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Asthma patients experience increased symptoms of anxiety, depression and fear during the COVID-19 pandemic

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Abstract

Population studies showed a decrease in psychological wellbeing during the COVID-19 pandemic. Asthma is associated with a negative effect on anxiety and depression, which might worsen during the COVID-19 lockdown. The aim of the study was to compare fear, anxiety and depression between asthma patients and patients wit hout asthma pre-COVID-19 and during COVID-19 pandemic.

This study compares fear, anxiety and depression in asthma patients and controls between pre-COVID-19 and during COVID-19 lockdown with a cross-sectional online survey. Participants were invited to fill out several questionnaires pertaining to fear, anxiety, depression, asthma control and quality of life.

Asthma patients (N = 37) displayed, during the course of the pandemic, a clinically relevant increase in anxiety (3.32 ± 2.95 vs. 6.68 ± 3.78; $p < 0.001$) and depression (1.30 ± 1.15 vs. 3.65 ± 3.31; $p < 0.001$), according to the hospital anxiety and depression levels (HADS) compared to pre-COVID-19 assessment. This was not seen in controls. Also, asthma patients displayed more anxiety about acquiring COVID-19 disease compared to controls ((5.11 ± 1.99 vs. 3.50 ± 2.79), $p = 0.006$).

Patients with asthma experienced an increase in anxiety and depression levels and were more afraid of acquiring COVID-19 disease compared to controls. Also, patients with asthma were more likely to avoid healthcare facilities due to fear of acquiring COVID-19 disease compared to controls. Therefore, we advise health care workers to address these possible negative effects on mental health by phone or e-consults.

Keywords

Anxiety, depression, Sars-CoV-2, asthma, e-Health

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Introduction

Asthma is a growing cause of morbidity in the Western world.[1] Chronic airway-inflammation and reversible airflow obstruction are key in the clinical presentation of wheezing, cough and dyspnea.[2]

In the Netherlands, the first COVID-19 case was reported on 27 February 2020. Various measures have been taken by the government since early March, resulting in a lockdown from 23 March through 1 June. Between 27 February and 1 June, 46,444 confirmed COVID-19 cases have been detected in The Netherlands and 6,056 patients have died due to COVID-19 infection.[3] The COVID-19 pandemic puts patients with respiratory disorders at risk for a severe disease course and death.[4]

Lockdowns may result in social isolation. Social isolation is known to have a negative impact on anxiety and depression levels.[5] As asthma itself is associated with a negative effect on anxiety and depression, the COVID-19 lockdown could result in an additional increase of anxiety and depression levels in asthma patients.[6] A deterioration of mental health in asthma patients and depression in allergic patients during the COVID-19 pandemic has recently been described.[7,8]

It is not clear whether or not asthma is a risk factor for severe COVID-19. Several recent studies have not identified allergic asthma as a risk factor per se. These studies actually indicate that type 2 inflammation, which is present in most asthmatic patients, might even be protective of severe COVID-19 disease.[9–12] This suggests that increased fear of COVID-19 in allergic asthma patients is unwarranted. However, authorities have long thought asthma patients to be at high risk for severe COVID-19 disease.[13]

It has been described in several studies that fear of COVID-19 is present in the population and that the COVID-19 pandemic has resulted in an increase in general anxiety.[14,15] Since asthma patients have a higher risk for acquiring viral respiratory tract infections (RTI), it is conceivable that they would experience more stress and anxiety toward acquiring COVID-19 disease compared to persons without asthma.[1,2] In our outpatient clinic, we have seen that asthma patients have contacted our physician assistants more often for help and advice during the COVID-19 pandemic. Also, severe asthma patients were less willing to pay a physical visit to a medical specialist.[16]

The objective here was to study fear for SARS-CoV-2 infections and clinically relevant anxiety and depression in patients with and without asthma during the COVID-19 pandemic.

Methods

Study design

This observational study (CALiFe, NL8576) was designed and reported according to the STROBE guideline.[17] This study is a follow-up from the "General Risk factors and Inflammatory parameters in Adult onset Asthma" study (GRANDMA; NCT03278561). This research was declared as outside the scope of the Medical Research Involving Human Subjects Act. Written informed consent of all subjects was collected.

Study population

All participants had been previously enrolled in the cross-sectional GRANDMA study, which included 52 adult patients with asthma, and 28 age- and sex-matched controls with no history of pulmonary disease. The aim of the GRANDMA study was to determine differences between childhood onset and adulthood onset asthma in terms of comorbidities, psychological burden and immunological parameters.

Asthma was diagnosed based on the presence of typical clinical symptoms and reversible airway obstruction (>12% improvement of forced expiratory volume in 1 second after bronchodilator) and/or bronchial hyperreactivity ($PD_{20} \leq 1.76$ mg/ml) and/or a FeNO > 50 parts per billion.[18] All patients were on step 3–4 medication according to the guidelines of the Global Initiative of Asthma (GINA). Controls were friends and relatives of included asthma patients, to rule out the bias of social background. All subjects were between 18 and 80 years of age. Exclusion criteria for all participants were: 1) Smoking history > 10 pack years; 2) Disease which could alter pulmonary function and/or the immune system; 3) Non-comprehension of the Dutch language; 4) Inability to perform pulmonary function tests or sputum induction. Controls were excluded from study participation if they were diagnosed with a pulmonary disease, or if lung function revealed the presence of asthma. Data collection of the pre-COVID-19 assessment took place in summer seasons between 1 June 2017 and 1 June 2019. Data collection of the COVID-19 lockdown assessment took place between14 April and 1 July 2020.

Table 1. Baseline demographics.

	Asthma (N = 37)	Controls (N = 18)	*P*-value
Gender, Female	24 (64.90)	10 (55.56)	0.51
Age, years	56.00 [33.00–63.00]	49.00 [29.50–63.00]	0.62
Body mass index, kg/m^2	26.21 [22.67–31.93]	27.46 [25.22–31.11]	0.39
T2 inflammation, N (%)	31 (83.78)		0.12
Allergy, N (%)	22 (59.50)	8 (44.4)	0.29
Smoking (quit/never)	24/13	15/3	0.22
Education level (primary/secondary/university)	1/13/23	1/2/15	0.20

Data shown in median [25th–75th] **or** absolute (%) counts.
T2 = Type 2.

Variables and outcome measures

From 12 April through 1 June 2020, participants were invited by email or post to fill out a short survey. The following surveys were sent out to all participants: 1) Hospital anxiety and depression scale (HADS): a 14-item scale with seven items each for anxiety and depression subscale. A subscale score $\geq$ 8 denotes anxiety or depression.[19] The minimal clinical important difference (MCID) for HADS-Anxiety is 1.32 and for HADS-depression 1.40[19]; 2) Three questions regarding avoidance of general practitioner (GP) or hospital care due to COVID-19, delay in asking for medical assistance due to COVID-19 and fear of becoming infected with SARS-CoV-2 at the GP's office or hospital to be answered with yes/no (Supplementary Material); 3) A 0–10 visual analog scale (VAS) on fear of becoming infected with COVID-19; 4) PCR-proven infection with SARS-CoV-2 yes/no. By responding to the survey, informed consent was given. Two reminders were sent out.

Asthma patients also completed the asthma control questionnaire (ACQ) to determine asthma control. The ACQ-6 consists of five questions on symptoms and one question on reliever medication. Scores were implied as followed; $\leq$0.75 = controlled asthma, 0.76–1.50 = partially controlled asthma, $\geq$1.50 = uncontrolled asthma.[20] Also, to measure asthma-related quality of life, asthma patients completed the mini asthma-related quality of life questionnaire (AQLQ). The mini-AQLQ consists of 15 questions and determines functional problems in adults with asthma. A lower score equals an increase in functional problems.[21]

Endpoints

Primary outcomes in this study were anxiety and depression scores as measured by HADS-Anxiety and HADS-Depression. Answers on the other questionnaires were used as secondary outcomes.

Statistical analyses

Differences between asthma and controls were evaluated with the chi-square-test, Student's-t-test or the Mann-Whitney-U-test depending on the variable and its distribution. Differences between time points were compared with a paired T-test as data were normally distributed. Associations between variables were calculated with Pearson's correlation coefficient. Data is shown in median [25th–75th] or mean $\pm$ standard deviation (SD). A p-value of <0.05 was deemed significant. Statistical analyses were conducted with SPSS 26.0 and GraphPad 8.4.2.

Results

Out of 81 invited persons, 55 (37 asthma vs. 18 controls) responded and were included in this study (67.90%). Reasons for non-participation were unknown.

No differences between the groups were found in pre-COVID-19 demographics in terms of sex, age, BMI or present allergies (Table 1).

ACQ did not differ significantly between pre-COVID-19 assessment and COVID-19 lockdown assessment (0.67 [0.03–1.25] vs. 1.00 [0.3–1.67], $p = 0.27$). This was the similar for AQLQ (6.09 [5.60–6.80] vs. 5.87 [5.24–6.33], $p = 0.31$). Asthma patients and controls had a similar frequency of PCR-proven SARS-CoV-2 infections (2.70% vs. 5.55%%, $p = 0.15$). However, fear of becoming infected with SARS-CoV-2 was higher in asthma patients compared to controls ((5.11 $\pm$ 1.99 vs. 3.50 $\pm$ 2.79), $p = 0.006$) (Figure 1).

HADS-Anxiety and HADS-Depression scores did not differ between asthma patients and controls at pre-

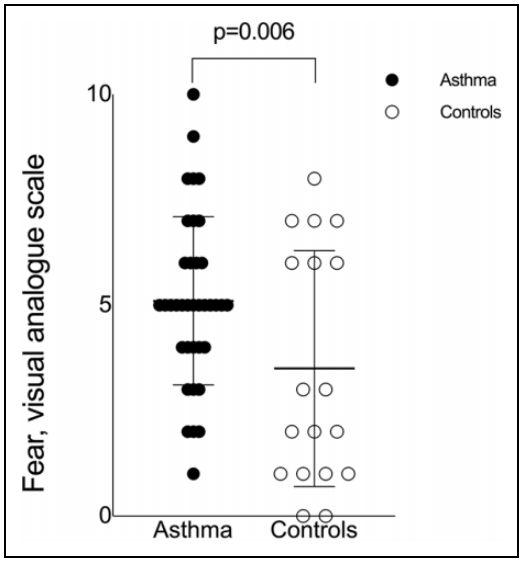

Figure 1. Fear of acquiring COVID-19 disease on a 0–10 visual analog scale.

COVID-19 assessment (Figure 1). Controls did not show a change in HADS-Anxiety nor HADS-Depression when pre-COVID-19 scores were compared to COVID-19 lockdown scores (Anxiety: 3.89 $\pm$ 1.35 vs. 2.72 $\pm$ 2.14, $p = 0.07$; Depression: 1.39 $\pm$ 1.72 vs. 1.67 $\pm$ 2.00, $p = 0.61$). In asthma patients, a significant increase was found for total HADS scores between pre-COVID-19 scores and COVID-19 lockdown scores ((4.65 $\pm$ 4.06 vs. 9.43 $\pm$ 6.68), $p < 0.001$). This increase was clinically relevant in the anxiety subscale ((3.32 $\pm$ 2.95 vs. 6.68 $\pm$ 3.78), $p < 0.001$), and the depression subscale ((1.30 $\pm$ 1.15 vs. 3.65 $\pm$ 3.31), $p < 0.001$) (Table 2). The total number of asthma patients with possible anxiety disorder according to HADS-Anxiety doubled, but was not statistically significant (5 (13.5%) vs. 10 (27.03%) $p = 0.07$), this was the same for HADS-Depression (0 (0.00%) vs. 5 (13.5%)). Controls did not show an increase in patients reaching the threshold for HADS-Anxiety (2 (11.11%) vs 0 (0.00%)) nor for HADS-Depression (0 (0.00%) vs. 0 (0.00%)).

Asthma patients were more likely to avoid their general practitioner (GP) and the hospital compared to controls (27% vs. 0%, $p = 0.02$) and more often showed fear of becoming infected with SARS-CoV-2 during visits to GP and the hospital compared to controls (24% vs. 0%, $p = 0.02$). In addition, they also appeared to delay medical care more often than controls, but this was not statistically significant (13.5% vs. 0%, $p = 0.10$).

Asthma patients who were more likely to avoid their GP and the hospital, scored higher on HADS-Anxiety compared to asthma patients who did not avoid these visits (8.30 $\pm$ 5.49 vs. 4.85 $\pm$ 2.63, $p = 0.014$). Asthma patients who were more likely to avoid their GP and the hospital also showed a tendency to contact their physician by e-consults ($r = 0.42$, $p = 0.010$). This was not seen for asthma patients who said they experienced fear of becoming infected with SARS-CoV-2 during these visits.

Discussion

In this study, we show an increase in scores of anxiety and depression in asthma patients during the COVID-19 lockdown. Also, we show that asthma patients experience more fear toward acquiring SARS-CoV-2 infection compared to patients without asthma.

Although most patients with asthma do not experience limitations in daily life, asthma patients with a higher disease burden do experience a reduced quality of life due to their asthma.[22] These asthma patients also are more prone to depression and anxiety.[6] The relationship between anxiety, depression and asthma has been widely studied, and no clear relationship has been found. However, reduced ability to attend social events, fatigue and asthma complaints might increase psychological stress. In combination with the asthmatic inflammation, this might increase cholinergic activity, leading to anxiety and depression.[23]

According to recent literature, we have found an increase in fear and anxiety in asthma patients compared to controls.[7] Our study adds fear of acquiring COVID-19 and avoidance of GP in asthmatics to this information. Increased anxiety at a population level, and in patients with chronic illnesses during the COVID-19 pandemic, has already been described.[14,24,25] More specifically, women were reported to be more anxious than men in a general Hongkong population.[25]

Previous studies in allergic patients also state the frequency of depression and an increase in post-traumatic stress due to the COVID-19 lockdown.[8] Our study shows comparable results for depression scores in asthma patients, who often have allergies as well. Although the percentages of clinically relevant allergies in asthma patients and controls in our study are comparable (59.50% vs. 44.40%, $p = 0.29$), we did find clinically relevant increased HADS-Depression scores in asthma patients and in controls.

Social distancing during the COVID-19 lockdown, combined with increased fear of getting infected with

Table 2. Scores for HADS, HADS-Anxiety and HADS-Depression pre-COVID-19 and during COVID-19 lockdown.

	Asthma pre-COVID-19	Asthma COVID-19 lockdown	*p*	Controls pre-COVID-19	Controls COVID-19 lockdown	*p*
HADS	4.65 ± 4.06	9.43 ± 6.68	<0.001	5.28 ± 3.55	4.39 ± 3.92	0.27
HADS-Anxiety	3.32 ± 2.95	6.68 ± 3.78	<0.001	3.89 ± 2.35	2.72 ± 2.14	0.07
HADS-Depression	1.30 ± 1.15	3.65 ± 3.31	<0.001	1.39 ± 1.72	1.67 ± 2.00	0.61

Data shown in mean ± SD.

SARS-CoV-2, could have a negative effect on anxiety and depression.[5–8] This is especially true for asthma patients, who are prone to anxiety and depression.[6,23] As asthma control and the asthma-related quality of life did not deteriorate between pre-COVID-19 and during the COVID-19 lockdown, we suggest that the increased HADS-Anxiety and HADS-Depression scores are related to the COVID-19 lockdown.

The HADS questionnaire is a patient-related outcome measure (PROM). This means that the minimal clinically important difference defines a threshold value of change, which is patient specific. Interpretation of minimal, clinically important changes in a PROM should therefore always be patient specific.[26] Our study shows no significant increase in numbers of patients reaching the threshold for both, HADS-Anxiety and HADS-Depression. However, numbers of patients reaching the threshold for HADS-Anxiety doubled, which showed a trend (5 (13.5%) vs. 10 (27.03%), $p = 0.07$). In a larger study population, this effect might have been statistically significant. Nevertheless, PROMs are patients specific, this increase should therefore not be neglected in clinical care of asthma patients.

While, in general, scores on HADS-Depression were quite low, they did increase with a minimal clinically important difference. This means that the increase is indeed important to address in the clinic, even though only five patients reached the threshold of mild depression.

Correlations between HADS-Anxiety and fear of getting infected with SARS-CoV-2, avoiding medical care facilities and fear of COVID-19 at these facilities, were not affected by these confounders. In asthma patients, the increased fear of acquiring COVID-19 disease may lead to a reduced infection rate among these patients in The Netherlands. As conflicting reports on COVID-19 risks and asthma might confuse asthma patients and increase their fear of acquiring COVID-19 disease, we suggest that information about the risks and COVID-19 in respiratory disease should be more patient and disease-specific.[9–13] This could reduce unnecessary fear of COVID-19 and avoidance of healthcare facilities.

Strengths of this study were the high response rate (67.9%) and the trustworthy baseline, as the threat of COVID-19 was not yet present at the time baseline scores were obtained. Moreover, patients from the GRANDMA study were mainly included in spring and summer, which parallels the season of the COVID-19 lockdown that was evaluated in the surveys. Also, asthma patients and controls did not differ on anxiety and depression scores at baseline. Controls were only free from respiratory diseases and not from other comorbidities, implying that asthma was the only discriminative factor between controls and asthma patients. In conjunction with the high response rate, the results obtained in this study are truly indicative of an increase in fear, anxiety and depression in the population of asthma patients.

Sample size might be a limitation of this study, as it was calculated from baseline data within the GRANDMA study, which was powered on immunological parameters. Therefore, baseline results on HADS within the GRANDMA study were less indicative and sample size in this follow-up is quite low. Also, patient-related outcome measures are prone to be overestimated and influenced by recall bias.[27] As sample size was thought to be a limitation of this study, we did not analyze differences between sexes, BMI and age.

As a practical implication of this study, we advise health care providers to address these possible negative effects on mental health by phone or e-consults. In this context, distribution of reliable scientific patient information on COVID-19 and asthma could be key in managing anxiety for COVID-19 in asthma patients.

In conclusion, asthma patients showed more fear of getting infected with COVID-19 compared to controls, and experienced an increase in anxiety and depression scores, without a statistically significant result in numbers of patients reaching thresholds during the COVID-19 lockdown compared to controls.

Increased anxiety scores were correlated with fear of becoming infected with SARS-CoV-2 and avoidance of medical care facilities during COVID-19.

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Author contributions

GMB conceived the idea of this follow-up study and set up the study under the close supervision of GB GT and RWH. GB conceived the idea of the original study. LH performed the study under the close supervision of GMB. GMB performed data-analysis under supervision of GT and JV. JV supervised data-analysis and interpretation. GMB and LH wrote the manuscript and all authors reviewed it during different phases. All authors approved the final version of the manuscript and are accountable for all aspects of the work.

Availability of data

Blinded data will be available upon request by the first author until 2 years after publication.

Consent to participate

Written informed consent of all subjects was collected.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval

This research was declared as outside the scope of the Medical Research Involving Human Subjects Act. Clinical Trial Registration: NL8576.

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Supplemental material

Supplemental material for this article is available online.

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