Misdiagnosis of Asthma in Patients with Anxiety/Depression

Anksiyete/Depresyon Hastalarda Yanlış Astım Tanısı

ABSTRACT

Objective: Anxiety/depression may lead to misdiagnosis of asthma if respiratory symptoms are prominent. In this study, we aimed to evaluate misdiagnosis due to anxiety and depression among patients diagnosed with asthma.

Material and Methods: This prospective study included patients who were previously diagnosed with asthma and evaluated by a psychiatrist through the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI). The patients were divided into two groups in terms of their BDI/BAI status as positive (mild, moderate or severe category) or negative (normal category). The groups were compared in terms of clinical characteristics, pulmonary function tests, asthma control tests (ACT), and atopy parameters.

Results: We identified 54 patients (32.7%) in BDI/BAI(+) group. Compared to that in BDI/BAI(-) group, patients in the BDI/BAI(+) group were more likely to have family history of asthma (37.0% vs. 65.7%, p<0.001). While total IgE and ACT were the tools with highest sensitivity (72% and 70%, respectively), skin prick test had the highest specificity (92%). Obstruction (88%) and reversibility (88%) had the highest positive predictive values.

Conclusion: The presence of dyspnea on the basis of asthma diagnosis may lead to misdiagnosis in some patients, especially in individuals with anxiety/depression. The history of patients presenting dyspnea symptoms should be taken carefully and examined in detail by spirometric and laboratory workup.

INTRODUCTION

Asthma is a chronic airway inflammatory disease that develops against direct or indirect stimuli with different severity of airway obstruction. The clinical presentation of the disease and intensity of symptoms vary over time (1). Asthma is estimated to affect approximately 10% of the European population (2). While spirometric pulmonary function tests (PFTs), serum total IgE level and prick test may contribute to the diagnosis, it is mainly based on anamnese: shortness of breath, wheezing, coughing, and chest tightness constitute critical features of asthma (3). Especially in the last 25 years, the number of patients diagnosed with asthma has increased significantly (4). However, this increase has been approached disputably, since a high prevalence of misdiagnosis of adult asthma has been reported in the literature (5). An estimated one-third of asthma patients are misdiagnosed. Evaluating the difference in healthcare resource use and costs between

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Nefes darlığı
Solunum fonksiyon testi

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misdiagnosis and confirmed cases of asthma can inform assessments of the burden of asthma misdiagnosis (6). Evidence-based guidelines, including from the Global Initiative for Asthma, recommend the diagnosis of asthma be confirmed by objective tests demonstrating either reversible airflow limitation or increased airway hyperresponsiveness (1). Despite these recommendations, studies suggest that asthma is diagnosed solely based on symptom history in over half of physician-diagnosed cases (7,8). Asthma may be misdiagnosed due to a number of conditions, including chronic obstructive pulmonary disease (COPD), upper respiratory tract infections, acute bronchitis, obesity, heart failure, and psychiatric disorders (9-12).

The physiological symptoms of anxiety mimic many diseases and can be elaborated as palpitation, difficult and/or rapid breathing, feeling of suffocation, increased heart rate, and tremor in hands and feet. Apart from these, patients also experience psychological symptoms such as distress, excitement, and sense of impending doom (12). Depression is a common and serious illness that affects individuals’ feeling, behaviors, and thoughts. Lack of energy, loss of interest or pleasure, lack of concentration, decreased self-confidence, feelings of guilt, pessimism, self-harm or suicidal thoughts, impaired sleep pattern, changes in appetite and decreased libido are common in depression (13). Anxiety, depression and panic attacks also cause asthma-like symptoms, confounding the diagnosis of asthma (1). Coexistence of psychiatric disorder and asthma may compromise asthma control and deteriorate asthma status in affected individuals. This may result in unnecessary hospitalization and inpatient treatment costs (14). In fact, anxiety and depression are more frequent in asthmatic patients compared to the general population and drug treatments for two diseases may interact with each other (14).

Anxiety/depression may lead to a misdiagnosis of asthma if respiratory symptoms are prominent. Therefore, a careful anamnesis is important in the diagnosis of asthma in such patients in addition to diagnostic tests (PFT, prick test, and reversibility test) (15).

In this study, we aimed to evaluate the misdiagnosis of asthma due to anxiety and depression.

MATERIAL AND METHODS

Study design and population

The study was planned in a prospective manner a single center. Ethical approval was obtained from the Ethics Committee of Dicle University Medical Faculty (Approval no: 206). All patients gave written informed consent. The study included 165 consecutive patients over the age of 18 years who were admitted to the pulmonary diseases outpatient clinic of our hospital between 01/06/2020 to 01/12/2020 and were previously diagnosed with asthma. Individuals who were examined by a pulmonologist at least one month ago and diagnosed with asthma and had a history of using inhaled medications for at least one months were eligible for the study. In our institution, those patients were also examined independently by another pulmonologist and psychiatrist to re-assess asthma diagnosis. We defined asthma as a history of variable respiratory symptoms and evidence of variable expiratory airflow limitation. The dyspnea symptoms of the patients who applied to the outpatient clinic were questioned. If the patient’s dyspnea was considered to be due to anxiety or diseases other than asthma, the patient was excluded from the study. Other exclusion criteria were as follows: being <18 years, respiratory infection or oral glucocorticoid use with in last month, concomitant anti-IgE medication or allergic immunotherapy, current asthma attack, any accompanying condition with shortness of breath (e.g., heart failure, hypertension, hypothyroidism, anemia), coexisting diseases that may compromise respiratory function (e.g., COPD, tuberculosis, pneumonia, bronchiectasis), those who were incompatible and unable to undergo PFT or correctly and regularly use asthma medications, and pregnant women.

Data collection

Age, gender, smoking status, body mass index (BMI), asthma control test (ACT), PFT, obstruction, reversibility test, Beck Anxiety Inventory (BAI), Beck Depression Inventory (BDI), history of asthma-related emergency room (ER) admission with in the last 1 year, and skin prick test (SPT) results were recorded. Total IgE levels were analyzed to evaluate the atopy status of the patients. The family history of asthma of the patients was recorded.

Scales and tests

Asthma Tests

Spirometry is the most widely used PFT (16). We used this tool to measure first-second forced expiratory volume (FEV1), peak flow rate (PEF), obstruction, and reversibility. ACT is a simple and reliable 5-item questionnaire that has five points for each. While a score of 25 points indicates full control, scores ≤19 points denotes the state that the asthma is not under control (17). SPT is performed with commercially available respiratory and food allergens, latex or (more rarely) drugs. It is used in the diagnosis of allergic rhinoconjunctivitis, bronchial asthma, atopic dermatitis, contact urticaria, and food/drug allergies. SPT results were recorded as positive or negative (18).

Psychiatric Tests

BDI is a 21-item self-report scale to measure emotional, cognitive, somatic and motivational components. Each question was given a score of 0, 1, 2, 3.A total score of 0 to 9 points shows none/minimal depression whereas higher scores reveal increasing severity of depression (mild: 10-18 points, moderate: 19-29 points, severe: 30-63 points) (19). Similarly, Beck Anxiety Inventory (BAI) measures the frequency of anxiety symptoms experienced by an individual with 21-item scored between 0 to 18 points, moderate: 19-29 points, severe: 30-63 points (20). The patients were divided into two groups in terms of their BDI/BAI status as positive (mild, moderate or severe category) or negative (normal category).

Statistical Analysis

Statistical analysis was performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). By calculating 0.05 margin of error and 0.80 effect power using G power, the minimum number of patient samples was determined and the number of samples greater than this number was reached. Descriptive statistics of continuous variables were shown with mean and standard deviation values. Shapiro-
Wilk test was performed to evaluate whether the data was distributed normally. Student t test was used to compare the BDI/BAI groups in terms of age, ACT, FEV1, BMI, PEF, and Total IgE levels. Categorical variables including SPT positivity, obstruction, reversibility, gender, smoking status, ER admission and presence of family history were compared via chi-square test. Statistically significant variables were tested through ROC curve analysis, where cut-off values, sensitivity, specificity, positive and negative predictive values were calculated. The hypotheses were bidirectional and an overall 5% Type-I error level was used to infer statistical significance.

RESULTS
Comparison of the study groups
We identified that there were 54 patients (32.7%) in BDI/BAI(+) group and 111 patients (67.3%) in BDI/BAI(-) group. The groups did not differ in age, smoking status or BMI while there were significantly more women in BDI/BAI(+) group (87.0%) compared to that in the BDI/BAI(-) group (72.1%, p=0.05). Compared to that in BDI/BAI(+) group, patients in the BDI/BAI(-) group were more likely to have family history of asthma (37.0% vs. 65.7%, p<0.001) whereas the groups were similar in asthma-related ER admission during previous year (46.3% vs. 40.5%, p=0.50), (Table 1).

The mean ACT score in the BDI/BAI(+) group was significantly lower than that in the BDI/BAI(-) group (15.9 vs. 19.3, respectively, p<0.001). BDI/BAI(+) and BDI/BAI groups did not show difference in terms of the mean FEV1 (87.7% vs. 83.3%, respectively) and the mean PEF (84.7% vs. 79.0%, respectively) values. Significantly less patients in BDI/BAI(+) group had evidence of obstruction (14.8%) and reversibility (14.8%) compared to those in BDI/BAI(-) group (57.7% and 54.1%, respectively; p<0.001 for each).

Positive SPT results were significantly more common in BDI/BAI(-) group (25.2%) than that in BDI/BAI(+) group (7.4%, p=0.04). The mean total IgE level was also significantly higher (278.4 IU/mL) in the BDI/BAI(-) group compared to that in the BDI/BAI (+) group (137.1 IU/mL, p<0.001), (Table 1).

Table 1: The comparison of the study groups by their demographic and clinical characteristics.

<table>
<thead>
<tr>
<th></th>
<th>BDI/BAI(+)</th>
<th>BDI/BAI(-)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>54 (32.7)</td>
<td>111 (67.3)</td>
<td>-</td>
</tr>
<tr>
<td>Age, yrs (mean ± SD)</td>
<td>39.3 ±11.5</td>
<td>39.3 ± 15.4</td>
<td>0.9</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>47 (87.0)</td>
<td>80 (72.1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never, n (%)</td>
<td>32 (59.2)</td>
<td>69 (62.2)</td>
<td>0.6</td>
</tr>
<tr>
<td>Former, n (%)</td>
<td>13 (24.1)</td>
<td>20 (18.0)</td>
<td></td>
</tr>
<tr>
<td>Current, n (%)</td>
<td>9 (16.7)</td>
<td>22 (19.8)</td>
<td></td>
</tr>
<tr>
<td>Family history of asthma, n (%)</td>
<td>20 (37.0)</td>
<td>73 (65.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Asthma-related ER admission within last year, n (%)</td>
<td>25 (46.3)</td>
<td>45 (40.5)</td>
<td>0.5</td>
</tr>
<tr>
<td>Body mass index, kg/m2 (mean ± SD)</td>
<td>28.0 ± 6.8</td>
<td>27.4± 6.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Total IgE, IU/mL (mean ± SD)</td>
<td>137.1 ± 204.3</td>
<td>278.4 ± 335.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skin prick test positivity, n (%)</td>
<td>4 (7.4)</td>
<td>28 (25.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Asthma control test score (mean ± SD)</td>
<td>15.9± 4.6</td>
<td>19.3 ± 3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1, % (mean ± SD)</td>
<td>87.7 ± 18.5</td>
<td>83.3 ± 18.4</td>
<td>0.15</td>
</tr>
<tr>
<td>PEF, % (mean ± SD)</td>
<td>84.7 ± 21.3</td>
<td>79.0 ± 21.3</td>
<td>0.09</td>
</tr>
<tr>
<td>Obstruction, n (%)</td>
<td>8 (14.8)</td>
<td>64 (57.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Reversibility, n (%)</td>
<td>8 (14.8)</td>
<td>60 (54.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; SD, standard deviation; ER, emergency room; FEV1, forced expiratory volume during first second; PEF, peak expiratory flow.

Table 2: Effects of the significant parameters on asthma diagnosis by ROC curve analysis.

<table>
<thead>
<tr>
<th></th>
<th>Cut-off value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACT score</td>
<td>17.5 points</td>
<td>70%</td>
<td>68%</td>
<td>82%</td>
<td>52%</td>
</tr>
<tr>
<td>Total IgE level</td>
<td>80 IU/mL</td>
<td>72%</td>
<td>77%</td>
<td>86%</td>
<td>57%</td>
</tr>
<tr>
<td>Family history</td>
<td>-</td>
<td>65%</td>
<td>62%</td>
<td>78%</td>
<td>47%</td>
</tr>
<tr>
<td>Obstruction</td>
<td>-</td>
<td>57%</td>
<td>85%</td>
<td>88%</td>
<td>49%</td>
</tr>
<tr>
<td>Reversibility</td>
<td>-</td>
<td>54%</td>
<td>85%</td>
<td>88%</td>
<td>52%</td>
</tr>
<tr>
<td>Skin prick test</td>
<td>-</td>
<td>25%</td>
<td>92%</td>
<td>87%</td>
<td>37%</td>
</tr>
</tbody>
</table>

ACT, asthma control test; PPV, positive predictive value; NPV, negative predictive value.
Asthma is a heterogeneous disease characterized by respiratory symptoms such as wheezing, shortness of breath, chest tightness and/or cough, and limitation of expiratory airflow. Comorbidities also contribute to the development of asthma. It is chronic airway inflammation associated with airway hyperresponsiveness and bronchoconstriction. Comorbid conditions such as anxiety or depression can exacerbate asthma symptoms and affect disease management. While asthma is a diagnosis made based on symptoms, there can be instances where patients are misdiagnosed, leading to potential mismanagement of their condition. Misdiagnosis can result from symptoms that overlap with other conditions, making it challenging to distinguish between conditions. In our study, we found that anxiety and depression were more prevalent in patients with asthma, indicating a possible coexistence of these conditions. The presence of anxiety and depression is associated with poorer asthma control, as these conditions can worsen asthma symptoms and affect quality of life. We observed that patients with asthma and anxiety or depression had lower ACT scores compared to those without these conditions, suggesting that these comorbidities may impact asthma control. This highlights the importance of considering mental health in the management of asthma. The relationship between asthma and anxiety/depression further supports the need for a comprehensive approach in treating patients with these conditions, as it is important to address both physical and mental health aspects for effective management. The presence of anxiety and depression in asthma patients can lead to a vicious cycle where both conditions worsen each other, highlighting the need for integrated care approaches. The use of validated instruments such as the ACT can help in the assessment and management of asthma control in patients with coexisting anxiety or depression. Our findings emphasize the importance of considering mental health in the treatment and management of asthma, and suggest that integrated care approaches may be beneficial for these patients. The identification and management of comorbid conditions can improve asthma control and quality of life in patients with asthma.
In this study we have observed that the treatment success of accurately diagnosed asthma patients were higher compared to others. We also would like to state that the diagnosis should be supported by obstruction, reversibility test, serum total IgE level, family history, and SPT. Individuals with negative or low results in these parameters and ACT should be consulted for psychiatric problems. In fact, severe anxiety was reported to deteriorate the course of asthma and control of episodes (35). Aaron et al. reported that 33% of patients did not need to use their asthma medication (23). Furthermore, Bryan Ng et al. emphasized that asthma was overdiagnosed with a consequent economic burden on the healthcare system in Canada (36). While we did not perform a pharmacoeconomic analysis, the fact almost one-third of our asthma patients had anxiety or depression may imply a substantial rate of asthma misdiagnosis, which could be potentially associated with unnecessary treatment expenditures and subsequent cost burden on the healthcare system.

There are certain limitations of this study. No asthma classification has been made regarding the severity of asthma in our patients. No bronchial provocation test was performed to evaluate the pathogenesis of dyspnea in subjects with anxiety/depression. Dyspnea is frequently reported as a concomitant disease with depression and anxiety, lack of analytical tests may contribute to the overrating of misdiagnosis. Dyspnea should be examined in detail by PFT, reversibility test, serum total IgE level, family history of asthma and SPT. Therefore, regular doctor control of patients is important. Further controlled studies are needed to clarify this subject.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Ethics:** This study was approved by the Dicle University Medical Faculty Non-Interventional Clinical Research Ethics Committee (Date: 20.09.2012, Number: 2012/206).

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**Approval of final manuscript:** All authors.

**REFERENCES**


3. Turkish Thoracic Society Guidelines for the Diagnosis and Treatment of Asthma. 2019;2-16.


