Gender differences in the perception of asthma and respiratory symptoms in a population sample of asthma patients in four Brazilian cities*

Diferenças entre os sexos na percepção de asma e sintomas respiratórios em uma amostra populacional em quatro cidades brasileiras

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Abstract

Objective: To evaluate the impact of asthma, by gender, in a population sample of asthma patients in Brazil. Methods: We conducted face-to-face interviews with 400 subjects (> 12 years of age) included in a national probability telephone sample of asthma patients in the Brazilian state capitals of São Paulo, Rio de Janeiro, Curitiba, and Salvador. Each of those 400 subjects completed a 53-item questionnaire that addressed five asthma domains: symptoms; impact of asthma on quality of life; perception of asthma control; exacerbations; and treatment/medication. Results: Of the 400 patients interviewed, 272 (68%) were female. In relation to respiratory symptoms, the proportion of women reporting extremely bothersome symptoms (cough with sputum, tightness in the chest, cough/shortness of breath/tightness in the chest during exercise, nocturnal shortness of breath, and nocturnal cough) was greater than was that of men. Daytime symptoms, such as cough, shortness of breath, wheezing, and tightness in the chest, were more common among women than among men. Women also more often reported that their asthma interfered with normal physical exertion, social activities, sleep, and life in general. Regarding the impact of asthma on quality of life, the proportion of subjects who reported that asthma caused them to feel that they had no control over their lives and affected the way that they felt about themselves was also greater among women than among men. Conclusions: Among women, asthma tends to be more symptomatic, as well as having a more pronounced effect on activities of daily living and on quality of life.

Keywords: Asthma/diagnosis; Asthma/prevention & control; Quality of life.

Resumo

Objetivo: Avaliar o impacto da asma em relação ao gênero em uma amostra populacional de pacientes asmáticos no Brasil. Métodos: Foram entrevistados pessoalmente 400 pacientes asmáticos com idade > 12 anos de uma amostra probabilística nacional por contato telefônico nas cidades de São Paulo, Rio de Janeiro, Curitiba e Salvador. Os indivíduos responderam um questionário de 53 questões relacionadas com cinco domínios da asma: sintomas; impacto da asma na vida; percepção do controle da asma; exacerbações; tratamento e medicación. Resultados: Dos 400 pacientes entrevistados, 272 (68%) eram do sexo feminino. Em relação aos sintomas respiratórios, uma maior proporção de mulheres relatou se sentir extremamente incomodada com seus sintomas (tosse com secreção, sensação de aperto no peito, tosse/falta de ar/sensação de aperto no peito durante exercícios, falta de ar noturna e tosse noturna) do que os homens. Sintomas diurnos, como tosse, falta de ar, chiado e sensação de aperto no peito, foram mais comuns nas mulheres que nos homens. Além disso, a asma interferiu mais frequentemente nos esforços físicos normais, atividades sociais, durante o sono e na vida em geral nas mulheres. Sobre o impacto da asma na qualidade de vida, as mulheres relataram mais frequentemente que os homens que a asma causava uma sensação de falta de controle sobre a própria vida e que eram afetadas na forma como se sentiam em relação a si mesmas. Conclusões: As mulheres asmáticas apresentam mais sintomas e são mais afetadas em suas atividades diárias e qualidade de vida.

Descritores: Asma/diagnóstico; Asma/prevenção & controle; Qualidade de vida.

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Introduction

Bronchial asthma is a chronic inflammatory disease characterized by airflow limitation that resolves spontaneously or with treatment. This inflammation also causes increased airway responsiveness. These pathophysiological changes cause recurrent episodes of wheezing, dyspnea, tightness in the chest, and cough, particularly at night and upon waking in the morning.

Asthma is one of the most prevalent chronic diseases worldwide and is the most common indication for hospitalization among children. In Brazil, the prevalence of asthma among children and adolescents is close to 20% and is high in all regions of the country. Environmental factors, including allergens, cigarette smoke, air pollution, and viral respiratory infections, are associated with asthma symptoms and severity. Some factors, such as family history, atopy, and gender, also play a role in the development and progression of asthma.

Current epidemiological studies suggest that there is a higher prevalence of asthma among males before puberty, after which asthma predominates among females. Women experience greater increases in the prevalence of and mortality from asthma over time, have a greater prevalence of bronchial hyperresponsiveness, and use healthcare services more often, including visits to the emergency room and hospitalizations, as well as reporting respiratory symptoms more often and poorer quality of life. Because asthma is a typical multifactorial disease, in which genetic, environmental, pathophysiological, and immunological factors play a role, the reasons for specific gender differences may also be multiple, such as differences in airway physiology and pathology, hormonal interference in women, differences in immune response to high-titer measles vaccine, risk of infectious diseases in childhood, and behavioral differences between men and women.

In Brazil, the prevalence of asthma and wheezing has been shown to be higher in two age groups of boys: 6–7 years and 10–12 years. In two other studies conducted in Brazil, girls aged 13–14 years had more respiratory symptoms than did boys of the same age. However, there are still few studies investigating the frequency of attacks, the impact of asthma, and the intensity of symptoms that affect men and women differently. Therefore, the objective of the present study was to evaluate, in a population sample of asthma patients in Brazil, the possibility of gender differences in five asthma domains: symptoms; impact of asthma on quality of life; perception of asthma control; exacerbations; and treatment/medication. This information will enhance the existing knowledge of how asthma affects men and women and can be useful for developing asthma management plans.

Methods

The Latin America Asthma Insight and Management survey was conducted in five Latin American countries (Argentina, Brazil, Mexico, Venezuela, and Puerto Rico) and followed the same design as that of the Asthma Insight and Management surveys conducted in the United States, Europe, Canada, Asia, and the Pacific region. The objective of the survey was to investigate asthma patients’ perception of their disease.

In Brazil, 4,545 households were selected from a national probability sample in four cities (São Paulo; Rio de Janeiro; Curitiba; and Salvador). The selected households were contacted by phone to investigate whether there were any subjects with physician-diagnosed asthma there. If there were two or more subjects with asthma in the household, only one of them was randomly selected for a scheduled face-to-face interview, which was conducted by trained professional interviewers. In total, 400 patients or parents/legal guardians of those aged 12–17 years were interviewed face to face (Figure 1). The questionnaire consisted of 53 questions concerning five major asthma domains: symptoms; impact of asthma on quality of life; perception of asthma control; exacerbations; and treatment/medication. Each interview lasted approximately 35 minutes.

Each domain addressed by the questionnaire was assessed at two time periods: the past 12 months and the past four weeks. For the past 12 months, history of exacerbations, symptoms of worsening disease, severe attacks, hospitalization, emergency room visits, and regular medical visits were assessed based on the recollection of respondents. In addition, still regarding the past year, the impact of asthma on patients’ lives was assessed by using questions concerning the frequency of asthma-related absences from school or work, as well as asthma-related limitation in activities of daily living, productivity on days when experiencing an asthma attack, and the
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Results

We interviewed 400 asthma patients in four Brazilian cities: 191 in São Paulo (47.8%); 144 in Rio de Janeiro (36.0%); 28 in Curitiba (7.0%); and 37 in Salvador (9.2%). Of those patients, 128 (32%) were male and 272 (68%) were female. There were no gender differences in age, smoking status, level of education, number of asthma patients in the household, passive smoking, presence of pets in the household, or adherence to maintenance medication in the past four weeks (Table 1). In relation to asthma control, as defined by GINA criteria, the gender proportion in the controlled asthma group (10.2% men vs. 8.8% women) and in the partially controlled asthma group (64.8% men vs. 52.6% women) was similar; however, a greater proportion of females was observed in the uncontrolled asthma group (25.0% men vs. 38.6% women; p = 0.02). We found no statistically significant gender difference for use of maintenance medication in the past four weeks (p = 0.56).

Table 2 shows that the proportion of women reporting cough with sputum, tightness in the chest, cough/shortness of breath/tightness in the chest during exercise, and nocturnal symptoms (shortness of breath and cough) was greater than that of men (p < 0.05). Women reported a greater frequency of these symptoms than did men (Table 3).

In comparison with men, women more often reported that their asthma interfered with normal physical exertion (p = 0.005), social activities (p = 0.001), sleep (p = 0.006), and life in general (p = 0.01), but not for sports/recreation (Table 4). The proportion of women who agreed with the statements “asthma causes me to feel that I have no control over my life” and “asthma affects the way I feel about myself” was significantly greater than that of men (Table 5).

Discussion

Our results suggest that, compared with men with asthma, women with asthma experience influence of the disease on quality of life. Activities of daily living were assessed by five questions concerning sports, recreation, physical exertion, social activities, sleep, and interference with life. Respondents scored each question on a 1-4 point scale, corresponding to the degree of asthma-related limitation in those activities (1: high interference; 2: some interference; 3: very little interference; and 4: no interference).

The frequency of daytime and nocturnal respiratory symptoms, its relationship with usual activities, and the use of rescue and maintenance medication were assessed for the past four weeks. On the basis of these assessments, patients were classified as having well-controlled asthma, partially controlled asthma, or uncontrolled asthma, as defined by the Global Initiative for Asthma (GINA). Those same parameters were also assessed for the worst month in the past 12 months.

The study was approved by the Research Ethics Committee of the Federal University of São Paulo Hospital São Paulo (CEP no. 238487 of April 5, 2013).

Statistical analysis

Numerical data are presented as mean and standard deviation, whereas categorical data are expressed as frequency and proportion. The chi-square test was used to compare categorical data between the groups (males and females), and the Student’s t-test was used to compare the means. The frequency of respiratory symptoms was rated from 1 to 4, with 1 and 4 meaning “every day” and “never”, respectively. The impact of asthma on sports, normal physical exertion, social activities, sleep, and life in general was scored from 1 to 4, with 1 and 4 meaning “asthma interfered a lot” and “asthma did not interfere at all”, respectively. Values of p < 0.05 were considered statistically significant.
a greater impact and frequency of respiratory symptoms and more often have asthma-related limitations in daily living. These differences have been the target of many studies, which investigate physiological, psychological, and environmental mechanisms related to asthma. In contrast to the literature, we found no gender differences in the prevalence of asthma even after stratification into different age groups.

It is known that, up to the age of 10-12 years, asthma is more prevalent among boys than among girls, and that, after puberty, it becomes more common among girls. It was not possible to assess age-related trends in asthma prevalence, because the sample consisted of individuals aged over 12 years.

The higher prevalence of asthma among women during their reproductive years coincides with increased bronchial hyperresponsiveness. Approximately 20-40% of women with asthma report worsening of their respiratory symptoms during the premenstrual and menstrual period. The mechanism of worsening of asthma during the menstrual cycle remains unknown, but suggestions include increased serum levels of progesterone, increased mucous secretions, increased synthesis of prostaglandins during the premenstrual period, and abnormal $\beta_2$-adrenergic

Table 1 - Demographic data of the 400 asthma patients interviewed in Brazil.*

| Data                          | Men   | Women | p     |
|------------------------------|-------|-------|-------|
| Age group                    |       |       |       |
| 12-17 years (n = 42)         | 13.8 ± 2.8 | 13.5 ± 2.2 | 0.67  |
| 18-40 years (n = 183)        | 28.7 ± 6.5 | 29.7 ± 6.2 |       |
| > 40 years (n = 175)         | 53.8 ± 11.1 | 53.0 ± 9.8 |       |
| Smoking status               |       |       |       |
| Smoker                       | 32 (25.0) | 64 (23.5) | 0.15  |
| Former smoker                | 39 (30.5) | 64 (23.5) |       |
| Nonsmoker                    | 56 (43.8) | 143 (52.9) |       |
| Level of education           |       |       |       |
| Illiterate/≤ 4 years of school | 21 (16.4) | 40 (14.8) | 0.60  |
| ≤ 9 years of school          | 22 (17.2) | 36 (13.3) |       |
| High school                  | 66 (51.6) | 158 (58.3) |       |
| College                      | 19 (14.8) | 37 (13.7) |       |
| Number of asthma patients in the household | 1.13 ± 0.36 | 1.24 ± 0.57 | 0.06  |
| Passive smoker as a child    | 64 (50.0) | 139 (51.1) | 0.49  |
| Passive smoker at home       | 47 (37.0) | 90 (33.3) | 0.13  |
| Pets                         | 63 (50.0) | 136 (50.0) | 0.33  |

*Values expressed as n (%) or mean ± SD.

Table 2 - Frequency and proportion of asthma patients who reported extremely bothersome respiratory symptoms in the past four weeks, by gender.*

| Symptoms                          | Men  | Women | p     |
|-----------------------------------|------|-------|-------|
| Daytime cough                     | 37 (29.1) | 98 (36.7) | 0.14  |
| Daytime shortness of breath       | 48 (38.4) | 116 (44.1) | 0.43  |
| Breathlessness/wheezing           | 49 (39.2) | 129 (48.5) | 0.23  |
| Cough with sputum                 | 34 (27.2) | 92 (36.7) | 0.01  |
| Tightness in the chest            | 34 (28.3) | 116 (46.0) | 0.005 |
| Cough/shortness of breath/tightness in the chest during exercise | 40 (33.3) | 110 (43.8) | 0.03  |
| Waking at night with shortness of breath | 54 (45.8) | 144 (57.6) | 0.01  |
| Waking at night with a cough      | 51 (41.1) | 138 (55.0) | 0.002 |

*Values expressed as n (%).

Table 3 - Respiratory symptom score during the worst month in the past 12 months, by gender (1: every day; 4: never).*

| Symptoms                          | Men  | Women | p     |
|-----------------------------------|------|-------|-------|
| Daytime cough                     | 2.38 ± 0.68 | 2.21 ± 0.74 | 0.03  |
| Daytime shortness of breath       | 2.77 ± 0.63 | 2.56 ± 0.78 | 0.007 |
| Breathlessness/wheezing           | 2.59 ± 0.68 | 2.39 ± 0.84 | 0.02  |
| Cough with sputum                 | 2.71 ± 0.70 | 2.60 ± 0.88 | 0.19  |
| Tightness in the chest            | 2.74 ± 0.69 | 2.51 ± 0.87 | 0.01  |
| Cough/shortness of breath/tightness in the chest during exercise | 2.73 ± 0.76 | 2.66 ± 0.89 | 0.47  |
| Nocturnal shortness of breath     | 2.58 ± 0.82 | 2.48 ± 1.03 | 0.33  |
| Nocturnal cough                   | 2.48 ± 0.85 | 2.44 ± 0.99 | 0.72  |

*Values expressed as mean ± SD.
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Table 4 - Asthma-related limitation in activities of daily living, as determined by the score (1: high interference; 4: no interference), by gender.

| Activities                   | Men          | Women        | p    |
|------------------------------|--------------|--------------|------|
| (n = 128)                    | (n = 272)    |              |      |
| Sports/recreation            | 2.62 ± 1.04  | 2.63 ± 1.08  | 0.93 |
| Normal physical exertion     | 2.74 ± 1.05  | 2.43 ± 1.01  | 0.005|
| Social activities            | 3.27 ± 0.94  | 2.89 ± 1.05  | 0.001|
| Sleep                       | 2.54 ± 1.05  | 2.22 ± 1.07  | 0.006|
| Interference with life       | 2.95 ± 0.98  | 2.65 ± 1.10  | 0.01 |

Values expressed as mean ± SD.

Table 5 - Frequency and proportion of asthma patients who agreed with any of the statements below, by gender.

| Statements                                                                 | Men       | Women      | p    |
|---------------------------------------------------------------------------|-----------|------------|------|
| (n = 128)                                                                 | (n = 272) |            |      |
| Asthma causes me to feel that I have no control over my life.              | 50 (39.1) | 141 (52.0) | 0.02 |
| I feel incapable because of asthma, compared with my friends.             | 33 (25.8) | 81 (29.8)  | 0.52 |
| Asthma affects the way I feel about myself.                               | 49 (38.3) | 147 (54.0) | 0.01 |
| At least once in my lifetime, I have had such a severe asthma episode     | 37 (28.9) | 100 (36.8) | 0.07 |
| that I thought my life was at risk.                                       |           |            |      |

Values expressed as n (%).

had a higher frequency of respiratory symptoms, such as cough and wheezing.\(^{(30,31)}\) One group of authors demonstrated a relationship between greater perception of shortness of breath and female gender,\(^{(10)}\) whereas another study showed that perception of dyspnea was dependent on bronchial responsiveness rather than on gender.\(^{(32)}\) Studies have shown that symptoms in men and women can be inherently different, representing a difference in the underlying mechanism of the disease or a difference in the perception of the symptom. Kauffmann & Becklake showed that, for any given FEV\(_1\) value, women experienced a greater degree of shortness of breath than did men.\(^{(13)}\) In addition, women had a more sensitive cough reflex to a given stimulus.\(^{(34)}\) On the basis of this information, some authors have argued that, compared with men, women have a greater perception of respiratory symptoms, especially shortness of breath.

Regarding activities of daily living, women experienced greater asthma-related limitation in normal physical exertion, social activities, and sleep, as well as higher interference with life. Given that they have a greater perception and frequency of respiratory symptoms, it is easy to understand that they develop more limitations in activities of daily living. These aspects directly affect the quality of life of women with asthma, explaining the fact that, compared with men, they have poorer quality of life, as described in previous studies.\(^{(8,12,35)}\)

The proportion of women who agreed that asthma caused them to feel that they had no control over their lives and that the disease affected the way they felt about themselves was also found to be greater. These results reflect how asthma reduces self-esteem in women with asthma. According to the results of a study, the correlation between dyspnea and the tendency toward social desirability is negative in men but positive in women.\(^{(11)}\) Psychologically, this could be explained by a certain repression. For men, being sick can be limiting in terms of social and professional relationships, and therefore, they tend to ignore their disease, especially in terms of social desirability. In contrast, for women, the disease may lead them to seek social support, which is reflected by a greater tendency toward social desirability. This interpretation is obviously only speculation, but it can explain the results obtained.
Quality of life impairment among women is not a characteristic only of asthma, but also of other chronic diseases. It has been suggested that the relationship between gender and quality of life in asthma is confounded by the higher levels of anxiety and depression among women. One group of authors found that, despite having lower mortality and higher life expectancy, women with asthma reported poorer health-related quality of life compared with men of the same age with asthma.

One of the explanations for the difference found between genders could be the greater exposure of women to risk factors, such as household environmental factors and presence of pets in the household, as well as less use of maintenance medication. However, in the present study, there were no significant gender differences in exposure to passive smoking as a child or at home, presence of pets, or use of maintenance medication. Nevertheless, even experiencing similar exposures, men and women can show different patterns of response to allergen exposure. Elderly males and females exposed to air pollution and showing high total IgE levels and airway hyperreactivity have been reported to have different responses to the same level of exposure: whereas women had a decrease in PEF in the morning, men were more likely to have symptoms such as cough. Although we found no significant differences for those variables, other forms of environmental exposure that were not investigated in the present study, such as exposure to gas used for cooking, may contribute to gender differences.

Another relevant finding was the great proportion of patients (36.8% of women and 28.9% of men) who reported that, at least once in their lifetime, they had had such a severe asthma episode that they thought their lives were at risk. The proportion of women who reported this feeling was greater than that of men, but the difference was not significant. Attention should be drawn to the fact that most asthma attacks can be considered preventable, since there is effective drug treatment for asthma and there are self-management plans for asthma control.

It is of paramount importance that health care professionals be cognizant of and understand the greater impairment in women than in men with asthma. Appropriate asthma management requires an ongoing partnership between the patient and her physician regarding physiological factors (e.g., sexual hormones, obesity, pregnancy, and depression) and non-physiological factors (e.g., smoking and drug adherence), all of which can contribute to improving asthma control. Asthma-related risks seem to be higher for women than for men, but the implementation of a specific management plan, including psychological support, could certainly help reduce the burden of asthma on women.

The present study has some limitations that are inherent in epidemiological studies. The sample for the study was selected via a probability sample and an initial telephone contact, in four Brazilian state capitals. Another limitation could be the fact that data were collected on the basis of information provided by patients rather than on information abstracted from medical records. However, the present study differs from other epidemiological studies, because asthma patients were defined only as those who had a physician-confirmed diagnosis of asthma. The second difference was the fact that all interviews were conducted face to face. In addition, the results found here are consistent with those found in the literature.

In conclusion, to our knowledge, this is the first study in Brazil that has shown clearly and in depth that, among women, asthma is more poorly controlled, causes greater interference with life, and is associated with a higher frequency of respiratory symptoms. These factors result in women experiencing poorer quality of life and greater social distress compared with men. Our study provides solid support for the clinical importance of physical and psychological differences between genders, as well as underlining the fact that there is a need to implement gender-specific approaches to asthma management. Future studies are needed to investigate gender differences in the development and progression of asthma.

References

1. Fanta CH. Asthma. N Engl J Med. 2009;360(10):1002-14. http://dx.doi.org/10.1056/NEJMoa0804579
2. Sole D, Wandalsen GF, Camelo-Nunes IC, Naspitz CK; ISAAC - Brazilian Group. Prevalence of symptoms of asthma, rhinitis, and atopic eczema among Brazilian children and adolescents identified by the International Study of Asthma and Allergies in Childhood (ISAAC) - Phase 3. J Pediatr (Rio J). 2006;82(5):341-6.
3. Mannino DM, Homa DM, Akinbami LJ, Moorman JE, Gwynn C, Redd SC. Surveillance for asthma—United States, 1980-1999. MMWR Surveill Summ. 2002;51(1):1-13.
4. Postma DS. Gender differences in asthma development and progression. Gend Med. 2007;4 Suppl 8:S133-46.

5. Asthma and respiratory symptoms in 6–7 yr old Italian children: gender, latitude, urbanization and socioeconomic factors. SIDIARI (Italian Studies on Respiratory Disorders in Childhood and the Environment). Eur Respir J. 1997;10(8):1780–6. http://dx.doi.org/10.1183/09031936.97.1081780

6. Strachan DP, Butland BK, Anderson HR. Incidence and prognosis of asthma and wheezing illness from early childhood to age 33 in a national British cohort. BMJ. 1996;312(7040):1195–9. http://dx.doi.org/10.1136/bmj.312.7040.1195

7. Manfreda J, Sears MR, Becklake MR, Chan-Yeung M, Dimich-Ward H, Siersted HC, et al. Geographic and gender variability in the prevalence of bronchial responsiveness in Canada. Chest. 2004;125(5):1657-64. http://dx.doi.org/10.1378/chest.125.5.1657

8. Osborne ML, Vollmer WM, Linton KL, Buist AS. Characteristics of patients with asthma within a large HMO: a comparison by age and gender. Am J Respir Crit Care Med. 1998;157(1):123-8. http://dx.doi.org/10.1164/ajrccm.157.1.96012063

9. Baibergenova A, Thabane L, Akhtar-Danesh N, Levine JS, Grunewald EJ, Fishman P. Gender differences in the perception of asthma and respiratory symptoms in a population sample of asthma patients in four Brazilian cities. J Bras Pneumol. 2014;40(6):591-598.

10. Brand PL, Rijcken B, Schouten JP, Koëter GH, Weiss ST, Postma DS. Perception of airway obstruction in a random population sample. Relationship to airflow hyperresponsiveness in the absence of respiratory symptoms. Am Rev Respir Dis. 1992;146(2):396-401. http://dx.doi.org/10.1164/ajrccm.146.2.396

11. Nowohbiski R, Furgal M, Polczyn R, de Barbaro B, Szczeklik A. Gender gap in psychogenic factors may affect perception of asthma symptoms. J Invest Allergol Clin Immunol. 2011;21(3):193-8. PMid:21548447

12. Wijnhoven HA, Kriegsman DM, Snoek FJ, Hesselink AE, de Rijk JN, Koëter GH, Weiss ST, Postma DS. Perception of airway obstruction in a random population sample. Relationship to airflow hyperresponsiveness in the absence of respiratory symptoms. Am Rev Respir Dis. 1992;146(2):396-401. http://dx.doi.org/10.1164/ajrccm.146.2.396

13. Osman M. Therapeutic implications of sex differences in asthma and atopy. Arch Dis Child. 2003;88(7):587-90. http://dx.doi.org/10.1136/adc.88.7.587

14. Holt EA, Moulton LH, Siberry G, Weiss ST, Postma DS. Perception of airway obstruction in a random population sample. Relationship to airflow hyperresponsiveness in the absence of respiratory symptoms. Am Rev Respir Dis. 1992;146(2):396-401. http://dx.doi.org/10.1164/ajrccm.146.2.396

15. Burgess JA, Abramson MJ, Gurrin LC, Byrnes GB, Matheson MC, May CL, et al. Childhood infections and the risk of asthma: a longitudinal study over 37 years. Chest. 2012;142(3):647-54. http://dx.doi.org/10.1378/chest.11-1432

16. Redline S, Gold D. Challenges in interpreting gender differences in asthma. Am J Respir Crit Care Med. 1994;150(5 Pt 1):1219-21. http://dx.doi.org/10.1164/ajrccm.150.5.9752543

17. Casagrande RR, Pastorino AC, Souza RG, Leone C, Solé D, Jacob CM. Asthma prevalence and risk factors in schoolchildren of the city of São Paulo, Brazil [Article in Portuguese]. Rev Saude Publica. 2008;42(3):517-23. http://dx.doi.org/10.1590/S0034-8910200800300018

18. Boechat JL, Rios JL, Sant’anna CC, França AT. Prevalência e gravidade de sintomas relacionados a asma em escolares e adolescentes no município de Duque de Caxias, Rio de Janeiro. J Bras Pneumol. 2005;31(2):111-7. http://dx.doi.org/10.1590/S1806-37132005000200005

19. Muino A, Menezes AM, Reichert FF, Duquia RP, Chatkin M. Wheezing phenotypes from birth to adolescence: a cohort study in Pelotas, Brazil, 1993–2004. J Bras Pneumol. 2008;34(6):347–55. PMid:18622500

20. de Luna Mde F, Fischer GB, Luna JR, Silva MG, Almeida PC, Chiesa D. Prevalences of asthma and rhinitis among adolescents in the city of Fortaleza, Brazil: temporal changes. J Bras Pneumol. 2013;39(2):128–37.

21. Kuschnir FC, Cunha AJ, Braga Dde A, Silveira HH, Barroso MH, Aires ST. Asthma in 13–14-year-old schoolchildren in the city of Nova Iguaçu, Rio de Janeiro State, Brazil: prevalence, severity, and gender differences [Article in Portuguese]. Cad Saude Publica. 2007;23(4):919-26. http://dx.doi.org/10.1590/S0100-65692007000400019

22. Gal despite: In展位. 2002;9:10.1186/1710-1492-9-11

23. Britton J, Pavord I, Richards K, Knox A, Wisnewski A, Wahedna I, et al. Factors influencing the occurrence of airway hyperreactivity in the general population: the importance of atopy and airway calibre. Eur Respir J. 1994;7(5):881–7. PMid:8050544

24. Agarwal AK, Shah A. Menstrual-linked asthma. J Asthma. 1997;34(6):539-45. http://dx.doi.org/10.3109/02707909709055398

25. Gibbs CJ, Cou tts II, Lock R, Finnegon OC, White RJ. Premenstrual exacerbation of asthma. Thorax. 1984;39(11):833-6. http://dx.doi.org/10.1136/thx.39.11.833

26. Janson C, Chinn S, Jarvis D, Burney P. Determinants of wheezing phenotypes from birth to adolescence: importance of inan androgen exposure. Lancet. 1988;2(8607):370–2. http://dx.doi.org/10.1136/s0140-6736(88)82837-1

27. Alberts WM. ‘Circa Menstrual’ rhythmicity and asthma. Chest. 1997;111(4):840–2. http://dx.doi.org/10.1378/chest.111.4.840

28. Tan KS. Premenstrual asthma: epidemiology, pathogenesis and treatment. Drugs. 2001;61(14):2079-86. http://dx.doi.org/10.1016/S0160-719X(01)00005-0

29. Troisi R, Speizer FE, Willett WC, Trichopoulos D, Rosner B, Menopause, postmenopausal estrogen preparations, and the risk of adult-onset asthma. A prospective cohort study. Am J Respir Crit Care Med. 1995;152(4 Pt 1):1183-8. http://dx.doi.org/10.1164/ajrccm.152.4.7551368

30. Janson C, Chinn S, Jarvis D, Burney P. Determinants of cough in young adults participating in the European Community Respiratory Health Survey. Eur Respir J. 2001;18(4):647-54. http://dx.doi.org/10.1183/09031936.01.0008701

31. Ishizuka T, Matsuzaki S, Aoki H, Yatomi M, Kamide K, Inagaki M. Gender differences in symptoms and FENO. Allergy Asthma Clin Immunol. 2011;7(1):15 http://dx.doi.org/10.1186/1710-1492-7-15

32. Stravinskaite K, Malakauskas K, Sitkauskiene B, Sakalauskas L. Gender differences in the perception of asthma and respiratory symptoms in a population sample of asthma patients in four Brazilian cities. J Bras Pneumol. 2014;40(6):591-598.
33. Kauffmann F, Becklake M. Maladies obstructives pulmonaires: un paradigme de la complexité des différences de santé entre hommes et femmes. Med Sci (Paris). 1996;12(2):209-33.

34. Dicpinigaitis PV, Rauf K. The influence of gender on cough reflex sensitivity. Chest. 1998;113(5):1319-21. http://dx.doi.org/10.1378/chest.113.5.1319

35. Belloch A, Perpi-á M, Martinez-Moragón E, de Diego A, Martinez-Francés M. Gender differences in health-related quality of life among patients with asthma. J Asthma. 2003;40(8):945-53. http://dx.doi.org/10.1081/JAS-120024595

36. Trawick DR, Holm C, Wirth J. Influence of gender on rates of hospitalization, hospital course, and hypercapnea in high-risk patients admitted for asthma: a 10-year retrospective study at Yale-New Haven Hospital. Chest. 2001;119(1):115-9. http://dx.doi.org/10.1378/chest.119.1.115

37. Boezen HM, Vonk JM, van der Zee SC, Gerritsen J, Hoek G, Brunekeef B, et al. Susceptibility to air pollution in elderly males and females. Eur Respir J. 2005;25(6):1018-24. http://dx.doi.org/10.1183/09031936.05.00076104

38. Kerkhof M, de Monchy JG, Rijken B, Schouten JP. The effect of gas cooking on bronchial hyperresponsiveness and the role of immunoglobulin Eur Respir J. 1999;14(4):839-44. http://dx.doi.org/10.1034/j.1399-3003.1999.14d20.x

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