



Research Article

The Association between Anxiety and Asthma in Asthmatic Patients at King Abdulaziz University Hospital in Jeddah, Saudi Arabia

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Abstract: Background: In prior research, the frequency of anxiety among asthmatic patients has been examined. However, the focus of our study is to explore the relationship between the severity of asthma and anxiety. Objectives: This study set out to determine how anxiety and asthma severity related to each other in patients receiving care at King Abdulaziz University Hospital in Jeddah, Saudi Arabia. Methods: This cross-sectional study took place at a tertiary care hospital in Jeddah, Saudi Arabia from 2021 to 2023, with approval from King Abdulaziz University Hospital's biomedical ethical committee (Reference No. 235-22). The study included 400 asthma patients, aged 14 or older, and based on PFT results. Patients with respiratory symptoms but not diagnosed with asthma were excluded. Information on the demographics of 185 asthma patients, as well as their asthma severity, anxiety levels, and GAD-7 scores were gathered. Results: The main results of the study showed that out of the total sample (n=185) 17.8% (p = 0.028) of the patients diagnosed with asthma had received the diagnosis generalized anxiety disorder by a medical professional in their lifetime. Additionally, higher proportion of patients who reported having total (57.4%, n = 35) or well (40.7%, n = 22) control of their asthma had minimal anxiety levels compared to those with mild to severe anxiety levels. Conclusion: The research emphasizes the significance of screening for anxiety among asthmatic patients and vice versa. There is a complex relationship between anxiety and asthma that warrants additional investigation and enhanced clinical awareness in the context of Saudi Arabia.

Keywords: Anxiety, Asthma, Asthmatic Patients, Mental health, Generalized Anxiety Disorder, GAD-7.

INTRODUCTION:

Over 200 million people worldwide suffer from asthma, a chronic noncommunicable disease characterized by persistent inflammation of the airways (1, 2). Asparagus is positioned as the 34th most significant cause of disease burden, according to the 2022 global asthma report (1). Over 383,000 people perished in 2015 due to asthma-related causes, impacting 235 million people globally, as reported by the World Health Organization (WHO) (3).

Previous research has suggested a correlation between asthma and psychological well-being (4, 5). Brain imaging of asthmatic patients has identified structural and functional alterations in the brain that may account for this correlation. A correlation between asthma and anxiety or depression has also been identified in investigations involving adults (6,

7). Anxiety and depression have been identified as risk factors for chronic asthma, both of which impede patients' ability to manage their condition and quality of life (8).

Due to the chronic nature of the condition and its detrimental impact on pulmonary function, there is an increased probability that individuals with asthma will experience cognitive dysfunction (10). In addition, empirical studies suggest a correlation between asthma and reduced volume of the hippocampus, a factor that potentially contributes to the onset of cognitive decline (11). Approximately three times more likely to develop sleep disturbances, anxiety, and melancholy than the general population are patients diagnosed with asthma and chronic obstructive pulmonary disease (COPD). On account of this, it is critical that treatment plans for asthma and COPD (12) include

early detection and multifaceted therapy for these conditions.

Significant mental and physical health impairments are frequently encountered by those with asthma, which increase their risk of morbidity and mortality and impede their ability to participate in social interactions and daily activities (13). Research has shown that anxiety significantly impacts the healthcare utilized by these individuals and their overall quality of life (14). Anxiety and the severity of asthma have also been linked in a number of investigations (13,14).

Over time, the percentage of adults in Saudi Arabia diagnosed with asthma by medical professionals has risen from 4% to 11% (15,16). 15%-25% of the population is affected by asthma, according to the Saudi Ministry of Health (18). More than half of asthmatic individuals, according to a Saudi study, suffer from uncontrolled asthma (19). Additionally, 45-64% of individuals with uncontrolled asthma were identified in two additional Saudi studies (20,21). Moreover, 70% of Saudi adults with asthma were uncontrolled, according to an epidemiological investigation on asthma management in the Middle East (22).

243 participants were recruited from outpatient facilities in Riyadh for a study conducted in Saudi Arabia. In individuals between the ages of 40 and 50, the researchers aimed to investigate the correlation between asthma and mental health outcomes. Aside from those with asthma, the participants were separated into two distinct categories. A correlation was identified between moderate cognitive impairment, anxiety, and depression, as stated by the results of a logistic regression analysis. In addition, a higher incidence of anxiety cases was observed in individuals with inadequately managed asthma, according to the study (19). The relationship between asthma and mental health outcomes, specifically anxiety, in Saudi Arabia requires additional study, as demonstrated by this research.

METHODOLOGY

Study design, setting, population

A cross-sectional study was undertaken at a tertiary care facility in Jeddah, Saudi Arabia, spanning the years 2021 to 2023. The research obtained clearance from the King Abdulaziz University facility's biomedical ethical committee (Reference No 235-

22). The research cohort comprised 400 individuals who had been diagnosed with asthma according to PFT findings; the minimal age of both male and female participants was 14 years. Excluding patients who presented with respiratory symptoms without a confirmed diagnosis of asthma from the study. 215 patients out of 400 declined to complete the questionnaire; 185 patients, in total, provided informed consent to partake in the research. The participants who received the questionnaire via WhatsApp and Google Forms were subsequently incorporated into the final study.

Data collection

In our research, we employed two assessment systems. To begin with, we utilised the Asthma Score Index, a tool that assessed both asthma control and symptoms. The GAD-7, the second system, was specifically developed to assess generalised anxiety.

Statistical Methodology

The investigation was carried out utilising IBM SPSS version 27 (IBM Corp., Armonk, N.Y., USA). A graphical representation of the findings was created using GraphPad Prism version 8 (GraphPad Software, Inc., San Diego, CA, USA). The attributes of the variables under investigation were delineated using descriptive statistics. For categorical and nominal variables, counts and percentages were employed, while for continuous variables, the mean and standard deviation were utilised. Furthermore, the researchers utilised a scoring system called the "General Anxiety Disorder (GAD-7)" to allocate a numerical value between 0 and 3 to each question.

Using the Cronbach's Alpha model, a reliability analysis was performed to investigate the properties of measurement scales and their constituent items. In order to ascertain the relationship between categorical variables, the research employed a chi-square test. Additionally, a General Linear Model univariate analysis was employed to determine significant predictors using the main effect as the model. The null hypothesis was rejected if the conventional p-value was less than 0.05.

RESULTS

In this research, the connection between anxiety symptoms and asthma symptoms, as well as the impact of anxiety symptoms on asthma severity, was assessed among 185 asthmatic patients in Jeddah, Saudi Arabia.

Table 1: Socio-demographic characteristics of the asthmatic patients (N = 185).

Demographics		Count	%
Total		185	100.0
Gender	Male	73	39.5
	Female	112	60.5
Nationality	Saudi	172	93.0
	Non-Saudi	13	7.0
Age	12-18 years	2	1.1
	19-30 years old	77	41.6
	More than 30 years	106	57.3
Educational level	Illiteracy	1	0.5
	Primary	7	3.8
	Secondary	32	17.3
	Intermediate	6	3.2
	Bachelor	3	1.6
	University	123	66.5
	Postgraduate	4	2.2
	Master	4	2.2
	PhD	2	1.1
Occupation	Others	3	1.6
	Student	27	14.6
	Employee	84	45.4
Income level	Unemployed	74	40.0
	Less than 2000	59	31.9
	2000-5999	43	23.2
	6000-9000	27	14.6
Have you been diagnosed with asthma by a specialist?	More than 9000	56	30.3
	Yes	154	83.2
Have you been diagnosed with generalized anxiety disorder by a professional?	No	31	16.8
	Yes	33	17.8
	No	152	82.2

The majority of the asthmatic patients were Saudi nationals (93.0%, n = 172), females (60.6%, n = 112), aged over 30 (57.3%, n = 106), had a university-level education (66.5%, n = 123), and were diagnosed by a specialist (83.2%, n = 154). However, they were not diagnosed with generalized anxiety disorder by a professional (82.2%, n = 152). In addition, nearly half of them (45.4%, n = 84) were employed, and nearly one-third (31.9%, n = 59) earned less than 2000 SR monthly, while approximately one-third (30.3%, n = 56) earned more than 9000 SR monthly.

Table 2: Asthma history of the asthmatic patients during the past four weeks (N = 185)

During the past four weeks:		Count	%
Total		185	100.0
How many times did asthma symptoms (wheezing, coughing, difficulty breathing, chest tightness) prevent you from performing and completing the required work, in the workplace/school and at home?	It never happened	63	34.1
	A little time	47	25.4
	Sometime	40	21.6
	Most of the time	28	15.1
	All the times	7	3.8
How many times have you had symptoms of difficulty breathing?	It never happened	58	31.4
	Once a day	7	3.8
	More than once a day	20	10.8
	Once or twice a week	69	37.3
How often did asthma symptoms (wheezing, coughing, shortness of breath, pain or tightness in the chest) cause you to wake up at night or wake up earlier than usual in the morning?	3 to 6 times a week	31	16.8
	It never happened	80	43.2
	Once a week	23	12.4
	2-3 nights a week	20	10.8
	4 or more nights a week	18	9.7
How many times did you use first aid sprays or steam sessions such as (Ventolin, Symbicort, or Albuterol)?	Once or twice a month	44	23.8
	I've never used it	62	33.5
	Once to twice a day	22	11.9
	3 or more times a day	20	10.8
	Once a week or less	40	21.6
How do you assess your asthma control?	2 to 3 times a week	41	22.2
	There is absolutely no control	8	4.3
	Poor control	21	11.4
	Fairly controlled	41	22.2
	Well controlled	54	29.2
	Totally in control	61	33.0

Figure 2 illustrates the asthma history of patients over the past four weeks. The results indicate that approximately 43.2% of patients (n=80) did not experience any asthma symptoms that disrupted their sleep at night or caused them to wake up earlier than usual in the morning. Additionally, 34.1% of patients (n=63) did not

report experiencing asthma symptoms that prevented them from completing work or other activities at home or in the workplace/school. Furthermore, 33.5% of patients (n=62) did not require the use of first aid sprays or steam sessions such as Ventolin, Symbicort, or Albuterol. However, 37.3% of patients (n=69) reported experiencing difficulty breathing once or twice a week. It is noteworthy that the majority of patients, 62.2% (n=105), reported their asthma conditions to be well to totally controlled.

On the other hand, the researchers evaluated the anxiety history and level among the asthmatic patients over the past two weeks (Figure 3).

Table 3: Anxiety history and level among the asthmatic patients during the past two weeks

During the past two weeks:	N	Min	Max	Mean	SD
How much have you experienced feeling angry, anxious, or extremely emotional?	185	0.00	3.00	1.12	0.9
How much have you suffered from the inability to stop or control anxiety?	185	0.00	3.00	0.79	0.9
How much have you suffered from excessive worry about different things?	185	0.00	3.00	0.89	0.9
How much difficulty have you had in relaxing?	185	0.00	3.00	1.09	0.9
How much have you suffered from such turmoil that it is difficult to remain calm?	185	0.00	3.00	0.60	0.8
How often have you become upset or irritable?	185	0.00	3.00	1.01	0.9
How much have you experienced a feeling of fear, as if something terrible might happen?	185	0.00	3.00	0.68	0.8

The results indicated that the majority of them experienced various symptoms, including feeling angry, anxious, or emotionally unstable (74.6%, n = 138), struggling with the inability to control their anxiety (84.3%, n = 156), worrying excessively about different things (81.6%, n = 151), having difficulty relaxing (76.2%, n = 141), feeling turmoil that makes it difficult to remain calm (87.5%, n = 162), becoming upset or irritable (76.2%, n = 141), and feeling fear as if something terrible might happen (83.8%, n = 155) for some days or never at all. The mean scores of 185 patients regarding their anxiety level and history during the past two weeks

are presented in Table 3.2.

The highest mean score of 1.12 (SD = 0.9, min = 0, max = 3) was observed for the experience of feeling angry, anxious, or extremely emotional, while the lowest score of 0.60 (SD = 0.8, min = 0, max = 3) was recorded for the experience of feeling turmoil that makes it difficult to remain calm. All the scores were below half the average of the minimum and maximum values. The distribution of anxiety level and history among the asthmatic patients is illustrated in Figure 4.

Table 4: Overall general anxiety disorder (GAD)-7 score and level of the asthmatic patients (N = 185).

Domain	N	Min	Max	Mean	SD
GAD-7	185	0.00	21.00	6.17	4.7
			Count		%
Total			185		100.0
GAD-7	Minimal anxiety		79		42.7
	Mild anxiety		69		37.3
	Moderate anxiety		28		15.1
	Severe anxiety		9		4.9

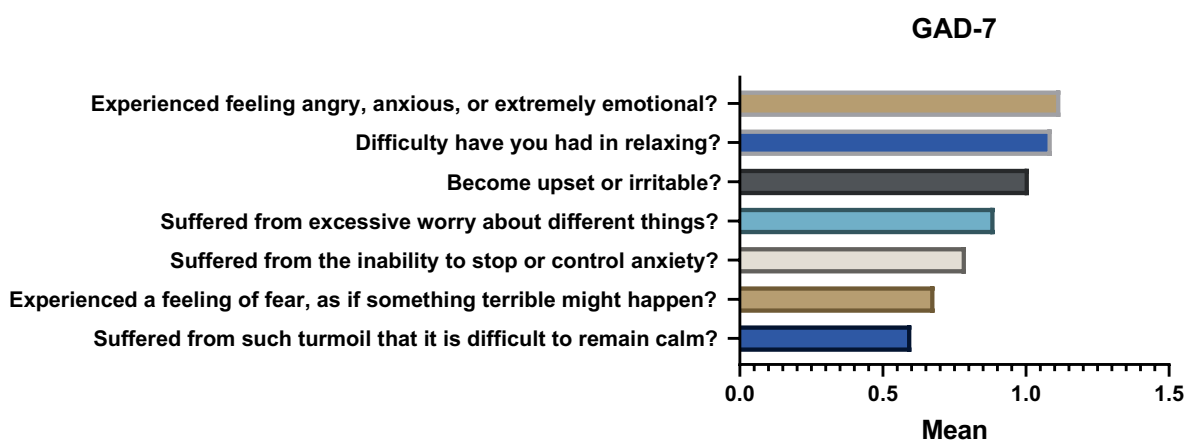


Figure 1: Distribution of anxiety level and history among the asthmatic patients (N = 185)

The Generalized Anxiety Disorder-7 (GAD-7) score and level of anxiety were assessed for asthmatic patients, and the results were then analyzed. It was found that the mean GAD-7 score was 6.17 (with a standard deviation of 4.7, a minimum of 0.00, and a maximum of 6.17). Furthermore, the results indicated that nearly half of the patients (42.7%, n = 79) had a minimal anxiety level, while only a small percentage (4.9%, n = 9) had a severe anxiety level.

Table 5. Reliability statistics of general anxiety disorder (GAD)-7 scores of asthmatic patients.

Reliability Statistics	Cronbach's Alpha	N of Items
GAD-7	0.898	7

Table 5 presents reliability statistics, which show a favorable Cronbach's alpha value of 0.898 for reaction (N = 7), indicating the reliability and internal consistency of the GAD-7 tool used to evaluate the level of general anxiety disorder among the asthmatic patients.

The study assessed the relationship between GAD-7 levels and socio-demographic factors of 185 asthmatic patients. Results showed a significant difference in GAD-7 levels based on a professional diagnosis of GAD, with a higher proportion of patients without a professional diagnosis having minimal anxiety levels (48.0%, n = 73) compared to those with mild to severe levels. Additionally, a higher number of patients with a professional diagnosis of GAD reported mild anxiety levels (57.6%, n = 19) compared to other levels. However, none of the other socio-demographic factors showed a significant association with GAD-7 levels (p > 0.05).

Table 6: Anxiety history and level among the asthmatic patients during the past two weeks

During the past two weeks	No never	Some days	More than half the days	Almost everyday
How much have you experienced feeling angry, anxious, or extremely emotional?	44(23.8)	94(50.8)	28(15.1)	19(10.3)
How much have you suffered from the inability to stop or control anxiety?	80(43.2)	76(41.1)	16(8.6)	13(7.0)
How much have you suffered from excessive worry about different things?	70(37.8)	81(43.8)	19(10.3)	15(8.1)
How much difficulty have you had in relaxing?	49(26.5)	92(49.7)	23(12.4)	21(11.4)
How much have you suffered from such turmoil that it is difficult to remain calm?	102(55.1)	60(32.4)	18(9.7)	5(2.7)
How often have you become upset or irritable?	54(29.2)	87(47.0)	32(17.3)	12(6.5)
How much have you experienced a feeling of fear, as if something terrible might happen?	95(51.4)	60(32.4)	25(13.5)	5(2.7)

The relationship between general anxiety disorder (GAD-7) levels and asthma history among asthmatic patients (N = 185) is presented in Table 6.

A significant association was observed between GAD-7 levels and personal asthma assessment, with a p-value of < 0.05 determined through a Chi-square test. Notably, a higher proportion of patients who reported having total (57.4%, n = 35) or well (40.7%, n = 22) control of their asthma had minimal anxiety levels compared to those with mild to severe anxiety levels.

The General Linear Model was used to determine the most significant predictor of GAD among asthmatic patients (Table 8).

Table 7: Association among the general anxiety disorder (GAD)-7 levels against asthma history of the asthmatic patients (N = 185).

During the past four weeks:		Total	GAD-7 Minimal anxiety	Mild anxiety	Moderate anxiety	Severe anxiety	p-value
Total		185	79(42.7%)	69(37.3%)	28(15.1%)	9(4.9%)	-
How many times did asthma symptoms (wheezing, coughing, difficulty breathing, chest tightness) prevent you from performing and completing the required work, in the workplace/school and at home?	It never happened	63	28(44.4%)	21(33.3%)	10(15.9%)	4(6.3%)	0.143
	A little time	47	25(53.2%)	15(31.9%)	6(12.8%)	1(2.1%)	
	Sometime	40	13(32.5%)	17(42.5%)	8(20.0%)	2(5.0%)	
	Most of the time	28	10(35.7%)	14(50.0%)	4(14.3%)	0(0.0%)	
	All the times	7	3(42.9%)	2(28.6%)	0(0.0%)	2(28.6%)	
How many times have you had symptoms of	It never happened	58	32(55.2%)	16(27.6%)	6(10.3%)	4(6.9%)	0.086

difficulty breathing?			%)	%)			
	Once a day	7	2(28.6%)	2(28.6%)	3(42.9%)	0(0.0%)	
	More than once a day	20	9(45.0%)	9(45.0%)	0(0.0%)	2(10.0%)	
	Once or twice a week	69	28(40.6%)	27(39.1%)	12(17.4%)	2(2.9%)	
			%)	%)			
	3 to 6 times a week	31	8(25.8%)	15(48.4%)	7(22.6%)	1(3.2%)	
			%)	%)			
How often did asthma symptoms (wheezing, coughing, shortness of breath, pain or tightness in the chest) cause you to wake up at night or wake up earlier than usual in the morning?	It never happened	80	44(55.0%)	25(31.3%)	9(11.3%)	2(2.5%)	0.198
	Once a week	23	5(21.7%)	12(52.2%)	4(17.4%)	2(8.7%)	
			%)	%)			
	2-3 nights a week	20	5(25.0%)	11(55.0%)	3(15.0%)	1(5.0%)	
			%)	%)			
	4 or more nights a week	18	7(38.9%)	5(27.8%)	4(22.2%)	2(11.1%)	
	Once or twice a month	44	18(40.9%)	16(36.4%)	8(18.2%)	2(4.5%)	
			%)	%)			
How many times did you use first aid sprays or steam sessions such as (Ventolin, Symbicort, or Albuterol)?	I've never used it	62	27(43.5%)	19(30.6%)	11(17.7%)	5(8.1%)	0.746
	Once to twice a day	22	10(45.5%)	10(45.5%)	2(9.1%)	0(0.0%)	
			%)	%)			
	3 or more times a day	20	9(45.0%)	9(45.0%)	1(5.0%)	1(5.0%)	
	Once a week or less	40	15(37.5%)	15(37.5%)	9(22.5%)	1(2.5%)	
			%)	%)			
	2 to 3 times a week	41	18(43.9%)	16(39.0%)	5(12.2%)	2(4.9%)	
			%)	%)			
How do you assess your asthma control?	There is absolutely no control	8	3(37.5%)	2(25.0%)	1(12.5%)	2(25.0%)	0.046 ^a
	Poor control	21	9(42.9%)	9(42.9%)	3(14.3%)	0(0.0%)	
	Fairly controlled	41	10(24.4%)	22(53.7%)	6(14.6%)	3(7.3%)	
			%)	%)			
	Well controlled	54	22(40.7%)	21(38.9%)	9(16.7%)	2(3.7%)	
			%)	%)			
	Totally in control	61	35(57.4%)	15(24.6%)	9(14.8%)	2(3.3%)	
			%)	%)			

^a-significant using Chi-Square Test at <0.05 level.

The results indicated that the most positively correlated factor with GAD was a patient's personal assessment of their asthma condition, which was found to be fairly controlled (B = 0.365, S.E. = 0.172, 95% C.I. = 0.026 – 0.704, p = 0.035). This suggests that a patient who personally assesses their asthma condition as "fairly controlled" has a 0.365 chance of exhibiting GAD. The second most significant predictor of GAD was a confirmed diagnosis of GAD by a professional (B = 0.364, S.E. = 0.165, 95% C.I. = 0.040 – 0.689, p = 0.028).

Table 8: Parameter Estimates for predictors of general anxiety disorder (GAD) among the asthmatic patients.

Parameter	B	S.E.	95% C.I.		p-value
			Lower Bound	Upper Bound	
			Intercept	1.604	
Have you been diagnosed with generalized anxiety disorder by a professional?=Yes	0.364	0.165	0.040	0.689	0.028 ^a
How do you assess your asthma control?=There is absolutely no control	0.555	0.319	-0.073	1.184	0.083
How do you assess your asthma control?=Poor control	0.007	0.216	-0.419	0.433	0.975
How do you assess your asthma control?=Fairly controlled	0.365	0.172	0.026	0.704	0.035 ^a
How do you assess your asthma control?=Well controlled	0.162	0.158	-0.150	0.475	0.307

^a-significant using General Linear Model at <0.05 level.

R Squared = 0.068 (Adjusted R Squared = 0.042).

DISCUSSION

The primary objective of our research was to assess the connection between anxiety and asthma in asthmatic patients at KAUH in Jeddah, Saudi Arabia. Of the 185 patients evaluated, (60.6% n=112) were female. This finding is consistent with a study conducted in 2021, which revealed that adult women are more likely to have asthma than

men.(23) Furthermore, a 2013 study revealed that women are almost twice as likely as men to experience anxiety disorders, underscoring the higher prevalence of anxiety and asthma in women.(24)

In our study, we found that 17.8% of the patients diagnosed with asthma had also been diagnosed

with generalized anxiety disorder by a medical professional. This finding has a 95% confidence interval and a p-value of 0.028. Furthermore, a previous systematic review and meta-analysis conducted in 2021 showed that patients with asthma were more likely to have comorbid anxiety disorders and anxiety symptoms than non-asthma controls. These results support our findings and highlight the strong association between asthma and anxiety.

When queried about the intensity of their asthma, the majority of patients (62.2%, n = 105) reported that their condition was effectively managed. Nonetheless, the patients' levels of anxiety and their anxiety history over the past two weeks, along with their overall general anxiety disorder score and level, showed that almost half of them experienced only minor anxiety (42.7%, n = 79), with a very small proportion exhibiting severe anxiety (4.9%, n = 9).

According to a study conducted in 2016, which examined the relationship between asthma and anxiety disorders in a large adult population, severe asthma was found to be strongly associated with a heightened risk of anxiety disorders. In contrast, non-severe asthma in the present was only linked to a higher risk of mood disorders, and non-severe asthma in the past was associated with a higher risk of both anxiety and somatoform disorders. These findings shed light on the connection between asthma severity and anxiety levels. It is worth noting that our study by Clearfield revealed that a significantly greater number of individuals with mild anxiety (57.6%, n = 19) had received a professional diagnosis of GAD compared to those with minimal, moderate, and severe levels of anxiety.

The relationship between General Anxiety Disorder (GAD)-7 scores and the history of asthma in patients (N = 185) was explored, with a formal tone. According to the Chi-square test at the <0.05 level, only the personal asthma assessment factor showed a significant association with the GAD levels. Specifically, a substantially larger number of patients who reported having total (57.4%, n = 35) and well (40.7%, n = 22) control over their asthma had minimal anxiety, compared to those with mild to severe anxiety. It is noteworthy that prior research has indicated that patients with asthma are more likely to experience anxiety, and there is a strong association between psychological illnesses and asthma outcomes, including poor control over asthma symptoms. (27)

The primary objective of this research was to expand the existing body of knowledge on anxiety in asthmatic patients in Saudi Arabia. However, the

study's limitations included a small sample size and patients who were unwilling to cooperate. We recommend that asthmatic patients be screened for anxiety, and vice versa.

CONCLUSION

In summary, it has been determined that individuals with asthma often experience anxiety. The outcomes of this research provide insight into the strong correlation between asthma and anxiety in those who have received a diagnosis. Overall, the study found that individuals with uncontrolled asthma have significantly higher levels of anxiety than those with controlled asthma, who have much lower anxiety levels. Further research on this topic may benefit anxious asthmatic patients by helping them better understand their condition and improve their quality of life.

Ethics approval and consent to participate

This study was authorized by the biomedical ethical committee of King Abdulaziz University Hospital, as evidenced by Reference No 235-22.

Consent for publication:

I, the undersigned, hereby give my consent for the publication of my identifiable details, encompassing my manuscripts, tables, and figures, in the aforementioned Journal and Article.

Availability of data and material:

The data supporting the findings of this study are available upon request from the lead authors.

Competing interests

The authors hereby affirm the absence of any financial interests or personal relationships that could potentially have exerted an influence on the work described in this paper, thereby declaring no competing interests.

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The authors confirm contribution to the paper as follows: study conception and design: Sulhi A. Alfakeh, Lamees B. Zamka, Malika M. Almadani ; data collection: Lamees B. Zamka, Malika M. Almadani, Raghad A. Shahbar, Shahd A. Alenaizan, Raghad A. Albaiti, Bayan A. Aloafi, Jana S. Alghamdi; analysis and interpretation of results: Sulhi A. Alfakeh, Lamees B. Zamka,; draft manuscript preparation: Lamees B. Zamka, Malika M. Almadani, Raghad A. Shahbar, Shahd A. Alenaizan, Raghad A. Albaiti, Bayan A. Aloafi. All authors reviewed the results and approved the final version of the manuscript.

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