Journal of Infection (2016) 72, 70—79

BIA British Infection Association

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Characteristics of herpes zoster-associated hospitalizations in Madrid (SPAIN) before vaccine availability

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Accepted 7 October 2015
Available online 20 October 2015

KEYWORDS
Chronic conditions;
Comorbidity;
Epidemiology;
Herpes zoster;
Hospitalization;
Immunosuppression;
Incidence

Summary *Objectives:* This study aimed to estimate the frequency of hospitalizations due to herpes zoster (HZ) and to describe their clinical characteristics by sex and age group.
Methods: Descriptive population-based cross-sectional study of hospital admissions due to HZ from 2003 to 2013 among residents in the Autonomous Community of Madrid. Sex, age, comorbidities, length of stay and outcomes were collected and described. Crude and age-adjusted cumulative incidence rates, and stratified by sex and age, were estimated. Robust Poisson regression analysis was used to calculate the incidence rate ratios by age group.
Results: 2039 hospitalizations were identified (51.0% in women). Complicated HZ caused 48.7% of them (50.9% in women). The hospitalization rate was 2.98/100,000 person-years and 7.19/1000 cases of HZ in primary care. Both rates were significantly higher in men, except in the extreme age groups. An immunosuppression-associated comorbidity was identified in 32.8% of the cases and was less common in patients ≥75 years of age. The median length of stay was 6 days, and in-hospital mortality was 1.4%.
Conclusions: Hospitalization rates due to HZ were higher in men and increased with age. In two out of every three cases, a comorbidity that potentially caused immunosuppression could not be identified. These cases could benefit from vaccination.

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http://dx.doi.org/10.1016/j.jinf.2015.10.003

Introduction

Herpes zoster (HZ) results from reactivation of the varicella-zoster virus in sensory ganglia after a long latency period following a primary varicella infection. Available evidence highlights that HZ and post-herpetic neuralgia result in a significant burden for patients, health care systems and societies,[1] and these burdens are expected to increase as the population ages.

Several risk factors have been identified, including ageing, female sex, genetic susceptibility, ethnicity, underlying cell-mediated immune disorders, immunotoxin exposure, mechanical trauma, psychological stress,[2] and certain chronic conditions.[3–8] The lifetime risk of HZ is estimated to be 10–30%, and the incidence increases markedly with age, affecting up to 50% of people who live to be 85 years old.[2,9]

The burden of hospitalizations related to HZ is significant and is very expensive, especially in populations older than 50 years of age, leading to an estimated average cost of more than 3500 € per hospitalization.[10,11] A recent systematic review found that the rates of HZ-related hospitalizations range widely worldwide, from 2 to 25/100,000 person-years.[12] In the Autonomous Community of Madrid, a previous analysis of hospital admissions showed that the incidence of hospitalizations with HZ increased significantly between 2003 and 2013 in both sexes, and the rate of primary diagnoses rose from 2.53 to 3.85 cases per 100,000 person-years.[13]

A live attenuated varicella-zoster virus vaccine has been demonstrated to significantly reduce the incidence of HZ as well as decrease the duration and severity of pain.[14] In terms of HZ prevention, the existing vaccine has been shown to be safe and effective for immunizing immunocompetent individuals 50 years of age or older who have no recent history of zoster.[15] This vaccine has been recently commercialized in our country (2014), but it is neither financed nor reimbursed by the public health care system.

Estimating the burden and cost of HZ, evaluating the overall impact of varicella immunization programmes and determining the most appropriate vaccination strategies necessitate a good understanding of the disease epidemiology.

The objectives of this study were to estimate the frequency of hospitalizations due to HZ (total and with or without complications) by person-year and by episodes of HZ in primary care and to describe their clinical characteristics, by sex and age group.

Materials and methods

We performed a descriptive population-based cross-sectional study of all hospital admissions due to HZ from 2003 to 2013 among residents in the Autonomous Community of Madrid (Spain).

Data were obtained from the hospital discharge MBDS (Minimum Basic Data Set). This database records all hospital admissions from public and private centres. Diagnoses are codified at discharge according to the Spanish version of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM).

All hospital admissions of residents in Madrid with HZ as the primary diagnosis, coded with any 053.xx ICD-9-CM codes, during an 11-year period (2003–2013) were selected. HZ was classified as uncomplicated (code 053.9) or complicated (the remaining 053.xx codes). Complicated HZ included: HZ with meningitis or other nervous system complications, HZ with ophthalmic or other specified complications, and those recorded with a diagnosis of HZ with an unspecified complication. Records with coincident admission and discharge dates were discarded after ensuring that they corresponded to patients accessing the hospital for therapy but not requiring hospitalization. Data collected from the MBDS were age at hospitalization, sex, codified diagnoses (primary and secondary), dates of admission and discharge to calculate the length of the hospital stay in days and outcome (discharge or death). Patient comorbidities were identified from codified secondary diagnoses (2nd to 13th); the pathologies that were considered included those potentially associated with the onset of HZ or its complications. According to the reviewed literature, these comorbidities included both haematological and non-haematological neoplasms, AIDS, transplantation, diabetes mellitus, COPD, asthma, rheumatologic diseases, depression and dementia. In addition, pathologies that may cause immunosuppression (i.e., malignancy, AIDS, transplantation, agranulocytosis, immune system diseases, and severe liver disease) were aggregated into a single variable to identify this condition (Supplementary Table 1).

Statistical methods

Total cumulative incidence rates of hospitalization and among sex and age subgroups were calculated. The denominator was the sum of the annual population of the Autonomous Community of Madrid for the study period obtained from the municipal records. The rates were adjusted by age using the direct method (European standard population). To estimate the rates of hospitalization by incident HZ episodes, information on cases assisted in primary care was obtained from the electronic clinical records available from 2005 to 2013. More detailed information about the collection and refinement of the data have been previously published.[16] Robust Poisson regression analysis was used to calculate the incidence rate ratio for each age group using the 0 to 14-year-old age group as the reference. The analysis was also performed by sex. A descriptive analysis was conducted stratified by sex and age group. Chi-squared and z tests were used to compare rates and proportions, and two-sided independent t-tests were used to compare the mean hospital stay lengths. All of the analyses were performed separately for complicated and uncomplicated HZ cases. Statistical significance was set at $p < 0.05$. Analyses were performed using SPSS 21.0 software.

Data were anonymous, and confidentiality was maintained at all times. Given the characteristics of the study and current Spanish legislation, prior consent of the patients and approval by an ethics committee were not required.

Results

In total, 2039 hospitalizations due to HZ were identified in the 11-year period, of which 48.9% were men, and 51.0%