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Original Article

Trends in hospitalizations for community-acquired pneumonia in Spain: 2004 to 2013

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ABSTRACT

Aim: To describe trends in the incidence and outcomes of community-acquired pneumonia (CAP) hospitalizations in Spain (2004–2013).
Methods: We used national hospital discharge data to select all hospital admissions for CAP as primary diagnosis. We analyzed incidence, Charlson comorbidity index (CCI), diagnostic and therapeutic procedures, pathogens, length of hospital stay (LOHS), in-hospital mortality (IHM) and readmission.
Results: We identified 959,465 admissions for CAP. Incidence rates of CAP increased significantly over time (from 142.4 in 2004 to 163.87 cases per 100,000 inhabitants in 2013). Time trend analyses showed significant increases in the number of comorbidities and the use of CAT of thorax, red cell transfusion, non-invasive mechanical ventilation and readmissions (all p values < 0.05). *S. pneumoniae* was the most frequent causative agent, but its isolation decreased over time. Overall median of LOHS was 7 days and it did not change significantly during the study period. Time trend analyses also showed significant decreases in mortality during admission for CAP. Factor associated with higher IHM included: older age, higher CCI, *S. aureus* isolated, use of red cell transfusion or mechanical ventilation and readmission.
Conclusions: The incidence and mortality of CAP have changed in Spain from 2004 to 2013. Although there was an increased incidence of hospitalization for this disease over time, we saw a significant reduction in IHM.

1. Introduction

Community-acquired pneumonia (CAP) is one of the most common infections requiring hospitalizations worldwide, resulting in a significant clinical and economic burden, especially in the elderly [1,2]. Both incidence and mortality, as well as costs associated with this disease vary, not only with age, but also with gender and comorbidity [3,4]. S. pneumonia is the leading causative agent in all age groups and is the major bacterial cause of adult CAP that requires hospitalization [5].

Although there is a high variability in published data of incidence of CAP, hospital admissions for pneumonia appears to be increasing [6–8], which may be due to their aging populations and a higher prevalence of concomitant diseases [9]. However, these trends are surprising in light of smoking cessation campaigns and increased uptake of influenza and pneumococcal vaccination among high risk groups [7]. In fact, in recent studies in U.S. it has been observed a substantial reduction in hospitalization for pneumonia after the introduction of 7-valent pneumococcal conjugate vaccine [10,11]. However, recent data of the burden of CAP are lacking for most European countries.

Despite the significant impact of this disease, studies conducted in Spain on the epidemiology of CAP are scarce, with figures of incidence varying, and sometimes with many years since its realization [12,13]. Administrative databases are attractive candidates for health services research, because the number of patient records is large and the acquisition cost is low [14]. Observational studies using these data can be used to understand disease patterns and burden of pneumonia [12,13].

A better understanding of the burden of CAP could help in planning preventive strategies and improving clinical management [15]. In this study, we used national hospital discharge data to examine trends in incidence and outcomes of CAP in Spain from 2004 to 2013. In particular,

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we analyzed patient comorbidities, diagnostic and therapeutic procedures, pneumonia pathogens and in-hospital outcomes, length of hospital stay (LOHS), in-hospital mortality (IHM) and readmissions.

2. Methods

We performed a retrospective, observational study using the Spanish National Hospital Discharge Database (CMBD, *Conjunto Mínimo Básico de Datos*), which is managed by the Spanish Ministry of Health, Social Services and Equality and compiles all public and private hospital data, covering >98% of hospital admissions [16]. The CMBD includes patient variables (sex, date of birth), admission and discharge dates, up to 14 discharge diagnoses, and up to 20 procedures performed during the hospital stay. The Spanish Ministry of Health, Social Services and Equality sets standards for record keeping and performs periodic audits of the database [16]. We analyzed data collected between January 1, 2004 and December 31, 2013 (10 complete years) for subjects aged 18 and over.

The criteria for diseases and procedures were defined according to the International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM), which is used in the Spanish CMBD. We selected admissions for patients with a primary diagnosis of CAP (ICD-9-CM codes: 480–488, 507.0–507.8).

Clinical characteristics included information on overall comorbidity at the time of diagnosis, which was assessed by calculating the Charlson comorbidity index (CCI) [17]. We used the comorbidities on the basis of the discharge diagnosis. This method has been described by Quan et al. [18]. We divided patients into three categories: “no disease”, “one disease” and “two or more diseases”.

Irrespectively of the position at the diagnoses coding list, we retrieved data about comorbidities, like acute myocardial infarction, congestive heart failure, vascular disease, cerebrovascular disease/hemiplegia/paraplegia, dementia, chronic pulmonary disease, pleuritic, liver disease, renal diseases, any type of malignancy, type 2 diabetes and obesity as described by Kornum et al. [19] using the enhanced ICD-9-CM. Respiratory failure was also identified (ICD-9-CM codes 518.81, 518.83, 518.84). In addition, we specifically identified the following procedures: computerized axial tomography (CAT) of thorax (ICD-9-CM code 87.41), bronchial fibroscopy (ICD-9-CM code 33.21–33.24), transbronchial biopsy (ICD-9-CM code 33.27), non-invasive mechanical ventilation (ICD-9-CM code 93.90), invasive mechanical ventilation (ICD-9-CM code 96.7, 96.70, 96.71, 96.72), thoracocentesis (ICD-9-CM code 34.91), and red cell transfusion (ICD-9-CM code 99.03, 99.04).

We analyzed pneumonia pathogens documented during hospitalizations for pneumonia using the following ICD-9 codes: 481 for *Streptococcus pneumonia*; 482.84 for *Legionella;* 482.41 and 482.42 for *Staphylococcus aureus;* 482.2 for *Haemophilus influenza*; and 482.1 for *Pseudomonas aeruginosa.*

We estimated the proportion of readmission (patients that had been discharged from the hospital within the previous 30 days), the median of LOHS and IHM. The variable “Readmission” was included in the database by the Ministry of Health before it was provided to us. This variable is “Yes” if the patient has been discharged from the same hospital in the previous 30 days before the actual admission. Given the anonymity of data we don't have information to identify is the same person is hospitalized more than once, we only have the variable provided to quantify the readmission rate. IHM is defined by the proportion of patients who died during admission for each year of study. Before the analysis, we checked the database for any missing data on the following variables: sex, date of birth, admission date, discharge date, and death during hospitalization. If any of these variables were missing, the record was deleted for the analysis. As all the databases undergo quality control at the Ministry of Health before being sent to the investigators, we only had to exclude <0.1% of records.

2.1. Statistical analysis

In order to assess time trends, the incidence rates of admissions for CAP were calculated per 100,000 inhabitants, according to sex, by dividing the number of cases per year, sex, and age group by the corresponding number of people in that population group, according to the data from the Spanish National Institute of Statistics, as reported on December 31 of each year [20].

A descriptive statistical analysis was performed for all continuous variables and categories. Variables are expressed as proportions, as means with standard deviations or as medians with interquartile ranges (LOHS). A bivariate analysis of variables according to year was performed using the χ^2 test for linear trend (proportions), ANOVA (means) and Kruskall-Wallis (medians), as appropriate. To asses time trend of incidence we used Poisson regression adjusted by age and sex when appropriate,

Lastly, we performed logistic regression analyses with mortality as a binary outcome using the independent variables and age, sex, CCI, readmission, diagnostic and therapeutic procedures, pathogens and year of admission for the entire population. Estimates were Odds Ratios (OR) with their 95% confidence intervals. Statistical analyses were performed using Stata version 10.1 (Stata, College Station, Texas, USA). Statistical significance was set at $p < 0.05$ (2-tailed).

2.2. Ethical aspects

Data confidentiality was maintained at all times in accordance with Spanish legislation. Patient identifiers were deleted before the database was provided to the authors in order to maintain patient anonymity. It is not possible to identify patients on an individual level, either in this article or in the database. Given the anonymous and mandatory nature of the dataset, it was not deemed necessary to obtain informed consent. The study protocol was approved by the ethics committee of the Universidad Rey Juan Carlos.

3. Results

From 2004 to 2013, we identified a total of 959,465 admissions for CAP as primary diagnosis in patients aged ≥18 years in Spain. Table 1 shows the incidence according to sex and age in these patients. Incidence increased significantly, from 142.4 cases per 100,000 inhabitants in 2004 to 163.87 in 2013. In both sexes a significant increase was observed over time, from 208.24 to 227.59 in males and from 92.17 to 116.28 in females (Fig. 1). In both sexes, an increase in incidence with increasing age was also observed. As can be seen in Table 1 higher incidences are found for men than women in all years and age groups.

Table 2 shows the characteristics and comorbidity of hospital admissions for pneumonia as primary diagnosis in Spain from 2004 to 2013. As can be seen in this table, Charlson comorbidity index increased significantly over time. Specifically, we observed an increase over time in the prevalence of congestive heart failure, pheripheral vascular disease, cerebrovascular diseases, hemiplegia/paraplegia, dementia, renal disease, cancer, type 2 diabetes and obesity, and a significant decrease in the prevalence of acute myocardial infarction, chronic obstructive pulmonary disease, pleuritic and liver disease.

Diagnostic tests are shown in Table 3. We detected a significant increase in use of CAT of thorax over the study period. However, a significant decrease in the use of bronchial fibroscopy was found reducing from 3.64% in 2004 to 3.15% in 2013.

The use of all therapeutics procedures (except invasive mechanical ventilation which showed a significant decrease) have significantly increased in the last ten years (Table 3). The use of non-invasive mechanical ventilation has shown an over four fold increase in patients over the study period, fron 0.76% to 3.26%

Of the pathogens analyzed the most commonly found was *S. pneumoniae*, followed by *Legionella*, *P. aeruginosa*, *H. influenza* and

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