaba mortalite oranı % 25 olarak bulundu.

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Sonuç: Yoğun bakım dışı bazı kliniklerde hastane kaynaklı pnömoni sürveyansının yapılması, empirik antimikrobiyal tedavi ve gerekli infeksiyon kontrol önlemlerinin alınabilmesi için yararlı bulunmuştur.

Anahtar sözcükler: Hastane kaynaklı pnömoni, yoğun bakım dışı dahili ve cerrahi klinikler, risk faktörleri, etyoloji ve antibiyotik duyarlılığı

Introduction

Hospital-acquired pneumonia (HAP) is defined as pneumonia that occurs 48 h or more after admission and was not incubating at the time of admission, according to the guidelines of the Joint Committee of the American Thoracic Society and Infectious Diseases Society of America (1). HAP is usually the second or third most frequent nosocomial infection (1-3).

HAP is associated with significant mortality (1). In the literature, it has been reported that approximately 60% of all deaths from nosocomial infections are due to HAP (4). Besides mortality, HAP increases hospital stay by an average of 7 to 9 days per patient and results in significant economic cost (1).

HAP is the most common nosocomial infection among intensive care unit (ICU) patients. In ICUs, nearly 90% of all episodes of HAP occur during mechanical ventilation; this type of HAP is known as ventilator-associated pneumonia (VAP) (1).

Until recently, most studies of HAP have centered on VAP because of its high incidence and mortality (1). In contrast, there are limited data on HAP developing in nonintubated patients or on healthcare-associated pneumonia (HCAP), and so information about this issue is lacking (1,5-10). In the present study, we aimed to determine the incidence, risk factors, etiology, and antibiotic susceptibility of HAP in non-ICU and nonintubated adult patients.

Materials and methods

The hospital in which the study was performed is a 732-bed teaching hospital with approximately 30,000 admissions per year. The prospective study was performed in the medical and surgical wards of the hospital between January 2006 and December 2007. Laboratory- and patient-based active surveillance methods were used. HAP was defined according to the standard definition of the Center for Disease Control (11). Patients in the ICU who were mechanically ventilated were not included in the study.

During the study period, infection control nurses visited the patients' wards daily. To assess HAP, they investigated the medical and nursing notes, microbiology reports, temperature charts, and antibiotic treatment charts of each case in the wards. If a patient had symptoms and signs of infection, the nurses also consulted with the patient's doctors. They met with an infection control doctor weekly to assess the hospital-acquired infections. If a patient was determined to have HAP, he or she was also seen by chest and infectious disease specialists**.** Data collected from each HAP patient included: age, gender, date of hospitalization, reason for admission, underlying diseases, immunosuppression (chemotherapy and corticosteroids), previous antibiotic therapy, and use of H2 receptor antagonists or antacids. Previous admission to the ICU, invasive procedures (nasogastric tube, endotracheal intubation, mechanical ventilation, tracheotomy, etc.), surgical operations, data of onset, isolated microorganisms, susceptibility patterns, and outcomes were also recorded.

Bacterial isolates were identified by conventional methods, and determination of antimicrobial susceptibility was carried out using the disk diffusion agar method. Antimicrobial susceptibilities were determined according to the Clinical and Laboratory Standards Institute (12).

To calculate nosocomial infection rates, the number of patients in the medical and surgical wards and the total number of patient-days were collected each month. The overall HAP rates per patient and per patient-days were calculated by dividing the total number of HAP cases in the medical and surgical wards by the total number of medical and surgical patient wards (×100) and patient-days (×1000), respectively (13).

Statistical analysis was conducted by using Student's t-test for numeric variables and chi-square and Fisher's exact test for categorical variables. Statistical significance was set to $P < 0.05$.

Results

During the study period, data on 57,133 patients with a total of 413,515 patient-days were analyzed. A total of 106 HAP episodes occurred in 99 patients. The infection rates per 100 patients and per 1000 patient-days were found to be 0.2% and 0.3%, respectively. The wards in which HAP episodes were detected are listed in Table 1.

A total of 106 HAP episodes occurred: 2 patients from internal medicine and 1 patient from the neurology department each had 2 episodes of HAP, 2 patients from the neurology department each had 3 episodes of HAP, and 94 patients each had 1 episode. The demographic characteristics and the intrinsic and the extrinsic risk factors of the 99 patients according to the first HAP episode are listed in Table 2. The mean interval from hospital admission to the first HAP episode was 18.7 ± 14.4 days (range, 3 to 90 days).

Table 1. Wards in which HAP episodes were detected (n = 106).

Departments	Number of episodes (%)
Medical	72 (68)
Internal medicine	41 (39)
Neurology	31 (29)
Surgical	34 (32)
Neurologic surgery	14 (13)
General surgery	12 (11)
Transplant unit	5 (5)
Ear, nose, and throat	3 (3)

Patients with HAP in medical wards were more likely to have greater comorbidity (cardiovascular disease and central nervous system disease), older age, neutropenia, immunosuppression, previous admission to the ICU, and longer stays than patients with HAP in surgical wards ($P < 0.05$). Comparisons of the demographic characteristics and some intrinsic and extrinsic risk factors between patients in medical wards and patients in surgical wards with HAP are listed in Table 3.

Table 2. The demographic characteristics and intrinsic and extrinsic risk factors of the 99 patients according to the first HAP episode (n = 99)*.

Demographics and intrinsic and extrinsic risk factors	Number of cases (%)
Age 58.7 ± 15.7**	
Gender (male)	72 (73)
Underlying diseases	92 (93)
Cardiovascular disease	47 (47)
Central nervous system disease	41 (41)
Malignancy	40 (40)
Diabetes mellitus	36 (36)
Neutropenia	28 (28)
Depressed level of consciousness	20 (20)
Chronic renal failure	20 (20)
Chronic obstructive lung disease	15 (15)
Trauma	5 (5)
Acute abdomen	5 (5)
Hepatic cirrhosis	2 (2)
Idiopathic thrombocytopenic purpura	1 (1)
Hospitalization >5 days	90 (91)
Antibiotic therapy	80 (81)
Previous endotracheal intubation	40 (40)
Nasogastric tube	38 (38)
H2 receptor antagonist and/or antacid	37 (37)
Surgery	34 (34)
Immunosuppression	32 (32)
Tracheotomy	9 (9)
Previous admission to ICU	6 (6)

*Patients may have multiple risk factors.
**Mean ± SD

A total of 109 microorganisms were isolated from 89 episodes of HAP. Twenty (22.47%) of these 89 HAP episodes were polymicrobial. Gram-negative species accounted for most of the monomicrobial infections, whereas a combination of *Staphylococcus aureus* and gram-negative species were the primary cause of polymicrobial infections. Overall, the most frequently isolated agents from HAP episodes were *Klebsiella pneumoniae* (23%), *Escherichia coli* (21%), *Staphylococcus aureus* (18%), *Pseudomonas aeruginosa* (12%), and *Acinetobacter baumannii*

Table 3. Comparison of the demographic characteristics and some intrinsic and extrinsic risk factors between patients in medical wards and patients in surgical wards with HAP.

Factor	Patients in medical wards, n = 65	Patients in surgical wards, n = 34	P-value
Age, year	63.6 ± 12.08*	49.7 ± 17.8*	<0.05
Gender (male)	47	25	NS
Cardiovascular disease	41	6	<0.05
Central nervous system disease	34	7	<0.05
Malignancy	29	11	NS
Diabetes mellitus	23	13	NS
Neutropenia	28	0	<0.05
Depressed level of consciousness	14	6	NS
Chronic renal failure	15	5	NS
Chronic obstructive lung disease	11	4	NS
The mean interval from hospital admission to the first HAP episode	20.9 ± 12.8*	14.5 ± 16.3*	<0.05
Antibiotic therapy	46	34	<0.05
Nasogastric tube	20	18	<0.05
H2 receptor antagonist and/or antacid	23	14	NS
Immunosuppression	28	4	<0.05
Previous admission to ICU	6	0	<0.05

NS: not significant
*Mean ± SD

(11%). These microorganisms were found to be the predominant causative microbiologic agents in both the immunosuppressive patients and the other patients. The percentages of the microorganisms isolated from HAP episodes are listed in Table 4. Sixty percent of *K. pneumoniae* and 57% of *E. coli* were ESBL-producing strains. Seventy percent of *S. aureus* were methicillin-resistant. Eight percent of *P. aeruginosa* and 58% of *A. baumannii* were carbapenem-resistant.

Twenty-five patients died of HAP and the crude mortality from HAP in 99 patients was found to be 25%. The demographic characteristics, some intrinsic and extrinsic risk factors, inappropriate initial antibiotic therapy, and the presence of multidrug-resistant (MDR) pathogens were compared between survivors and non-survivors. Non-survivors were more likely to have had inappropriate initial antibiotic therapy and multidrug-resistant (MDR) pathogens than survivors ($P < 0.05$).

Table 4. Percentage of the microorganisms isolated from HAP episodes (n = 109).

Microorganisms	Percentage
Klebsiella pneumoniae	23
Escherichia coli	21
Staphylococcus aureus	18
Pseudomonas aeruginosa	12
Acinetobacter baumannii	11
Stenotrophomonas maltophilia	5
Enterobacter cloacae	5
Coagulase negative staphylococci	4
Streptococcus pneumoniae	1
Proteus mirabilis	1

Discussion

Cumulative incidence rates for HAP were estimated in the range of 0.5% to 1% cases per 100 patients and a rate of 0.8 cases per 1000 patient-days for U.S. hospitals, with the incidence increasing by as

much as 6- to 20-fold in mechanically ventilated patients (14). Although the incidence of HAP was higher in intubated patients, it was reported that around half of all cases were detected outside of the ICU (6). In a prospective multicenter study of 12 Spanish academic hospitals evaluating HAP in patients admitted to conventional medical, surgical, and trauma wards, the incidence of HAP ranged from 1.3 to 5.9 cases per 1000 hospital admissions, with a mean of 3.1 ± 1.4 per 1000 hospital admissions (5). In a study from Japan, the incidence rate of HAP in nonventilated patients was estimated at 0.9% per 100 patients (8). The incidence rates in ICU and in non-ICU patients reported from a Turkish study were 9.5% and 0.5%, respectively (10). In our study, the infection rate per 100 patients and per 1000 patient-days for HAP in medical or surgical wards was found to be 0.2% and 0.3%, respectively. These results show that there may be variations in the rates of infections in nonventilated general ward patients among hospitals because of the characteristics of the patient population and the hospital setting.

Several studies have established a number of risk factors for the development of HAP in nonventilated patient populations. These risk factors are: advanced age, male gender, severity of illness, chronic lung disease, trauma/head injury, depressed level of consciousness, poor nutritional status, coma, impaired airway reflexes, neuromuscular disease, obesity, endotracheal intubation, nasogastric tube, bronchoscopy, immunosuppressive therapy, thoracic or upper abdominal surgery, duration of surgery, duration of hospitalization, large-volume aspiration, oropharyngeal colonization with gram-negative bacilli, antibiotic therapy, reflux esophagitis, and previous pneumonia (5,14,15). The risk factors for HAP found in our study were mostly in accordance with those previously reported (5,14,15). The intrinsic risk factors observed in this study are as follows: most patients were male; 56% of patients were 60 years or older; and 92% had comorbidity, primarily including cardiovascular disease, cerebrovascular disease, malignancies, and diabetes mellitus. The extrinsic risk factors were prolonged hospitalization and antibiotic usage in most of the cases, instrumentation (endotracheal intubation in 40% of the cases and a nasogastric tube in 38% of the cases), H2 receptor antagonist and/or antacid usage in 37% of the cases, and surgery and immunosuppression in 33% of the cases.

In the present study, a particularly great number of HAP episodes occurred in medical wards. This result was similar to those in the Spanish multicenter study, but contrary to others reported (16,17). The explanation for our finding could be that, compared with the patients with HAP in surgical wards, those in medical wards were older patients and had greater comorbidity, neutropenia, immunosuppression, previous admission to the ICU, and longer stays.

Early-onset bacterial HAP occurs during the first 4 days of the hospital stay and is more frequently caused by *Streptococcus pneumonia, Haemophilus influenzae*, or methicillin-susceptible *S. aureus*. Conversely, late-onset HAP occurs after 4 days and is more commonly caused by *Klebsiella, Acinetobacter* spp., *P. aeruginosa*, or methicillin-resistant *S. aureus* (MRSA) (17,18). Few data are available about bacteriology in patients with HAP and HCAP who are not mechanically ventilated (1,19). In the Spanish multicenter study, although most of the patients were hospitalized for more than 5 days, the most frequent pathogens were *S. pneumoniae*, *L. pneumophila*, *Aspergillus* spp., *P. aeruginosa*, and several *Enterobacteriaceae* species (5). In a recent study of 10 Asian countries (20), MRSA, *Acinetobacter* species, ESBL-producing *E. coli* and *Klebsiella,* and *P. aeruginosa* were found to be the most common pathogens causing HAP and VAP. According to prospectively collected hospital-wide surveillance data at the University of North Carolina, in general, the bacteriology of nonventilated patients was similar to that of ventilated patients, including infection with MDR pathogens such as MRSA, *P. aeruginosa*, *Acinetobacter* species, and *K. pneumoniae.* It was also reported that some organisms like MRSA and *K. pneumoniae* were more common in nonventilated than in ventilated patients, whereas *P. aeruginosa, Stenotrophomonas maltophilia*, and *Acinetobacter* species were more common in patients with VAP (19). Similarly to the Asian and University of North Carolina studies, in this study, the most commonly isolated pathogens from HAP episodes in the medical and surgical wards were *K. pneumoniae, E. coli, S. aureus, P. aeruginosa,* and *A. baumannii*, and those were mostly MDR. Emergence of drug-resistant

pathogens could be related to prior inappropriate antibiotic use such as overly frequent use or misuse of antibiotics, severity of underlying diseases, long duration of hospitalization, and lack of effective hospital infection control in these units.

The crude mortality rates reported for HAP, including VAP, have ranged between 30% and 88.9% (1,9). However, it was reported that many of these patients with HAP died of their underlying diseases rather than pneumonia (1). In the present study, the crude mortality rate was found to be 25%. This was lower than in some other studies (8,9), whereas it was in accordance with the Spanish multicenter study (5). It has been stated that the absence or presence of risk factors for MDR pathogens should be initially questioned for better outcomes and administration of early, appropriate antibiotic therapy in adequate doses; according to local surveillance data, this has been associated with lower mortality rates (1).

In summary, this is one of the few studies of HAP in general medical and surgical wards in nonventilated patients as far as we know. HAP occurred mainly in general medical ward patients. Most patients were old and had comorbidity, prolonged hospitalization, and antibiotic usage. *Klebsiella pneumoniae*, *Escherichia coli*, and *Staphylococcus aureus* were identified as the most common organisms. These were mostly MDR. We think that surveillance of HAP in non-ICU and nonintubated adult patients provides valuable guidance for empirical antimicrobial therapy and infection control measures for some wards.

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