

N. SANTOS¹, A. BUGALHO DE ALMEIDA¹, A. COVAS², L. PRATES², M. MORAIS-ALMEIDA^{1,3}

Trends of asthma hospitalization and hospital mortality in mainland Portugal

¹Immunoallergy Department, CUF Descobertas Hospital and CUF Infante Santo, Lisbon, Portugal

²Administração Central dos Serviços de Saúde / Health Services Central Administration, Portugal

³Center for Research in Health Technologies and Information Systems, Faculty of Medicine, University of Porto, Porto, Portugal

KEY WORDS

asthma; epidemiology; hospitalization; mortality; trend

Corresponding author

Mário Morais-Almeida
Immunoallergy Department, CUF
Descobertas Hospital
Rua Mário Botas, 1998-018 Lisbon,
Portugal
E-mail: mmoraisalmeida@netcabo.pt
Phone: +351 917 232 267

Summary

Aim. To evaluate nationwide asthma hospitalizations and hospital mortality from the year 2000 to 2010. **Methods.** Data from the Health Services Central Administration of the Portuguese Ministry of Health on hospital admissions and hospital mortality in the National Health Service in mainland Portugal, from January 1st 2000 to December 31st 2010, were analysed. Cases with bronchial asthma as a main diagnosis were selected. **Results.** We found a mean frequency of asthma hospitalizations of 2.5 / 1000 hospital admissions, 28.1 / 100,000 inhabitants (66.6/100,000 in < 19 years old). The global frequency of hospital admissions decreased 18.6% from 2000 to 2010 ($r = -0.85$, $p = 0.002$), and 47.0% in those aged 0 to 2 years old ($r = -0.77$, $p = 0.008$). There were 261 hospital deaths attributed to asthma (68.5% > 65 years old), accounting for an in-hospital mortality of 8.0 / 1000 asthma hospitalizations and 2.4 / 1,000,000 inhabitants, with no change throughout the years. **Conclusions.** Asthma hospitalization rates have decreased, especially in younger children. Mortality remained unchanged, particularly in the elderly; this might be explained by deficient control in this age group.

Introduction

Asthma is a chronic inflammatory disorder of the airways associated with widespread, but variable, airflow obstruction within the lung, that is often reversible either spontaneously or with treatment (1). There are over 300 million people with asthma worldwide (1) and an estimated 695,000 Portuguese with current asthma (defined as “self-report of asthma and one of the following: at least one medical appointment due to asthma in the last 12 months; current use of asthma medication; or asthma symptoms in the last 12 months), with a prevalence of 6.8% in this population (2). Of Portuguese preschool children, 9.4% had four or more episodes of wheezing in the previous year (3). The World Health Organization has estimated that 15 million disability-adjusted life years (DALYs) are lost annually due to asthma, representing 1% of the total global disease burden; moreover, annual worldwide deaths from asthma have been estimated at 250,000 (1).

Awareness of this gave rise to the 2001 National Asthma Control Programme (PNCA) of the Portuguese National Health Authority. This was inspired by the Global Initiative for Asthma (GINA) and set up to reduce asthma morbidity and mortality and improve asthmatics' quality of life and well-being (4). Two of the PNCA evaluation parameters were the number of hospitalizations due to asthma and the annual mortality.

As a previous study has depicted the regional differences of hospital admissions and mortality from asthma (5), our aim was to evaluate nationwide asthma hospitalizations and hospital mortality from the year 2000 to 2010, with a particular focus on the evolution of these parameters in different age groups.

Methods

Data from the Health Services Central Administration of the Portuguese Ministry of Health on global and asthma hospital

admissions and hospital mortality in the National Health Service in mainland Portugal, from January 1st 2000 to December 31st 2010, were analysed.

Cases with bronchial asthma as a main diagnosis (ICD, ninth revision, 493x) were selected, excluding all those in which bronchial asthma was recorded in a secondary position.

Hospital admissions, hospital stay days, days spent in intensive care units (ICU), mortality and costs are reported according to year and age group, in crude frequency and adjusted to the number of inhabitants.

Data on year and age-adjusted population resident in mainland Portugal were retrieved from the National Institute of Statistics (6). Spearman Rank Correlation (7) was used to evaluate yearly variation and considered statistically significant for a p-value < 0.05.

Results

Hospital admissions

From January 1st 2000 to December 31st 2010 there were 32,504 asthma hospitalizations, with a mean of 2955 hospitalizations per year, 2.5 per 1000 hospital admissions, and a mean annual asthma hospitalization rate of 28.1 per 100,000 inhabitants living in mainland Portugal.

Asthma hospitalization frequency was higher in children aged 5 years old or younger (134.9 per 100.000 inhabitants), with an age-specific frequency of 66.6 per 100,000 children and adolescents aged under 19 years old (**table 1**). Females accounted for 18,112 (55.7%) of asthma hospitalizations. Asthma hospitalization rates in children aged 0 to 5 years old was 1.6 higher in boys (172.9 vs. 110.8 per 100,000 girls aged under 6 years old), while in those aged 66 or older it was 2.1 times more frequent in women (42.1 vs. 19.7 per 100,000 men aged over 65 years old) (**figure 1**). Hospitalizations were consistently less frequent during the summer, peaking in the months of December and January (**figure 2**).

Table 1 - Age-specific asthma hospitalization frequency and mean annual asthma hospitalization rate per 100,000 inhabitants in mainland Portugal.

Age (years)	Total frequency	Mean annual frequency	Per 100,000 inhabitants
0-2	4668	424.4	131.3
3-5	4946	449.6	138.4
6-12	4953	450.3	59.1
13-18	911	82.8	11.8
19-40	4078	370.7	11.0
41-65	6677	607.1	18.9
> 65	5909	537.2	29.7

Figure 1 - Age and gender-specific mean annual hospitalization rate per 100,000 inhabitants.

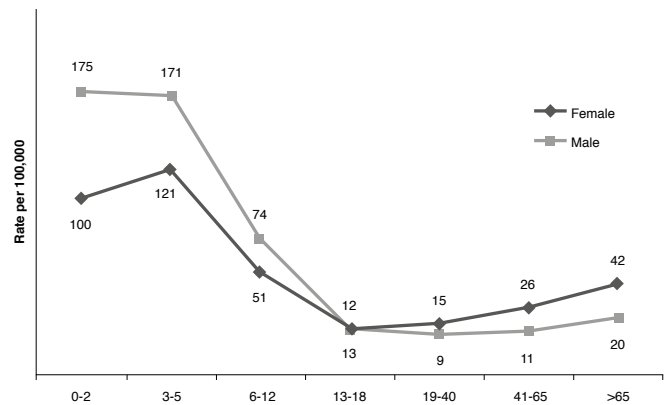
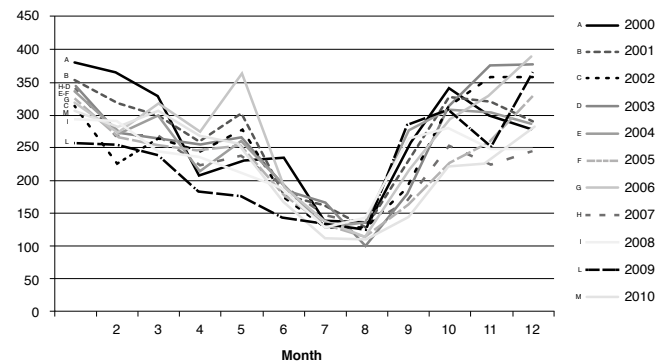


Figure 2 - Asthma hospitalization frequency according to month of discharge.



Hospital stay days

The total number of hospital stay days was 185,146, with a mean (SD) stay of 5.9 (0.29) days, which increased with age (r = 0.89, p = 0.01), ranging from 2.9 days in the 3 to 5-year-old group to 9.7 days in those aged over 65 years old.

Days spent in an intensive care unit (ICU) comprised a total of 5122 days, representing 2.8% of all asthma hospital stay days, ranging from 2.2% in those aged 41 to 65 years old to 4.2% of all asthma stay days in children 3 to 5 years old.

Mortality

During this 11 year period there were 261 deaths attributed to asthma in hospitalized patients, 149 (57.1%) in females, with a frequency of 8.0 per 1000 asthma hospitalizations and a mean

annual asthma hospital mortality of 2.4 per 1,000,000 inhabitants. People aged older than 65 accounted for 68.5% of asthma hospital mortality, while the paediatric age group accounted for 1.9% (**table 2**).

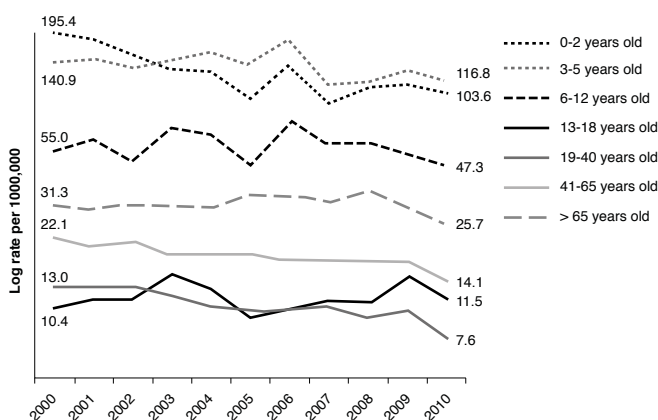
Table 2 - Age-specific asthma hospital mortality frequency and mean annual asthma hospital mortality rates per 1,000 asthma hospitalizations and per 1,000,000 inhabitants in mainland Portugal.

Age (years)	Total frequency	Mean annual frequency	Per 1,000 Hospitalizations	Per 1,000,000 inhabitants
0-2	1	0.1	0.2	0.3
3-5	0	0.0	0.0	0.0
6-12	2	0.2	0.4	0.3
13-18	2	0.2	2.2	0.3
19-40	25	2.3	6.1	0.7
41-65	52	4.7	7.8	1.5
> 65	178	16.1	30.1	8.9

Costs

A total 36,602,995 € was spent in asthma hospitalizations, with a mean cost of 1184 € per hospitalization and of 198 € per hospital stay day, ranging from 117 € in those aged 41 to 65 years old, to 285 € in adults between 19 and 40 years old.

Figure 3 - Yearly variation in age-specific asthma hospitalization rate per 100,000 inhabitants.



Yearly variation

Throughout the years, there has been an overall decrease in asthma hospitalization rate ($r = -0.85$, $p = 0.002$), with 18.6% less hospitalizations in 2010 compared to the year 2000 and a more important decrease in those aged 0 to 2 years old ($r = -0.77$, $p = 0.008$, -47.0%), 19 to 40 years old ($r = -0.87$, $p < 0.001$, -41.5%) and 41 to 65 years old ($r = -0.98$, $p < 0.001$, -36.2%) (**figure 3**). There were no significant timeline changes in overall mortality rate ($r = 0.19$, $p = 0.578$), mortality rate in the oldest age group ($r = 0.40$, $p = 0.225$), mean hospital stay days ($r = 0.07$, $p = 0.838$) or mean cost per patient ($r = 0.35$, $p = 0.286$) (**table 3**).

Table 3 - Yearly variation (2000-2010) in asthma hospitalization rate per 100,000 inhabitants, asthma hospital mortality rate per 1,000,000 inhabitants, mean hospital stay days and mean cost per patient (€).

Year	Hospitalization rate	Mortality rate	Hospital stay days	Cost per patient
2000	31.2	2.1	5.69	1,108
2001	30.8	2.1	5.86	1,122
2002	29.1	1.5	6.21	1,181
2003	29.8	2.9	5.51	1,218
2004	28.7	2.3	6.03	1,277
2005	26.2	3.0	6.39	1,192
2006	30.5	2.0	5.61	1,105
2007	25.6	2.1	6.31	1,252
2008	26.4	2.2	5.95	1,198
2009	25.7	1.6	5.67	1,155
2010	25.4	3.0	5.87	1,230

Discussion

This study describes hospitalization rates attributed to asthma in mainland Portugal from the year 2000 to 2010. We found a mean frequency of asthma hospitalizations of 2.5 per 1000 hospital admissions, 28.1 per 100,000 inhabitants and 66.6 per 100,000 inhabitants aged under 19 years old, which was lower than the one reported from 1995 to 1999 in the United States (76 per 100,000 Caucasian inhabitants) using a similar methodology (8).

The seasonal predominance of asthma hospitalizations during winter is in agreement with other northern hemisphere countries (9) and is probably related to a higher frequency of respiratory infections as a cause for asthma exacerbation in all age groups.

The frequency of hospital admissions from asthma decreased 18.6% from the year 2000 to 2010, in accordance with the trend for decrease in asthma hospitalizations worldwide (8). We found a particularly important decrease in the number of hospital admissions in younger children, where hospitalizations remain the highest. In the study by *Brandão et al* (10), severe asthma was the only predictive factor for hospital admission in children aged 4 to 19 years old. In 124 Portuguese children with asthma, the three most significant independent risk factors for hospital admission were previous hospitalization, environmental tobacco exposure and atopy (11). We have previously reported in a nationwide population-based study that 24.5% of Portuguese preschool children had current wheezing and 9.4% had four or more episodes of wheezing in the previous year, while only 5% referred an asthma diagnosis and 4% of these were treated with inhaled corticosteroids (3,12). This underdiagnosis and undertreatment of asthma in preschool children, along with recurrent hospitalizations (13), might explain the higher rates of asthma-related hospital admissions in this age group. On the other hand, tobacco smoke restrictions in Portugal since 2008 might be a positive factor influencing the decrease in hospitalizations.

During this 11-year period there were 261 deaths attributed to asthma in hospitalized patients, accounting for an in-hospital asthma mortality of 8.0 per 1000 asthma hospitalizations (0.8%) and 2.4 per 1,000,000 inhabitants. This frequency is in accordance with the reported < 1% found in other studies, namely in the United Kingdom (0.4%) (14), United States (0.5%) (15) and Spain and Latin America (0.8%) (16). The former study (16) showed that female gender, out of hospital cardiopulmonary arrest and arterial pH < 7.3 during hospitalization were strongly associated with asthma mortality. *Watson et al* (14) found that women and those over 45 years old had the highest rate of death, possibly reflecting asthma prevalence, while *Woods et al* (17) reported worse outcomes in men. In our study, 55.7% of asthma hospitalizations and 57.1% of asthma deaths occurred in women, which is not in favour of a higher risk for mortality in the female gender, although a comparative study was not possible. However, while only 24.9% of asthma hospital admissions occurred in those aged over 65 years old, 68.5% of in-hospital mortality were in this age group, which might be related to other frequent comorbidities in the elderly, namely cardiovascular disease and diabetes, decreased asthma control and deficient awareness of their asthma control level. This is in line with results found in the Portuguese National Asthma Survey, performed in 2010, where lack of asthma control was significantly more frequent in females and in the elderly (18,19). Despite previous studies showing a downward trend in asthma deaths, less significant in those aged 65 or older (20), we could not find an improvement in mortality either in the total or elderly population.

The main limitation of this study is the fact that we excluded patients with asthma as a secondary diagnosis, even when the main diagnosis was respiratory insufficiency, failure or arrest (possible complications of an asthma exacerbation) or respiratory infection (a frequent cause for exacerbation). This methodology probably leads to an underreporting of asthma hospitalizations, which is much lower than the 3.9% prevalence of lifelong hospitalization in children aged 6 to 17 years old from a population-based nationwide *Portuguese* survey (21). However, including other diagnosis would introduce distorting factors in the analysis and hamper comparability with other studies. Another limitation results from the confidentiality of data supplied by the Health Services Central Administration, from which it is not possible to assess if one given patient has been hospitalized more than once. It would have been interesting to evaluate if the high frequency of hospital admissions in children is due to recurrent hospitalization, as suggested in other studies (10), as this information would impact on future strategies for decreasing hospitalization rates in these age groups.

The strengths of the study are the inclusion of nationwide data on asthma hospitalization and mortality over a period of 11 years, the categorization in different age groups and the analysis according to the population for a given age group and year, which allowed for the calculation of rates per 100,000 inhabitants and comparability with other studies in different populations.

As asthma hospitalization rates vary inversely with inhaled corticosteroid use, implying that most hospitalizations are preventable (22,23), the Portuguese National Health Service in 2011 produced a recommendation for physicians focusing on asthma control (24), with frequency of prescription of inhaled corticosteroid per diagnosed asthma patient being an evaluation parameter of the implementation of this recommendation. Despite the observed reduction in asthma hospitalizations, possibly due to the impact of the National Asthma Control Programme started in 2001 (4), an effort to further reduce hospitalization rates and especially mortality needs to be pursued, with particular attention to the older patients with asthma (25).

References

1. From the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA) 2015. Available from: <http://www.ginasthma.org> (accessed on 20th July, 2015).
2. Sa-Sousa A, Morais-Almeida M, Azevedo LF, Carvalho R, Jacinto T, Todo-Bom A, et al. Prevalence of asthma in Portugal - The Portuguese National Asthma Survey. *Clin Transl Allergy*. 2012;2(1):15.
3. Pereira AM, Morais-Almeida M, Santos N, Nunes C, Almeida Fonseca J. Wheezing in preschool children in Portugal - prevalence, characterization and association with rhinitis. *Rev Port Imunoalergologia*. 2014;22(3):215-26.
4. Programa Nacional de Controlo da Asma - Direção-Geral de Saúde. 2000.

5. Bugalho de Almeida A, Covas A, Prates L, Fragoso E. Asthma hospital admission and mortality in mainland Portugal 2000-2007. *Rev Port Pneumol*. 2009;15(3):367-83.
6. Statistics Portugal (Instituto Nacional de Estatística). Available from: <http://www.ine.pt> (accessed on 26th November, 2011).
7. Wessa P. Spearman Rank Correlation (v1.0.0) in Free Statistics Software (v1.1.23-r7): Office for Research Development and Education; 2009. Available from: http://www.wessa.net/rwasp_spearman.wasp (accessed on 1st November, 2011).
8. Lang DM, Polansky M, Sherman MS. Hospitalizations for asthma in an urban population: 1995-1999. *Ann Allergy Asthma Immunol*. 2009;103(2):128-33.
9. Roy SR, McGinty EE, Hayes SC, Zhang L. Regional and racial disparities in asthma hospitalizations in Mississippi. *J Allergy Clin Immunol*. 2010;125(3):636-42.
10. Brandão HV, Cruz CS, Guimarães A, Camargos PAM, Cruz AA. Predictors of hospital admission due to asthma in children and adolescents enrolled in an asthma control program. *J Bras Pneumol*. 2010;36(6):700-6.
11. Gaspar A, Morais-Almeida M, Nunes C. Epidemiologia da asma grave. *Rev Port Imunoalergologia*. 2006;14(Suppl. 2):27-41.
12. Pereira AM, Morais-Almeida M, Santos N, Nunes C, Bousquet J, Almeida Fonseca J. Severity of rhinitis and wheezing is strongly associated in preschoolers: A population-based study. *Pediatr Allergy Immunol*. 2015. doi: 10.1111/pai.12430 *Pediatr Allergy Immunol*. 2015;26(7):618-27.
13. Macy ML, Stanley RM, Sasson C, Gebremariam A, Davis MM. High turnover stays for pediatric asthma in the United States: analysis of the 2006 Kids' Inpatient Database. *Med Care*. 2010;48(9):827-33.
14. Watson L, Turk F, James P, Holgate ST. Factors associated with mortality after an asthma admission: A national United Kingdom database analysis. *Respir Med*. 2007;101(8):1659-64.
15. Krishnan V, Diette GB, Rand CS, Bilderback AL, Merriman B, Hansel NN, et al. Mortality in patients hospitalized for asthma exacerbations in the United States. *Am J Respir Crit Care Med*. 2006;174(6):633-8.
16. Javier Rodrigo G, Plaza V, Bardagí Forn S, Perpiñá Tordera M, Salas J. Factors associated with mortality in patients hospitalized in Spain and Latin America for acute severe asthma in 1994, 1999, and 2004. *J Bras Pneumol*. 2008;34(8):546-51.
17. Woods SE, Brown K, Engel A. The influence of gender on adults admitted for asthma. *Gend Med*. 2010;7(2):109-14.
18. Sa-Sousa A, Morais-Almeida M, Azevedo LF, Carvalho R, Todo-Bom A, Loureiro C, et al. The Portuguese national asthma survey – Over 40% of asthma patients are controlled. *Allergy*. 2011;66(Suppl. 94):571.
19. Sa-Sousa A, Amaral R, Morais-Almeida M, Araújo L, Azevedo LF, Bugalho-Almeida A, et al. Asthma control in the Portuguese National Asthma Survey. *Rev Port Pneumol*. 2015;21(4):209-13.
20. Campbell MJ, Cogman GR, Holgate ST, Johnston SL. Age specific trends in asthma mortality in England and Wales, 1983-95: Results of an observational study. *BMJ*. 1997;314(7092):1439-41.
21. Ferreira-Magalhães M, Sá-Sousa A, Morais-Almeida M, Azevedo LF, Azevedo I, Pereira AM, et al. High prevalence of hospitalisation for asthma in a population-based paediatric sample. *Arch Dis Child*. 2015;100(5):507-8.
22. Adams RJ, Fuhlbrigge A, Finkelstein JA, Lozano P, Livingston JM, Weiss KB, et al. Impact of inhaled antiinflammatory therapy on hospitalization and emergency department visits for children with asthma. *Pediatrics*. 2001;107(4):706-11.
23. Suissa S, Ernst P, Kezouh A. Regular use of inhaled corticosteroids and the long term prevention of hospitalisation for asthma. *Thorax*. 2002;57(10):880-4.
24. Abordagem e controlo da asma - Norma nº 016/2011 de 27/09/2011 atualizada a 14/06/2012. Available from: <http://www.dgs.pt> (accessed on 15th July, 2013).
25. Pite H, Pereira AM, Morais-Almeida M, Nunes C, Bousquet J, Fonseca JA. Prevalence of asthma and its association with rhinitis in the elderly. *Respir Med*. 2014;108(8):1117-26.

Conflicts of interest: none

Funding source: self-funded