

## Clinical characteristics and prognosis in near-fatal asthma patients in Salvador, Brazil\*

Características clínicas e prognóstico em pacientes com asma quase fatal em Salvador, Bahia\*

Eduardo Vieira Ponte, Adelmir Souza-Machado, Carolina Souza-Machado, Rosana Franco, Álvaro Augusto Cruz

### Abstract

**Objective:** To determine the frequency of near-fatal asthma in a group of severe asthma patients, as well as the clinical characteristics and prognosis of these patients within a one-year follow-up period. **Methods:** A prospective study involving 731 low-income patients with severe asthma treated at a referral outpatient clinic located in the city of Salvador, Brazil. The patients were submitted to spirometry at admission, received medications for asthma, and were monitored regarding the frequency of asthma exacerbations during the follow-up period. A subsample of 511 patients also completed questionnaires regarding asthma symptoms and asthma-related quality of life. **Results:** Of the 731 patients studied, 563 (77%) were female. The median age was 47 years, and 12% were illiterate. Most of the patients had rhinitis, and 70 patients (10%) reported near-fatal asthma prior to admission. Of these 70 patients, 41 (59%) reported having been intubated previously. The patients reporting a history of near-fatal asthma at admission were more likely to have asthma exacerbations during the follow-up period and to respond poorly to therapy than were those not reporting such a history. At the end of the follow-up period, the scores on the two questionnaires were similar between the two groups of patients. **Conclusions:** The frequency of near-fatal asthma was high in this group of low-income patients with severe asthma. The patients with a history of near-fatal asthma had a worse prognosis than did those without such a history, although both groups had received the same kind of treatment. Curiously, the intensity of symptoms and the quality of life at the end of the study were similar between the two groups.

**Keywords:** Asthma/prevention and control; Asthma/complications; Quality of life; Prognosis.

### Resumo

**Objetivo:** Determinar a frequência de asma quase fatal em um grupo de pacientes com asma grave, assim como as características clínicas e o prognóstico desses pacientes em um ano de seguimento. **Métodos:** Estudo prospectivo envolvendo 731 pacientes de baixa renda com asma grave tratados em um ambulatório de referência para asma na cidade de Salvador (BA). Os pacientes realizaram espirometria na admissão do estudo, receberam medicações para asma e foram monitorizados quanto à frequência de exacerbações durante o seguimento. Uma subamostra de 511 pacientes também respondeu questionários de sintomas e de qualidade de vida relacionada a asma. **Resultados:** Dos 731 pacientes estudados, 563 (77%) eram do sexo feminino, com mediana de idade de 47 anos, e 12% não eram alfabetizados. A maioria dos pacientes apresentava rinite, e 70 (10%) relataram asma quase fatal antes da admissão. Desses 70 pacientes, 41 (59%) relataram terem sido intubados previamente. Os pacientes com asma quase fatal na admissão eram mais propensos a exacerbações de asma durante o acompanhamento e tiveram menor resposta ao tratamento do que aqueles sem asma quase fatal. Os resultados dos questionários no final do acompanhamento foram semelhantes nos dois grupos de pacientes. **Conclusões:** A frequência de asma quase fatal foi alta nesta população de pacientes com asma grave e de baixa renda. Os pacientes com histórico de asma quase fatal tiveram um pior prognóstico que aqueles sem esse histórico, embora tenham recebido o mesmo tratamento. Curiosamente, a intensidade dos sintomas e a qualidade de vida no final do estudo foram semelhantes entre os dois grupos de pacientes.

**Descritores:** Asma/prevenção e controle; Asma/complicações; Qualidade de vida; Prognóstico.

\* Study carried out at the Center of Excellence in Asthma, Federal University of Bahia, Salvador, Brazil.

Correspondence to: Eduardo Vieira Ponte. Programa para o Controle da Asma na Bahia, Rua Carlos Gomes, 270, 7º andar, CEP 40060-330, Salvador, BA, Brasil.

Tel. 55 11 2575-3324. E-mail: evponte@yahoo.com.br

Financial support: This study received financial support from the *Fundação de Amparo à Pesquisa do Estado da Bahia* (FAPESB, Bahia Research Foundation).

Submitted: 5 February 2011. Accepted, after review: 25 May 2011.

## Introduction

Although patients with asthma generally present with mild, intermittent symptoms, 20% of asthma patients present with symptom profiles that are associated with severe disease.<sup>(1)</sup> In comparison with other asthma patients, those with severe asthma have a poorer quality of life,<sup>(2)</sup> are at a higher risk of death,<sup>(3)</sup> and require greater health care expenditures.<sup>(4,5)</sup> Fortunately, treatment with inhaled corticosteroids and long-acting  $\beta_2$  agonists provides symptom control and improves the quality of life of such patients.<sup>(6)</sup>

A near-fatal asthma attack is characterized by asthma exacerbation accompanied by an increase in PaCO<sub>2</sub>, a need for orotracheal intubation, or cardiopulmonary arrest. Patients with near-fatal asthma should receive advanced life support in an ICU. The risk of death is higher in patients with a history of near-fatal asthma.<sup>(7)</sup> Deaths from asthma can be prevented by treatment with inhaled corticosteroids.<sup>(8)</sup> In some countries, government strategies aimed at optimizing the treatment of asthma have reduced the number of hospitalizations, the number of near-fatal asthma attacks, and the mortality from asthma.<sup>(9-11)</sup>

Although fatal and near-fatal attacks of asthma can be prevented, patients with severe asthma rarely receive the best treatment available. Studies have demonstrated that 10-60% of patients experiencing a near-fatal asthma exacerbation were not using inhaled corticosteroids regularly at the time of the attack.<sup>(12-15)</sup> After the attack, 35% of such patients continue to use inhaled corticosteroids irregularly and are not followed by a specialist.<sup>(7,15,16)</sup> Impaired perception of the severity of the symptoms and functional changes probably contributes to poor adherence to treatment in patients with a history of near-fatal asthma.<sup>(17-19)</sup>

According to the results of one study,<sup>(20)</sup> the prevalence of asthma in Brazil is high. In the city of Salvador, the capital of the state of Bahia, the estimated prevalence of asthma in adolescents is 25%.<sup>(20)</sup> The *Programa para o Controle da Asma e Rinite Alérgica na Bahia* (ProAR, Bahia State Asthma and Allergic Rhinitis Control Program) was launched in 2003 with the purpose of treating severe asthma patients via the Brazilian Unified Health Care System. The patients treated via the ProAR belong to the lower socioeconomic classes.<sup>(21)</sup> Therefore, they

cannot afford the inhaled corticosteroids and long-acting  $\beta_2$  agonists that are recommended in order to control moderate and severe asthma. Patients enrolled in the ProAR receive those medications for free, as well as receiving multidisciplinary treatment. A study involving a cohort of patients followed via the ProAR demonstrated that the rate of adherence to the treatment provided was 85%,<sup>(22)</sup> and that the number of hospitalizations was reduced by 90%.<sup>(21)</sup> A cohort of patients with severe asthma provides a good opportunity to study near-fatal asthma. The objective of the present study was to determine the frequency of near-fatal asthma in a group of severe asthma patients, as well as the clinical characteristics and prognosis of these patients within a one-year follow-up period.

## Methods

This was a prospective study involving patients who, between January of 2003 and December of 2007, were admitted to the ProAR referral outpatient clinic, located in the city of Salvador, Brazil. The inclusion criteria were having been diagnosed with severe uncontrolled asthma, in accordance with the Global Initiative for Asthma criteria, and being over 12 years of age. The exclusion criteria were having been diagnosed with respiratory comorbidities and having any severe extrapulmonary disease. The patients who reported having required ICU admission prior to enrollment in the study were classified as having a history of near-fatal asthma. The study design was approved by the Research Ethics Committee of the Federal University of Bahia School of Medicine Climério de Oliveira Maternity Hospital, and all participating patients gave written informed consent.

All of the patients were followed for one year. A total of 731 patients met the inclusion and exclusion criteria. Those patients were evaluated at five separate visits, designated V1, V2, V3, V4, and V5, with a 3-month interval between visits. During V1, the patients received an inhaled corticosteroid (beclomethasone or budesonide), a long-acting  $\beta_2$  agonist (formoterol), and a short-acting  $\beta_2$  agonist (albuterol). In addition, the patients underwent spirometry (Koko spirometer; PDS Instrumentation Inc., Louisville, CO, USA) and were interviewed about emergency room visits and hospitalizations for asthma attacks in the previous year, as well as

about their lifetime history of ICU admissions for asthma attacks. During the subsequent visits, the patients received the asthma medications and were interviewed about any emergency room visits, hospitalizations, and ICU admissions for asthma attacks occurring since their previous visit. During each of the five visits, the patients received multidisciplinary treatment, provided by physicians, nurses, pharmacists, social workers, psychologists, and physical therapists. During each visit, the doses of the asthma medications were adjusted, when necessary, at the discretion of the physician on duty, with the objective of achieving total control of asthma symptoms.

We also evaluated a subsample composed of the first 511 patients who appeared for V5 by reviewing the medications prescribed during the follow-up period, by administering the Asthma Control Questionnaire (ACQ) to assess the intensity of asthma symptoms in the last 7 days,<sup>(23)</sup> and by administering the Asthma Quality of Life Questionnaire (AQLQ) to assess asthma-related quality of life in the last 14 days.<sup>(24)</sup> In addition, the patients were clinically evaluated by a pulmonologist in order to determine whether they had experienced any asthma symptoms in the last 14 days. The patients also underwent spirometry after the treatment. A trained technician who was blinded to the clinical status of the patients administered the ACQ and the AQLQ.

Statistical analysis was performed in order to compare patients with a history of near-fatal asthma and those without. The chi-square test and Fisher's exact test were used in order to analyze categorical variables, and the Mann-Whitney test was used for ordinal and continuous variables. The logistic regression analysis was adjusted for age, gender, and FEV<sub>1</sub> in order to compare patients with a history of near-fatal asthma and those without in terms of prognosis and treatment response. In order to evaluate disease exacerbation during the study, the primary outcome measure was the need for emergency room treatment for asthma attacks. Other outcome measures, such as the need for hospitalization and the need for ICU admission, were also analyzed. The indicators of uncontrolled asthma at the end of the one-year follow-up period were the presence of asthma symptoms, as assessed by the pulmonologist during V5, and an ACQ score > 1.14.<sup>(25)</sup> Because

the patients had not been using inhaled corticosteroids before the study outset, we were able to create an index to assess treatment response. A > 90% reduction in the number of emergency room visits for asthma attacks during the study period in comparison with the patient-reported number of emergency room visits in the year preceding the study outset was considered to constitute good treatment response. The statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA). Categorical and continuous variables are expressed as absolute values (with proportions) and as medians (with interquartile ranges), respectively.

## Results

Table 1 shows the initial clinical characteristics of the 731 patients under study. Of the 731 patients studied, 563 (77%) were female. The median age was 47 years, and 12% were illiterate. Most of the patients presented with rhinitis. The proportion of patients who reported near-fatal asthma prior to enrollment in the study was 10%. Of those, 59% reported having been intubated and submitted to mechanical ventilation during their ICU stay. The initial pulmonary function test results were worse in the patients with a history of near-fatal asthma than in those without. There were no significant differences between the groups regarding age, gender, obesity, smoking history, level of education, or rhinitis.

Table 2 shows the improvement in asthma severity after enrollment in the study. The groups of patients with and without a history of near-fatal asthma were analyzed separately. In both groups, the number of asthma exacerbations requiring emergency room treatment and the number of asthma exacerbations requiring hospitalization were reduced by the treatment provided. However, pulmonary function improved only in the patients who had no history of near-fatal asthma.

As can be seen in Table 3, the logistic regression analysis showed that the risk of asthma exacerbation requiring emergency room treatment, hospitalization, or ICU admission during the follow-up period was higher in the patients with a history of near-fatal asthma than in those without. Treatment response was lower in the patients with a history of near-

**Table 1** – Characteristics of the 731 patients with severe asthma, categorized by the history of near-fatal asthma prior to enrollment in the study.<sup>a</sup>

Characteristics	All	With near-	Without near-	p
	patients (n = 731)	fatal asthma (n = 70)	fatal asthma (n = 661)	
Female gender	563 (77)	54 (77)	509 (77)	0.98
Age, years <sup>b</sup>	47 (37-57)	50 (39-58)	47 (36-57)	0.44
Duration of asthma symptoms, years <sup>b</sup>	28 (17-42)	31 (19-45)	27 (16-42)	0.20
Body mass index <sup>c</sup> > 35 kg/m <sup>2</sup>	46 (9)	4 (8)	42 (9)	0.75
Illiterate patients <sup>d</sup>	71 (12)	3 (6)	68 (13)	0.10
Smoking history > 10 pack-years <sup>e</sup>	85 (13)	7 (11)	78 (13)	0.55
Rhinitis <sup>f</sup>	588 (81)	58 (83)	530 (81)	0.71
FEV <sub>1</sub> < 60% of the value predicted at visit 1 <sup>g</sup>	284 (43)	34 (57)	250 (42)	0.03
History of mechanical ventilation	41 (6)	41 (59)	0 (0)	-

<sup>a</sup>Values expressed as n (%), except where otherwise indicated. <sup>b</sup>Values expressed as median (interquartile range). <sup>c</sup>Data available for 527 patients. <sup>d</sup>Data available for 592 patients. <sup>e</sup>Data available for 656 patients. <sup>f</sup>Data available for 724 patients. <sup>g</sup>Data available for 654 patients.

fatal asthma than in those without (OR = 0.4; 95% CI: 0.2-0.7), because the proportion of patients with a history of near-fatal asthma who presented with a > 90% reduction in the number of emergency room visits because of asthma attacks during the follow-up period was lower. In the present study, 11 patients died during the follow-up period. However, the logistic regression analysis showed no association between near-fatal asthma and death.

Table 4 shows that the scores on the ACQ and AQLQ, which were administered to the subsample of patients during V5 (after one year of follow-up and treatment), were similar between the groups of patients with and without a history of near-fatal asthma. The proportion of patients who reported having no symptoms of asthma during the appointment with the pulmonologist and the proportion of patients with controlled asthma (as assessed by the ACQ) were also similar between the two groups. The doses of the asthma medications prescribed during the study period were also similar between the two groups. After treatment,

severe airway obstruction continued to be more common in the patients with a history of near-fatal asthma.

## Discussion

The frequency of near-fatal asthma in the present study was 10%, which is unacceptably high, given that this condition carries considerable risk. Near-fatal asthma can be prevented with inhaled corticosteroids.<sup>(9-11)</sup> In Brazil, the government plays a fundamental role in facilitating access to inhaled corticosteroids because individuals with low incomes cannot afford those medications. A study conducted by our study group demonstrated that free distribution of inhaled corticosteroids and long-acting  $\beta_2$  agonists to patients with severe asthma is cost-effective, meaning that the government saves money that would otherwise be spent on hospitalizations, as well as improving the quality of life of patients in this population.<sup>(26)</sup>

In the present study, the treatment recommended in the current asthma guidelines

**Table 2** – Indicators of asthma severity before and during follow-up via the Bahia State Asthma and Allergic Rhinitis Control Program. Salvador, Brazil.<sup>a</sup>

Indicator	History of near-fatal asthma			No history of near-fatal asthma		
	(n = 69)		p*	(n = 657)		p*
	Year preceding inclusion	Year of study		Year preceding inclusion	Year of study	
Emergency room visits <sup>b</sup>	8 (4-34)	1 (0-5)	< 0.01	6 (2-24)	0 (0-2)	< 0.01
Hospitalizations <sup>b</sup>	1 (0-2)	0 (0-0)	< 0.01	0 (0-1)	0 (0-0)	< 0.01
FEV <sub>1</sub>	57 (47-73)	59 (50-73)	0.26	66 (49-80)	69 (55-83)	< 0.01

<sup>a</sup>Values expressed as median (interquartile range). <sup>b</sup>Number of episodes per patient per year. \*The Wilcoxon test.

**Table 3** - Relative risk for severe events in patients with a history of near-fatal asthma in a sample of patients with severe asthma (n = 726).<sup>a</sup>

Severe asthma-related event	Relative risk (95% CI)
Emergency room treatment during the follow-up period	2.4 (1.4-4.2)
Hospitalization during the follow-up period	3.7 (1.6-8.5)
ICU admission during the follow-up period	20 (1.8-231)
> 90% reduction in the number of emergency room visits <sup>b</sup>	0.4 (0.2-0.7)
Death during the follow-up period	0.6 (0.1-5.2)

<sup>a</sup>Logistic regression adjusted for age, gender, and pulmonary function test results. <sup>b</sup>Relative to the year preceding enrollment.

reduced the number of emergency room visits and hospitalizations for asthma attacks in patients with and without a history of near-fatal asthma. However, the risk of having exacerbations was higher in the patients with a history of near-fatal asthma than in those without. In addition, the chance of reducing the number of asthma exacerbations during the study period was lower in the patients with a history of near-fatal asthma than in those without. These data indicate that patients with a history of near-fatal asthma have worse prognoses.

Although the patients with a history of near-fatal asthma had more exacerbations and lower treatment response during the study period, the scores on the ACQ and AQLQ, administered during V5, were similar between the two groups of patients. The proportion of patients who, during V5, reported having no

asthma symptoms was also similar between the two groups, as was the proportion of patients with controlled asthma, as assessed by the ACQ score. This result leaves room for speculation. It is possible that patients with a history of near-fatal asthma respond slowly to treatment, given that the patients with a history of near-fatal asthma investigated in the present study had a larger number of exacerbations; however, by the end of the one-year follow-up period, those patients had achieved symptom control that was similar to that achieved by the patients without such a history. Another possibility is that the level of control of asthma symptoms between episodes of exacerbation is similar between the two groups, although patients with a history of near-fatal asthma are more susceptible to exacerbations. In addition, it is possible that patients with a history of near-fatal asthma have difficulty perceiving the severity of their condition and the degree of airway obstruction, as has been described in various studies.<sup>(17-19)</sup>

Although the treatment provided in the present study was appropriate for patients with severe asthma, the proportion of patients who were unable to achieve total control of asthma symptoms, as assessed during V5, was quite high. It is likely that multiple factors contributed to that situation, including the prescription of insufficient doses of inhaled corticosteroids, noncompliance with the treatment prescribed, and the presence of refractory asthma. By improving the quality of the treatment provided to asthma patients, the first two factors can be controlled, and total asthma control can be achieved by many of the patients who remained with symptoms at V5.

**Table 4** - Medications used during the study and indicators of controlled asthma at the final visit during the study period.<sup>a</sup>

Variable	With near-fatal asthma	Without near-fatal asthma	p
	(n = 51)	(n = 460)	
Budesonide > 800 µg/day	44 (86)	384 (83)	0.66
Long-acting β <sub>2</sub> agonist	46 (90)	391 (85)	0.33
Controlled asthma: clinical evaluation	18 (35)	190 (41)	0.38
ACQ score <sup>b</sup>	2.2 (1.4-3.1)	2.0 (1.1-2.7)	0.11
Controlled asthma: ACQ score < 1.14 <sup>c</sup>	9 (18)	109 (24)	0.24
AQLQ score <sup>b</sup>	3.8 (2.8-5.5)	3.8 (2.7-5.1)	0.99
FEV <sub>1</sub> < 60% of predicted <sup>d</sup>	22 (52)	132 (33)	0.01

ACQ: Asthma Control Questionnaire; and AQLQ: Asthma Quality of Life Questionnaire. <sup>a</sup>Values expressed as n (%), except where otherwise indicated. <sup>b</sup>Values expressed as median (interquartile range). <sup>c</sup>Data available for 466 patients. <sup>d</sup>Data available for 437 patients.

The findings of the present study indicate that near-fatal asthma represents the highest degree of asthma severity. We find it surprising that patients with a history of near-fatal asthma have been reported to have more in common with patients with mild or moderate asthma than do those with severe asthma, as assessed by parameters such as pulmonary function, atopy, and presence of inflammatory cells in sputum and blood.<sup>(27)</sup> Therefore, near-fatal asthma attacks can occur not only patients with severe asthma but also those who have mild or moderate asthma that goes untreated.

A history of near-fatal asthma was not associated with higher mortality in the present study. This is probably due to the fact that the study did not have sufficient power for that analysis, given that the prospective follow-up lasted only one year, and there were only 11 deaths. Studies involving a longer follow-up period, a larger sample size, or a combination of the two are needed in order to reach definitive conclusions regarding this issue. The diagnostic criteria for near-fatal asthma also merit discussion. The usual definition of near-fatal asthma is asthma exacerbation with severe respiratory failure, characterized by increased PaCO<sub>2</sub> or by respiratory arrest. In the present study, the patients were not evaluated in the ICU, in order to assess the severity of respiratory failure. However, in Brazil, public ICUs have few beds available, and most of those beds are reserved for cases that are more severe. In addition, 59% of the patients who were classified as having a history of near-fatal asthma in the present study reported having undergone orotracheal intubation. Therefore, it is very likely that those patients were classified appropriately.

In conclusion, the frequency of a history of near-fatal asthma was high in this group of low-income patients with undertreated severe asthma in the city of Salvador, Brazil. The patients with a history of near-fatal asthma had a worse prognosis than did those without. We found it curious that the patients with a history of near-fatal asthma did not differ significantly from those without such a history in terms of the post-treatment intensity of symptoms and quality of life.

## References

- Smith DH, Malone DC, Lawson KA, Okamoto LJ, Battista C, Saunders WB. A national estimate of the economic costs of asthma. *Am J Respir Crit Care Med.* 1997;156(3 Pt 1):787-93.
- Ekici A, Ekici M, Kara T, Keles H, Kocyigit P. Negative mood and quality of life in patients with asthma. *Qual Life Res.* 2006;15(1):49-56.
- Mitchell I, Tough SC, Semple LK, Green FH, Hessel PA. Near-fatal asthma: a population-based study of risk factors. *Chest.* 2002;121(5):1407-13.
- Stock S, Redaelli M, Luengen M, Wendland G, Civello D, Lauterbach KW. Asthma: prevalence and cost of illness. *Eur Respir J.* 2005;25(1):47-53.
- Franco R, Nascimento HF, Cruz AA, Santos AC, Souza-Machado C, Ponte EV, et al. The economic impact of severe asthma to low-income families. *Allergy.* 2009;64(3):478-83.
- Suissa S, Ernst P. Inhaled corticosteroids: impact on asthma morbidity and mortality. *J Allergy Clin Immunol.* 2001;107(6):937-44.
- Ishihara K, Hasegawa T, Okazaki M, Katakami N, Sakamoto H, Umeda B, et al. Long-term follow-up of patients with a history of near fatal episodes; can inhaled corticosteroids reduce the risk of death from asthma? *Intern Med.* 1995;34(2):77-80.
- Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med.* 2000;343(5):332-6.
- Zar HJ, Stickells D, Toerien A, Wilson D, Klein M, Bateman ED. Changes in fatal and near-fatal asthma in an urban area of South Africa from 1980-1997. *Eur Respir J.* 2001;18(1):33-7.
- Bellido Casado J, Plaza V, Bardagi S, Cosano J, López Viña A, Martínez Moragón E, et al. Is the incidence of near-fatal asthma decreasing in Spain? [Article in Spanish]. *Arch Bronconeumol.* 2006;42(10):522-5.
- Souza-Machado C, Souza-Machado A, Franco R, Ponte EV, Barreto ML, Rodrigues LC, et al. Rapid reduction in hospitalisations after an intervention to manage severe asthma. *Eur Respir J.* 2010;35(3):515-21.
- Turner MO, Noertjojo K, Vedal S, Bai T, Crump S, Fitzgerald JM. Risk factors for near-fatal asthma. A case-control study in hospitalized patients with asthma. *Am J Respir Crit Care Med.* 1998;157(6 Pt 1):1804-9.
- Schmitz T, von Kries R, Wjst M, Schuster A. A nationwide survey in Germany on fatal asthma and near-fatal asthma in children: different entities? *Eur Respir J.* 2000;16(5):845-9.
- Plaza V, Serrano J, Picado C, Sanchis J; High Risk Asthma Research Group. Frequency and clinical characteristics of rapid-onset fatal and near-fatal asthma. *Eur Respir J.* 2002;19(5):846-52.
- Dhuper S, Maggiore D, Chung V, Shim C. Profile of near-fatal asthma in an inner-city hospital. *Chest.* 2003;124(5):1880-4.
- Kesten S, Chew R, Hanania NA. Health-care utilization after near-fatal asthma. *Chest.* 1995;107(6):1564-9.
- Magadle R, Berar-Yanay N, Weiner P. The risk of hospitalization and near-fatal and fatal asthma in relation to the perception of dyspnea. *Chest.* 2002;121(2):329-33.
- Kikuchi Y, Okabe S, Tamura G, Hida W, Homma M, Shirato K, et al. Chemosensitivity and perception of dyspnea in patients with a history of near-fatal asthma. *N Engl J Med.* 1994;330(19):1329-34.
- Barreiro E, Gea J, Sanjuás C, Marcos R, Broquetas J, Milic-Emili J. Dyspnoea at rest and at the end of

- different exercises in patients with near-fatal asthma. *Eur Respir J*. 2004;24(2):219-25.
20. Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet*. 2006;368(9537):733-43.
  21. Ponte E, Franco RA, Souza-Machado A, Souza-Machado C, Cruz AA. Impact that a program to control severe asthma has on the use of Unified Health System resources in Brazil. *J Bras Pneumol*. 2007;33(1):15-9.
  22. Santos Pde M, D'Oliveira A Jr, Noblat Lde A, Machado AS, Noblat AC, Cruz AA. Predictors of adherence to treatment in patients with severe asthma treated at a referral center in Bahia, Brazil. *J Bras Pneumol*. 2008;34(12):995-1002.
  23. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J*. 1999;14(4):902-7.
  24. Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. *Eur Respir J*. 1999;14(1):32-8.
  25. Sastre J, Olaguibel J, Vega JM, Del Pozo V, Picado C, Lopez Viña A. Cut-off points for defining asthma control in three versions of the Asthma Control Questionnaire. *J Asthma*. 2010;47(8):865-70.
  26. Franco R, Santos AC, do Nascimento HF, Souza-Machado C, Ponte E, Souza-Machado A, et al. Cost-effectiveness analysis of a state funded programme for control of severe asthma. *BMC Public Health*. 2007;7:82.
  27. Romagnoli M, Caramori G, Braccioni F, Ravenna F, Barreiro E, Siafakas NM, et al. Near-fatal asthma phenotype in the ENFUMOSA Cohort. *Clin Exp Allergy*. 2007;37(4):552-7.

## ***About the authors***

---

### ***Eduardo Vieira Ponte***

Collaborator. Bahia State Asthma and Allergic Rhinitis Control Program, Salvador, Brazil.

### ***Adelmir Souza-Machado***

Professor. Institute of Health Sciences, Federal University of Bahia, Salvador, Brazil.

### ***Carolina Souza-Machado***

Professor. Federal University of Bahia School of Nursing, Salvador, Brazil.

### ***Rosana Franco***

Physician. Octávio Mangabeira Specialized Hospital, Bahia State Health Department, Salvador, Brazil.

### ***Álvaro Augusto Cruz***

Professor. Federal University of Bahia School of Medicine, Salvador, Brazil.