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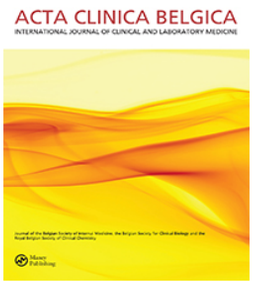

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Original Paper

Asthma exacerbations: factors related to longer hospital stay

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Background: Hospital admissions account for a significant part of asthma cost, but with significant differences between geographic areas.
Aims: The aim of our study is to analyse hospital admissions due to asthma, as well as the factors associated with longer hospital stays.
Methods: A review was retrospectively carried out on all admissions of patients over 18 years old due to exacerbation of asthma occurring in our hospital between the years 2000 and 2010. The personal characteristics of each patient, the asthma personal history, characteristics of every exacerbation, as well as the treatment before admission and after hospital discharge were recorded.
Results: During the study period, there were 2163 hospital admissions in 1316 patients (mean age 62.6 years; mean hospital stay 11.6 days). The admissions mainly occur in winter, in the 56–75-year age group, and in patients with severe asthma. Female sex, higher comorbidity, a greater number of emergencies due to asthma in the previous year, and baseline treatment with theophylline were independently associated to longer hospital stay.
Conclusions: The management of asthma in our population seems improvable. There appears to be a need to optimise both the diagnosis and treatment of the disease, and to identify risk factors as important as tobacco habits. As regards exacerbations, the hospital stay and mortality must be significantly reduced.

Keywords: Asthma, Exacerbations, Hospital admissions, Length of stay, Risk factors

Introduction

Asthma is a highly prevalent disease that involves increased health care costs, as well having a high impact on the quality of life of the patients and their families. Hospital admissions account for a significant part of these costs. Among the European Union (EU) member states, asthma accounted for an average of 53 hospital admissions per 100,000 inhabitants in 2009.[1–3] The annual direct and indirect costs in the 28 EU countries due to asthma are estimated at 34 billion euros.[2,3]

The prognosis of the disease seems to have improved in the last few years, but with significant differences between geographic areas.[2,3] In Spain, a slight downward trend is observed in the mortality due to asthma, although hospital admissions continue to increase, particularly in elderly women.[4,5]

The majority of exacerbations that lead to a hospital admission are deemed to be preventable, suggesting a lack of control and inadequate management of the disease.[6,7]

Various factors have been associated with longer hospital stays in admissions due to asthma, although there are significant differences between different geographical areas and health care models.[8–10]

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The aim of this study is to analyse hospital admissions due to asthma in our health area, as well as the factors associated with longer hospital stays.

Material and methods

A review was retrospectively carried out on all admissions of patients over 18 years old due to exacerbation of asthma occurring in our hospital between the years 2000 and 2010. These data were gathered by two members of the research team, by reviewing the clinical records. In cases where there were discrepancies in the evaluation of any data, the decision was made by consensus with the rest of the group members.

Cases were excluded where the reason was due to another specific cause, such as pulmonary embolism or pneumonia.

The personal characteristics of each patient were recorded, including age (classified into four groups: from 18 to 35 years, from 36 to 55 years, from 56 to 75 years, and greater than 75 years), gender, body mass index (BMI), classifying the patients as normal weight when they had a BMI less than 25 kg/m^2, as overweight with a BMI greater than or equal to 25, and obese with a BMI greater than or equal to 30.[11] Comorbidity was evaluated according to the Charlson index, [12] and smoking classified as active smokers, ex-smokers or never smoked.

An analysis was performed on the asthma personal history, including the baseline treatment, lung function, based on the forced expiratory volume (FEV1) as a percentage of the reference value, the baseline severity of the asthma according to the Global Initiative for Asthma (GINA) 2006 criteria,[13] having attended any hospital emergency department (ED), and admissions due to asthma in the previous year. For the exacerbations, an analysis was made that included the season of the year (taking the months of January to March as winter, April to June as spring, July to September as summer and October to December as autumn), duration of hospital stay (including from the time the patient arrived in the ED until discharge), and treatment after hospital discharge.

Previous year, visits to the ED were stratified into three groups, one group consisting of those who did not make any visit to the ED in the previous year, another group that made one to three visits and a last group that made four or more visits to the ED in the previous year.

A mean prolonged stay was defined as a duration longer than that of the mean of our population.

The Clinical Research Ethics Committee of Galicia at our institution approved the protocol.

Statistical analysis

These data were tested for normal distribution using the Kolmogorov–Smirnov test. The Student *t* test was used for the comparison of the two category of continuous variables when these had a normal distribution, and the Mann–Whitney *U* test when they had a non-parametric distribution. For the comparison of continuous variables of more than two categories, we used ANOVA in the normal distribution variable and the Kruskal Wallis test when the distribution was non-Gaussian. The comparison of the categorical variables was performed using the Chi-squared test. The adjusted Odds Ratios of the increase in the mean hospital stay were calculated depending on variables that were significant in the univariate analysis.

Results

There were 2163 hospital admissions by 1316 patients during the study period. The mean age was 62.6 years (Standard deviation (SD): 18.7). The median hospital stay was 9 days (Interquartile range: 6–13), and the mean stay was 11.6 days (SD: 8.6). For this study, two cases were excluded from this study as the hospital stay was longer than one year due to social criteria; thus reducing the analysis to the 2,161 remaining admissions.

The highest number of admissions was in the year 2010, with 255 episodes, and the least was in 2006 with 138

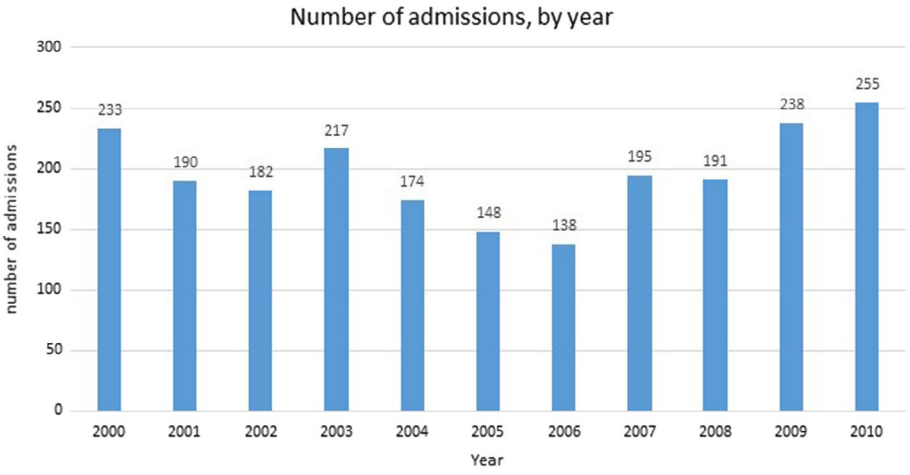

Figure 1 Number of admissions, by year

Table 1 Characteristics of patients and length of hospital stay

Hospital stay, mean (SD)	11.6 (8.6)
Hospital stay, median (IQR)	9 (6–13)
Age, mean (SD)	62.6 (18.7)
Gender, n (%)	
Male	550 (25.5)
Age, n (%)	
18–35 years	274 (12.7)
36–55 years	366 (16.9)
56–75 years	898 (41.6)
Over 75 years	623 (28.8)
Season, n (%)	
Winter	721 (33.4)
Spring	528 (24.4)
Summer	321 (14.9)
Autumn	591 (27.3)
Asthma severity, n (%)	
Intermittent	287 (13.3)
Mild	286 (13.2)
Moderate	346 (16.0)
Severe	741 (34.3)
Unclassified	501 (23.2)
Smoking, n (%)	
Never	1037 (48.0)
Current	292 (13.5)
Former	248 (11.5)
Not available	584 (27.0)
Charlson index, n (%)	
0	580 (26.8)
1	763 (35.3)
2	426 (19.7)
≥3	3691 (18.1)
FEV1 (% of reference value), n (%)	
≥80%	397 (18.4)
60–80%	286 (13.2)
<60%	396 (18.3)
Not available	1082 (50.1)
Arterial blood gases, median (interquartile range)	
pO_2 (mmHg)	58.2 (52.3–65.8)
pCO_2 (mmHg)	38.4 (34.2–44.0)
pH	7.43 (7.40–7.46
BMI, n (%)	
Normal weight	324 (14.9)
Overweight	364 (16.8)
Obesity	394 (18.2)
Not available	1082 (50.1)
Emergency last year, n (%)	
0	1361 (62.9)
1	484(22.4)
≥2	316 (14.6)
Hospital admissions last year, n (%)	
0	1196 (55.3)
1–3	853 (39.4)
≥4	112 (5.2)

Notes: SD: standard deviation; IQR: interquartile range; BMI: body mass index.

episodes (Figure 1). Taking into account that the population over 18 years old in our hospital catchment area was 327,965 patients in half the study period, it assumes an admission rate per 100,000 inhabitants that varies between a minimum of 42.1 in the year 2006 and a maximum of 77.7 in the year 2010.

The characteristics of the patients admitted are shown in Table 1. It is noted that the admissions mainly occur, in winter (33.4% of the total) in the 56–75-year age group (41.6% of the total), and in patients with severe asthma (34.3% of the total).

It should be pointed out that no spirometry results could be obtained from the clinical history in 50% of the patients, and in 27% of the clinical histories, there were no data on smoking habits (Table 1).

As regards patient treatment, it is highlighted that 39% of the patients were not on any baseline control treatment, and more than 14% of this group were still without treatment on discharge (Table 2).

It should be mentioned that 4.9% of the hospital admissions were admitted to ICU, and 2.6% died during admission (Table 2).

There was an independent association with a hospital stay longer than the mean stay, as well and being female, a higher comorbidity, a greater number of emergency visits due to asthma in the previous year, and a baseline treatment with theophylline (Table 3).

Discussion

Hospital admissions due to asthma are an objective indicator of the morbidity of the disease in a determined area. In our health area, there appears to be an increasing trend in the number of hospital admissions in the last few years, unlike that observed in the majority of developed western countries.[3,5] The Netherlands appears to be another exception in this regard, where there is still an increase in hospital admissions due to asthma, despite the high rate in the use of inhaled corticosteroids.[14] In a recent publication from the Basque Country (Spain), an increase was observed in the hospital admissions due to asthma in the population greater than 64 years old, and a decrease in those less than 15 years old.[15]

Several factors could be associated with this increase in hospital admissions due to asthma. On the one hand, the management of the disease does not appear to be optimal in our population, as indicated by the fact that more than half the patients with a hospital admission due to asthma had no spirometry in the clinical history. This lack of use of spirometry has also been mentioned in other populations, despite the fact that an objective periodic evaluation of lung function is a recommendation in the guidelines.[3] In a study conducted in the USA, spirometry was used in 76% of patients consulting specialists in asthma, while it dropped to 38% in family medicine.[16] The situation appears to be a little better in France, where in a study of family doctors, 19% of asthmatics lacked spirometry.[17] In Canada, spirometry in the diagnosis was used in the diagnosis of 52% of Primary Care patients.[18] In Qatar, the situation is worse, with only 37.2% of asthmatics with a spirometry performed in the 5 years prior to the study.[19]

It is also worth noting that in 27% of the clinical histories of asthma patients, there was no record on tobacco habits. This figure is similar to that mentioned in a study conducted in the Clinic de Barcelona Hospital, where in 27.1% of the hospital discharge reports made no explicit mention of tobacco habits of the patients admitted to this hospital.[20] In the study by Nieva et al., at the time of

Table 2 Characteristics of asthma exacerbation and type of treatment

	n (%)
Fever	
<37.9	1764 (81.6)
≥37.9	397 (18.4)
ICU	106 (4.9%)
Death	57 (2.6)
Treatment before admission	
Beta-2 agonists	1099 (50.9)
ICS	358
Combination ICS-LABA	927 (42.9)
LTRA	267 (12.4)
Some controller	1318 (60.8)
Theophylline	147 (6.8)
Anticholinergic	792 (36.6)
OCS	303 (14)
DOT	248 (11.5)
Treatment after hospital discharge	
Beta-2 agonists	1130 (52.3)
ICS	380
Combination ICS-LABA	1459 (67.5)
LTRA	324 (15)
Some controller	1855 (85.6)
Theophylline	129 (6)
Anticholinergic	1046 (48.4)
OCS	1458 (67.5)
DOT	300 (13.9)

Notes: ICU: intensive care unit; ICS: inhaled corticosteroids; LABA: long acting beta-2 agonists; LTRA: leukotriene receptor antagonist; OCS: oral corticosteroids; DOT: domiciliary oxygen therapy.

Table 3 Factors related to longer hospital stay, multivariate analysis.

	OR (CI 95%)
Gender	
Male	1
Female	1.59 (1.15–2.19)
Severity	
Intermittent	1
Mild	0.87 (0.51–1.48)
Moderate	0.91 (0.51–1.60)
Severe	1.60 (0.93–2.77)
Charlson index	
0	1
1	1.54 (1.00–2.36)
2	2.04 (1.25–3.33)
≥3	1.92 (1.11–3.29)
Emergency visits last year	
0	1
1–3	1.48 (1.08–2.03)
≥4	2.24 (1.05–4.79)
Theophylline as baseline treatment	
No	1
Yes	1.98 (1.18–3.31)

Notes: OR: odds ratio; CI: confidence interval.

discharge, the patients were also asked if they remembered being questioned about their tobacco habits during admission, and only 30.8% of them mentioned this. This discrepancy between recent memory and that recorded in the clinical history suggests that there may be some inaccuracy in the discharge report, as such that the investigation into tobacco habits by health professionals could even be less than that reflected in the discharge reports.[20]

Likewise, 40% of the patients did not receive any treatment to control the disease, and even after admission, more than 14% of the patients did not follow any treatment. This under-use of medication to control the disease has also been observed in other countries like Japan, where less than 10% of asthmatic patients are being treated with these drugs.[21–23] In this regard, the best data appear in California, where more than 78% of patients receive treatment to control the asthma.[23] These results are in concordance with the low level of asthma control observed in the Spanish population, where only 36% of asthmatics are well controlled.[6]

Another possible cause of the increase in hospital admissions due to asthma could be the increase in prevalence in the population of the area studied. This seems likely, given the increase in asthma prevalence in the Spanish population in the past few years.[24]

The admissions are predominantly female. This finding seems reasonable, given the higher prevalence of asthma in women.[3] Other factors possibly related to the higher probability of hospital admissions in women have also been mentioned in the literature, such as greater expression of symptoms of the disease in females [25]; the fact that women are normally more exposed than men to cleaning products and other irritants in the workplace and at home [26,27]; higher female life expectancy, making their admission due to asthma more likely,[28] a different perception of the disease, leading to a higher probability of hospital admission in women, although with less severity of the exacerbation,[29] and more psychiatric comorbidity that increases the use of health resources.[30,31]

The higher number of admissions in the winter period is in agreement with that mentioned in the literature, and is mainly associated with virus infections, which are the main cause of exacerbation of asthma.[15,32]

Hospital mortality is slightly high compared to other populations, where there are mortality rates less than 1%.[10,33,34]

The hospital stay seems prolonged in our patients compared to that reported in the literature.[10,28,35] Factors independently related to a longer hospital stay were being female, greater comorbidity, having more emergency consultations in the year prior to the current admission, and baseline treatment with theophylline.

In a publication with a population from the Basque Country, a higher incidence in admissions was also reported in the population over 64 years old.[15] Various factors can complicate the evolution of asthma in advanced ages. On the one hand, the comorbidities in themselves lead to a poorer prognosis, and at the same time, they can lead to undertreatment, in order to avoid the secondary effects of these. Functional impairment reduces the mobility capacity of the respiratory apparatus, the response to bronchodilator treatment is reduced with age, the immune capacity is impaired, or the perception of reduced symptoms that may lead to a delay in the request for health care assistance with the subsequent aggravation of the disease.[36]

As observed in other diseases, a higher comorbidity is associated with an increase in hospital stay in asthma exacerbations.[37]

The worse prognosis in patients with emergency consultations in the previous year is a constant in the literature.[38,39] This is clearly associated with a poorer control of the asthma, which leads to a worse prognosis for these patients.[39]

We hope that we can reduce the hospital admission rates due to asthma in the near future, for several reasons. On the one hand, the arrival of new biological treatments, with a different profile from those already available, may be useful in some selected.[40] On the other hand, a better classification of the patients, particularly the approach based on endotypes, would lead to a better understanding of the pathophysiological process that would make an optimal treatment redundant.[41] Another aspect is the increasing availability of healthcare in day hospitals that are being introduced in our region and could help to reduce hospital admissions, particularly the most severe patients.[42] Finally, home hospitalisation may also help in reducing the conventional hospital admission rates.[43]

On being retrospective, our study has some limitations, since the data missing in the medical records cannot be analysed, as well as the other data that could be relevant, such as stress factors or unexpected exposure to noxes/allergens. Although the asthma diagnosis based on hospital discharge record is shown to be highly reliable, it also does not allow us to confirm the final diagnosis. A recent Canadian study has analysed this aspect, observing that admissions with the primary discharge diagnosis of asthma had a positive predictive value of 90% of being asthma-related.[44]

Conclusion

The management of asthma in our population is frankly improvable, both in the outpatient setting and during hospital admission. In the management of patients in a baseline situation, there appears to be a particular need to optimise the diagnosis of the disease, as such that all patients should have lung function tests, to identify risk factors so important as tobacco habits, to adjust the control treatment of the disease to that recommended in the guidelines. As regards exacerbations, the hospital stay and mortality must be significantly reduced during admission. More attention to the factors associated to an extended hospital stay could help improve these results.

Compliance with ethical standards

This study was carried out without any external funding.

The Clinical Research Ethics Committee of Galicia at our institution approved the protocol.

Notes on contributors

Francisco-Javier Gonzalez-Barcala conceived and designed the study, and analysed and interpreted the data. He drafted the submitted article and approved the final version of the article.

Uxio Calvo-Alvarez acquired data, revised the article critically and approved the final version of the study.

Francisco-Javier Salgado-Castro analysed and interpreted the data, drafted the submitted article and approved the final version of the article.

David Facal analysed and interpreted the data, drafted the submitted article and approved the final version of the article.

Maria-Teresa Garcia-Sanz acquired the data, revised the article critically and approved the final version of the article.

Xavier Muñoz conceived and designed the study, and analysed and interpreted the data. The author drafted the submitted article and approved the final version of the article.

Nuria Garcia-Couceiro acquired the data, revised the article critically and approved the final version of the article.

Olalla Paz-Neira acquired the data, revised the article critically and approved the final version of the article.

Esther San-Jose conceived and designed the study, analysed and interpreted the data and approved the final version of the article.

Luis Valdes-Cuadrado conceived and designed the study, analysed and interpreted the data and approved the final version of the article.

Jose-Martin Carreira conceived and designed the study, analysed and interpreted the data, drafted the submitted article and approved the final version of the article.

Conflict of interest

No potential conflict of interest was reported by the authors.

References

1 Gonzalez Barcala FJ, la Fuente-Cid RD, Alvarez-Gil R, Tafalla M, Nuevo J, Caamaño-Isorna F. Factors associated with a higher prevalence of work disability among asthmatic patients. J Asthma. 2011;48:194–9.
2 Bousquet J, Addis A, Adcock I, Agache I, Agusti A, Alonso A, et al. Integrated care pathways for airway diseases (AIRWAYS-ICPs). Eur Respir J. 2014;44:304–23.
3 The Global Initiative for Asthma (GINA) [Internet]. [cited 2015 Dec 15]. Available from: http://www.ginasthma.org.
4 Gonzalez-Barcala FJ, Aboal J, Carreira JM, Rodriguez-Alvarez MX, Puga A, Sanjose E, et al. Trends of asthma mortality in Galicia from 1993 to 2007. J Asthma. 2012;49:1016–20.
5 Gonzalez-Barcala FJ, Aboal J, Valdes L, Carreira JM, Alvarez-Dobaño JM, Puga A, et al. Trends in adult asthma hospitalization: gender-age effect. Multidiscip Respir Med. 2011;6:82–6.
6 González Barcala FJ, la Fuente-Cid RD, Alvarez-Gil R, Tafalla M, Nuevo J, Caamaño-Isorna F. Factors associated with asthma control in primary care patients: the CHAS study. Arch Bronconeumol. 2010;46:358–63.
7 Hasegawa K, Sullivan AF, Tovar Hirashima E, Gaeta TJ, Fee C, Turner SJ, et al. A multicenter observational study of US adults with acute asthma: who are the frequent users of the emergency department? J Allergy Clin Immunol Pract. 2014;2:733–40.
8 Becerra BJ, Banta JE, Ghamsary M, Martin LR, Safdar N. Burden of mental illness on hospital and patient outcomes among asthma hospitalizations. J Asthma. 2016;53:392–7.
9 Pai S, Mancuso CA, Loganathan R, Boutin-Foster C, Basir R, Kanna B. Characteristics of asthmatic patients with and without repeat

emergency department visits at an inner city hospital. J Asthma. 2014;51:627–32.
10 Bugalho de Almeida A, Covas A, Prates L, Fragoso E. Asthma hospital admission and mortality in mainland Portugal 2000–2007. Rev Port Pneumol. 2009;15:367–83.
11 Available from: http://www.who.int/mediacentre/factsheets/fs311/en/ [updated 2014 15 Aug .
12 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–83.
13 Available from: http://www.ginasthma.org/local/uploads/files/GINA_Report_072007_1.pdf [updated 2014 15 Aug].
14 Gupta R, Anderson HR, Strachan DP, Maier W, Watson L. International trends in admissions and drug sales for asthma. Int J Tuberc Lung Dis. 2006;10:138–45.
15 Altzibar JM, Tamayo-Uria I, De Castro V, Aginagalde X, Albizu MV, Lertxundi A, et al. Epidemiology of asthma exacerbations and their relation with environmental factors in the Basque Country. Clin Exp Allergy. 2015;45:1099–108.
16 Nathan RA, Meltzer EO, Blaiss MS, Murphy KR, Doherty DE, Stoloff SW. Comparison of the Asthma in America and Asthma Insight and Management surveys: did asthma burden and care improve in the United States between 1998 and 2009? Allergy Asthma Proc. 2012;33:65–76.
17 Guittet L, Blaisdell CJ, Just J, Rosencher L, Valleron AJ, Flahault A. Management of acute asthma exacerbations by general practitioners: a cross-sectional observational survey. Br J Gen Pract. 2004;54:759–64.
18 To T, Guan J, Zhu J, Lougheed MD, Kaplan A, Tamari I, et al. Quality of asthma care under different primary care models in Canada: a population-based study. BMC Fam Pract. 2015 Feb;16:309. Available from: https://www.ncbi.nlm.nih.gov/pubmed/?term=to+T%2C+Guan+J%2C+Zhu+J%2C+et+al
19 Ibrahim WH, Suleiman NN, El-Allus F, Suleiman J, Elbuzidi AA, Guerrero MD, et al. The burden of adult asthma in a high GDP per capita country: the QASMA study. Ann Allergy Asthma Immunol. 2015;114:12–7.
20 Nieva G, Gual A, Mondon S, Walther M, Saltó E. Evaluation of brief intervention for smoking cessation in hospitalized patients. Med Clin (Barc). 2007;128:730–2.
21 Aït-Khaled N, Enarson DA, Bencharif N, Boulahdib F, Camara LM, Dagli E, et al. Implementation of asthma guidelines in health centres of several developing countries. Int J Tuberc Lung Dis. 2006;10:104–9.
22 Murase K, Tomii K, Chin K, Tsuboi T, Sakurai A, Tachikawa R, et al. The use of non-invasive ventilation for life-threatening asthma attacks: changes in the need for intubation. Respirology. 2010;15:714–20.
23 Eisner MD, Boland M, Tolstykh I, Mendoza G, Iribarren C. Intensive care unit admission for asthma: a marker for severe disease. J Asthma. 2005;42:315–23.
24 Urrutia I, Aguirre U, Sunyer J, Plana E, Muniozguren N, Martínez-Moratalla J. Changes in the prevalence of asthma in the Spanish cohort of the European Community Respiratory Health Survey (ECRHS-II)]. Arch Bronconeumol. 2007;43:425–30.
25 Schatz M, Clark S, Camargo CA Jr. Sex differences in the presentation and course of asthma hospitalizations. Chest. 2006;129:50–55.
26 Mendonça EM, Algranti E, de Freitas JB, Rosa EA, dos Santos Freire JA, de Paula Santos Ud U, et al. Occupational asthma in the city of São Paulo, 1995–2000, with special reference to gender analysis. Am J Ind Med. 2003;43:611–617.
27 Dimich-Ward H, Camp PG, Kennedy SM. Gender differences in respiratory symptoms – does occupation matter? Environ Res. 2006;101:175–183.
28 Chen Y, Stewart P, Johansen H, McRae L, Taylor G. Sex difference in hospitalization due to asthma in relation to age. J Clin Epidemiol. 2003;56:180–187.
29 Baibergenova A, Thabane L, Akhtar-Danesh N, Levine M, Gafni A, Leeb K. Sex differences in hospital admissions from emergency departments in asthmatic adults: a population-based study. Ann Allergy Asthma Immunol. 2006;96:666–72.
30 Woods SE, Sorscher J, King J, Hasselfeld K. Young adults admitted for asthma: does gender influence outcomes? J Womens Health (Larchmt). 2003;12:481–5.
31 ten Brinke A, Ouwerkerk ME, Zwinderman AH, Spinhoven P, Bel EH. Psychopathology in patients with severe asthma is associated with increased health care utilization. Am J Respir Crit Care Med. 2001;163:1093–6.
32 Brzezińska-Pawłowska OE, Rydzewska AD, Łuczyńska M, Majkowska-Wojciechowska B, Kowalski ML, Makowska JS. Environmental factors affecting seasonality of ambulance emergency service visits for exacerbations of asthma and COPD. J Asthma. 2015;15:1–7.
33 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;174:633–8.
34 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;101:1659–64.
35 Pascal L, Fuhrman C, Durif L, Nicolau J, Charpin D, Dujols P, et al. Trends in hospital admissions for asthma in France, 1998–2002. Rev Mal Respir. 2007;24:581–90.
36 Busse PJ, Mathur SK. Age-related changes in immune function: effect on airway inflammation. J Allergy Clin Immunol. 2010;126:690–9.
37 Diamantea F, Kostikas K, Bartziokas K, Karakontaki F, Tsikrika S, Pouriki S, et al. Prediction of hospitalization stay in COPD exacerbations: the AECOPD-F score. Respir Care. 2014;59:1679–86.
38 Griswold SK, Nordstrom CR, Clark S, Gaeta TJ, Price ML, Camargo CA Jr. Asthma exacerbations in North American adults: who are the "frequent fliers" in the emergency department? Chest. 2005;127:1579–86.
39 Schatz M, Meckley LM, Kim M, Stockwell BT, Castro M. Asthma exacerbation rates in adults are unchanged over a 5-year period despite high-intensity therapy. J Allergy Clin Immunol Pract. 2014;2:570–4.e1.
40 Mitchell PD, El-Gammal AI, O'Byrne PM. Emerging monoclonal antibodies as targeted innovative therapeutic approaches to asthma. Clin Pharmacol Ther. 2016;99:38–48.
41 Lötvall J, Akdis CA, Bacharier LB, Bjermer L, Casale TB, Custovic A, et al. Asthma endotypes: a new approach to classification of disease entities within the asthma syndrome. J Allergy Clin Immunol. 2011;127:355–60.
42 Cots F, Raventòs J, Ausín P, Chiarello P, Balcells E, Castells X, et al. The day hospital: analysis of results, costs and management of pneumology resources. Arch Bronconeumol. 2013;49:54–62.
43 Gonzalez Barcala FJ, Pose Reino A, Paz Esquete JJ, La Fuente Cid RD, Masa Vazquez LA, Alvarez Calderon P, et al. Hospital at home for acute respiratory patients. Eur J Intern Med. 2006;17:402–7.
44 Canadian Institute for Health Information [Internet]. Ottawa: CIHI data quality study of the 2005e2006 discharge abstract database. 2009. https://secure.cihi.ca/free_products/DAD_DQ_study_2005_2006_August_2009_e.pdf [cited 2016 Dec 8].