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THE DUAL BURDEN OF ASTHMA AND ANXIETY: FROM SHARED MECHANISMS TO COMPREHENSIVE CARE

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ABSTRACT

Asthma is a prevalent chronic respiratory disease affecting over 300 million people globally, characterized by episodic or persistent symptoms and airflow limitation due to bronchoconstriction, airway wall thickening, and increased production of mucus. This disease often coexists with anxiety, which significantly affects patient outcomes. Anxiety, identified as the strongest predictor of dyspnea in asthma, exacerbates the perception of symptoms, impairs cognitive function, and reduces coping mechanisms. This review explores the association between asthma and anxiety, including biological and psychological mechanisms such as inflammatory pathways, neuroimmune interactions, genetic factors, and autonomic dysregulation. Elevated inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) indicate a common inflammatory mechanism that contributes to the comorbidity. Epidemiological studies highlights a bidirectional relationship, with each condition increasing the risk of developing the other. This relationship is evident across all age groups, with higher prevalence among women and younger adults. The presence of anxiety in asthma patients leads to poorer asthma control, more frequent exacerbations, and overuse of healthcare services, significantly burdening both patients and healthcare systems. Effective management strategies, including cognitive-behavioral therapy (CBT), mindfulness-based stress reduction (MBSR), pharmacological treatments, and breathing techniques, have shown promise in reducing the impact of anxiety on asthma. Additionally, integrated pharmacotherapy, telemedicine, physical exercise programs, and peer support are valuable tools in addressing

the complex relationship between anxiety and asthma. By addressing both conditions simultaneously, patients can achieve better asthma control and an improved quality of life.

KEYWORDS: *Anxiety, Asthma, Cognitive-behavioral therapy, Inflammatory markers.*

INTRODUCTION

Asthma is a common, non-communicable, and chronic respiratory disease that can result in episodic or persistent symptoms (e.g. shortness of breath, wheezing, chest tightness, cough) and airflow limitation (due to bronchoconstriction, airway wall thickening, and increased mucus), affecting over 300 million worldwide.[1][2] This disease involves interactions between neural, endocrine, immune, behavioural and psychological processes.[3] Anxiety is the strongest predictor of dyspnoea in asthma and is more strongly association with asthma-related health condition than lung function.[4][5] Anxiety does not only worsen cognitive function and coping mechanisms but also enhances the perception of symptoms experienced by asthmatic patients.[6][7] Recent reviews have demonstrated that patients who have been diagnosed with asthma are significantly at a higher risk of developing psychological conditions such as generalized anxiety disorder, panic disorder and agoraphobia, including anxiety related to symptoms, anxiety related to asthma-triggers, and anxiety related to therapy.[8] Observational studies revealed a high prevalence of anxiety in asthmatic patients with up to 30% in children and adolescents and 34% in adults. Such comorbidity can lead to adverse outcomes, such as poor asthma control, symptomatic exacerbation, significantly reduced quality of life and increased utilization of emergency services.[9] [10]

Possible mechanisms linking anxiety with asthma

Biological mechanisms

Inflammatory pathways

- Previous research studies investigated the role of systemic inflammation in linking asthma and anxiety. Inflammatory markers like interleukin-6 (IL-6) and C-reactive protein (CRP) were found to be elevated in individuals with both conditions. This suggests a shared inflammatory pathway that may contribute to the comorbidity of asthma and anxiety, with inflammation potentially affecting both respiratory and central nervous system functions.[11]

- Pro-inflammatory cytokines have been involved in the pathogenesis of allergy-related disorders, such as asthma.[12] Studies have indicated a potential association between

emotional illnesses, including anxiety disorders, and cytokines such as interleukin (IL)-6, tumour necrosis factor-alpha, IL-10, and monocyte chemoattractant protein-1/CCL2.[13][14]

- Another study on salivary cortisol, alpha-amylase, and pro-inflammatory cytokines suggested that these factors might have a role in the development of generalized anxiety disorder in asthmatic patients.[15]

- In one study, asthmatic patients were categorized as having high or low chronic life stress. Following the Trier Social Stress Test, low-stress patients had increased glucose metabolism in the anterior insula, decreased glucose metabolism in the mid-cingulate cortex, and higher levels of airway inflammation as measured by fraction of exhaled nitric oxide (FeNO) than high-stress patients. Additionally, poor asthma control was associated with worsening internalizing disorder symptoms (anxiety and depression). IL-17 pathway cytokine expression in sputum could serve as markers for the association between psychological stress and inflammation related to asthma.[16]

Neuroimmune interactions

- An earlier research study suggested that early-life stressors could prime the immune system, leading to a higher susceptibility to both asthma and anxiety later in life. The research indicated that the stress response may alter immune function in ways that predispose individuals to chronic inflammatory conditions like asthma and anxiety disorders.[17]

Genetic factors

- Genetic studies suggest shared genes and potential causal links between asthma and anxiety disorders.[18] Genetic polymorphisms in the serotonin transporter gene have been identified, associated with both asthma and anxiety. This finding suggests a genetic overlap between the two conditions, indicating that shared genetic factors may contribute to their comorbidity. Sentinel SNP: rs1709393 has a significant association with anxiety disorders and asthma, and the NR3C1 gene considerably alters the trait anxiety level in asthmatic patients.[19]

Psychological mechanisms

- In asthmatic patients, health anxiety and catastrophizing over asthma symptoms are important indicators of anxiety disorders.[20]

- Avoidance behaviors, which are more common in anxiety disorders, have been linked to worsen asthma control and more symptomatology. Patients may, for example, refrain from engaging in activities that they believe would trigger an asthma attack. This will result in less physical activity and social isolation, both of which can worsen anxiety.[21]

- Anxiety can lead to hypervigilance about bodily sensations, resulting in overuse of asthma medications and increased side effects. This over-reliance on medications can lead to a cycle of anxiety about symptoms and side effects, complicating asthma management.[22]

Hypoxia and Brain function

- Repetitive experiences with hypoxia and hypercapnia due to asthma may sensitize neural circuits that control fear responses, such as neurons in the amygdala and locus coeruleus, to overreact and to enhance fearful perceptions of conditioned stimuli such as the sensation of breathlessness.[22] [23] [24] [25]

Autonomic dysregulation

- Asthma and anxiety are both associated with autonomic nervous system (ANS) dysregulation, particularly increased sympathetic activity. This can result in heightened stress responses and anxiety symptoms, creating a feedback loop that exacerbates asthma.[26][27]

Epidemiological data

- Van Lieshout and Macqueen reviewed the prevalence of anxiety disorders among adolescents with asthma. Their findings indicate that adolescents with asthma are at an elevated risk for developing anxiety disorders. The authors suggest that the chronic nature of asthma, coupled with the psychosocial stressors of adolescence, may contribute to this increased risk, highlighting the need for early mental health interventions in this population.[28]

- Chen conducted a meta-analysis supporting the hypothesis that asthma in early adolescence is associated with an increased risk of developing unipolar depression and bipolar disorder in later stages of life.[29]

- Sarah and colleagues conducted a scoping review to assess the nature of the research on mental health and self-management in adolescents aged 11 to 24. They synthesized the relationships between the literatures and found that stress, anxiety, and depression are linked to worse asthma outcomes and may affect self-management.[30]

- A study conducted by Del Giacco revealed that individuals with lifetime anxiety disorder are at a four-fold higher risk of developing asthma, in particular uncontrolled and severe asthma. Similarly, asthmatic patients have twice the risk of developing an anxiety condition, confirming the possibility of a bidirectional relationship between anxiety and asthma, either of which can be the cause or consequence of the other.[2]

- A Population based study was conducted in Taiwan to assess the bidirectional relationship between asthma and anxiety. The study analyzing 22,797 individuals newly diagnosed with asthma and comparing them to matched controls, identified that female gender, older age, rural residence, prednisone use, asthma and depression increased the risk of anxiety. Conversely, anxiety, older age, rural residence, and prednisone use were found to increase the risk of developing asthma.[31]

- Another study focused on individuals with severe asthma demonstrated that those with concurrent anxiety had worse asthma control, increased dyspnea, and more frequent exacerbations. This study highlighted the bidirectional relationship, where anxiety exacerbates asthma symptoms and vice versa.[27]

- A cross-sectional study in Riyadh examined the prevalence of anxiety among middle-aged and elderly individuals with asthma. The study revealed significantly higher rates of anxiety and depression in asthma patients, especially those with poorly controlled asthma. Middle-aged individuals were particularly susceptible to anxiety, indicating a need for targeted mental health interventions in this group.[26]

Clinical implications

1. Exacerbation of symptoms

Anxiety can lead to heightened perceptions of asthma symptoms, such as breathlessness and chest tightness. This can make patients more prone to panic during asthma attacks, worsening their symptoms and leading to a vicious cycle of anxiety and asthma exacerbations. For example, the association between anxiety and worsening asthma symptoms has been documented in studies showing that anxious patients often experience more frequent and severe asthma attacks.[27][32]

2. Impact on asthma control

Anxiety negatively affects asthma control, often leading to poorer outcomes. One study revealed that asthmatic patients with comorbid anxiety tend to have lower scores on the Asthma Control Test (ACT) and experience more significant functional impairments. In such cases, patients are more likely to overuse short-acting beta-agonists or avoid necessary treatments due to fear of side effects.[32]

3. Poor treatment adherence

Patients with high anxiety levels often exhibit poor adherence to prescribed asthma management plans. For instance, a study found that anxious individuals were less likely to use maintenance inhalers regularly, resulting in uncontrolled asthma.[32]

4. Hospitalizations and Emergency visits

Anxiety in asthma patients is associated with increased hospitalizations and emergency room visits due to the misinterpretation of mild symptoms as severe asthma attacks. These patients are also more likely to have repeated visits to healthcare facilities due to ongoing concerns about their symptoms.[27]

Management

Cognitive-Behavioral Therapy (CBT)

- Cognitive Behavioral Therapy (CBT) helps asthma patients recognize and modify maladaptive thoughts related to breathing difficulties, reducing panic and anxiety. The therapy focuses on breaking the cycle of hyperventilation and fear that exacerbates asthma symptoms.
- An asthma patient might constantly worry about experiencing a sudden asthma attack, leading to heightened anxiety levels. Through CBT, they learn to recognize these fears as

exaggerated. For instance, a therapist might help them identify how the fear of an attack prevents them from engaging in activities they enjoy.

- By restructuring these thoughts and practicing relaxation techniques, the patient can reduce both anxiety and asthma exacerbations.
- A recent meta-analysis highlighted the effectiveness of CBT in reducing comorbid anxiety.[10]

Mindfulness-Based Stress Reduction (MBSR)

- MBSR, including practices like meditation and breathing exercises, can reduce stress-related exacerbations in asthma patients. MBSR teaches patients to focus on the present moment through meditation and controlled breathing.
- For asthma patients, mindfulness reduces the anxiety-driven exacerbation of symptoms by promoting relaxation and stress management.
- An individual with asthma might experience worsening symptoms when stressed. Through MBSR, they practice mindfulness meditation to stay grounded in the present moment, reducing the impact of stress on their asthma. For example, a patient who feels anxious about their breathing can use focused breathing techniques learned in MBSR to calm themselves during a flare-up. This method has shown promise in reducing stress-related exacerbations in asthma patients.
- Studies highlight that MBSR helps improve both mental and physical well-being, reducing anxiety and improving asthma control by minimizing the stress-induced hyperreactivity of the airways.[33]

Pharmacological treatments

- Selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines are often prescribed to manage anxiety in asthma patients. However, due to potential respiratory side effects, their use must be carefully monitored.
- Current guidelines recommend low dose starting SSRIs for the patient and gradually increasing the dose to avoid adverse effects.[27]

Integrated pharmacotherapy

- Pharmacological treatment combining anxiety and asthma medications is crucial for patients with both conditions.

- A patient suffering from both asthma and anxiety might struggle to balance their medications.
- Selective serotonin reuptake inhibitors (SSRIs) are commonly used to manage anxiety without worsening asthma symptoms, while inhaled corticosteroids control inflammation in the airways.
- Integrated pharmacotherapy ensures that the combination of these medications does not interfere with the management of either condition. Regular follow-ups with healthcare providers allow for adjustments to dosage and medication types to optimize both mental and physical health.[34]

Telemedicine and Internet-based therapies

- Internet-delivered Cognitive Behavioral Therapy (iCBT) and other telemedicine options provide accessible mental health support for asthma patients experiencing anxiety.
- These remote interventions allow for consistent psychological care, helping patients manage their anxiety and asthma symptoms simultaneously.
- A patient with severe asthma who also experiences anxiety might have limited access to in-person therapy. Using telemedicine, they participate in internet-delivered CBT (iCBT) sessions from the comfort of their home. These sessions teach them coping strategies for managing anxiety without exacerbating their asthma.
- A study showed that patients who used iCBT experienced significant improvements in anxiety and asthma control compared to those who received standard care indicating that telemedicine reduces the barrier of access to mental health services, improves patient adherence, and enhances overall asthma management.[35]

Physical exercise programs

- Regular physical activity improves lung function and reduces anxiety levels, creating a positive feedback loop in asthma management.
- A tailored aerobic exercise program might involve low-impact activities like swimming or walking, specifically designed for an asthma patient with anxiety. Over time, regular physical exercise can help reduce airway inflammation and improve lung capacity, while also lowering anxiety levels.
- For instance, yoga, which combines physical movement with controlled breathing, can help patients manage both their asthma and anxiety by promoting relaxation and improving respiratory function.

- Exercise programs are designed to the patient's physical capabilities, ensuring that activities do not trigger asthma symptoms while providing the mental health benefits of reduced stress and anxiety.[36]

Breathing techniques (e.g., Buteyko method)

- Breathing retraining, such as the Buteyko method, teaches asthma patients to manage hyperventilation and anxiety by focusing on controlled, slow breathing. This technique reduces panic attacks and prevents anxiety-related asthma exacerbations by stabilizing breathing patterns.
- A patient who tends to hyperventilate during an asthma attack learns the Buteyko method, which emphasizes shallow nasal breathing to prevent over-breathing. By practicing this technique, the patient can reduce panic and regain control of their breathing during an asthma episode.
- Studies have shown that the Buteyko method not only helps in managing anxiety but also reduces the need for rescue inhalers.[34]

Biofeedback

- Biofeedback techniques teach patients to control physiological functions like heart rate and muscle tension.
- For asthma patients, biofeedback can help them recognize and manage anxiety symptoms before they escalate into an asthma attack. For instance, a patient who notices increased heart rate due to anxiety can use relaxation techniques to lower it, thus preventing an asthma attack.
- Studies suggest that biofeedback reduces anxiety and improves asthma outcomes by promoting relaxation and better autonomic regulation.[37]

Psychological counseling

- A patient with persistent anxiety related to asthma management might attend regular psychological counseling sessions. These sessions help the patient explore the emotional impact of living with a chronic condition, develop coping mechanisms, and address any underlying mental health concerns.
- Over time, the patient learns to manage anxiety more effectively, leading to fewer asthma exacerbations and improved overall quality of life.[38]

Peer support programs

- Peer support groups, including group therapy and online communities, help asthma patients share experiences and coping strategies.
- This social support reduces anxiety by offering a sense of belonging and understanding.
- For example, a patient who is anxious about using an inhaler in public might gain confidence after hearing how others in their group handle similar situations. This sense of community can alleviate the isolation that often accompanies chronic conditions like asthma, thereby reducing anxiety and improving overall asthma control.[38]

CONCLUSION

The complex relationship between asthma and anxiety reveals significant implications for patient health and management strategies. Asthma, affecting millions globally, not only presents respiratory challenges but also significantly intertwines with psychological conditions, particularly anxiety. The comorbidity of asthma and anxiety can exacerbate symptoms, leading to poor asthma control, frequent exacerbations, and reduced quality of life. Epidemiological data emphasizes the bidirectional nature of asthma and anxiety, with each condition potentially exacerbating the other. Clinical implications point towards integrated care models as effective strategies for managing these comorbid conditions. Effective management strategies, including cognitive-behavioral therapy, mindfulness-based stress reduction, pharmacological treatments, and telemedicine, have demonstrated success in mitigating anxiety's impact on asthma. Tailored interventions focusing on the specific needs of asthmatic patients with anxiety, combined with regular follow-ups and holistic care, can significantly improve outcomes. Future research should continue to explore the underlying mechanisms and develop innovative, accessible treatments to optimize care for patients affected by both asthma and anxiety.

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