

A Worldwide Perspective of Nursing Home-Acquired Pneumonia Compared With Community-Acquired Pneumonia

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BACKGROUND: Nursing home-acquired pneumonia (NHAP) is the leading cause of death among long-term care patients and the second most common cause of transfers to acute care facilities. The aim of this study was to characterize the incidence, microbiology, and outcomes for hospitalized patients with community-acquired pneumonia (CAP) and NHAP. **METHODS:** A secondary analysis of 5,160 patients from the Community-Acquired Pneumonia Organization database was performed. World regions were defined as the United States and Canada (I), Latin America (II), and Europe (III). **RESULTS:** From a total of 5,160 hospitalized patients with CAP, NHAP was identified in 287 (5.6%) patients. Mean age was 80 y. NHAP distribution by region was 6% in region I, 3% in region II, and 7% in region III. Subjects with NHAP had higher frequencies of neurological disease, diabetes mellitus, congestive heart failure, and renal failure than did subjects with CAP ($P < .001$). ICU admission was required in 32 (12%) subjects. Etiology was defined in 68 (23%) subjects with NHAP and 1,300 (27%) with CAP. The most common pathogens identified in NHAP included *Streptococcus pneumoniae* (31%), *Staphylococcus* species (31%), and *Pseudomonas aeruginosa* (7%). Presentation of NHAP more frequently included pleural effusions (34% vs 21%, $P < .001$) and multilobar involvement (31% vs 24%, $P < .001$). Thirty-day hospital mortality was statistically greater among subjects with NHAP than among those with CAP (42% vs 18%, $P < .001$). **CONCLUSIONS:** Worldwide, only a very small proportion of hospitalized patients with CAP present with NHAP; the poor outcomes for these patients may be due primarily to a higher number of comorbidities compared with patients without NHAP. *Key words:* pneumonia; respiratory infections; clinical epidemiology; quality of life; nursing homes. [Respir Care 2014;59(7):1078–1085. © 2014 Daedalus Enterprises]

Introduction

In many countries, the aging of the population has led to increases in the number of disabled elderly persons, many of whom reside in nursing homes. It is estimated that, over

the next 30 y, 40% of adults will spend some time in a long-term care facility before dying.¹

Nursing home-acquired pneumonia (NHAP) is the second most common infection among long-term care patients and is responsible for the majority of transfers to emergency departments.² More than 4 million NHAP cases are reported annually at a median incidence rate of 1–3.2 per 1,000 patient-days and 600,000 emergency department admissions. Moreover, the mortality rates associated with

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NHAP are also higher than those associated with community-acquired pneumonia (CAP) and range from 5 to 40%.²

There is little agreement, however, about the approach to managing NHAP. Patients with NHAP often suffer from more severe disease, with many comorbidities and functional status as the major determinants of survival.³ The appropriate management of NHAP remains questionable because of the controversial status of its microbial etiology. Data from the United States⁴⁻⁶ indicate an excess of multidrug-resistant (MDR) pathogens in patients with NHAP, but studies from Europe do not confirm this.⁷⁻⁹ Furthermore, the term NHAP does not have the same meaning for all countries, and this could explain discrepancies observed in patients' comorbidity patterns (especially aspiration), microbial etiology, diagnostic and treatment capabilities, and management policies.

In an attempt to investigate some of the controversies in the field of NHAP, we performed a secondary analysis of the Community-Acquired Pneumonia Organization (CAPO) database¹⁰ to evaluate the frequency of NHAP in hospitalized patients with CAP in different regions of the world and to compare severity, microbial patterns, and outcomes between the two groups of hospitalized subjects.

Methods

The CAPO Database

This database contains information regarding the management of 5,160 patients with CAP from 43 hospitals in 12 countries from June 2001 through September 2009. The study was approved by an ethics committee in each country, and informed consent was waived because this was a retrospective observational study. In each participating center, primary investigators randomly selected one or more subjects from a list of hospitalized patients with a diagnosis of CAP. Data were collected on a case report form and then entered into a computer and transferred electronically to the CAPO coordinating center at the University of Louisville Clinical and Translational Research Support Center (Louisville, Kentucky). A sample of the data collection form is available at <http://www.caposite.com>. Validation of data quality was performed at the study center before each case was entered into the CAPO database.

The collected specimens included oropharyngeal swabs for polymerase chain reaction and culture for virus and atypical pathogens; sputum and blood for culture; acute and convalescent serum samples for antibody titer determination for *Mycoplasma pneumoniae* (acute immunoglobulin (Ig) G titer > 1:64, IgM titer > 1:16), *Chlamydia pneumoniae* (acute IgG titer > 1:512, IgM titer > 1:10), and *Legionella pneumophila* (acute IgG, IgM, or IgA titer > 1:256); or a 4-fold increase in either IgG or IgM in the convalescent specimen by immunofluorescent antibody as-

QUICK LOOK

Current knowledge

Nursing home-acquired pneumonia (NHAP) is the leading cause of death among long-term care patients and the second most common reason for readmission to acute care facilities.

What this paper contributes to our knowledge

Worldwide, only a very small proportion of hospitalized community-acquired pneumonia patients present with NHAP. Poor outcomes are due primarily to a higher number of comorbidities compared with patients without NHAP.

say. Urine specimens for *L. pneumophila* type 1 antigen detection and *S. pneumoniae* antigen were also collected. The samples were all collected according to the doctor's decisions and as part of each center's microbiological workup.

Definitions

Subjects were considered to have definitive CAP if they met the criteria by having a new pulmonary infiltrate on chest radiograph at time of hospitalization plus at least one of the following: (1) a new or increased cough, (2) an abnormal temperature (< 35.6°C or > 37.8°C), or (3) an abnormal serum leukocyte count (leukocytosis, left shift, or leukopenia) as defined by local laboratory values.

The cause of CAP was declared if one of the following conditions was met: (1) positive findings for a bacterial pathogen in blood cultures or (2) pathogen from endotracheal aspirate, bronchoscopy sample (protected brush or lavage), pleural fluid, or sputum cultures. Sputum cultures were restricted to sputum samples according to local hospital microbiology laboratory policy (eg, specimens must have < 25 squamous epithelial cells).

Severity of disease was evaluated using the Pneumonia Severity Index and CURB-65 (confusion, urea nitrogen, breathing frequency, blood pressure, ≥ 65 y of age) score. Clinical stability was defined following the American Thoracic Society guidelines for CAP,¹ and the criteria for clinical stability were evaluated daily during the first 7 d of hospitalization. In-hospital all-cause mortality was defined as the total mortality during hospitalization. CAP-related mortality was defined as death due primarily to pulmonary infection during hospitalization.

Study regions were defined as United States/Canada (region I), Latin America (region II), and Europe (region III), as has been done in a previous study by CAPO investigators.¹⁰

NURSING HOME-ACQUIRED COMPARED WITH COMMUNITY-ACQUIRED PNEUMONIA

Table 1. Incidence of NHAP

| | Globally | United States/ Canada (Region I) | Latin America (Region II) | Europe (Region III) |
|--------------------|--------------|--|---------------------------------|------------------------|
| CAP, <i>n</i> (%) | 4,873 (94.4) | 1,534 (94.1) | 1,383 (97.0) | 1,900 (92.8) |
| NHAP, <i>n</i> (%) | 287 (5.6) | 97 (5.9) | 43 (3.0) | 147 (7.2) |

NHAP = nursing home-acquired pneumonia
CAP = community-acquired pneumonia

NHAP is included under the concept of health care-associated pneumonia,⁶ referring only to those subjects who presented with pneumonia at the emergency departments and who also resided in a nursing home or long-term care facility. These subjects may have received intravenous antibiotics prior to admission, but we do not have data for all the subjects. The other risk factors for health care-associated pneumonia are not included in the NHAP group of subjects (hospitalization for ≥ 2 d in the preceding 90 d, family member with multidrug-resistant pathogen, chronic dialysis within 30 d, and home wound care).

Statistical Analysis

Categorical variables were described with counts and percentages. For continuous variables, the mean \pm SD was presented. Relationships between categorical variables were studied using the chi-square test or Fisher exact test when necessary. Comparison of continuous variables between 2 groups was carried out using the *t* test for unpaired data.

Univariate and multivariate logistic regression analyses were performed to predict 30-d mortality (dependent variable). In the logistic regression models, we adjusted for region. The Hosmer-Lemeshow goodness-of-fit test was performed to assess the overall fit of the models.

All tests were two-tailed, and significance was set at 5%. All analyses were performed using SPSS 18.0 (SPSS, Chicago, Illinois).

Results

During the study period, 5,160 adults with pneumonia were reviewed; 287 (5.6%) had NHAP. The proportions of NHAP among CAP subjects for each region of the world are depicted in Table 1.

Demographics

The characteristics of subjects with NHAP and CAP are compared in Table 2. Subjects with NHAP were older (80.4 ± 13.5 y vs 63.8 ± 18.9 y, $P < .001$), with 87.1%

Table 2. Characteristics of Subjects

| Variables | CAP (<i>n</i> = 4,817) | NHAP (<i>n</i> = 287) | <i>P</i> |
|---|----------------------------|---------------------------|----------|
| Age, mean \pm SD, y | 63.8 \pm 18.9 | 80.4 \pm 13.5 | < .001 |
| Gender, male, <i>n</i> (%) | 2,927 (60.8) | 137 (47.7) | < .001 |
| Smoking status, <i>n</i> (%) | | | .001 |
| Current | 572 (26.5) | 14 (15.7) | |
| Ex-smokers | 700 (32.4) | 20 (22.5) | |
| Nonsmokers | 887 (41.1) | 55 (61.8) | |
| Liver disease, <i>n</i> (%) | 279 (5.9) | 13 (4.6) | .37 |
| Neurological disease, <i>n</i> (%) | 509 (10.7) | 104 (36.4) | < .001 |
| COPD, <i>n</i> (%) | 1,230 (25.5) | 79 (27.5) | .45 |
| Cancer, <i>n</i> (%) | 470 (9.9) | 31 (10.9) | .57 |
| HIV infection, <i>n</i> (%) | 214 (4.4) | 2 (0.7) | .002 |
| Diabetes mellitus, <i>n</i> (%) | 839 (17.6) | 64 (22.5) | .035 |
| Congestive heart failure, <i>n</i> (%) | 848 (17.8) | 78 (27.5) | < .001 |
| Renal disease, <i>n</i> (%) | 507 (10.7) | 53 (18.7) | < .001 |
| Cerebrovascular disease, <i>n</i> (%) | 618 (13) | 125 (44) | < .001 |
| Aspiration, <i>n</i> (%) | 253 (5.3) | 57 (20) | < .001 |
| Prior admission for CAP, <i>n</i> (%) | 404 (8.5) | 40 (14.1) | .001 |
| Time from symptoms until presentation, mean \pm SD d | 5.6 \pm 5.8 | 4 \pm 4.9 | .009 |
| Prior antibiotics, <i>n</i> (%) | 783 (16.3) | 54 (18.9) | .24 |

CAP = community-acquired pneumonia
NHAP = nursing home-acquired pneumonia
HIV = human immunodeficiency virus

> 65 y. Subjects with NHAP were more often women, smoked less frequently, and had greater comorbidity compared with patients with CAP.

In the NHAP group, a higher proportion of subjects in region III had cerebrovascular disorders (59% vs 37% vs 24.7% for II and I, $P < .001$), and more subjects in region II had congestive heart failure (42% vs 21.6% vs 27% for II [$P < .001$], I [$P = .72$], and III [$P = .002$], respectively) and neurological disease (58% vs 26% vs 37% for II, I, and III, respectively, $P < .001$). At the time of admission, more NHAP compared with CAP subjects had been hospitalized for CAP in the previous year (14.1% vs 8.5%, $P = .001$).

Etiology

Etiology was defined in 68 (24%) subjects with NHAP and 1,333 (27%) subjects with CAP (Table 3). Blood cultures positive for pathogens considered causative of pneumonia were found in 1,366 subjects (35%), and sputum culture results were positive for 135 subjects (4%) in the cohort. In subjects with NHAP, 68 blood cultures and 14 sputum culture samples were positive for etiologic pathogen.

Overall, in subjects with NHAP, *S. pneumoniae* and *Staphylococcus* species (methicillin-resistant *Staphylococ-*

Table 3. Etiological Diagnosis

| | CAP (n = 4,817), n (%) | NHAP (n = 287), n (%) | P |
|---------------------------------|------------------------------|-----------------------------|--------|
| Pathogen detected | 1,333 (28%) | 68 (23%) | .18 |
| Mixed | 124 (2.5) | 14 (5) | .02 |
| <i>Streptococcus pneumoniae</i> | 451 (37) | 17 (32) | .39 |
| <i>Staphylococcus aureus</i> | 19 (1.6%) | 3 (5.6%) | .064 |
| MRSA | 38 (3) | 9 (17) | < .001 |
| MSSA | 40 (3) | 6 (11) | .01 |
| GNB | 150 (12) | 11 (20) | .10 |
| <i>Moraxella catarrhalis</i> | 28 (2.3) | 3 (5.6) | .14 |
| <i>Haemophilus influenzae</i> | 87 (7) | 0 | .047 |
| <i>Mycoplasma pneumoniae</i> | 30 (2.5) | 0 | .64 |
| <i>Chlamydia pneumoniae</i> | 11 (1) | 0 | > .99 |
| <i>Legionella pneumophila</i> | 61 (5) | 2 (3.7) | .65 |
| <i>Klebsiella pneumoniae</i> | 38 (3) | 0 | .40 |
| <i>Pseudomonas aeruginosa</i> | 50 (4) | 4 (7.4) | .29 |
| <i>Escherichia coli</i> | 19 (1.6) | 2 (3.7) | .25 |
| <i>Proteus</i> species | 2 (0.2) | 2 (3.7) | .01 |
| Influenza A virus | 228 | 1 | < .001 |

CAP = community-acquired pneumonia
 NHAP = nursing home-acquired pneumonia
 MRSA = methicillin-resistant *S. aureus*
 MSSA = methicillin-sensitive *S. aureus*
 GNB = Gram-negative bacteria

cus aureus [MRSA] and methicillin-sensitive *S. aureus*) were the most frequent causative pathogens. *Staphylococcus* species and especially MRSA were the most frequent pathogens in subjects with NHAP in region I (29.2% [$P < .001$] vs 12.5% [$P = .005$] vs 4.5% [$P = .61$]). Apart from *L. pneumophila* (two cases) in region III, atypical pathogens were rarely found in subjects with NHAP.

Pneumonia with polymicrobial etiology was more frequent in subjects with NHAP than in those with CAP, especially in region I (5.2% vs 3.1%, $P = .01$).

Severity Assessment

NHAP was associated with more severe pneumonia, assessed according to the Pneumonia Severity Index (137 ± 35.4 vs 87.1 ± 43.8 , $P < .001$). The proportion of subjects classified as CURB-65 classes 3–5 was ~4-fold higher in the NHAP group (14.6% vs 4%, $P < .001$). The severity indices for regions I–III are presented in Table 4.

Patients with NHAP presented more frequently with confusion (41.1% vs 12.8%, $P < .001$), such as with multilobar infiltration (31% vs 24.2%, $P = .01$) and with pleural effusion (28.2% vs 19.3%, $P < .001$).

The presentation of NHAP was more severe in Europe, with more patients (20.4%) belonging to CURB65 3–5 classes instead of 9.3% in Latin America and 8.3% in the

United States ($P < .001$, $P = .2$, and $P < .001$, respectively).

Outcomes

Generally, clinical stability was reached after a mean of 4.8 ± 2.5 d of hospitalization. The mean time to clinical stability was 5.9 ± 2.5 d for subjects with NHAP compared with 4.7 ± 2.5 d for those with CAP ($P < .001$). The mean hospital stay of the cohort was 10 ± 11 d (Table 5).

Similar percentages of subjects in both groups required ICU admission (11.9% vs 11.1%, $P = .70$). A higher proportion of subjects with NHAP were admitted to the ICU in region II than in the other parts of the world (28% vs 14.4% vs 4% for II [$P = .09$], I [$P = .92$], and III [$P = .40$], respectively), although the CAP-related mortality was even higher in these subjects (32.6% vs 10.3% vs 17% for II, I, and III, respectively, $P < .001$).

The overall hospital mortality rate was 9.3%, with NHAP mortality significantly higher than CAP mortality (26.1% vs 8.3%, $P < .001$). Additionally, the 1-month mortality was even higher for subjects with NHAP (41.5% vs 18.1%, $P < .001$) compared with those with CAP.

Predictors of 30-d Mortality

The multivariate analysis revealed that sex, neoplastic disease, cerebrovascular disease, renal disease, neurological disease, aspiration, breathing frequency > 30 breaths/min, multilobar pneumonia, and NHAP were independently associated with increased 30-d mortality.

Discussion

The most important findings of this comparative report of NHAP are as follows: (1) Subjects with NHAP constituted only 5% of hospitalized CAP patients in the CAPO database. (2) Although they presented with more severe pneumonia than did CAP subjects, NHAP subjects received ICU care with the same frequency. (3) Comparing regions, the presentation of NHAP was more severe in Latin America, the proportion of subjects admitted to the ICU was higher, and mortality was also highest. (4) *S. pneumoniae* was the most frequent pathogen in both groups in all regions of the world except the United States and Canada, where MRSA was the prominent microorganism.

Presentation and Severity

Subjects with NHAP presented as expected with more comorbidities, especially with higher frequency of aspiration as a consequence of neurological disorder (eg, dementia, Alzheimer disease, or psychotropic medications) and mental confusion as a crucial symptom.

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Table 4. Severity of CAP-NHAP by Regions

| Severity Indices | Globally (CAP, <i>n</i> = 4,817; NHAP, <i>n</i> = 287) | Latin America (CAP, <i>n</i> = 1,383; NHAP, <i>n</i> = 43) | United States/Canada (CAP, <i>n</i> = 1,534; NHAP, <i>n</i> = 97) | Europe (CAP, <i>n</i> = 1,900; NHAP, <i>n</i> = 147) |
|----------------------------------|--|--|---|--|
| Pneumonia Severity Index | | | | |
| CAP | 87 | 80.3 ± 45.1 | 84.2 ± 43.0 | 94.5 ± 42.5 |
| NHAP | 137 | 147.1 ± 37.1 | 128.5 ± 32.0 | 139.7 ± 36.0 |
| <i>P</i> | < .001 | < .001 | < .001 | < .001 |
| CURB-65 | | | | |
| <i>P</i> | < .001 | .037 | < .001 | < .001 |
| Classes 0–1 | | | | |
| CAP, <i>n</i> (%) | 4,337 (90) | 1,235 (89.5) | 1,474 (96.2) | 1,572 (83.1) |
| NHAP, <i>n</i> (%) | 237 (83) | 38 (88.4) | 89 (91.8) | 164 (74.8) |
| <i>P</i> | < .01 | .83 | .031 | .01 |
| Class 2 | | | | |
| CAP, <i>n</i> (%) | 330 (7) | 104 (7.5) | 35 (2.3) | 191 (10.1) |
| NHAP, <i>n</i> (%) | 8 (3) | 1 (2.3) | 0 | 7 (4.8) |
| <i>P</i> | .005 | .20 | .13 | 0.035 |
| Classes 3–5 | | | | |
| CAP | 193 (4) | 39 (3) | 23 (1.5) | 128 (6.7) |
| NHAP | 42 (15) | 4 (9.3) | 8 (8.3) | 20 (20.4) |
| <i>P</i> | < .001 | .02 | < .001 | < .001 |
| Confusion | | | | |
| CAP | 616 (13) | 193 (14) | 158 (10.3) | 265 (13.9) |
| NHAP | 118 (41) | 30 (69.8) | 37 (38.1) | 51 (34.7) |
| <i>P</i> | < .001 | < .001 | < .001 | < .001 |
| Time respiratory symptoms | | | | |
| CAP | 5/6, 5/8 | 6.6 ± 6.8 | 5.2 ± 5.2 | 5 ± 5.2 |
| NHAP | 4, 4/9 | 4 ± 2.4 | 3.8 ± 5.5 | 4 ± 5.1 |
| <i>P</i> | .009 | .26 | .35 | .35 |
| Multilobar infiltration | | | | |
| CAP | 1,178 (24) | 95 (28.6) | 460 (30.1) | 310 (16.3) |
| NHAP | 89 (31) | 18 (41.9) | 36 (37.1) | 35 (23.8) |
| <i>P</i> | .01 | .060 | .15 | .02 |
| Pleural effusion | | | | |
| CAP | 993 (21) | 224 (16.2) | 297 (19.4) | 407 (21.5) |
| NHAP | 81 (28) | 6 (14) | 25 (25.8) | 50 (34) |
| <i>P</i> | < .001 | .69 | .13 | < .001 |

CAP = community-acquired pneumonia
 NHAP = nursing home-acquired pneumonia
 CURB-65 = confusion, urea nitrogen, breathing frequency, blood pressure, ≥65 y of age

The NHAP presentation was more severe than the CAP presentation, as assessed by the CURB-65 score, which has better performance accuracy in predicting mortality in patients with NHAP.¹¹ Particularly in Europe, 20% of NHAP cases belonged to CURB-65 classes 3–5 (see Table 4). These differences reflect the differences in healthcare system tactics and the assessment of severity of NHAP worldwide. A novel prognostic system termed SOAR (systolic blood pressure, oxygenation, age, and respiratory rate) is an alternative for better identification of severe NHAP.^{12,13} One common limitation to all these scoring models is that not one takes into

consideration the functional status of nursing home residents.^{3,12}

Although NHAP was more severe than CAP, the proportion of subjects admitted to the ICU was similar, except in region II (28% vs 18%, *P* = .09). We found that subjects with NHAP are older with a higher frequency of comorbidities. Therefore, they are more likely to have treatment restrictions, such as do-not-resuscitate orders, precluding mechanical ventilation or vasopressor support.¹⁴ It is possible that, in Latin America (region II), patients do not have these restrictions for social reasons.

Table 5. Outcomes by Regions

| Outcome | Globally | | P | United States/Canada | | P | Latin America | | P | Europe | | P |
|------------------------------|--------------------|-------------------|--------|----------------------|------------------|--------|--------------------|------------------|--------|--------------------|-------------------|--------|
| | CAP (n = 4,817) | NHAP (n = 287) | | CAP (n = 1,534) | NHAP (n = 97) | | CAP (n = 1,383) | NHAP (n = 43) | | CAP (n = 1,900) | NHAP (n = 147) | |
| In-hospital mortality, n (%) | 402 (8.3) | 75 (26.1) | < .001 | 88 (5.7) | 17 (17.5) | < .001 | 166 (12) | 19 (44.2) | < .001 | 148 (7.8) | 39 (39) | < .001 |
| 30-d mortality, n (%) | 871 (18.1) | 119 (41.5) | < .001 | 350 (22.8) | 44 (45.4) | < .001 | 237 (17.1) | 22 (51.2) | < .001 | 284 (14.9) | 53 (36.1) | < .001 |
| CAP-related death, n (%) | 237 (4.9) | 49 (17.1) | < .001 | 45 (2.9) | 10 (10.3) | < .001 | 100 (7.2) | 14 (32.6) | < .001 | 92 (4.8) | 25 (17) | < .001 |
| Hospital stay, mean ± SD | 10.1 ± 11.1 | 10.1 ± 8.1 | > .99 | 9.2 ± 14.4 | 9.4 ± 8.5 | .90 | 10.7 ± 9.3 | 10 ± 7.2 | .64 | 10.5 ± 9 | 10.7 ± 8.1 | .83 |
| Admission to ICU, n (%) | 573 (11.9) | 32 (11.9) | .70 | 216 (14.1) | 14 (14.4) | .92 | 248 (17.9) | 12 (27.9) | .10 | 109 (5.7) | 6 (4.1) | .40 |
| Stability d, mean ± SD | 4.7 ± 2.5 | 5.9 ± 2.5 | < .001 | 4.1 ± 2.6 | 5.2 ± 2.7 | < .001 | 5.2 ± 2.5 | 6.3 ± 2.3 | .004 | 4.8 ± 2.4 | 6.2 ± 2.3 | < .001 |
| Readmission, n (%) | 55 (1.1) | 5 (1.7) | .36 | 28 (1.8) | 2 (2.1) | .24 | 8 (0.6) | 0 | .62 | 19 (1) | 3 (1) | .24 |

CAP = community-acquired pneumonia
 NHAP = nursing home-acquired pneumonia

Another reason is the heterogeneity of the population residing in nursing homes and the level of care in these institutions.

Etiology

The 2005 American Thoracic Society/Infectious Diseases Society of America guidelines recommend that a patient with NHAP receive empirical therapy, including antibiotics directed against MDR microorganisms (MRSA and *P. aeruginosa*).⁶ The validity of these antimicrobial guidelines for the treatment of nursing home patients has been most challenging because the microbiology of NHAP varies widely among published reports, according to study design, severity of illness, and colonization with resistant organisms due to prior hospitalization.¹⁵

Our results confirm the previously published etiologic difference between NHAP from the United States and Europe.⁷ In particular, *Staphylococcus* species were identified as the prominent pathogen in the United States (52%) as opposed to *S. pneumoniae* in Europe (46%) and Latin America (25%). Moreover, *S. aureus* and MRSA were significantly higher in the NHAP group than in the CAP group globally.

Studies from the United States indicate an excess of MDR pathogens in subjects with NHAP.^{1,2} In a study by El-Solh et al¹⁶ conducted in 52 NHAP subjects who failed initial antimicrobial therapy, *S. aureus* (including MRSA strains) was found in 33%, enteric Gram-negative bacilli in 24%, and *P. aeruginosa* in 14% of isolates.

In contrast, a recent Spanish study by Polverino et al¹⁷ spanning 10 y of clinical experience confirmed the predominance of *S. pneumoniae* (58%), with MRSA representing only 5% of all isolates. In agreement, an older study by Lim et al¹⁸ and the CAPNETZ study¹⁹ also reported that the most common pathogen in NHAP was *S. pneumoniae* (55%). In a study of similar design from Japan, Maruyama et al²⁰ identified *C. pneumoniae*, *S. pneu-*

moniae, *S. aureus*, and influenza virus as frequent causative agents of pneumonia in nonintubated institutionalized elderly persons. Interestingly, atypical pathogens accounted for 37% of all isolates.

The identification of *L. pneumoniae* in region III in subjects with NHAP (9.1%) as the only atypical pathogen is associated with the greater frequency of atypical pathogens in CAP in this region as well. However, it should be noted that outbreaks of *Legionella* infection have been reported in nursing homes.³ Prospective clinical and environmental surveillance of nursing homes has revealed previously unsuspected *Legionella* infection because of colonization of the facilities' water supply by *Legionella*.²¹

Viral infection in nursing homes is seasonal.^{22,23} In the present study, we also found seasonality of the H1N1 epidemic in NHAP cases, particularly in region II (39% vs 13%, *P* = .16).

Outcomes

Thirty-d mortality was far higher in NHAP subjects compared with CAP subjects (41.5% vs 18%, *P* < .001); 51% of NHAP subjects in region II died, although 28% of all NHAP subjects were admitted to the ICU.

The higher mortality seen in subjects with NHAP may be due to the presence of dementia and other neurological disorders leading to atypical presentations of pneumonia and a delay in diagnosis and treatment. In one study of CAP subjects > 65 y old, the functional status for activities of daily living was the best mortality predictor²⁴; other studies reached similar conclusions.^{17,18,20}

Another reason for the higher mortality is the higher incidence of MDR bacteria and thus the administration of inappropriate empirical antibiotic treatment. In recent studies,²⁵⁻²⁷ enteral tube feeding (as well as poor functional status and aspiration) was predictive of MDR pathogens in NHAP. However, it is a fact that, in clinical practice, the poor functional status and advanced age of these patients

lead doctors to decide on treatment restrictions, managing pneumonia as a terminal event for a disabled adult.

Although the reasons are unknown, it is believed that differences in the populations of hospitalized patients with NHAP between countries and regions result in differences in rates of mortality. In an attempt to identify prognostic factors for mortality by multiregression analysis, we found that comorbidities such as cancer, neurological disease, renal disorder, cerebrovascular disease, and aspiration were significantly associated with death.

As in a recent United Kingdom study by Chalmers et al²⁷ and a Spanish study by Rello et al²⁸ referring to pneumococcal severe health care-associated pneumonia, we did not find a relationship between MDR pathogens and excess mortality.

One strength of the present study is the generalizability of the CAPO database study population, with an overall mortality rate of > 10%. The results of our multivariate analysis were consistent with published literature indicating an increased risk for mortality in CAP patients with neurological disease, aspiration, multilobar infiltrates, and NHAP.⁸

The study has several limitations, including the retrospective design and the enrollment of nonconsecutive subjects with CAP. Furthermore, the subjects who were enrolled were limited to the specialized type of patients seen by each principal investigator. The study was limited to the five processes of care that were reviewed. Other processes of care, such as whether to perform a special procedure (eg, bronchoscopy or parapneumonic effusion drainage) or when to admit to an ICU, were not available in the database and may have been significant. Other important elements not available in our database were information about the functional status of the subjects and data regarding treatment restrictions. Furthermore, the proportion of subjects with an etiology identified was low and did not exceed 30%, a proportion that was expected because of the difficulty in obtaining sputum specimens from elderly patients with confusion.

Conclusions

NHAP represents a small proportion of CAP and, in terms of etiology, severity, and outcomes, varies globally, representing heterogeneity of administrative structures and treatment policies. As a consequence, the management of these patients must take into account risk factors for mortality, functional status of the patient, and microbiology of the community. This is one of the reasons for the low compliance of doctors for the American Thoracic Society/Infectious Diseases Society of America guidelines for health care-associated pneumonia²⁹ and the need for validation and re-evaluation for the NHAP category.

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