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Are psychiatric disorders associated with worse asthma control and quality of life in asthma patients?

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Summary
Background: Achieving good asthma control has become the major goal of asthma treatment. Studies have reported a high rate of psychiatric disorders among asthma patients, though the impact of these disorders on asthma control and quality of life remains unexplored. This study evaluated the prevalence of psychiatric disorders in 406 adult asthma patients, and associations between psychiatric status, levels of asthma control, and asthma-related quality of life.
Methods: Consecutive asthma patients presenting to the asthma clinic underwent a brief, structured psychiatric interview, completed the Asthma Control Questionnaire (ACQ) and Asthma Quality of Life Questionnaire (AQLQ), and reported the frequency of bronchodilator use in the past week. All patients underwent standard pulmonary function testing.
Results: A total of 34% ($n = 136$) of patients had one or more psychiatric diagnosis, including major depression (15%), minor depression (5%), dysthymia (4%), panic

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disorder (12%), generalized anxiety disorder (5%), and social phobia (4%). Though there were no differences in pulmonary function, patients with versus without psychiatric disorders had worse ACQ and AQLQ scores and reported greater bronchodilator use, independent age, sex and asthma severity.
Conclusions: Results suggest that psychiatric disorders are prevalent among asthmatics and are associated with worse asthma control and quality of life. Physicians should be aware of the potential risk of poorer asthma control and functional impairment in this population.

Introduction

Asthma remains one of the most prevalent chronic respiratory disorders, affecting 100–150 million people worldwide.[1,2] The cost of caring for asthma has been calculated by the World Health Organization to exceed that of AIDS/HIV and tuberculosis combined.[1] These figures highlight the scope of the burden associated with this disease and its impact on quality of life. The high burden of asthma appears to be related to poor asthma control, which is associated with more frequent asthma symptomatology (dyspnea, wheezing, nocturnal waking symptoms), bronchodilator use, functional impairment (absenteeism, participation in social and physical activities), and worse pulmonary function.[3,4] Given that asthma can be well controlled for the majority of patients,[5,6] identifying those patients who may be at greater risk for poorly controlled asthma and worse quality of life therefore represents an important goal for clinical research.

Several psychosocial and emotional factors have been found to be associated with poor asthma control and worse asthma-related quality of life, including anxiety, depression, and inappropriate (e.g., avoidant) coping skills.[7–12] However, relatively few studies have evaluated the impact of *chronic* psychopathology, i.e., psychiatric disorders, on levels of asthma control and quality of life. Interestingly, rates of certain psychiatric disorders (e.g., panic disorder, major depression) among asthmatics have been reported to be at least double those observed in the general population,[9,12–16] suggesting a need to better understand the impact of such disorders on levels of asthma control and related outcomes.

The purpose of the present study was twofold: (1) to evaluate the prevalence of psychiatric disorders in a large group of adult asthma outpatients and (2) to evaluate associations between psychiatric disorders and levels of asthma control and asthma-related quality of life. It was hypothesized that asthmatics with comorbid psychiatric disorders would have worse asthma control and asthma-related quality of life relative to asthmatics without psychiatric disorders, and that these associations would be independent of age, sex, and asthma severity.

Materials and methods

Study subjects

Participants were recruited from consecutive adult patients presenting to the asthma clinic of Hôpital du Sacré-Coeur de Montréal from June 2003 to March 2004. Patients were eligible if they had a primary clinical diagnosis of asthma, were at least 18 years of age or older, and were fluent in either English or French. A total of 935 patients presented to the asthma clinic, of which 825 were contacted to participate (88%). A total of 385 were excluded ($n = 126$ due to existence of comorbid disease (e.g., chronic obstructive pulmonary disease) that conferred greater risk for morbidity than asthma; $n = 127$ due to ''new'' or unconfirmed asthma or occupational asthma; $n = 103$ were under the age of 18; $n = 22$ due to language criteria (did not speak English or French fluently enough to reliably complete the assessments); $n = 7$ due to missing data), which yielded a total sample of 440 eligible patients. Only 34 patients declined to participate, which resulted in a final sample of 406 patients (92% participation rate). This project was approved by the Ethics Committee of Hôpital du Sacré-Cœur de Montréal.

Study design

Patients were screened on the day of their asthma clinic visit to verify eligibility. Participants underwent a demographic and medical history interview, including asking patients to report the frequency of bronchodilator use in the past week, followed by a brief, structured psychiatric interview (Primary Care Evaluation for Mental Disorders, PRIME-MD) administered by a trained clinical research

assistant. Patients completed the questionnaires assessing asthma control (Asthma Control Questionnaire—ACQ) and quality of life (Asthma Quality of Life Questionnaire—AQLQ) and underwent standard spirometry to measure pulmonary function. Asthma diagnoses were confirmed by chart evidence of a 20% fall in FEV_1 after methacholine challenge and/or bronchodilator reversibility in FEV_1 of $\geqslant$20% predicted.[17] Asthma severity was determined according to 1997 NHLBI guidelines[18] that categorize asthma severity into four categories (mild intermittent, mild persistent, moderate persistent, and severe persistent) based on clinical symptoms, medication usage, and pulmonary function. Medical history, including medication status and dosage was self-reported and verified by chart review.

Measures

Psychiatric assessment

Participants underwent a brief, structured psychiatric interview using the Primary Care Evaluation of Mental Disorders (PRIME-MD),[19] which is a well-validated screening instrument designed to detect the most common Diagnostic and Statistical Manual of Mental Disorders—4th Edition (DSM-IV)[20] disorders in primary care settings. It uses diagnostic algorithms to generate diagnoses based on DSM-IV criteria that have been shown to be of comparable reliability as longer structured interviews.[19,21] The PRIME-MD takes between 10 and 20 min to administer and score, and consists of a 27-item patient self-report questionnaire, followed by a 12 page structured interview that is used to follow-up patient responses. It has been used successfully in previous studies assessing the prevalence of psychiatric disorders in asthma patients.[9,15]

Asthma control and quality of life assessment

To assess asthma control, participants completed the ACQ,[22] reported the frequency (number of times in the last week) of bronchodilator use, and underwent standard spirometry to assess pulmonary function (forced expiratory volume in one second, FEV_1). The ACQ evaluates asthma control according to standard criteria specified by international guidelines.[6] Respondents are asked to recall their symptoms, activity limitations, and bronchodilator use in the last week. One additional question assessing spirometry results (FEV_1, % Pred.) is completed by the research assistant. The ACQ contains 7 items rated on a 7-point scale (0 = good control, 6 = poor control). To assess asthma quality of life, participants completed the AQLQ.[23] The AQLQ evaluates asthma quality of life across four domains: activity limitation, symptoms, emotional distress, and environmental stimuli. It contains 32 items rated on a 7-point scale (1 = maximal impairment, 7 = no impairment). Both the ACQ and AQLQ have demonstrated very good measurement properties, including high intraclass correlation coefficients between 0.90 and 0.95 and good construct, cross-sectional and longitudinal validity,[22–25] and have been validated in Quebec French.[26]

Pulmonary function testing

Rescue medication was withheld for at least 4 h before pulmonary function tests. FEV_1 and forced vital capacity (FVC) were assessed before administration of 200 μg salbutamol using a metered-dose inhaler or 500 μg terbutaline using a Turbuhaler®. Predicted values of FEV_1 and FVC were calculated from reference values for patients less than[27] and greater[28] than 70 years, respectively, yielding % predicted FEV_1 and % predicted FEV_1/FVC.

Analyses

Group differences in categorical variables were examined using Pearson's χ^2 test statistics. Group differences in continuous variables were examined using *t*-tests. All tests were two-sided and significance was set at 0.05. General Linear Models controlling for sex, age, smoking status and asthma severity were used to compare individual item, subscale, and total scores on the ACQ and AQLQ questionnaire, as well as frequency of bronchodilator use in the last week. Data analysis was performed using SAS v8.2 (SAS Institute, Cary NC).

Results

Sample characteristics

A total of 406 asthma outpatients participated in the present study. Participants were 62% female and had a mean age of 50 ($\pm$14.5) years.

Prevalence of psychiatric disorders

A total of 34% of patients met diagnostic criteria for one or more psychiatric disorder (Table 1). A total of 25% of patients met diagnostic criteria for one or more anxiety disorder, the most common of which was panic disorder at 12%. A total of 20% of patients met diagnostic criteria for one or more mood disorders, the most common of which was major

depressive disorder at 15%. It is noteworthy that 36% of patients reported a lifetime history of panic attacks. Despite a high rate of current psychiatric morbidity in this sample, only 13% ($n = 19/136$) of psychiatric patients reported currently being under the care of a mental health professional.

Sociodemographic and patient characteristics

Sociodemographic and patient characteristics presented as a function of psychiatric group (asthmatics with and without one or more cormorbid psychiatric disorder) are presented in Table 2. There were significantly more women and current smokers in the psychiatric group and significantly fewer patients who had never smoked in the psychiatric group. There were no other significant differences between groups.

Table 1 Prevalence of DSM-IV psychiatric disorders.

$N = 406$	% (n)
Any psychiatric disorder	34 (136)
Anxiety disorders	25 (103)
Panic disorder	12 (49)
Generalized anxiety disorder	5 (21)
Social anxiety disorder	4 (18)
Other anxiety disorder	11 (45)
Mood disorders	20 (81)
Major depressive disorder	15 (59)
Minor depressive disorder	5 (22)
Dysthymia	4 (18)
Bipolar disorder	1 (1)
History of panic attacks	36 (146)
Psychiatric patients under care of mental health professional*	13 (19)

*Includes psychologist or psychiatrist.

Medical characteristics and medications

Medical characteristics and asthma medications presented as a function of psychiatric group are presented in Table 3. There were significantly more patients taking benzodiazepines and antidepressants in the psychiatric group relative to the non-psychiatric group. There were no other significant group differences in medical characteristics, asthma severity classification, or the proportion of patients taking various asthma medications.

Asthma control and quality of life

Asthma control and quality of life data presented as a function of psychiatric group are shown in Table 4. There were no differences between groups in pre-bronchodilator FEV_1, measured in liters or as a percentage of predicted values (% predicted); nor were there any differences in FEV_1/FVC (% predicted). However, asthmatics with cormorbid psychiatric disorders reported significantly more bronchodilator use in the last week, independent of age, sex and smoking status and asthma severity, compared to non-psychiatric asthmatics. Asthmatics with comorbid psychiatric disorders also had significantly higher scores on the ACQ,

Table 2 Sociodemographic and patient characteristics as a function of psychiatric group.

% (n)	No-psych $n = 270$	Psych $n = 136$	χ^2	P
Age (yr)*	51 ± 14.5	48 ± 14.5	1.64	0.10
Sex (female)	57 (154)	71 (97)	7.82	0.005
Ethnicity (Caucasian vs. all other ethnic groups)	92 (248)	96 (130)	1.97	0.16
Married/living together	70 (180)	62 (84)	2.95	0.09
Years of education*	13 ± 3.7	13 ± 4.2	0.78	0.44
Employed	63 (160)	54 (74)	2.41	0.12
Smoking status			8.73	0.01
Never smoked	51 (138)	40 (55)		
Past smoker	40 (109)	42 (57)		
Current smoker	9 (23)	18 (24)		
Pack-years* †	11 ± 20.0	13 ± 20.0	−0.07	0.48

*Values are $M \pm SD$; results are t-tests.
†Pack-years = average number of packs (20 cigarettes) smoked per day multiplied by the number of years smoked.

Table 3 Medical characteristics and medications as a function of psychiatric group.

% (*n*)	No-psych $n = 270$	Psych $n = 136$	χ^2	*P*
Hypertension	26 (71)	20 (27)	2.05	0.15
Diabetes	7 (20)	7 (9)	0.09	0.77
BMI (kg/m^2)*	27±5.0	28±6.3	−0.10	0.33
Atopic	60 (159)	67 (90)	1.93	0.17
Medications-asthma				
Short-acting bronchodilators	95 (259)	95 (130)	0.03	0.87
Long-acting bronchodilators	53 (142)	49 (66)	0.49	0.48
Inhaled corticosteroids (ICS)	73 (197)	78 (106)	1.84	0.28
†ICS dose (μg)*	500 (0–2500)	500 (0–2000)	−0.96	0.34
Oral corticosteroids	12 (31)	12 (16)	0.01	0.92
Anti-leukotrienes	12 (33)	13 (17)	0.01	0.91
Medications-psychotropic				
Benzodiazepines	10 (27)	23 (31)	12.3	0.0004
Antidepressants	4 (11)	20 (27)	26.8	0.0001
Asthma severity classification			2.86	0.41
Mild intermittent	1 (3)	0		
Mild persistent	12 (29)	8 (10)		
Moderate persistent	55 (139)	56 (69)		
Severe persistent	32 (81)	36 (45)		
Asthma duration (yr)*	20.3±15	18.4±15	1.09	0.28

†Median (range) flucatisone propionate equivalent, result is a *t*-test (data available for 222 non-psych and 104 psych participants).

*Value is M±SD; result is a *t*-test.

Table 4 Pulmonary function, bronchodilator use, and ACQ and AQLQ scores as a function of psychiatric group.

M±SD	No-psych $n = 270$	Psych $n = 136$	*F*	*P*
FEV_1 (l)*	2.3±0.88	2.3±0.80	0.00	0.97
FEV_1, % predicted*	76.1±20.7	78.1±19.1	0.78	0.38
FEV_1/FVC, % predicted*	86.3±12.5	88.7±13.1	3.19	0.08
Bronchodilator use (#times in last week)†	9.4±1.0	13.7±1.5	5.14	0.02
ACQ (total)†	1.6±0.06	2.0±0.09	11.6	0.0007
Q 1: Nocturnal waking	0.3±0.09	1.3±0.12	6.2	0.01
Q 2: Waking symptoms	1.3±0.09	1.7±0.13	5.7	0.01
Q 3: Activity limitation	1.1±0.09	1.8±0.12	20.6	0.0001
Q 4: Shortness of breath	1.8±0.09	2.5±0.13	18.4	0.0001
Q 5: Wheezing	1.6±0.09	2.0±0.13	6.2	0.01
Q 6: Bronchodilator use	1.1±0.09	1.4±0.11	3.6	0.06
Q 7: % FEV_1	2.9±0.09	2.7±0.13	2.92	0.08
AQLQ (total)†	5.3±0.08	4.6±0.12	25.1	0.0001
Activity limitation	5.1±0.10	4.4±0.13	20.2	0.0001
Symptoms	5.3±0.08	4.6±0.12	20.6	0.0001
Environmental stimuli	5.0±0.10	4.3±0.15	14.7	0.0002
Emotional distress	5.7±0.08	4.9±0.13	24.9	0.0001

FEV—forced expiratory volume; FVC—forced vital capacity; ACQ—Asthma Control Questionnaire; AQLQ—Asthma Quality of Life Questionnaire.

*Adjusted values controlling for smoking status, asthma severity; ±SEM.

†Mean ACQ and AQLQ total scores, subscale scores and individual items adjusted controlling for sex, age, smoking status, and asthma severity; ±SEM.

indicating significantly worse asthma control, relative to non-psychiatric asthmatics (Table 4). With the exception of question 7 (% predicted FEV_1) and a marginally significant trend for question 6 (bronchodilator use), asthmatics with comorbid psychiatric disorders exhibited significantly higher scores on each individual item of the ACQ, indicating that in the last week, asthmatics with comorbid psychiatric disorders experienced more nocturnal waking due to asthma; worse asthma symptoms in the morning; greater limitations in their daily activities; greater shortness of breath due to asthma; and greater wheezing relative to non-psychiatric asthmatics. These findings were statistically significant even after controlling for sex, age, smoking status and asthma severity.

Asthmatics with comorbid psychiatric disorders also had significantly lower scores on the AQLQ, both for the total scale score and each of the four subscales (Table 4). Therefore, asthmatics with comorbid psychiatric disorders reported significantly worse asthma quality of life, both in general and in relation to their symptomatology, being limited in their daily activities, in response to environmental stimuli, and in regards to feelings of emotional distress. These findings were significant after controlling for sex, age, smoking status and asthma severity. Moreover, all differences between the mean total and subscale scores on the AQLQ for asthmatics with versus without psychiatric disorders were also clinically significant as they all exceeded 0.5 (range 0.7–0.8), where differences of $\geqslant$0.5 have been defined previously as clinically significant for this population.[22]

Discussion

The results of the present study indicate a high rate (34%) of psychiatric disorders among adult asthmatics. Consistent with hypotheses, asthmatics with comorbid psychiatric disorders have worse asthma control and quality of life, independent of sex, age, smoking status and asthma severity, relative to asthmatics without psychiatric disorders. Though objective measures of pulmonary function were comparable between groups, asthmatics with psychiatric disorders reported greater use of short-acting bronchodilators in the last week, also suggesting poorer asthma control in this population of asthmatics.

Compared to point prevalence rates in the general population, rates of both anxiety and mood disorders were at least double those observed in the general population (25% and 20% versus 1–13% and 2–9%, respectively [20,29]). Moreover, rates of certain psychiatric disorders, including panic disorder and major depressive disorder, were as much as six times more prevalent among asthmatics relative to the general population.[20,29] These findings are consistent with previous reports suggesting a high rate of psychiatric disorders, particularly mood (range 14–41%)[9,12,14,15] and anxiety (range 9–24%)[13–15,30] disorders, among adult asthmatics.

To our knowledge, this is the first study to indicate a strong and independent association between psychiatric disorders and worse asthma control and quality of life. This study is consistent with the relatively few studies finding associations between actual psychiatric disorders and asthma morbidity, including worse asthma control and adherence to inhaled steroids[8]and worse quality of life.[9]However, the present study strengthens previous reports by finding associations between psychiatric disorders and worse asthma control and quality of life independent of asthma severity. It also strengthens previous reports by including a large sample size (over 400) of adult asthmatics with confirmed asthma. Previous studies assessing the prevalence of psychiatric disorders either had small sample sizes (less than 110),[8,12–14]did not include assessments of asthma morbidity,[13–16] or failed to measure pulmonary function,[8,9,13–16] potentially limiting the generalizability, strength and clinical relevance of the findings.

The association between psychiatric disorders and poor asthma control and asthma-related quality of life could occur through several pathways including behavioral pathways, such as disorganized self-care and poor health behaviors; cognitive or perceptual pathways, such as biased symptom reporting; or through the direct physiological effects of depression and anxiety on the autonomic nervous (ANS) and immune systems which increase asthma symptomatology.

Previous studies have found consistent relationships between psychiatric disorders, particularly mood and anxiety disorders, and increased rates of smoking,[31–33] which may complicate asthma management[34,35] and quality of life.[36] There is also evidence showing that asthmatics reporting greater levels of psychological distress (e.g., anxiety, depression) misuse medication.[8,37] Of course, nonadherence to asthma medications has been directly linked to several indices of poor outcome, including increased use of emergency services[38] and near-fatal asthma attacks.[39] Though we did not measure medication adherence in the current study, future research should include measures of treatment adherence to help elucidate the mechanisms of

poorer asthma control in asthmatics with psychiatric disorders.

Findings of worse asthma control and quality of life in asthma patients with psychiatric disorders could also have occurred through cognitive or perceptual pathways, whereby psychiatric patients may have been more likely to over-report the frequency and/or severity of asthma symptoms as a result of their negative mood states. Previous studies have shown that psychiatric patients may be ''hyper-sensitive'' to changes in bodily sensations, which may contribute to distorted symptom perceptions in this population.[40,41] However, there is evidence from asthma studies showing that overperception of asthma symptoms may occur independently of emotional or psychiatric factors.[42,43] The fact that physicians rely so heavily upon patient self-reports of their symptoms suggests that the potential influence of negative mood states on symptom perception should be taken into account when evaluating levels of asthma control and quality of life in patients with suspected or known psychiatric morbidity.

Poorer asthma control in asthmatics with psychiatric disorders could also occur through direct effects of chronic psychological stress on the ANS and immune systems. Chronic psychological stress (as is the case in patients with psychiatric disorders) has been linked to both ANS dysregulation and reduced immunocompetence in asthmatics. Several studies have reported associations between certain emotional states (e.g., depression, hopelessness) and increased cholinergically mediated airway reactivity in asthmatics.[44–46] It has also been suggested that asthmatics who experience chronic psychological stress may be in a chronic proinflammatory state. Evidence for this association comes from two studies which found that examination stress was associated with increased production of proinflammatory superoxides and increased cytokine production by lymphocytes among asthmatics.[47,48] Although these studies suggest plausible mechanisms by which chronic psychopathology and psychological stress may affect asthma control, this research is still in its infancy and future research is needed to fully elucidate the nature and significance of these associations.

The present study may be limited by the fact that the sample was drawn from a tertiary asthma clinic; therefore, findings may not generalize to asthmatics treated in primary care. The present study may also be limited by the fact that most measures of asthma control and quality of life were based on self-report assessments, which may be subject to recall bias. However, the instruments used in the present study (ACQ and AQLQ) have both been shown to be valid evaluative and discriminative tools with excellent measurement properties.[22–25] Moreover, a recent study by Juniper et al.[24] found that the self-report questionnaire version of the ACQ demonstrated superior reliability and discriminative validity than did a daily diary version of the scale, which was thought to be less subject to recall bias. Similarly, the AQLQ has shown strong correlations between the four subscales of the questionnaire and several relevant asthma outcomes, including asthma severity, asthma control, medication requirements, and overall quality of life.[23] The AQLQ has also been argued to measure the component of asthma ''most important to patients,''[23] suggesting that self-report instruments may provide potentially valuable information not always captured by traditional (medical) assessments.

Finally, this study may be limited by the cross-sectional nature of the design. We therefore cannot conclude that psychiatric disorders among asthmatics *cause* worse asthma control and quality of life, because the reverse may be equally plausible: that poor asthma control and quality of life leads to greater psychiatric morbidity. As such, prospective studies are needed to better delineate these relationships. It may also be beneficial to conduct intervention trials designed to treat comorbid psychiatric disorders among asthmatics, and evaluate the efficacy and effectiveness of such interventions on both psychiatric and asthma outcomes. To our knowledge, there have been no controlled treatment outcome studies of empirically validated interventions (i.e., pharmacotherapy and/or cognitive-behavioral therapy) in patients with both asthma and psychiatric disorders. It is noteworthy that the NHLBI guidelines for asthma treatment recommended referral of asthmatics to mental health professionals when stress appears to interfere with medical management of asthma.[18] Though more patients with psychiatric disorders were taking psychotropic medications, alarmingly few (13%) reported being under the care of a mental health professional. This suggests that greater efforts should be made to improve referral and follow-up of these patients to appropriate treatment providers.

In conclusion, the results of this study highlight the high prevalence of psychiatric disorders among adult outpatient asthmatics, and the range of increased morbidity that may be associated with it. These findings also suggest that physicians may want to consider the potential impact of negative mood states when assessing levels of asthma control and implementing treatment strategies. It

may be that psychiatric morbidity is associated with increased symptom perception and/or symptom reporting, which may be falsely interpreted as poor asthma control by both patients and physicians. Nonetheless, physicians still rely heavily upon patient reports of symptoms when making treatment decisions, and should be aware of the heightened symptomatology, greater functional impairment, and poorer asthma control in this population.

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