Hospital Admissions for Herpes Zoster in Portugal Between 2000 and 2010

Internamentos Hospitalares por Herpes Zoster em Portugal entre 2000 e 2010

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ABSTRACT

Introduction and Objectives: Herpes zoster and post-herpetic neuralgia increasing incidence is related to ageing. These conditions can be very debilitating and have an important impact in patients’ quality of life. In an ageing population like the Portuguese, is expected that the burden of herpes zoster and post-herpetic neuralgia rises, nevertheless, a specific surveillance system for zoster does not exist in the country, and data regarding the incidence of herpes zoster and the burden of the disease in Portugal in the last decades was not found.

In Portugal, the vaccine is still not available. Scaling the burden of disease is important to support public health policies regarding zoster vaccination.

Material and Methods: We carried out a retrospective analysis from encoded information from the Portuguese Ministry of Health database for hospital admissions which included all individuals with a primary diagnosis of Herpes Zoster (ICD-9-CM 053), who were discharged between 2000 and 2010.

Results: In Portugal, between 2000 and 2010, 1 706 hospital admissions with primary diagnosis of herpes zoster occurred. The majority of the patients were elderly. Eleven percent of the patients had potentially severe immunocompromise. The predominant disease was uncomplicated herpes zoster, followed by nervous system and ophthalmic herpes zoster. Mean hospital stay length was 9.3 days, increasing with age. There was a 1% case fatality rate. Considering the 2000-2009 period and the adult population only, the average annual incidence rate of hospitalization with primary diagnosis of herpes zoster in Portugal was 1.9/100 000 inhabitants, increasing with age.

Conclusion: This study confirms that, in Portugal, severe herpes zoster is related to ageing and associated with significant morbidity, mortality and health resources allocation.

Keywords: Herpes Zoster; Hospitalization Length of Stay; Patient Admission; Patient Discharge; Portugal.

RESUMO

Introdução e Objetivos: O aumento da incidência de herpes zoster e da nevralgia pós-herpética estão associados ao envelhecimento da população. Estas patologias podem ser francamente debilitantes e ter um grande impacto na qualidade de vida dos doentes. Numa população envelhecida como a portuguesa, é esperado que o impacto do herpes zoster e da post-herpética neuralgia aumentem. No entanto, não existe no país nenhum sistema específico de monitorização da doença e não foram encontrados dados epidemiológicos portugueses nas últimas décadas. A vacina contra o herpes zoster, já recomendada noutros países europeus, ainda não se encontra disponível em Portugal. Conhecer o impacto do herpes zoster é importante para fundamentar medidas de saúde pública relacionadas com a vacinação.

Material e Métodos: Procedeu-se a uma análise retrospectiva da base de dados da Administração Central dos Sistemas de Saúde com a informação clínica codificada dos internamentos hospitalares de todos os indivíduos com o diagnóstico principal de herpes zoster (ICD-9-CM 053) e que tiveram alta entre 2000 e 2010.

Resultados: Em Portugal, entre 2000 e 2010, ocorreram 1 706 internamentos hospitalares com o diagnóstico principal de herpes zoster. A maioria dos doentes era idosa. Do total de internados, 10,6% tinham formas potencialmente graves de imunocompromisso. A doença predominante de herpes zoster sem complicações, seguido de herpes zoster do sistema nervoso e oftalmico. A duração média dos internamentos foi de 9,3 dias, aumentando com a idade. A letalidade intra-hospitalar foi de 1%. Considerando o período de 2000-2009 e apenas a população adulta, a média anual da incidência dos internamentos hospitalares com o diagnóstico principal de herpes zoster foi de 1,9 por 100 000 habitantes, aumentando com a idade.

Conclusão: Este estudo confirma que, em Portugal, as formas graves de herpes zoster estão relacionadas com a idade e associadas a significativa morbidade, mortalidade e utilização de recursos em saúde.

Palavras-chave: Herpes Zoster; Hospitalização; Portugal; Tempo de Internamento.

INTRODUCTION

Herpes zoster (HZ), also known as shingles, is the clinical manifestation of the reactivation of latent varicella zoster virus (VZV), which as a primary infection causes varicella or chickenpox.1,2

HZ is a potentially serious and debilitating condition usually characterized by a unilateral vesicular rash affecting a dermatome and can be accompanied by acute pain.2,3

The most frequent and debilitating complication of HZ is post-herpetic neuralgia (PHN), a persistent neuropathic pain syndrome often defined as pain that persists for ≥ 90 days after the onset of HZ rash.2,4

HZ, and particularly PHN, can have a devastating impact


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the incidence of HZ and PHN rises, nevertheless, a specific surveillance system for zoster does not exist in the country, and data regarding the incidence of HZ and the burden of the disease in Portugal in the last decades was not found.

In Portugal, the vaccine is still not available. Scaling the programmatic vaccination of the elderly population to HZ during their lifetime and this risk rate roughly doubles with each decade of life after 50 years reaching 50% in those aged ≥ 85 years. Incidence rates range from approximately 3/1 000 inhabitants per year at the age of 50 to 9/1 000 at the age of 65 and 10/1 000 at the age of 80.

On average, 10–20% of HZ patients will develop PHN, which can persist for years or even decades after the HZ rash has gone, with rates of 25–50% reported in patients over 50 years old, depending on the definition used. 

The second most frequent are the ophthalmic complications.

Studies refer need for inpatient care for 1.3% to 4.4% of HZ cases, and almost 2% of PHN. Hospitalization rates increased with age, reaching more than 15% of the cases for 80+ patients. Data regarding the rate of hospitalization due to HZ in immunocompromised patients population was not found.

While antiviral therapy reduces the severity and duration of HZ, it does not prevent PHN, which remains a poorly controlled condition, even after standard therapeutic approach. 

In terms of zoster prevention, the existing vaccine showed to be safe and effective for immunization of immunocompetent individuals with no history of recent zoster. The preventive effect of the vaccine has been associated to a boost on host cell-mediated immunity to VZV.

In the elderly, vaccination significantly decreased shingles incidence, the development of PHN and its severity, and reduced the burden of both diseases.

The programmatic vaccination of the elderly population is actually considered cost-effective in some countries like Canada, US, UK, Netherlands and is also recommended in Austria, Australia and Greece. Portugal assists to an accelerated demographic ageing process. Portuguese individuals over 65 years old increased 18.2% in the last decade, from 16.4% of total population in 2001 to 19.0% in 2011. People reached an average life expectancy of 82.1 years for women and 76.1 for men between 2008 and 2010.

In an ageing population like the Portuguese, is expected that the burden of HZ and PHN rises, nevertheless, a specific surveillance system for zoster does not exist in the country, and data regarding the incidence of HZ and the burden of the disease in Portugal in the last decades was not found.

In Portugal, the vaccine is still not available. Scaling the burden of disease is important to support public health policies regarding zoster vaccination.

This study aimed to characterize the incidence of hospital admission with HZ between 2000 and 2010 and analyze the patient’s characteristics over that period.

**RESULTS**

**Patient characteristics**

In Portugal, there were 1 706 hospital admissions with HZ encoded as the primary diagnosis between 2000 and 2010, with an annual frequency that ranged from 131 episodes in 2000 to 182 in 2010, with average of 155 episodes (SD 15.2) per year (Fig. 1).

The 1 706 cases with primary diagnostic of HZ represented 26.4% of the total 6 474 episodes with HZ encoded as primary or secondary diagnosis during that period (Table 1).
From the 1,706 episodes, 54% of the patients were women (N = 922) and 46% men (N = 784).

The average age was 57.1 years (SD: 25.2), with a median age of 64 years. The average age was 55.4 (SD: 25.3) for men and 60.0 (SD: 24.8) for women (p < 0.001). The greatest age was 98 years for women and 99 for men and the lowest was 0 years for both genders (Fig. 2).

Regarding the distribution of the episodes by age group, 12.4% were pediatric patients and 31.2% were adults (18-59 years) and 56.4% were 60 years and older. From all the cases, 40.6% were patients aged 70 years and older and 19.4% were patients aged 80 years and older.

Incidence rate

Considering the 2000-2009 period and the adult population only, the average annual incidence rate of hospitalization with primary diagnosis of HZ in Portugal was 1.9/100,000 inhabitants. This incidence rate showed a consistent increase with age, ranging from 0.5/100,000 for the 18-29 age group to 0.7/100,000 for the 30-49 age group, 1.7/100,000 for the 50-64 age group, 2.8/100,000 for the 65-74 age group, 5.5/100,000 for the 75-84 age group and 8.8/100,000 for the 85 and older age group.

Type of disease

Regarding the type of HZ disease, 49.5% of the episodes were for HZ without complications, 21.0% for nervous system disease, 16.6% for ophthalmic disease, 9.8% for HZ with other complications and 3.2% for otologic disease. (Table 2)

Immune status

Regarding the immune status, 10.6% of the patients were immunocompromised (N = 180). From these, 48.9% were HIV/AIDS patients (N = 88), 40.6% were transplant patients (N = 73) and 10.6% were oncologic patients on chemotherapy (N = 19).

From the immunocompromised patients, 56.7% were male and 42.3% were female. The average age was 41.6 years (SD 25.4) and 63% of the patients were 30 to 64 years old. When comparing to the immunocompetent patients, predominance of male gender (p = 0.02) and younger age
ARtIGO ORIGINAL

The last decade was marked by an evident demographic ageing, predisposing the population to an increase on HZ incidence and burden. On the other hand, the first zoster vaccine became available. These two motives led to several studies regarding the incidence and burden of the disease in different settings.10,11,14,27-30

This study focused on the most severe HZ episodes and showed that, in Portugal, during the 2000-2009 period, 1 706 hospital admissions with primary diagnosis of HZ occurred. The majority of the patients were elderly. Eleven percent of the patients had potentially severe immunocompromise. The predominant disease was uncomplicated HZ, followed by nervous system and ophthalmic HZ. Mean hospital stay length was 9.3 days, increasing with age. There was a 1% case fatality rate. Considering the 2000-2009 period and the adult population only, the average annual incidence rate of hospitalization with primary diagnosis of HZ in Portugal was 1.9/100 000 inhabitants, increasing with age.

Our study has potential limitations. The Portuguese Ministry of Health database is essentially administrative. The clinical information is coded from discharge documents; this work is carried out exclusively by medical doctors who

Table 1 – Frequency of cases, gender distribution, length of hospital stay, case fatality rate and percentage of cases with HZ as primary diagnosis (HZ) per age group.

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Gender</th>
<th>Frequency (N)</th>
<th>% of total N</th>
<th>Hospital stay (days)</th>
<th>Case Fatality Rate</th>
<th>Primary diagnosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Masc.</td>
<td>Fem.</td>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>%</td>
</tr>
<tr>
<td>0-14</td>
<td>102</td>
<td>87</td>
<td>189</td>
<td>11.1%</td>
<td>6.3</td>
<td>3.8</td>
</tr>
<tr>
<td>15-29</td>
<td>59</td>
<td>46</td>
<td>105</td>
<td>6.2%</td>
<td>7.6</td>
<td>6.1</td>
</tr>
<tr>
<td>30-39</td>
<td>62</td>
<td>53</td>
<td>115</td>
<td>6.7%</td>
<td>7.5</td>
<td>4.7</td>
</tr>
<tr>
<td>40-49</td>
<td>64</td>
<td>64</td>
<td>128</td>
<td>7.5%</td>
<td>8.4</td>
<td>5.6</td>
</tr>
<tr>
<td>50-59</td>
<td>101</td>
<td>106</td>
<td>207</td>
<td>12.1%</td>
<td>9.2</td>
<td>6.6</td>
</tr>
<tr>
<td>60-69</td>
<td>119</td>
<td>150</td>
<td>269</td>
<td>15.8%</td>
<td>9.5</td>
<td>9.3</td>
</tr>
<tr>
<td>70-79</td>
<td>168</td>
<td>194</td>
<td>362</td>
<td>21.2%</td>
<td>10.4</td>
<td>9.7</td>
</tr>
<tr>
<td>80-89</td>
<td>92</td>
<td>186</td>
<td>278</td>
<td>16.3%</td>
<td>11.1</td>
<td>8.9</td>
</tr>
<tr>
<td>90-99</td>
<td>17</td>
<td>36</td>
<td>53</td>
<td>3.1%</td>
<td>12.3</td>
<td>12.9</td>
</tr>
<tr>
<td>Total</td>
<td>784</td>
<td>922</td>
<td>1706</td>
<td>100.0%</td>
<td>9.3</td>
<td>8.2</td>
</tr>
</tbody>
</table>

(p < 0.001) was evident.

From these patients, 76.6% had uncomplicated HZ (N = 136).

Hospital stay

The average length of stay for the admissions encoded with HZ as the primary diagnosis was 9.3 days (SD 8.2).

The hospital stay length showed a weak positive correlation with age (Pearson = 0.195, p < 0.001) and a significant difference between age groups (p = 0.004) (Table 1).

Hospital stays >17 days (percentile 90) were more frequent (p<0.001) for patients 65+ (OR 2.48; CI95%1.75-3.52) and for patients with complicated HZ (OR 2.34; CI 95%1.65-3.34).

The total 1706 admissions with primary HZ diagnosis accounted for 15898 days of inpatient treatment in Portugal during the 2000-2010 periods. These correspond to an average of 1 445 annual inpatient treatment days. Of these inpatient days, 65% were related to patients aged 60+.

Outcome

Patients who deceased in the hospital had an average age of 76.8 (SD 13.6), being significantly older (p < 0.001) then the survivors.

Regarding the intra-hospitalar mortality for the admissions with primary diagnosis of HZ, this study revealed a 1% case fatality rate (N = 17). From these patients, 9 were male. Ages ranged from 46 to 93 years, with mean age of 76.8 years (SD 18.1). From the deceased patients, 6 were admitted for uncomplicated HZ; 6 for HZ with nervous system complications including 3 with meningitis; 4 for HZ with ophthalmic complications and 1 for HZ with other complications.

DISCUSSION

The last decade was marked by an evident demographic ageing, predisposing the population to an increase on HZ incidence and burden. On the other hand, the first zoster vaccine became available. These two motives led to several studies regarding the incidence and burden of the disease in different settings.10,11,14,27-30

This study focused on the most severe HZ episodes and showed that, in Portugal, during the 2000-2009 period, 1 706 hospital admissions with primary diagnosis of HZ occurred. The majority of the patients were elderly. Eleven percent of the patients had potentially severe immunocompromise. The predominant disease was uncomplicated HZ, followed by nervous system and ophthalmic HZ. Mean hospital stay length was 9.3 days, increasing with age. There was a 1% case fatality rate. Considering the 2000-2009 period and the adult population only, the average annual incidence rate of hospitalization with primary diagnosis of HZ in Portugal was 1.9/100 000 inhabitants, increasing with age.

Our study has potential limitations. The Portuguese Ministry of Health database is essentially administrative. The clinical information is coded from discharge documents; this work is carried out exclusively by medical doctors who...
have been formally trained in hospital coding, to make the process more rigorous. The Ministry of Health carries out regular audits, both internal and external, of this codification process.

We included patients of all ages in the study and didn’t exclude patients with underlying immunosuppressive conditions. Due to methodological limitations, we could just identify as immunocompromised the patients with HIV/AIDS, transplant or oncologic disease submitted to chemotherapy. Comparing to other studies, we present a lower percentage of immunocompromised patients, a fact that can be related to this methodological difference.

Data for calculating incidence rates was only accessible for adults (> 17 years) and for the period between 2000-2010, and so we could not calculate incidence rates for pediatric patients and for year 2011.

Apart from these limitations, the methodologies are similar to those which have been used in other countries. One advantage of this study is that it covers a period of 10 years, a fact that can minimize the impact of years that deviate from the norm.

Comparing our study to the studies cited above, the main difference found was in the incidence rate of the episodes. We observed a 1.9/100,000 inhabitants average annual incidence rate of hospitalization with primary diagnosis of HZ in Portugal. Although methods were not identical, this rate is lower than the observed in all the other studies, ranging from 4.4/100,000 in England and Wales to

| Table 2 – Number of herpes zoster (HZ) admissions, average age, average hospital stay and case fatality rate per type of HZ disease encoded. |
|---------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|-----------------|
| ICD-9 Code                      | Gender         | Age (years)    | Hospital Stay (days) | Mortality |
|                                 | N   | %   | Masc | Fem | Mean | SD | Média | SD | N   | Rate |
| 053.0 HZ with meningitis         | 93  | 5.5%| 50   | 43  | 47.9 | 26.5 | 17.1 | 14.6 | 3   | 3.2% |
| 053.10 HZ with unspecified nervous system complication | 9   | 0.5%| 4    | 5   | 69.6 | 25.5 | 11.9 | 11.8 | 1   | 11.1% |
| 053.11 Geniculate HZ            | 122 | 7.2%| 52   | 70  | 58.2 | 20.4 | 8.5  | 6.5  | 0   | 0.0% |
| 053.12 Postherpetic trigeminal neuralgia | 21  | 1.2%| 6    | 15  | 59.1 | 19.9 | 6.6  | 4.9  | 0   | 0.0% |
| 053.13 Postherpetic polyneuropathy | 44  | 2.6%| 19   | 25  | 69.6 | 16.1 | 11.4 | 9    | 1   | 2.3% |
| 053.14 HZ myelitis              | 3   | 0.2%| 2    | 1   | 64.7 | 18   | 28   | 4    | 0   | 0.0% |
| 053.19 HZ with other nervous system complications | 64  | 3.8%| 28   | 36  | 63.2 | 18.8 | 10   | 9    | 1   | 1.6% |
| Total Nervous System HZ         | 356 | 21.0%| 161  | 195 | 61.2 | 19.8 | 9.5  | 8    | 6   | 1.7% |
| 053.20 HZ dermatitis of eyelid   | 148 | 8.7%| 68   | 80  | 57.8 | 27   | 8.6  | 7.2  | 3   | 2.0% |
| 053.21 HZ keratoconjunctivitis  | 45  | 2.6%| 18   | 27  | 60.1 | 25.1 | 8.7  | 7    | 0   | 0.0% |
| 053.22 HZ iridocyclitis         | 9   | 0.5%| 6    | 3   | 73.7 | 11.6 | 6.6  | 4    | 0   | 0.0% |
| 053.29 HZ with other ophthalmic complications | 82  | 4.8%| 43   | 39  | 60.9 | 25.5 | 9.8  | 7.8  | 1   | 1.2% |
| Total Ophthalmic HZ             | 284 | 16.6%| 135  | 149 | 59.6 | 26   | 8.9  | 7.3  | 4   | 1.4% |
| 053.71 Otitis externa due to HZ | 54  | 3.2%| 22   | 32  | 56.5 | 22.8 | 9.1  | 6.1  | 0   | 0.0% |
| 053.79 HZ with other specified complications | 137 | 8.0%| 70   | 67  | 53.1 | 26.8 | 11.2 | 11.8 | 1   | 0.7% |
| 053.8 HZ with unspecified complication | 31  | 1.8%| 17   | 14  | 57.1 | 24.3 | 9.8  | 14.4 | 0   | 0.0% |
| 053.9 HZ without mention of complication | 844 | 49.5%| 379  | 465 | 56.4 | 25.9 | 8.2  | 5.8  | 6   | 0.7% |
| Total HZ                        | 1706| 100%| 784  | 922 | 57.1 | 25.2 | 9.3  | 8.2  | 17  | 1.0% |
8.4/100,000 in Spain, 10.34/100,000 in Italy, 11.6.1/100,000 in the US and 28/100,000 in Australia, in patients aged 50+. This difference can be due to real differences on the incidence of HZ but, in our opinion, differences on admission criteria for HZ and difficulties regarding the access of the elderly to the health care system should be considered when comparing Portugal to the other studied countries.

Regarding the length of the hospital stay, our average was 9.3 days, within the average lengths observed in the other studies of 6.8 days in Australia, in 6.8 patients aged 50+, 7.8 to 8 days in Italia, 8.3 days in Taiwan, and 10.8 days in the UK.

Relating to case fatality rate, our average (1%) was once more within the values observed in the other studies: 0.5% in the UK, 1.9% in the US and 3.6% in Spain. This difference can be due to real differences on the scale the burden of disease in our country.

CONCLUSION
This study confirms that, in Portugal, severe Herpes Zoster is related to ageing and associated with significant morbidity, mortality and health resources allocation.

Knowledge of the incidence rate of HZ and PHN in primary care settings would be fundamental to completely scale the burden of disease in our country.

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CONFLICT OF INTEREST
The authors have no competing interests to declare.

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REFERENCES