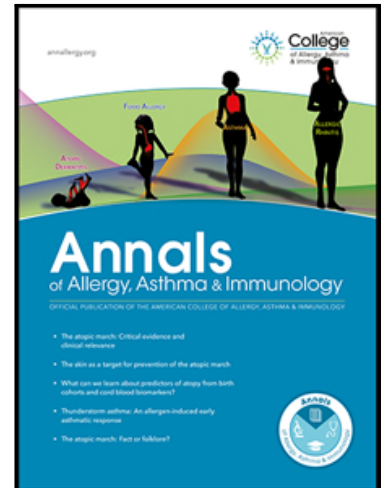


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COVID-19 Related Anxiety Is Associated with Uncontrolled Asthma in Adults

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Abbreviations/Acronyms:

ACT: Asthma Control Test

CI: Confidence Interval

OR: Odds Ratio

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There is evidence that the COVID-19 pandemic, its mitigation strategies, and resulting life changes are associated with detrimental effects on physical and mental health. Adults in the US were three times more likely to meet the criteria for moderate/serious mental distress in April 2020 than in 2018 (70.4% vs. 22.0%).¹ Although there is evidence linking stress with asthma exacerbation,² studies addressing the impact of the COVID-19 pandemic on anxiety among adults with asthma are limited. We examined the associations of COVID-19 related anxiety with asthma control in adults.

An online, cross-sectional study was conducted with US adults (≥ 18 years old) with a current self-reported physician diagnosis of asthma.³ Study invitations were shared online (e.g., social media, email contacts in the networks of the researchers, ResearchMatch) and participants opted in for an incentive drawing.³ Anxiety was measured using a 5-point Likert scale to capture participants' responses to 8 questions on participants' experiences in the last 2 weeks.⁴ These questions were developed in the Coronavirus Health and Impact Survey Initiative which was launched early in the pandemic.⁵ Responses were summed for a score ranging from 8-40 with higher values indicating higher anxiety. Anxiety scores were first dichotomized at the median (22) as high (above median) or low (at or below median) and then categorized into quartiles (8-17, 18-22, 23-26, and 27-40) to examine the dose-response association of anxiety with uncontrolled asthma. Participants also completed the asthma control test (ACT), answered

questions about health care utilization and the level of life changes during the pandemic. The study was approved by the University of Kansas Medical Center's IRB.

As of December 19, 2020, 909 surveys were received, of which 873 had complete data on the main variables. Chi-squared statistics were used to examine associations of anxiety (high vs low) with participant characteristics. Binary logistic regression models examined associations of anxiety level as a dichotomous variable or as an ordinal variable (quartiles) with uncontrolled asthma (ACT score ≤ 19). Multiple logistic regression analysis was performed to adjust for potential confounding variables identified a priori including age, education, gender, race/ethnicity, residential area, home ownership, and having confirmed/suspected COVID-19. Statistical analysis was performed in SAS 9.4 and p-value < 0.05 indicated statistical significance.

Participants were mostly female (83%), white (80%), urban (60%), with at least a college degree (69%), and mean age of 45 ± 15 years. Among participants, 13% and 15% self-quarantined with and without COVID-19 symptoms, respectively; 14% lost their job; 21% had reduced ability to earn money, 25% had confirmed/suspected COVID-19, and 2% were hospitalized due to COVID-19. Almost 57% had a self-reported asthma episode/attack since the pandemic, 29% contacted their healthcare provider for urgent symptoms, and 43% had uncontrolled asthma (ACT ≤ 19).

Most participants reported being worried about themselves and family/friends becoming infected with COVID-19, and about their own physical and mental/emotional health. Almost 48% of participants had high anxiety score. Less educated and those who were renting or reported living with family were more likely to experience significantly higher levels of anxiety. Additionally, participants who self-quarantined, had confirmed/suspected COVID-19, and those

exposed to others with confirmed/suspected COVID-19 reported significantly higher levels of anxiety.

Participants with higher anxiety levels were more likely to report having uncontrolled asthma (Figure 1). In adjusted multiple logistic regression models, participants with high anxiety were twice as likely to have uncontrolled asthma compared with counterparts reporting low levels of anxiety (OR: 2.00, 95% CI: 1.45, 2.74). In additional analyses treating anxiety as an ordinal variable (quartiles), we observed a significant dose-response direct relationship of COVID-19 related anxiety with the odds of uncontrolled asthma ($p < 0.0001$). Compared to participants in the lowest anxiety quartile, the odds of uncontrolled asthma were 1.64 (95% CI=1.06, 2.53), 1.78 (95% CI=1.12, 2.85), and 3.83 (95% CI=2.41, 6.09) for those in the 2nd, 3rd, and 4th anxiety quartiles, respectively, after adjusting for covariates including having confirmed/suspected COVID-19.

Adults with asthma are significantly impacted by the pandemic, experiencing high levels of anxiety. For example, findings from a national sample of adults in the US suggest increased physical and mental symptoms among those with chronic respiratory conditions during the COVID-19 pandemic as compared to others.⁶ Our study, with a geographically diverse adult asthma population and differing levels of asthma control, supports these findings and also demonstrates a significant, detrimental, dose-response effect of COVID-19 related anxiety on asthma control. Acute stress is associated with an increase in sympathetic nervous system responses, cortisol, and inflammatory responses in people with asthma.⁷ Chronic negative stress may impact asthma in multiple ways. Chen and Williams postulate that chronic stress impacts asthma by altering the magnitude of airway inflammatory response to irritants, allergens, and infections.² Others demonstrated that chronic negative stress induces inflammatory changes

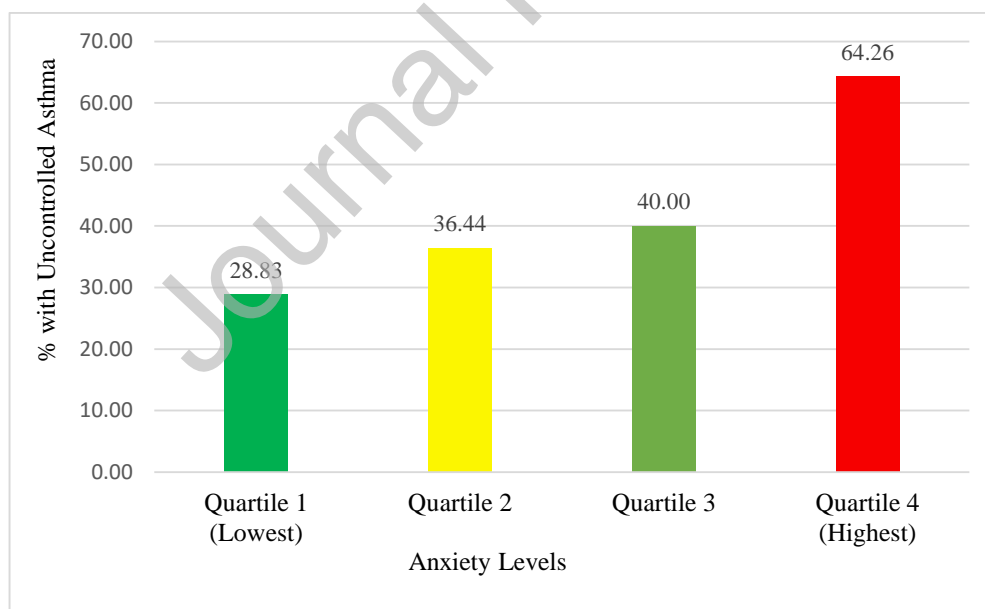
which reduces glucocorticoid receptor responsiveness.⁸ Both of these mechanisms can lead to difficult-to-treat, uncontrolled asthma. Our study has the typical limitations of the cross-sectional design, including the inability to rule out whether poor asthma control leads to increased anxiety (i.e., reverse causation), selection bias, and relying on self-report of asthma. Further, the anxiety scale used was developed during the emerging COVID-19 crisis to provide researchers with consistent measurement tools. Therefore, our findings should be interpreted with caution as reliability, validity, and cut points of the instrument have not yet been established. In addition, we could not assess if COVID-related anxiety was additive to existing chronic anxiety/stress, or if anxiety and asthma symptoms were confused. Moreover, although we were able to achieve geographic diversity in our sample, well-educated white females were overrepresented.

The COVID-19 pandemic has disproportionately impacted people with chronic diseases including asthma; these impacts were both physically and psychologically. While asthma-related ED visits and hospitalizations appeared to be lower during COVID-19, we must consider the avoidant healthcare behaviors people developed during the COVID-19 pandemic. Our findings underscore the need for healthcare providers to assess for the ongoing psychological impact of the pandemic and refer to mental health specialists. Equally important are efforts among policy makers to improve access to mental health services for all, especially during a pandemic.

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Figure 1: Percentage with Uncontrolled Asthma by Anxiety Levels (Quartiles)



P-values for overall differences and for a dose-response association were <0.0001