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High levels of anxiety during the COVID-19 pandemic as a risk factor of clinical worsening in patients with severe asthma

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Clinical Implications

- Mental health can have a significant role in managing chronic diseases, particularly during the global pandemic. High levels of trait and state anxiety are a potential risk factor for loss of asthma symptom control and decline in disease-related quality of life.

Mental disorders are some of the most commonly reported chronic conditions found in asthmatics, and recent reports suggest that anxiety may negatively affect their disease control and quality of life.[1,2] The current pandemic of coronavirus disease 2019 (COVID-19), which emerged in late 2019, has severely affected both physical and psychological health of people around the world.[3] Since the first reports of severe respiratory syndrome coronavirus 2, it has proven to be highly contagious and potentially dangerous. From the beginning, it was considered especially threatening to vulnerable populations such as patients with chronic respiratory conditions, which could naturally lead to increased levels of stress and anxiety. The aim of our study was to assess levels of anxiety and its impact on disease control and quality of life in patients with severe asthma who were treated in our tertiary allergology center in the early months of the COVID-19 pandemic.

We surveyed all of the severe asthma patients undergoing biological treatment with omalizumab, mepolizumab, and benralizumab in the National Severe Asthma treatment Program during their visits in March and June 2020. Our aim was to assess patients on their first visit after the COVID-19 pandemic declaration by the World Health Organization. We asked each patient to complete the State-Trait Anxiety Inventory (STAI), a validated tool for measuring anxiety in adults as both a temporary condition (state) and a general, long-standing personal quality (trait).[4] All patients completed a 15-item questionnaire (COVID-19 survey) developed by the authors to assess concerns regarding the impact of COVID-19 on patients' anxiety, asthma, and quality of life using multiple choice, visual analog, and five-point Likert scales. We used hospital records to acquire information about medical history and performed statistical analysis of the data using Statistica (TIBCO Software Inc, Palo Alto, California, USA).

All 88 patients surveyed provided complete questionnaire responses, except for one patient who erroneously omitted the trait part of the STAI questionnaire. Thus, 87 had complete medical data available, including changes in the Asthma Control Questionnaire (ACQ) and Mini Asthma Quality of Life Questionnaire (mAQLQ) compared with the last visit before the global pandemic announcement.

A total of 40 patients demonstrated an increase in the ACQ score (46%), 15 reported no change (17%), and 32 experienced a reduction in ACQ (37%). Asthma-related quality of life appeared to be even more visibly affected; 53 patients had a reduced mAQLQ score (62%), 15 were unchanged (18%), and 17 had an increased score (20%). Mean changes in ACQ and mAQLQ scores were 0.214 and −0.248, respectively. Moreover, 22 patients showed a significant decline in symptom control and 18 in quality of life, defined as changes exceeding the minimal clinically important difference of 0.5 points in ACQ and mAQLQ, respectively.[5] No patients experienced an exacerbation in the next 3 months after the assessment. Mean STAI scores were 44.82 for state and 42.14 for trait anxiety; most patients reported in the COVID-19 survey that the current pandemic considerably affected their responses. Thirty patients qualified as having high state anxiety (34%), whereas seven had high trait anxiety (8%) (Tables I and II).

The high state anxiety group included a higher proportion of patients with both a significant ACQ increase (53.3% vs 10.5%) and mAQLQ decrease (30.0% vs 15.8%) compared with those with low to moderate state anxiety (Table I). A similar tendency could be observed in asthmatics with high trait anxiety (57.1% vs 21.5% for a significant ACQ increase and 28.6% vs 20.3% for an mAQLQ decrease) compared with the rest of the group (Table II).

Linear regression analysis showed that both state and trait anxiety were significantly associated with the change in ACQ ($P < .001$ and $P < .01$, respectively), but not the mAQLQ scores. Mean change in ACQ was −0.24, −0.18, and +0.98 for patients with a low, moderate, and high level of state anxiety, respectively (Table I). Logistic regression results suggested that a high level of state anxiety may prove to be a risk factor for a significant decline (exceeding the minimal clinically important difference) in ACQ (odds ratio = 9.71; $P < .001$) and mAQLQ (odds ratio = 2.29; $P = .008$) compared with the low or moderate state anxiety group. Regression analyses were adjusted for age, sex, and treatment length.

Anxiety and mental comorbidities are commonly associated with poor asthma control, but to date, few studies approached this subject in a clinical setting, most commonly in adolescents.[6-8] Our observations showed that a major event, such as the rise of a global pandemic, may significantly affect patients' level of anxiety, which can reflect on their quality of life and disease control. In previously published studies, the outbreak of severe respiratory syndrome coronavirus 2 was shown to cause a spectrum of mental health issues, including anxiety.[9] Our analyses confirmed that high levels of anxiety are associated with worse asthma control in the population of severe asthmatics and may be a risk factor for significant worsening of disease control and asthma-related quality of life.

We believe that the major strengths of our analysis were the use of a specialized anxiety-oriented scale and the study group, because severe asthmatics are rarely the subject of trials focusing on anxiety in asthma, although they are potentially the most vulnerable group in whom anxiety and stress can have clinically significant consequences.

TABLE I. Baseline demographic and clinical characteristics of study group, grouped by anxiety state status

		State-Trait Anxiety Inventory: State		
Variable	**Overall (n = 87)**	**Low (n = 7)**	**Moderate (n = 50)**	**High (n = 30)**
Age, y, (mean [SD])	56.103 (±11.891)	57.571 (±12.067)	56.080 (±10.665)	55.800 (±14.021)
Male, n (%)	34 (39.1)	5 (71.4)	20 (40.0)	9 (30.0)
Biological treatment, mo (mean [SD])	29.000 (±24.180)	30.857 (±27.865)	30.500 (±25.110)	26.300 (±22.262)
Biological agent				
Omalizumab, n (%)	45 (51.7)	2 (28.6)	24 (48.0)	19 (63.3)
Mepolizumab, n (%)	33 (37.9)	5 (71.4)	19 (38.0)	9 (30.0)
Benralizumab, n (%)	9 (10.3)	0 (0.0)	7 (14.0)	2 (6.7)
ACQ on day of assessment	1.491 (±1.381)	1.443 (±1.971)	1.048 (±1.086)	2.241 (±1.392)
ACQ change (mean [SD])	0.214 (±1.123)	-0.243 (±0.873)	-0.184 (±0.583)	0.983 (±1.439)
ACQ significant increase, n (%)	22 (25.3)	1 (14.3)	5 (10.0)	16 (53.3)
mAQLQ on day of assessment	4.114 (±2.198)	5.214 (±2.227)	4.138 (±2.383)	3.817 (±1.807)
mAQLQ change (mean [SD])	-0.248 (±1.061)	-0.514 (±1.775)	-0.069 (±0.802)	-0.492 (±1.226)
mAQLQ significant decline, n (%)	18 (20.7)	1 (14.3)	8 (16.0)	9 (30.0)
Clinical asthma control				
Controlled, n (%)	30 (34.5)	5 (71.4)	21 (42.0)	4 (13.3)
Partially controlled, n (%)	20 (23.0)	0 (0.0)	14 (28.0)	6 (20.0)
Uncontrolled, n (%)	37 (42.5)	2 (28.6)	15 (30.0)	20 (66.7)

ACQ, Asthma Control Questionnaire; *mAQLQ*, mini Asthma Quality of Life Questionnaire; *SD*, standard deviation.
The ACQ ranges for controlled, partially controlled, and uncontrolled asthma were 0-0.75, 0.76-1.49, and ≥1.5, respectively. Changes exceeding the minimal clinically important difference of 0.5 points were considered significant in both mAQLQ decline and ACQ increase.

TABLE II. Baseline demographic and clinical characteristics of study group, grouped by anxiety trait status

	State-Trait Anxiety Inventory: Trait		
Variable	**Low (n = 24)**	**Moderate (n = 55)**	**High (n = 7)**
Age, y (mean [SD])	55.667 (±10.557)	55.473 (±12.456)	62.000 (±12.517)
Male, n (%)	9 (37.5)	22 (40.0)	3 (42.8)
Biological treatment, mo (mean [SD])	27.646 (±25.057)	24.826 (±23.700)	27.703 (±28.867)
Biological agent			
Omalizumab, n (%)	10 (41.7)	30 (54.5)	4 (57.1)
Mepolizumab, n (%)	12 (50.0)	20 (36.4)	1 (14.3)
Benralizumab, n (%)	2 (8.3)	5 (9.1)	2 (28.6)
ACQ on day of assessment	1.087 (±1.289)	1.573 (±1.424)	2.186 (±1.185)
ACQ change (mean [SD])	−0.212 (±0.732)	0.235 (±1.104)	0.957 (±1.072)
ACQ significant increase, n (%)	4 (16.7)	13 (23.6)	4 (57.1)
mAQLQ on day of assessment	4.763 (±2.324)	3.916 (±2.174)	3.257 (±1.667)
mAQLQ change (mean [SD])	−0.108 (±1.256)	−0.327 (±1.026)	−0.094 (±0.729)
mAQLQ significant decline, n (%)	4 (16.7)	12 (21.8)	2 (28.6)
Clinical asthma control			
Controlled, n (%)	13 (54.2)	16 (29.1)	1 (14.3)
Partially controlled, n (%)	3 (12.5)	16 (29.1)	1 (14.3)
Uncontrolled, n (%)	8 (33.3)	23 (41.8)	5 (71.4)

ACQ, Asthma Control Questionnaire; *mAQLQ*, mini Asthma Quality of Life Questionnaire; *SD*, standard deviation.
The ACQ ranges for controlled, partially controlled, and uncontrolled asthma were 0-0.75, 0.76-1.49, and ≥1.5, respectively. Changes exceeding the minimal clinically important difference of 0.5 points were considered significant in both mAQLQ decline and ACQ increase.

Moreover, the timing of assessments was advantageous, because all patients were evaluated soon after the announcement of the global pandemic, which universally affected the world with the high potential to cause stress and anxiety in vulnerable patients with chronic diseases. A major limitation of the study was the lack of a measure of anxiety before COVID-19 was declared a pandemic. Moreover, worsening of asthma caused by other COVID-related factors, such as increased levels of stress and depression, or greater exposure to household allergens as a result of the widespread shutdown, may have affected the changes in ACQ and AQLQ scores. As a result, it is impossible to rule out that the increased levels of anxiety may actually have been caused by a loss of asthma control unrelated to the patients' emotional state. However, the study group was composed of long-observed patients with stable disease who were receiving biological treatment. Moreover, most patients reported in the

COVID-19 survey that the changes brought on by the pandemic affected their perceived psychological well-being.

Our results show that high levels of anxiety may be a risk factor for clinical worsening in patients with severe asthma. Regular screening of severe asthmatics using the STAI questionnaire could be a valuable addition in asthmatic patient care. Further studies are required to assess whether an intervention aimed at reducing anxiety could prove effective in improving asthma control.

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