

# The relationship between the severity of asthma and comorbidities with anxiety and depressive disorders

## Relação entre a gravidade da asma e comorbidade com transtornos de ansiedade e depressão

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### Abstract

**Objective:** There is evidence that asthma is associated with increased frequency of psychiatric symptoms and mental disorders. Our aim was to assess the frequency of anxiety and depressive disorders in a sample of asthmatic outpatients and observe if there is any relationship between this comorbidity and the severity of asthma. **Method:** Sixty-two consecutive patients of two outpatient asthma clinics located in university hospitals were evaluated. Psychiatric diagnoses were assessed with the Mini-International Neuropsychiatric Interview 4.4 Version. **Results:** Twenty-seven patients (43.5%) met criteria for at least one psychiatric diagnosis. The most frequent diagnoses were major depression (24%), generalized anxiety disorder (20.9%) and panic disorder/agoraphobia spectrum disorders (17.7%). We found no significant differences in the prevalence of anxiety disorders and depression between the groups with mild/moderate and severe asthma. Despite the high frequency of depression and anxiety disorders, only 4 (6.5%) patients were under psychiatric treatment and 13 (20.9%) patients were taking benzodiazepines. Twelve of 15 (80%) patients who reported present use of psychotropic medication were not under psychiatric treatment at the moment of the study. **Conclusions:** Our results support the high morbidity of anxiety and depressive disorders in asthmatic patients, independent of the severity of asthma.

**Keywords:** Respiratory tract diseases; Respiratory insufficiency; Pulmonary disease (Specialty); Anxiety; Panic disorder

### Resumo

**Objetivo:** Existem evidências de que a asma está associada a um aumento da presença de sintomas psiquiátricos e de transtornos mentais. O objetivo do presente estudo é o de averiguar a frequência de transtornos de ansiedade e depressão em uma amostra de pacientes asmáticos ambulatoriais e observar se há relação deste tipo de comorbidade com a gravidade da asma. **Método:** Sessenta e dois pacientes consecutivos de dois ambulatórios universitários especializados em asma foram examinados. Os diagnósticos psiquiátricos foram obtidos em entrevista com a utilização do Mini-International Neuropsychiatric Interview 4.4 Version. **Resultados:** Vinte e sete (43,5%) pacientes preencheram os critérios para ao menos um diagnóstico psiquiátrico. Os diagnósticos mais frequentes foram depressão maior (24,0%), transtorno de ansiedade generalizada (20,9%) e transtornos do espectro pânico/agorafobia (17,7%). Não encontramos diferenças significativas na prevalência de transtornos de ansiedade e depressão entre os grupos com asma leve/moderada e com asma grave. Apesar da alta frequência de depressão e transtornos de ansiedade, apenas 4 (6,5%) pacientes estavam em tratamento psiquiátrico e 13 (20,9%) estavam usando benzodiazepínicos. Doze dos 15 (80,0%) pacientes em uso de medicação psicotrópica não estavam em tratamento psiquiátrico no momento do estudo. **Conclusão:** Nossos resultados demonstram a elevada comorbidade de transtornos de ansiedade e depressão em pacientes asmáticos, independente da gravidade da asma.

**Descritores:** Doença respiratória; Insuficiência respiratória; Doença pulmonar (Especialidade); Ansiedade; Transtorno de pânico

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## Introduction

Asthma is a respiratory disease characterized by reversible airways obstruction, airway inflammation, and hyperreactive airways,<sup>1</sup> varying from a very mild disorder to a disabling and life-threatening condition.<sup>2</sup> There is also some evidence that asthma is associated with increased psychiatric symptoms and mental disorders.<sup>3-5</sup> Shavitt et al. found in 107 asthmatic outpatients that the prevalence of agoraphobia and panic disorder were higher (13.1% and 6.5%, respectively) than in the general population.<sup>5</sup> According to Brinke et al., patients with severe asthma and a comorbid psychiatric disorder had almost 11-fold increased risk for two or more asthma exacerbations and almost 5-fold increased risk for two or more hospitalizations during the past year as compared with patients with severe asthma without psychiatric disorder.<sup>2</sup>

The aim of the present study is to assess the frequency of anxiety and depressive disorders, in a sample of asthmatic outpatients. We also want to examine if there is any relationship between these comorbidities and the severity of asthma. Our first hypothesis is that asthmatic patients have a high morbidity of anxiety disorders and depression, especially panic/agoraphobia spectrum disorders. Our second hypothesis is that current severe asthma is associated with a higher frequency of these disorders.

## Method

Sixty-two consecutive outpatients at their routine consultation at two different clinics (the Outpatient Asthma Unit of Severino Sombra Hospital, Universidade Severino Sombra, Vassouras-RJ, and Outpatient Asthma Unit of Clementino Fraga Filho General Hospital, Universidade Federal do Rio de Janeiro), were selected from May 2003 to June 2004. Asthma was defined by recurrent episodes of dyspnea with diffuse wheezing and either a 20% improvement in forced expiratory volume in 18 s (FEV1) following a nebulized beta-2-agonist bronchodilator or a 20% decrease in FEV1 after the metacoline bronchoprovocation test.<sup>6</sup> Patients with other chronic lung diseases were excluded. All patients invited to participate in this trial accepted our invitation. There was no refuse to answer any question.

Patients were asked to participate in the study and signed a voluntary written informed consent to participate in the study, which was approved by our local Research Ethics Committee.

The 4.4.version of the Mini-International Neuropsychiatric Interview (MINI)<sup>7</sup> (a short structured interview designed to explore each of the necessary criteria for the main Axis I diagnoses of DSM-IV<sup>8</sup>) was the principal diagnostic instrument. The social-demographic features, history of current or previous psychiatric treatment, and family history of psychiatric disorders were obtained in an ordinary clinical interview.

The patients of the sample were classified in mild, moderate and severe asthma, according to the criteria of GINA (Global Initiative for Asthma, World Health Organization, 1999).<sup>9</sup>

### 1. Data analysis

The Epi Info program 6.04b version (CDC, OMS, 1997) was used to analyze the results. The  $\chi^2$ -test was used in the analysis of categorical variables, and Yates' correction was applied when one of the cells was  $< 5$ . Values of  $p < 0.05$  were accepted as significant differences. Student's t-test was also used for the analysis of continuous variables. To compare the differences between the groups regarding the frequency of generalized anxiety disorder, panic disorder and agoraphobia, Fisher Exact Test was used.

## Results

The sample ( $n = 62$ ) was divided by gender and included 41 women (66.1%) and 21 men (33.9%). Their ages ranged from 20 to 82, with a mean ( $\pm$  S.D.) age of 52.8 ( $\pm$  14.7) years. Fifty-five (88.7%) of the patients had at least 5 years of asthma diagnosis. The educational level was 8 years of studying for 47 (75.8%) patients, 12 years of studying for 10 (16.1%) patients and more than 12 years for 5 (8.1%) patients. Our sample had 26 (41.9%) patients with an active remunerated occupation, 5 (8.1%) with active non-remunerated occupation, and 31 (50.0%) patients inactive. Twenty-seven patients (43.5%) met criteria for at least one psychiatric diagnosis explored by the MINI, which mainly included major depression ( $n = 15$ , 24.2%); generalized anxiety disorder ( $n = 13$ , 20.9%); panic disorder/agoraphobia spectrum disorders ( $n = 11$ , 17.7%), panic disorder with or without agoraphobia ( $n = 8$ , 12.9%), agoraphobia without panic disorder ( $n = 3$ , 4.8%), obsessive-compulsive disorder ( $n = 2$ , 3.2%), social anxiety disorder ( $n = 2$ , 3.2%), and psychosis ( $n = 1$ , 1.6%).

Thirteen (48.1%) of the 27 patients with current psychiatric diagnosis had other mental comorbid disorder. Among depressive patients, 10 of 15 (66.6%) had a comorbid anxiety disorder. A high frequency of comorbidity with anxiety or depressive disorders was also found in TAG (9 of 13, 69.2%) and panic disorder/agoraphobia spectrum disorders (8 of 11, 72.7%) patients.

Four (6.5%) patients were under psychiatric treatment and 15 (24.2%) reported previous psychiatric treatment. Fifteen (24.2%) patients were taking some psychotropic drug. Of these 15, 13 (86.6%) were taking only benzodiazepines. One patient reported use of antipsychotic and other reported use of a tricyclic antidepressant. Twelve out of 15 (80%) patients who reported present use of psychotropic medication were not under psychiatric treatment in the moment of the study.

The sample ( $n = 62$ ) was divided into two groups according to the severity of asthma: 41 (66.1%) had mild/moderate asthma and 21 (33.8%) had severe asthma. These groups were compared in relation to socio-demographic features and prevalence of anxiety and depressive disorders. In the socio-demographic features, except for age, no significant differences were found between the two groups. There were no significant differences in the prevalence of anxiety and depressive disorders between the groups (Table 1).

## Discussion

A high frequency of anxiety disorders and depression was found in asthmatic patients in our study, confirming our first hypothesis. Fifteen (24.1%) patients of the sample had a major depression disorder and 21 (33.8%) had an anxiety disorder diagnosed by the MINI.

Our hypothesis that current severe asthma was associated with a higher prevalence of anxiety disorders and depression was not confirmed. In our sample, 41 (66.1%) had mild/moderate asthma and 21 (33.8%) had severe asthma. Anxiety disorders and depression were both highly frequent without significant differences between the two groups (mild, moderate, and severe asthma).

Several theories have been proposed as an attempt to explain the apparent increased risk of the development of panic disorder in patients with asthma. A cognitive explanation posits that longitudinal experience with respiratory diseases such as asthma may generate fearful or catastrophic beliefs about respiratory symptoms, which, in turn, provoke panic attacks.<sup>10-11</sup> Biological theories posit that repetitive experiences with hypoxia and hypercapnia may also sensitize neural circuits that control fear responses, such as neurons in the amygdala and locus caeruleus, to overreact to either subsequent episodes

**Table 1 - Comparison of social-demographic and clinical features according to asthma severity level**

	Mild/Moderate asthma (n = 41)	Severe asthma (n = 21)		Data analysis
Mean age (± SD)	49.6 ± 14.6	59.0 ± 12.9	Confidence Interval = 22.5-65.9	p = 0.015 <sup>1</sup>
Sex			$\chi^2 = .045$ df = 1	p = 0.432 <sup>2</sup>
Male	29.3% (12)	42.9% (9)		
Female	70.7% (29)	57.1% (12)		
Educational level	More than 12 years = 9 (21.9%)	More than 12 years = 6 (28.6%)	$\chi^2 = .039$ df = 1	p = 0.747 <sup>2</sup>
Occupation	Working = 21 (51.2%)	Working=10 (47.6%)	$\chi^2 = .106$ df = 1	p = 0.133 <sup>2</sup>
Psychiatric disorders	43.9% (18)	42.9% (9)	$\chi^2 = .026$ df = 1	p = 0.848 <sup>2</sup>
Major depression	22.0% (9)	28.6% (6)	$\chi^2 = .044$ df = 1	p = 0.793 <sup>2</sup>
Anxiety disorders	34.1% (14)	33.3% (7)	$\chi^2 = .035$ df = 1	p = 0.826 <sup>2</sup>
Generalized anxiety disorder	19.5% (8)	23.8% (5)		p = 0.748 <sup>3</sup>
Panic disorder	14.6% (6)	9.5% (2)		p = 0.705 <sup>3</sup>
Agoraphobia	3.2% (2)	1.6% (1)		p = 1.000 <sup>3</sup>

<sup>1</sup> t Test; <sup>2</sup> Chi-square test; <sup>3</sup> Fisher exact test

of hypoxia and hypercapnia due to asthma or to fearful perceptions of conditioned stimuli such as the sensation of breathlessness.<sup>12-13</sup> Patients with anxiety and asthma may have additive respiratory abnormalities, which may create a vicious cycle of anxiety and fear that provokes increased respiratory abnormalities, which, in turn, precipitates fear that is set off by both biological and cognitive factors. Our data showed that the severity of asthma is not a main variable in this relationship, but the presence or not of asthma alone is enough to increase the risk of anxiety and depressive disorders.

Another major finding was that despite the high frequency of depression and anxiety disorders, only 4 (6.5%) patients were under psychiatric treatment and 13 (20.9% of the sample) were taking benzodiazepines. Twelve out of 15 (80%) patients who reported current use of psychotropic medication were not under psychiatric treatment in the moment of the study. The high frequency of use of benzodiazepines among our patients suggests that panic-agoraphobic disorder patients may have a high tendency to use psychotropic drugs without a proper diagnosis, in order to reduce their anxiety symptoms. The use of benzodiazepines without a specific diagnosis may lead to a higher difficulty in diagnosing panic disorder and therefore impede the treatment.

In a previous study,<sup>14</sup> we found a high psychiatric morbidity (61.6%) in a sample of 90 asthmatic patients, mainly panic disorder/agoraphobia spectrum disorders (40.7%), generalized anxiety disorder (24.4%), major depression (33.7%) and social phobia (9.3%). In this first study, we found a high frequency of agoraphobia without panic disorder (26.8%). On the other hand, in the present study, the frequency of this disorder was low (n = 3, 4.8%). Perhaps this difference was related to the use of more restrictive criteria. In our present study, phobic symptoms such as discomfort in places or situations related exclusively to worry of having an asthma crisis were not considered as agoraphobia. Others studies have also found a lower frequency of agoraphobia without panic disorder than the frequency found in our previous study.<sup>10,15</sup>

We had some methodological limitations in our trial. The main ones were: the lack of a control group with other chronic disease; the fact that our sample had a large age range (between 20 and 82 years); the fact that our sample has high probability of different respiratory and psychiatric influences; and that lifetime psychiatric diagnoses were not investigated. Therefore, it was not possible to describe the relationship between asthma and anxiety and depression in the last five-year period.

## Conclusions

Our study is consistent with previous findings suggesting that asthma is associated with a significantly increased likelihood of depression and anxiety disorders not being related to the severity of asthma. It is essential to perform a careful psychiatric evaluation in asthmatic patients in order to minimize the impact of these disorders in the course of asthma. As well, early diagnosis and treatment of psychiatric disorders may avoid self-medication in that population.

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