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Correlation Between Anxiety Disorders and Asthma Severity Indices in Asthmatic Children

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Abstract

Background: Anxiety and depression in patients with asthma have been linked to frequent exacerbations, increased use of healthcare resources, and poor asthma control.
Objectives: In the current study, we examined the correlations between asthma and symptoms of depression/anxiety in adolescents with asthma referred to Masih Daneshvari and Mofid hospitals during 2020 - 2021.
Methods: The current observational, cross-sectional study was conducted by administering the Spence Children Anxiety Scale and a demographic information checklist among 105 subjects. Asthma severity was measured using forced expiratory volume in 1 second (FEV1), FEV1/forced vital capacity (FVC), the number of short-acting β-2 agonists used per week or month, the number of night awakenings per week or month, having asthma symptoms in daily activities, the number of asthma attacks needing oral corticosteroids per year, and the number of disease exacerbations per week or month. Data were analyzed, and the correlation between the variables was investigated through linear regression and ordinal logistic regression.
Results: Patients with a mean age of 11.3 ± 2.5 years showed a mean overall anxiety score of 14 ± 9 out of 114. There was a significant negative correlation between the overall score of anxiety disorders and FEV1 and FEV1/FVC ($P < 0.001$). There was also a direct correlation between the overall score of anxiety disorders and the frequency of using β-2 agonists, the number of night awakenings, interference with normal functions, and exacerbation frequency ($P < 0.001$).
Conclusions: Our findings indicated a significant association between anxiety disorders and asthma in children. Considering the high prevalence of asthma in Iran than the global average, studying the underlying mechanisms of anxiety and psychological and environmental variables in children with asthma can aid in developing effective psychological therapies.

Keywords: Asthma, Psychiatric Morbidity, Depression, Anxiety, Adolescent

1. Background

Asthma is the most common respiratory disorder. The prevalence, severity, and duration of hospitalization in patients with asthma have increased in recent years (1). Asthma is often characterized by limitations in physical activity, negative impacts on social life and relationships, challenges in finding and maintaining employment, and a decreased quality of life (2). More than 80% of asthma-related deaths occur in low and middle-income countries, and almost 25,000 children die yearly (3). In Iran, asthma affects 13.14 % of people under 18 and 7.48% of people of all ages, which is higher than the global average (4).

Asthma is one of the most common chronic inflammatory disorders in adolescence, with various consequences, including poor school performance and social work disorders. Thus, it can be a serious health issue (5-7). The prevalence of asthma in children is currently increasing. In 2001, 8.7% of children had asthma, and by 2009, this number had risen to 9.6%. This upward trend is expected to continue, with the CDC predicting that by 2025, more than 400 million people will have asthma (8). Its prevalence and severity are linked to factors such as exposure to allergic materials and lifestyle changes, particularly regarding physical activity. There is a correlation between asthma prevalence and reaction to allergenic materials, especially air dust particles (9).

Anxiety and depression are up to six times more common in people with asthma than in the general population (10). Also, 16 % of people with asthma in the UK have panic disorder (11), compared to 1% in the general population (12). In patients with psychiatric or behavioral disorders, abnormal breathing patterns can cause asthma-like symptoms (13). Several studies have discovered a link between asthma and anxiety disorders among young people and adults (14, 15). One study found a close association between anxiety, depression, and poor asthma control. Another study revealed that children with well-controlled asthma were not at an elevated risk of anxiety, depression, or low self-esteem (16). Prior research has shown a high prevalence of asthma and mood disorders in adolescents (17).

2. Objectives

Because the association between anxiety disorders and asthma severity indicators has not been extensively investigated in Iran, we herein investigated this association in children with asthma who were referred to Masih-Daneshvari and Mofid hospitals during 2020 - 2021.

3. Methods

3.1. Subjects

The sample size was calculated based on the formula provided for regression analysis by Tabachnick and Fidell: Sample size = 50 + 8* (number of independent variables) (18). As the number of independent variables was 9, the minimum sample required was 122. Considering the conditions of the coronavirus pandemic, lockdowns, and the need to refer patients, finally, 105 patients completed the study, and the rest refused to continue. Hence, about 13% of the patients lost the follow-up, but since Tabachnick and Fidell recommended a sample size of at least 80 for regression analysis, the statistical power of this study was appropriate (19).

The study group consisted of 105 children with asthma (31 males and 74 females) aged between 6 and 18 years (mean ± SD: 11.3 ± 2.5) who were followed up in the Pediatric Allergy and Immunology Departments of Masih-Daneshvari and Mofid hospitals, Shahid Beheshti University of Medical Sciences during 2020 - 2021. In this study, 6-18-year-old children who had asthma symptoms (chronic cough, tightness in the chest, wheezing, and shortness of breath) were evaluated. After performing a complete physical examination, if they had inclusion criteria, they entered the study with their parent's written informed consent. For inclusion in the study, the person would have asthma confirmed by spirometry, no heart disease (heart failure, heart valve failure, severe heart valve stenosis, and heart attack), lack of severe lung disease (cystic fibrosis, chronic obstructive pulmonary disease, and chronic and severe pulmonary bronchitis), and no history of chronic disease. This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1400.223).

3.2. Study Design

Diagnosis and severity of asthma were described prospectively based on the global initiative for asthma guideline (20). The children were administered Spence Children's Anxiety Scale (SCAS) (parent report). Besides an overall anxiety score, six areas, including separation anxiety, social anxiety, panic, generalized anxiety, social phobia, and obsessive-compulsive disorder (OCD), were also evaluated based on the questionnaire utilized in this study. Duration of asthma, asthma symptoms, and the number of emergency department visits were also recorded for asthmatic children. The sociodemographic characteristics of patients were recorded in a separate questionnaire.

The SCAS consists of 44 items, of which 6 are filler items. Only 38 anxiety items are scored. The 6 filler items are not scored. The responses are scored on a 4-point scale ranging from 0 to 3 (never = 0, sometimes = 1, often = 2, always = 3). This yields a maximum possible score of 114. The total score is the sum of items: 1 + 2 + 3 + 4 + 5 + 6 + 7 + 8 + 9 + 10 + 12 + 13 + 14 + 15 + 16 + 18 + 19 + 20 + 21 + 22 + 23 + 24 + 25 + 27 + 28 + 29 + 30 + 32 + 33 + 34 + 35 + 36 + 37 + 39 + 40 + 41 + 42 + 44. Alternatively, the total score may be computed by summing all the subscale scores if no missing items exist. The positive filler items not computed in total or subscale scores include items 11, 17, 26, 31, 38, and 43. A T-score of less than 60 (a percentile score less than 85%) shows the "normal" range. A T-score of 60 or more (top 15% or more) suggests higher-than-normal anxiety but not necessarily in the clinical range. For this reason, the term "elevated" anxiety is used. A total score of 65 means that the child's score is in the top 6% of children. A total score of 70 means that the child's score is in the top 2% of children. Cronbach's alpha for the SCAS total score was 0.92. Cronbach's alphas were 0.70 for separation anxiety, 0.72 for social phobia, 0.71 for OCD, 0.82 for panic/agoraphobia, 0.57 for physical injury fears, and 0.74 for generalized anxiety (21).

3.3. Statistical Analysis

Statistical analysis was performed by SPSS 25.0 (Chicago, IL). Frequency, percentage, mean, and standard deviation were used to describe the data. After converting the distribution of total scores and social anxiety scores to normal distribution (by converting SQRT), we used the linear regression test. We used ordinal logistic regression analysis for other scores whose distribution did not allow normal distribution. All analyses were performed based on linear and ordinal logistic regression adjusted for age and sex. Also, forced expiratory volume in 1 second (FEV1) and FEV1/forced vital capacity (FVC) were entered into the model individually and again in a separate model, and their effects on the questionnaire scores were measured. A P-value of less than 0.05 was considered statistically significant, and a P-value between 0.05 and 0.07 was in the borderline range.

4. Results

The study included 105 subjects, including 31 (29.5%) males and 74 (70.5%) females. The mean age was 11.3 ± 2.5 years, ranging from 7 to 16.

Patients' mean total anxiety score was 14 ± 9 out of 114, with a median of 13 (2,49). A total score of less than 60 is in the normal range. We examined the correlation between FEV1 and the squared total score using linear regression. There was a statistically significant inverse correlation between FEV1 and the overall score, so by one unit increase in FEV1, the overall score decreased by 0.029 ($P < 0.001$).

Likewise, we examined the correlation between FEV1/FVC and the overall score, showing a statistically significant negative correlation with a coefficient of 0.057 ($P < 0.001$). Examination of the correlation between the total score and the frequency of using short-acting β-2 agonists showed a statistically significant direct correlation with a coefficient of 0.9 ($P < 0.001$). Additionally, a significant correlation with a coefficient of 0.92 was found between the number of night awakenings per month and the total score ($P < 0.001$). Likewise, we assessed the correlation between symptom interference in routine activities and the total score and found a statistically significant positive correlation with a coefficient of 1.56 ($P < 0.001$). However, linear regression analysis found no correlation between the yearly number of asthma exacerbations requiring treatment with oral corticosteroids and the total score of the questionnaire (P = 0.184).

In the next step, we evaluated the patients' various areas of anxiety, including separation anxiety, social anxiety, panic, generalized anxiety, social phobia, and OCD (Table 1).

Table 1. Patients' Scores on Various Types of Anxiety

	Mean ± SD	Median (Range)
Separation anxiety	3 ± 3	3 (0 - 11)
Social anxiety	3 ± 2	3 (0 - 12)
Obsessive-compulsive disorder	0 ± 1	0 (0 - 6)
Panic	1 ± 1	1 (0 - 6)
Generalized anxiety	2 ± 2	2 (0 - 9)
Social phobia	3 ± 3	2 (0 - 15)

Ordinal logistic regression analysis investigated the correlation between separation anxiety scores and other variables. The results of the correlation between asthma-related variables and separation anxiety scores are seen in Table 2 and described as follows. A regression coefficient of 0.028 showed a statistically significant association between separation anxiety score and FEV1. The separation anxiety score decreased by 0.028 when the FEV1 variable increased by one unit (P = 0.001). The separation anxiety score had a negative association with FEV1/FVC, with a regression coefficient of 0.056 (P = 0.001). Furthermore, the separation anxiety score increased by 0.808 (P = 0.001) for a single unit increase in the frequency of using short-acting β-2 agonists during the week. Similarly, there was a statistically significant association between the separation anxiety score and the frequency of night awakenings per month (regression coefficient of 0.62, P = 0.001) and the interference of symptoms in routine activities (regression coefficient of 1.25, P = 0.001). In addition, the separation anxiety score had a significant association with the number of pulmonary exacerbations needing corticosteroid medication and the frequency of symptom exacerbations (regression coefficients of 0.715 and 0.808, respectively; P = 0.001).

Using linear regression after controlling for age and gender, we observed a significant negative association between social anxiety disorder (SAD) score and FEV1/FVC. Accordingly, the SAD score decreased by 0.029 units (P = 0.003) for every unit increase in FEV1/FVC. There was also a statistically significant association between the SAD score and the frequency of using short-acting β-2 agonists over the week (regression coefficient of 0.43 and $P < 0.001$). Furthermore, the SAD score had a statistically significant direct correlation with the frequency of waking up at night during the month, interference of symptoms in normal activities, and the frequency of symptoms during the week (regression coefficients of 0.41, 0.74, and 0.43, respectively; P = 0.001). According to ordinal logistic regression analysis, the OCD score had no statistically significant correlation with other asthma-related variables. Although the OCD score decreased by 0.001 per unit increase in FEV1, the association was insignificant (P = 0.872).

Likewise, we examined the correlation between variables and panic scores. As observed, FEV1 and FEV1/FVC variables had no significant correlation with panic scores. In contrast, for one unit increase in using short-acting β-2 agonists, the panic score increased by 0.67 (P = 0.001). Also, for a one-time increase in the number of night awakenings, the panic score increased by 0.39 (P = 0.066), which was significant in the borderline range. Hence, it can be claimed that the panic score significantly correlated with the number of night awakenings. Further studies with a higher sample size are needed to validate these results.

There was also a direct correlation between the panic score and the number of symptom exacerbations during the week (regression coefficient of 0.67, P = 0.001). We also discovered a significant correlation between the FEV1 and FEV1/FVC variables and the generalized anxiety score (regression coefficients of 0.048 and 0.12, respectively; P = 0.001). Moreover, the frequency of using short-acting β-2 agonist, frequency of night awakenings, interference of symptoms with routine activities, number of pulmonary exacerbations requiring corticosteroids, and frequency of symptom exacerbations had a significant direct correlation with the generalized anxiety score (regression coefficients of 1.45, 1.6, 2.3, 1.8, and 1.45, respectively; P = 0.05). Finally, the social phobia score had a significant negative association with FEV1 (regression coefficient of 0.04, P = 0.001). Also, the frequency of using short-acting β-2 agonists during the week, frequency of night awakenings during a month, interference of symptoms with routine activities, and frequency of symptom exacerbations during the week were directly related to the social phobia score (regression coefficients of 1.16, 1.05, 1.69, and 1.16, respectively; $P < 0.001$) (Table 2).

5. Discussion

In this study, we examined 105 asthmatic patients aged 6 to 18, referred to Mofid and Masih Daneshvari hospitals in Tehran between 2020 and 2021 to investigate the correlation between asthma-related variables and anxiety scores. Our results show a negative correlation between the overall score of anxiety disorders and FEV1 and FEV1/FVC. There was also a direct correlation between the overall score of anxiety disorders and the frequency of using short-acting β-2 agonists, the number of night awakenings, interference with daily tasks, and the frequency of symptom exacerbations. In detail, separation anxiety, social anxiety, OCD, panic, generalized anxiety score, and SAD had a substantial association with asthma-related symptoms.

Asthma is one of the most frequent chronic childhood disorders, affecting 9.5% of the world's under-18 population and 13% in Iran (22). This chronic inflammatory disease of the airways causes frequent pulmonary exacerbations, which can result in panic in children. Therefore, anxiety in children with asthma should be considered (23). Previous studies in patients with asthma have reported that experiencing greater levels of negative emotion leads to decreased lung function (24). Anxiety disorders, particularly panic disorders, are prevalent in children with asthma, with a reported frequency of 33% (25). While anxiety affects 7% of children in the general population, it affects four to five times more children with asthma (26). Anxiety disorders in childhood can reflect adolescent anxiety and other mental disorders, and they can continue to adulthood (27).

Evidence suggests that anxiety disorders in children are linked to adulthood disorders, including depression, panic, agoraphobia, and physical illness (28). Prolonged respiratory problems can lead to catastrophic beliefs about the symptoms of respiratory disease, which can lead to panic attacks, and children who experience more negative emotions are more likely to have asthma attacks (29). Our findings revealed a negative correlation between FEV1 and FEV1/FVC and separation anxiety, SAD, and generalized anxiety. Only FEV1 revealed a negative correlation with the OCD and social phobia scores. Anxiety in asthmatics exposes them to a variety of behavioral and social disorders (30). Previous research has also discovered a link between asthma and anxiety or depression, leading to recommendations in national and international guidelines to evaluate comorbid mental

Table 2. Findings Based on Ordinal Logistic Regression and Linear Regression

	Coefficient	Std. Coefficient	Std. Err.	P-Value
Based on Ordinal Logistic Regression (Separation Anxiety Score)				
FEV1	-0.028	-0.263	0.019	0.001
FEV1/FVC	-0.056	-0.335	0.034	0.001
Use of short-acting β-2 agonists	0.808	0.564	0.237	0.001
Number of night awakenings per month	0.62	0.447	0.333	0.001
Symptom interference in routine activities	1.25	0.419	0.667	0.001
Number of pulmonary exacerbations needing corticosteroid medication	0.715	0.154	1.386	0.001
Frequency of symptom exacerbations	0.808	0.546	0.237	0.001
Based on Linear Regression (Total Score)				
FEV1	-0.029	-0.347	0.06	< 0.001
FEV1/FVC	-0.057	-0.373	0.111	< 0.001
Number of asthma exacerbations			4.601	0.184
Requiring treatment with oral corticosteroids during the year				0.184
Use of short-acting β-2 agonists	0.9	0.706	0.682	< 0.001
Number of night awakenings per month	0.92	0.609	0.993	< 0.001
Symptom interference in routine activities	1.56	0.544	2.071	< 0.001
SAD				
FEV1/FVC	-0.029	-0.333	0.031	0.003
Frequency of using short-acting β-2 agonists over the week	0.43	0.569	0.216	< 0.001
Frequency of night awakenings during the month	0.41	0.457	0.305	< 0.001
Interference of symptoms in normal activities	0.74	0.452	0.603	< 0.001
Frequency of symptoms during the week	0.43	0.569	0.216	< 0.001
Panic Scores				
Short-acting β-2 agonists	0.67	0.342	0.121	0.001
Number of night awakenings	0.39	0.312	0.16	0.066
Number of symptom exacerbations during the week	0.67	0.342	0.121	0.001
Social Phobia				
FEV1	0.04	0.323	0.02	0.001
Using short-acting β-2 agonists during the week	1.16	0.489	0.269	< 0.001
Frequency of night awakenings during a month	1.05	0.446	0.352	< 0.001
Interference of symptoms with routine activities	1.69	0.333	0.747	< 0.001
Frequency of symptom exacerbations during the week	1.16	0.489	0.269	< 0.001
Generalized Anxiety Score				
FEV1	0.048	0.357	0.014	0.001
FEV1/FVC	0.12	0.479	0.026	0.001
Short-acting β-2 agonists	1.45	0.622	0.181	0.05
Frequency of night awakenings	1.6	0.611	0.239	0.05
Interference of symptoms with routine activities	2.3	0.479	0.52	0.05
Number of pulmonary exacerbations requiring corticosteroid medication	1.8	0.193	1.098	0.05
Frequency of symptom exacerbations	1.45	0.622	0.181	0.05

Abbreviations: FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; SAD, social anxiety disorder.

health impairment in patients with severe asthma (31, 32). Although the underlying mechanisms of anxiety and asthma have not been precisely identified, studies have shown that anxiety and depression may worsen with the disease's severity (33). According to a recent study by Montalbano et al., the quality of life impairment and internalizing behavioral problems, particularly the subscale including anxiety and depressive symptoms, are more common in children with severe asthma than in non-severe asthma, and no sex differences were identified (34).

In two meta-analysis studies, reviewing 901 studies, children with chronic diseases were found to be more anxious than the average level (35, 36). Due to the prevalence of psychological and behavioral problems in children with asthma, they are at higher risk for developing and worsening anxiety disorders (26). In a cohort study, Goodwin et al. discovered that severe and persistent asthma among 5-year-old children significantly increased the risk of mental problems between the ages of 5 and 17, while the risk of mental disorders in children with mild and improved asthma did not increase (37). The inability to perform the desired physical function causes a person to suffer from anxiety and depression (38). In asthma, chronic inflammation and high levels of proinflammatory cytokines affect glucocorticoid and corticosteroid-releasing hormone receptors and alter the hypothalamic-pituitary-adrenal (HPA) axis, impairing neurotrophic factor secretion. These reactions eventually cause damage to the hippocampus and decrease monoamine content in the brain (39, 40). Panek et al. also discovered that glucocorticoid receptor gene (NR3C1) haplotypes (ER22/23EK, N363S, BclI) were linked to mood and anxiety issues in asthma patients (40).

On the other hand, more anxiety leads to weaker control over the disease (41). Studies have shown that anxiety in children with asthma can affect self-care behaviors (42) and treatment adherence (42). Hospitalization (43), medical expenses (44), and parental anxiety (45) are among the problems caused by the disease that can harm the quality of life of children with the disease (46). According to the current study, asthma negatively impacts mental health, particularly anxiety disorders. The frequency of short-acting β-2 agonists consumption, the number of night awakenings, interference of symptoms in daily tasks, frequency of pulmonary exacerbations requiring oral corticosteroid therapy, and frequency of symptoms flare-ups were all found to be positively correlated with separation anxiety and generalized anxiety scores. There was also a positive link between social anxiety and short-acting β-2 agonist use, the frequency of waking up at night, the interference of symptoms with routine tasks, and the frequency of symptom exacerbation. The number of short-acting β-2 agonists administered and the number of symptom exacerbations are directly connected to the panic score. These results align with research conducted by Kullowatz et al. on 90 asthmatic patients. Their findings revealed that the incidence of anxiety and depression in asthma patients has a major impact on patients' quality of life (47).

Similarly, Mancuso et al. found that 45% of patients with asthma were positive for depressive symptoms, and depression was significantly associated with a lower quality of life score (48). In this regard, de Miguel Diez et al.'s research, which used two SF-36 questionnaire indicators and interviewed adults with asthma and bronchitis, found that healthy people had higher mental health scores than asthmatics (49). According to Ahmadiafshar et al.'s research, students with asthma symptoms had a higher level of anxiety. They also reported higher rates of depression among students with asthma in a parallel study (50). This correlation has been validated in other research (51, 52). However, previous research has found conflicting results and reported no link between mental disorders and asthma (16, 53). In one study, adolescents with asthma had a higher frequency of anxiety and depression, but this correlation was insignificant regarding age, gender, and asthma severity (54).

Concomitant stress caused by respiratory disorders can be a factor in developing anxiety disorders or depression. Consistent with this notion, some studies have found a link between anxiety and poorly controlled asthma (41, 55). According to Garg and Silverberg, children with allergy disorders are likelier to have at least one psychological and behavioral issue (56). In the study by Kohlboeck et al., children with asthma were nearly three times more likely than children without asthma to have emotional symptoms, and asthma was not linked to emotional symptoms (57). These differences may be the result of different measuring tools or sampling methods. In addition, some contributing factors, such as the ethnic, environmental, and cultural background of the study population, may explain these diverse outcomes. However, further studies with a larger sample size are needed to evaluate the associations of demographic variables, particularly gender, with mental health in patients with asthma.

5.1. Conclusions

Asthma has various negative physical, psychological, social, and economic effects. Asthma prevalence in Iran is higher than the global average, causing a severe public health hazard. The current research found significant associations of separation anxiety, social anxiety, OCD, panic, generalized anxiety score, and SAD with asthma-related symptoms in children aged 6 - 18. Therefore, it is necessary to consider asthma's psychological and environmental aspects, which may worsen the disease and its consequences. However, further research with a larger sample size is needed to identify the underlying mechanisms of anxiety in children with asthma, which can lead to successful psychological therapies.

Footnotes

Authors' Contribution: M. R., P. P., V. R., and P. H. conceived and designed the evaluation and drafted the manuscript. P. P., M. KG., M. V., N. E., S. S., and H. S. participated in designing the evaluation, performed parts of the statistical analysis, and helped to draft the manuscript. P. P., A. M., M. M., and S. V. re-evaluated the clinical data, revised the manuscript, performed the statistical analysis, and revised the manuscript. A.S. re-analyzed the clinical and statistical data and revised the manuscript. All authors read and approved the final manuscript.

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References

1. Lucas SR, Platts-Mills TA. Physical activity and exercise in asthma: relevance to etiology and treatment. *J Allergy Clin Immunol*. 2005;**115**(5):928–34. [PubMed ID: 15867847]. https://doi.org/10.1016/j.jaci.2005.01.033.
2. Stanescu S, Kirby SE, Thomas M, Yardley L, Ainsworth B. A systematic review of psychological, physical health factors, and quality of life in adult asthma. *NPJ Prim Care Respir Med*. 2019;**29**(1):37. [PubMed ID: 31636268]. [PubMed Central ID: PMC6803647]. https://doi.org/10.1038/s41533-019-0149-3.
3. Jameson JL, Fauci AS, Longo DL, Kasper DL, Loscalzo J, Hauser SL. *Harrison's principles of internal medicine*. **Vol. 1**. 19th ed. New York: McGraw-Hill; 2015.
4. Entezari A, Mehrabi Y, Varesvazirian M, Pourpak Z, Moin M. A systematic review of recent asthma symptom surveys in Iranian children. *Chron Respir Dis*. 2009;**6**(2):109–14. [PubMed ID: 19411572]. https://doi.org/10.1177/1479972309103884.
5. Liu A. Childhood Asthma. In: Kliegman RM, Berhman RE, Jenson HB, Stanton BF, editors. *Nelson Textbook of pediatrics*. 18th ed. Philadelphia: Saunders Elsevier; 2007. 143 p.
6. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald JM, et al. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J*. 2008;**31**(1):143–78. [PubMed ID: 18166595]. https://doi.org/10.1183/09031936.00138707.
7. Thombs BD, Roseman M, Kloda LA. Depression screening and mental health outcomes in children and adolescents: a systematic review protocol. *Syst Rev*. 2012;**1**:58. [PubMed ID: 23176742]. [PubMed Central ID: PMC3563607]. https://doi.org/10.1186/2046-4053-1-58.
8. Centers for Disease Control and Prevention. Vital signs: asthma prevalence, disease characteristics, and self-management education: United States, 2001–2009. *MMWR Morb Mortal Wkly Rep*. 2011;**60**(17):547–52. [PubMed ID: 21544044].
9. Meyer A, Gunther S, Volmer T, Taube K, Baumann HJ. A 12-month, moderate-intensity exercise training program improves fitness and quality of life in adults with asthma: a controlled trial. *BMC Pulm Med*. 2015;**15**:56. [PubMed ID: 25947010]. [PubMed Central ID: PMC4431028]. https://doi.org/10.1186/s12890-015-0053-8.
10. Thomas M, Bruton A, Moffat M, Cleland J. Asthma and psychological dysfunction. *Prim Care Respir J*. 2011;**20**(3):250–6. [PubMed ID: 21674122]. [PubMed Central ID: PMC6549858]. https://doi.org/10.4104/pcrj.2011.00058.
11. Goodwin RD, Fergusson DM, Horwood LJ. Asthma and depressive and anxiety disorders among young persons in the community. *Psychol Med*. 2004;**34**(8):1465–74. [PubMed ID: 15724877]. https://doi.org/10.1017/s0033291704002739.
12. Jenkins R, Bebbington P, Brugha T, Farrell M, Gill B, Lewis G, et al. The National Psychiatric Morbidity Surveys of Great Britain – strategy and methods. *Psychol Med*. 1997;**27**(4):765–74. https://doi.org/10.1017/S003329179700531X.
13. Moes-Wójtowicz A, Wójtowicz P, Postek M, Domagała-Kulawik J. [Asthma as a Psychosomatic Disorder: The Causes, Scale of the Problem, and the Association with Alexithymia and Disease Control]. *Adv Respir Med*. 2012;**80**(1):13–9. Polish. https://doi.org/10.5603/arm.27612.
14. Lee YC, Lee CT, Lai YR, Chen VC, Stewart R. Association of asthma and anxiety: A nationwide population-based study in Taiwan. *J Affect Disord*. 2016;**189**:98–105. [PubMed ID: 26432033]. https://doi.org/10.1016/j.jad.2015.09.040.
15. Lind N, Nordin M, Palmquist E, Nordin S. Psychological distress in asthma and allergy: the Vasterbotten Environmental Health Study. *Psychol Health Med*. 2014;**19**(3):316–23. [PubMed ID: 23767935]. https://doi.org/10.1080/13548506.2013.806814.
16. Letitre SL, de Groot EP, Draaisma E, Brand PL. Anxiety, depression and self-esteem in children with well-controlled asthma: case-control study. *Arch Dis Child*. 2014;**99**(8):744–8. [PubMed ID: 24812302]. https://doi.org/10.1136/archdischild-2013-305396.
17. Afshar H, Roohafza H, Rajabi F, Attari A, Feizi A, Hassanzadeh-Keshteli A, et al. Psychological Profile in a General Population in Central Iran. *Int J Body Mind Culture*. 2016;**3**(1):12–21.
18. Tabachnick BG, Fidell LS. *Using Multivariate Statistics*. Boston, MA: Allyn and Bacon; 2001.
19. Tabachnick BG, Fidell LS, Ullman JB. *Using multivariate statistics*. Boston, MA: Pearson; 2013.
20. National Institutes of Health National Heart, Lung, and Blood Institute. *NHLBI/WHO Workshop Report: Global Strategy for Asthma Management and Prevention*. 2002. Available from: https://ginasthma.org/wp-content/uploads/2019/01/2002-GINA.pdf.
21. Essau CA, Muris P, Ederer EM. Reliability and validity of the Spence Children's Anxiety Scale and the Screen for Child Anxiety Related Emotional Disorders in German children. *J Behav Ther Exp Psychiatry*. 2002;**33**(1):1–18. [PubMed ID: 12389796]. https://doi.org/10.1016/s0005-7916(02)00005-8.

22. Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. *NCHS Data Brief*. 2012;(94):1–8. [PubMed ID: 22617340].
23. Vuillermin PJ, Brennan SL, Robertson CF, Carlin JB, Prior M, Jenner BM, et al. Anxiety is more common in children with asthma. *Arch Dis Child*. 2010;**95**(8):624–9. [PubMed ID: 20522474]. https://doi.org/10.1136/adc.2009.166967.
24. von Leupoldt A, Ehnes F, Dahme B. Emotions and respiratory function in asthma: a comparison of findings in everyday life and laboratory. *Br J Health Psychol*. 2006;**11**(Pt 2):185–98. [PubMed ID: 16643693]. https://doi.org/10.1348/135910705X52462.
25. Katon WJ, Richardson L, Lozano P, McCauley E. The relationship of asthma and anxiety disorders. *Psychosom Med*. 2004;**66**(3):349–55. [PubMed ID: 15184694]. https://doi.org/10.1097/01.psy.0000126202.89941.ea.
26. Dudeney J, Sharpe L, Sicouri G, Lorimer S, Dear BF, Jaffe A, et al. Attentional Bias in Children with Asthma with and without Anxiety Disorders. *J Abnorm Child Psychol*. 2017;**45**(8):1635–46. [PubMed ID: 28066857]. https://doi.org/10.1007/s10802-017-0261-1.
27. Pine DS, Helfinstein SM, Bar-Haim Y, Nelson E, Fox NA. Challenges in developing novel treatments for childhood disorders: lessons from research on anxiety. *Neuropsychopharmacology*. 2009;**34**(1):213–28. [PubMed ID: 18754004]. [PubMed Central ID: PMC2794358]. https://doi.org/10.1038/npp.2008.113.
28. Woodward LJ, Fergusson DM. Life course outcomes of young people with anxiety disorders in adolescence. *J Am Acad Child Adolesc Psychiatry*. 2001;**40**(9):1086–93. [PubMed ID: 11556633]. https://doi.org/10.1097/00004583-200109000-00018.
29. Chen E, Miller GE. Stress and inflammation in exacerbations of asthma. *Brain Behav Immun*. 2007;**21**(8):993–9. [PubMed ID: 17493786]. [PubMed Central ID: PMC2077080]. https://doi.org/10.1016/j.bbi.2007.03.009.
30. Blackman JA, Gurka MJ. Developmental and behavioral comorbidities of asthma in children. *J Dev Behav Pediatr*. 2007;**28**(2):92–9. [PubMed ID: 17435459]. https://doi.org/10.1097/01.DBP.0000267557.80834.e5.
31. Sastre J, Crespo A, Fernandez-Sanchez A, Rial M, Plaza V; Investigators of the CONCORD Study Group. Anxiety, Depression, and Asthma Control: Changes After Standardized Treatment. *J Allergy Clin Immunol Pract*. 2018;**6**(6):1953–9. [PubMed ID: 29454162]. https://doi.org/10.1016/j.jaip.2018.02.002.
32. Galic K, Dodaj A, Corluka-Cerkez V, Lasic V, Pejic R, Simic J, et al. Study of depression and anxiety in patients with asthma and chronic obstructive pulmonary disease. *Psychiatr Danub*. 2019;**31**(Suppl 1):112–7. [PubMed ID: 30946729].
33. Kewalramani A, Bollinger ME, Postolache TT. Asthma and Mood Disorders. *Int J Child Health Hum Dev*. 2008;**1**(2):115–23. [PubMed ID: 19180246]. [PubMed Central ID: PMC2631932].
34. Montalbano L, Ferrante G, Montella S, Cilluffo G, Di Marco A, Bozzetto S, et al. Relationship between quality of life and behavioural disorders in children with persistent asthma: a Multiple Indicators Multiple Causes (MIMIC) model. *Sci Rep*. 2020;**10**(1):6957. [PubMed ID: 32332757]. [PubMed Central ID: PMC7181655]. https://doi.org/10.1038/s41598-020-62264-9.
35. Pinquart M, Shen Y. Behavior problems in children and adolescents with chronic physical illness: a meta-analysis. *J Pediatr Psychol*. 2011;**36**(9):1003–16. [PubMed ID: 21810623]. https://doi.org/10.1093/jpepsy/jsr042.
36. Pinquart M, Shen Y. Anxiety in children and adolescents with chronic physical illnesses: a meta-analysis. *Acta Paediatr*. 2011;**100**(8):1069–76. [PubMed ID: 21332786]. https://doi.org/10.1111/j.1651-2227.2011.02223.x.
37. Goodwin RD, Robinson M, Sly PD, McKeague IW, Susser ES, Zubrick SR, et al. Severity and persistence of asthma and mental health: a birth cohort study. *Psychol Med*. 2013;**43**(6):1313–22. [PubMed ID: 23171853]. [PubMed Central ID: PMC3857579]. https://doi.org/10.1017/S0033291712001754.
38. Basaran S, Guler-Uysal F, Ergen N, Seydaoglu G, Bingol-Karakoc G, Ufuk Altintas D. Effects of physical exercise on quality of life, exercise capacity and pulmonary function in children with asthma. *J Rehabil Med*. 2006;**38**(2):130–5. [PubMed ID: 16546771]. https://doi.org/10.1080/16501970500476142.
39. Jacobson L. Hypothalamic-pituitary-adrenocortical axis regulation. *Endocrinol Metab Clin North Am*. 2005;**34**(2):271–92. [PubMed ID: 15850842]. https://doi.org/10.1016/j.ecl.2005.01.003.
40. Panek M, Pietras T, Szemraj J, Kuna P. Association analysis of the glucocorticoid receptor gene (NR3C1) haplotypes (ER22/23EK, N363S, BclI) with mood and anxiety disorders in patients with asthma. *Exp Ther Med*. 2014;**8**(2):662–70. [PubMed ID: 25009637]. [PubMed Central ID: PMC4079411]. https://doi.org/10.3892/etm.2014.1734.
41. Di Marco F, Verga M, Santus P, Giovannelli F, Busatto P, Neri M, et al. Close correlation between anxiety, depression, and asthma control. *Respir Med*. 2010;**104**(1):22–8. [PubMed ID: 19733042]. https://doi.org/10.1016/j.rmed.2009.08.005.
42. Guevara JP, Wolf FM, Grum CM, Clark NM. Effects of educational interventions for self management of asthma in children and adolescents: systematic review and meta-analysis. *BMJ*. 2003;**326**(7402):1308–9. [PubMed ID: 12805167]. [PubMed Central ID: PMC161636]. https://doi.org/10.1136/bmj.326.7402.1308.
43. Hsu J, Qin X, Beavers SF, Mirabelli MC. Asthma-Related School Absenteeism, Morbidity, and Modifiable Factors. *Am J Prev Med*. 2016;**51**(1):23–32. [PubMed ID: 26873793]. [PubMed Central ID: PMC4914465]. https://doi.org/10.1016/j.amepre.2015.12.012.
44. Akinbami LJ, Moorman JE, Garbe PL, Sondik EJ. Status of childhood asthma in the United States, 1980-2007. *Pediatrics*. 2009;**123 Suppl 3**:S131–45. [PubMed ID: 19221156]. https://doi.org/10.1542/peds.2008-2233C.
45. van de Loo KF, van Gelder MM, Roukema J, Roeleveld N, Merkus PJ, Verhaak CM. Prenatal maternal psychological stress and childhood asthma and wheezing: a meta-analysis. *Eur Respir J*. 2016;**47**(1):133–46. [PubMed ID: 26541526]. https://doi.org/10.1183/13993003.00299-2015.
46. Miadich SA, Everhart RS, Borschuk AP, Winter MA, Fiese BH. Quality of Life in Children With Asthma: A Developmental Perspective. *J Pediatr Psychol*. 2015;**40**(7):672–9. [PubMed ID: 25680363]. [PubMed Central ID: PMC4505073]. https://doi.org/10.1093/jpepsy/jsv002.
47. Kullowatz A, Kanniess F, Dahme B, Magnussen H, Ritz T. Association of depression and anxiety with health care use and quality of life in asthma patients. *Respir Med*. 2007;**101**(3):638–44. [PubMed ID: 16891108]. https://doi.org/10.1016/j.rmed.2006.06.002.
48. Mancuso CA, Peterson MG, Charlson ME. Effects of depressive symptoms on health-related quality of life in asthma patients. *J Gen Intern Med*. 2000;**15**(5):301–10. [PubMed ID: 10840265]. [PubMed Central ID: PMC1495457]. https://doi.org/10.1046/j.1525-1497.2000.07006.x.
49. de Miguel Diez J, Garcia RJ, Hernandez Barrera V, Rodriguez PR, Maestu LP, Garrido PC. Mental health among adults with asthma and chronic bronchitis. A population-based study in Spain. *Respir Med*. 2012;**106**(7):924–32. [PubMed ID: 22534040]. https://doi.org/10.1016/j.rmed.2012.03.021.
50. Ahmadiafshar A, Ghoreishi A, Afkhami Ardakani S, Khoshnevis P, Faghihzadeh S. Anxiety Disorder Among Adolescents with Asthma in Zanjan. *J Adv Med Biomed Res*. 2020;**28**(126):33–40. https://doi.org/10.30699/jambs.28.126.33.
51. Asnaashari AMH, Talaei A, Baghban Haghighi M. Evaluation of psychological status in patients with asthma and COPD. *Iran J Allergy Asthma Immunol*. 2012;**11**(1):65–71. [PubMed ID: 22427478].
52. Amelink M, Hashimoto S, Spinhoven P, Pasma HR, Sterk PJ, Bel EH, et al. Anxiety, depression and personality traits in severe, prednisone-dependent asthma. *Respir Med*. 2014;**108**(3):438–44. [PubMed ID: 24462260]. https://doi.org/10.1016/j.rmed.2013.12.012.
53. Brunner WM, Schreiner PJ, Sood A, Jacobs Jr DR. Depression and risk

of incident asthma in adults. The CARDIA study. *Am J Respir Crit Care Med*. 2014;**189**(9):1044–51. [PubMed ID: 24456492]. [PubMed Central ID: PMC4098106]. https://doi.org/10.1164/rccm.201307-1349OC.

54. Lu Y, Mak KK, van Bever HP, Ng TP, Mak A, Ho RC. Prevalence of anxiety and depressive symptoms in adolescents with asthma: a meta-analysis and meta-regression. *Pediatr Allergy Immunol*. 2012;**23**(8):707–15. [PubMed ID: 22957535]. https://doi.org/10.1111/pai.12000.
55. Sundbom F, Malinovschi A, Lindberg E, Alving K, Janson C. Effects of poor asthma control, insomnia, anxiety and depression on quality of life in young asthmatics. *J Asthma*. 2016;**53**(4):398–403. [PubMed ID: 26666333]. https://doi.org/10.3109/02770903.2015.1126846.
56. Garg N, Silverberg JI. Association between childhood allergic disease, psychological comorbidity, and injury requiring medical attention. *Ann Allergy Asthma Immunol*. 2014;**112**(6):525–32. [PubMed ID: 24713577]. https://doi.org/10.1016/j.anai.2014.03.006.
57. Kohlboeck G, Koletzko S, Bauer CP, von Berg A, Berdel D, Kramer U, et al. Association of atopic and non-atopic asthma with emotional symptoms in school children. *Pediatr Allergy Immunol*. 2013;**24**(3):230–6. [PubMed ID: 23590416]. https://doi.org/10.1111/pai.12056.