Asthma, much more than a respiratory disease: influence of depression and anxiety

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SUMMARY

OBJECTIVE: The goals of this study are to compare self-reported depression and anxiety in subjects diagnosed of asthma and healthy controls.
METHODS: We designed a case-control study. Subjects were recruited using a consecutive sampling method from a single institution. Two groups were created: Asthma and healthy controls. Data of medical history and demographic background were collected from the medical record. Self-reported depression level was assessed using Beck's depression inventory (BDI). Self-reported anxiety was measured with the "State-trait anxiety inventory" (STAI).
RESULTS: Fifty-one subjects with asthma, and fifty healthy patients were included in this study. BDI scores (p<0.001) were higher for asthma (10.22±7.3) than in the control group (5.2±6.56). STAI state (p<0.001) was higher in asthma (42.61±11.5) than in controls (34.88±9.25). STAI trait (p<0.001) showed higher scores in asthma (43.14±10.89) than in controls (34.62±9.19).
CONCLUSIONS: These study findings showed that BDI, and STAI trait and state scores are significantly higher in subjects who suffer from asthma than healthy controls.
KEYWORDS: Depression. Anxiety. Asthma.

INTRODUCTION

Depression and anxiety are considered "common mental disorders". Globally, the total number of people with depression was estimated to exceed 300 million in 2015 (4.5% of the world's population). Up to nearly 40% of the population are affected at some point by an anxiety disorder[1]. The consequences of both conditions in terms of loss of health are substantial and have a considerable effect on a patient's health-related quality of life (HRQL). Depression is considered the single largest contributor to global disability around

the world. The most common underlying disorder in those who attempt suicide is depression.

Depressive disorders are characterized by symptoms as sadness, loss of interest or pleasure, feelings of worthlessness or guilt, sleep difficulties, fatigue, appetite or weight changes, feelings of tiredness, psychomotor disturbances, poor ability to concentrate, and even suicidality[2]. Depression can be long-lasting or recurrent, causing impairment to daily life activities.

Anxiety is associated with physical and psychological discomfort. All anxiety disorders share common symptoms, such

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as fear, anxiety, and avoidance. Other anxiety-related symptoms include fatigue, restlessness, irritability, sleep disturbances, reduced concentration, lack of memory, and muscle tension. Depression and anxiety often co-occur. Up to 90% of patients with anxiety develop symptoms of depression, and nearly 85% of patients with depression show some kind of anxiety symptom[3].

The prevalence of depression and anxiety is two to three times higher in people with chronic medical conditions than in healthy peopl[4]. People with a long-term condition and depression or anxiety have worse health status than people with depression or anxiety alone, and even than people with any combination of long-term conditions without depression[5].

Asthma is considered a chronic heterogeneous disease. Its pathogenesis involves various cells and mediators of inflammation, and it is characterized by airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation, totally or partially reversible, either spontaneously or due to the action of the medication[6].

In 2017, the worldwide prevalence of asthma was around 3.5% with a reported incidence of 0.56%[7]. Asthma may disturb daily activities, as well as the patient's quality of life (QoL)[8]. It carries an economic burden, due to an often increment of the emergency care use, hospital admission, as well as work absenteeism. In addition, it can potentially cause early disability and premature death. The mean cost per patient per year is high, and can vary among countries, according to Nunes et al, in Europe is $USD 1,900, different from the USA, in which estimated mean is estimated around $USD 3,100[9]. People with asthma are more prone to emotional disorders, even when their symptoms are controlled[10]. Different authors, reported a high prevalence of anxiety and depression[11,12]. Labor et al. reported that 24.5% of asthma patients were depressed, and 44% had symptoms of anxiety[11].

Del Giacco et al, reported that anxiety may be a predisposing factor for developing asthma, and also, having asthma may predispose a higher risk of having an anxiety disorder, establishing the possibility of a bidirectional association between anxiety and asthma[13].

Besides, anxiety and depression have been associated with increased asthma exacerbations and emergency visits[14]. Depression acts as an independent co-morbid factor in asthma[15].

We hypothesized that people with asthma, had the worst levels of Self-perceived depression, anxiety trait, and state when compared to healthy people. So, the main objective of this research was to determine self-perceived depression and anxiety trait and state levels in a subset of asthma patients compared to healthy controls.

METHODS

Study design

A case-control study of a non-probability consecutive sampling method from a medical center was performed to compare self-assessed depression severity, anxiety trait, and anxiety state in patients diagnosed with asthma and healthy controls. All the data collection was supervised by the same researcher. The guidelines for reporting observational studies, stated by the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) were followed[16].

This study was approved by the ethics committee of clinic research of Galicia (Spain). The Helsinki declaration as well as all national and international ethical standards for human experimentation were respected[17]. Also, all participants signed the informed consent before their inclusion in the present research.

Analytic analysis

Sample size calculation

T-tests for differences between 2 different means were used to determine the sample size calculation by the G*Power 3.1.9.2 software and based on the BDI as the main outcome measurement of a pilot study (n=28 participants) with 2 groups (mean±SD), 14 patients with asthma (9.28±6.16 points) and 14 healthy controls (4.92±3.64 points). Furthermore, the followed parameters were used for the sample size calculation with an effect size of 0.86, α error of 0.01, and power (1-β error) of 0.90. Thus, the required total sample size was 84 participants, 42 for each group, necessary to achieve an actual power of 0.901. Finally, considering a possible 15% loss to follow-up, a total sample of 98 participants, 49 subjects for each group, was required for the present study.

Participants

A consecutive sampling method was used to recruit participants from the pneumology department of the Complexo Hospitalario de Ourense (Ourense, Spain). Two groups were established: Asthma (case group) and healthy patients (control group). Asthma patients were diagnosed and classified according to the GEMA (Spanish Group for Asthma Management) guidelines[6]. Healthy matched-paired participants were included, as the control group. The inclusion criteria were being older than 18 years old, agreement to sign informed consent, and lack of history of psychiatric. For the control group, healthy participants older than 18 years old were included, without chronic respiratory disease, or known psychiatric medical history and agreement to sign informed consent. Exclusion criteria: not complying with the inclusion criteria described above.

Descriptive data

Descriptive data such as sex, age, weight, height, body mass index (BMI; calculated by the Quetelet index as kg/m^2), and smoke habit were collected.

Outcome measurements

Self-perceived depression, anxiety trait, and state were considered as the primary outcomes.

Self-reported depression was assessed using the "Beck´s depression inventory (BDI-II)", which has become one of the most widely used instruments for assessing the severity of depression worldwide. It contains 21 items, scored by a 4-point Likert scale (0-3). The final results range from 0 to 63 points. Greater scores suggest increased depression severity. Scores between 0–10 indicate no signs of depression; 11–16 indicate mild depression; 17–20 indicate borderline depression; 21–30 indicate moderate depression; 31–40 indicate serious depression; and, 41 or higher indicate extreme depression. Anything over 17 points requires professional treatment[18]. This tool was validated in Spanish, with a Cronbach's α=0.87 and a high diagnostic validity (ROC=0.91) in the general population[19].

The State-Trait Anxiety Inventory (STAI) is a self-reported scale used for the assessment of anxiety state and trait in research and clinical practice. The STAI consists of two 20-item scales (S-Anxiety measuring anxiety as an emotional state, and T-Anxiety measuring anxiety as a personal characteristic or trait)[20]. Each item is scored by a 4-point Likert scale (1–4). Spanish version of the STAI was used. The final score was converted to a digit (0–80) as described for *Buela-Casal*, to be uniform with the original Y-version of the STAI[21]. Higher scores suggest higher levels of anxiety. This test has a good internal consistency, with a Cronbach´s α=0.92 for anxiety state (95%IC 0,91–0,93) and a Cronbach´s α=0.91 for anxiety trait (95%IC 0.90–0.92.)[22] and a Test-retest reliability coefficients on initial development ranged from 0.31 to 0.86[20].

Statistical analysis

Statistical analyses were performed by the SPSS 24.0 version (IBM–Windows; Armonk–NY: IBM Corp) using an α error of 0.01 in conjunction with a 99% confidence interval (CI).

Considering quantitative data, the test of Kolmogorov-Smirnov was applied to determine normality distribution. All data were described by the mean±standard deviation (SD) and range (minimum–maximum values). Regarding the parametric data (Kolmogorov-Smirnov p≥0.05), between-groups differences were compared by the Student t-tests for independent samples, and for the non-parametric data (Kolmogorov-Smirnov p<0.05), between-groups differences were compared by the Mann-Whitney U tests for independent samples.

For categorical data, frequencies were used to describe these data values and categorical between-groups differences were analyzed by the Fisher exact tests for the age dichotomous variable and the Chi-square (χ^2) test for the depression categories polytomous variable using bar graphs to show this distribution.

RESULTS

The study population included 101 participants, 37 men and 64 women. 11 participants (10.9%) were smokers, 21 (20.8%) former smokers, and 69 (68.3%) non-smokers. The control group was formed by 50 healthy participants, 64% female and 36% male, with a mean age of 42.84±15.69. They were not having chronic medication. In the asthma group, there were 51 patients, 62.7% female and 37.3% male, with a mean age of 59.76±17.7 years. According to Table 1, there were statistically

Table 1 Sociodemographic and clinical characteristics of the sample population.

	Sample	Control	Asthma	
	Mean±SD (range) n=52	Mean±SD (range) n=50	Mean±SD (range) n=51	p-value
Age (years)	51.39±18.45 (18–95)	42.84±15.69 (19–83)	59.76±17.17 (18–95)	<0.001*
Weight (Kg)	72.59±13.83 (43–115)	70.37±13.9 (47–115)	74.76±13.51 (43–109)	0.111†
Height (m)	1.66±0.1 (1.45–1.90)	1.69±0.92 (1.50–1.89)	1.63±0.10 (1.45–1.90)	0.003*
BMI (Kg/m^2)	26.31±4.79 (17.59–45.78)	24.48±3.42 (17.59–33.79)	28.09±5.27 (18.13–45.78)	<0.001*
Sex (female/male)	64/37	32/18	32/19	1.000‡
Smoker (no/yes/former)	69/11/21	38/7/5	31/4/16	0.026§

BMI: body mass index; SD: standard deviation; p<0.01 with a 99% confidence interval was considered statistically significant. *Mann-Whitney U test was used. †Student t-test for independent samples test was used. ‡Fisher exact test was used. §Chi-squared (χ^2) test was used.

Table 2. Depression and anxiety score differences between asthma and healthy participants.

	Sample Mean±SD (range) n=52	Control Mean±SD (range) n=50	Asthma Mean±SD (range) n=51	p-value
STAI-State	38.78±11.10 (21–71)	34.88±9.25 (21–66)	42.60±1.50 (21–71)	<0.001*
STAI-Trait	38.92±10.91 (20–69)	34.62±9.19 (20–65)	47.13±10.89 (20–69)	<0.001†
BDI	7.73±7.35 (0–36)	5.20±6.56 (0–36)	10.21±7.30 (0–27)	<0.001†

BDI: beck depression inventory; SD: standard deviation; STAI: state-trait anxiety inventory; p<0.01 with a 99% confidence interval was considered statistically significant. *Student *t*-test for independent samples test was used. †Mann-Whitney *U* test was used.
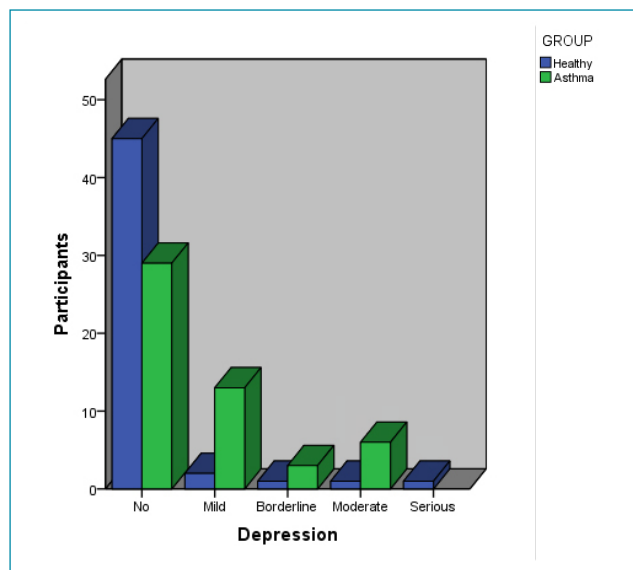

Figure 1. Depression categories between asthma and healthy subjects.

significant differences (p<0.01) between asthma and healthy participants for age, height and BMI, but not for weight, sex and smoker habits (p>0.01).

Regarding Table 2, state and trait anxiety as well as anxiety scores were greater in patients who suffer from asthma with respect to healthy participants, showing statistically significant differences (p<0.001). In addition, the Chi-squared (χ^2) test showed statistically significant differences (p=0.002) detailing more presence of mild, borderline, and moderate depression categories in patients with asthma versus healthy subjects according to Figure 1.

DISCUSSION

Psychological issues are very common in asthma and have a significant impact on quality of life, even if the asthma symptoms are under adequate clinical control[8,23].

In the present study, we found a higher self-reported anxiety state and trait scores in patients with asthma compared to healthy people, consistent with the data previously published[24,25]. Also found higher BDI scores in asthma patients, compared to controls and a direct correlation between the severity of depressive symptoms and asthma severity. The exact connection between asthma and anxiety/depression is still not fully explained. Regarding anxiety in asthma, even when disease control is reached, these patients could experience continuous distress, having presented the risk of future exacerbations, and fear of a crisis and reduced pulmonary function. Chronic psychological distress may cause a pro-inflammatory condition and be associated with increased superoxide and cytokine and leukocyte production. According to Veres et al., neurokinins and P substance (asthma pulmonary neurogenic inflammation byproducts) have a direct action on the central nervous system, inducing anxiety states[26].

Regarding depression and asthma, as a possible pathophysiological mechanism, Marini et al. described that the pro-inflammatory state noted in certain asthma phenotypes is similar to that induced by pro-inflammatory cytokine treatments in humans such as corticosteroids, long known to be associated with depressive symptoms[27]. Also, hypothalamic-pituitary-adrenal axis dysregulation, noted in major depression, have been described in asthma as a result of the inhaled corticosteroids[28,29].

This study had some limitations and should be taken into consideration in future studies. First, to recruit participants a consecutive sampling method was used and could be improved. Second, a larger sample size could be necessary to achieve more reliable results.

CONCLUSIONS

Asthma subjects showed higher scores of self-reported depression, anxiety state, and anxiety trait than controls.

AUTHORS' CONTRIBUTIONS

RHR: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **ÓÁCI:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **RDQ:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **RBBV:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **CCL:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **MSA:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **MELI:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **DLL:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

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