

## Beyond The Lungs: A Case Series on The Interplay Between Psychiatric Disorders and Asthma Management

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### Introduction

Asthma and psychiatric disorders can complicate diagnosis when they co-occur. Individuals with asthma have a higher prevalence of anxiety disorders (1). Both conditions may exacerbate each other, with emotional distress triggering asthma attacks and poorly controlled asthma increasing anxiety. Current evidence has recognised the utility of fractional exhaled nitric oxide (FeNO) as a biomarker of type 2 inflammation in chronic airway diseases such as asthma (2). However, its interpretation in patients with psychiatric comorbidities remains complex due to the bidirectional influence of psychological states on FeNO levels (3). We present three cases of asthma with psychiatric disorders (Table 1): **Case 1:** A 23-year-old female with a three-year history of uncontrolled bronchial asthma, allergic rhinitis, and bipolar disorder. Reported difficulty differentiating between asthma and panic attack symptoms. FeNO test: 71 parts per billion (ppb), and the lung function test (LFT) was normal (Table 1). **Case 2:** 21-year-old female with asthma and allergic rhinitis since childhood, ACT score declined since being diagnosed with major depressive disorder 2 years ago. She can recognise the symptoms indicative of panic attacks, distinct from asthma. Her LFT was normal. **Case 3:** 17-year-old female with history of childhood asthma, allergic rhinitis, class I obesity, and major depressive disorder. She reported difficulty in differentiating between asthma and panic attack symptoms. Unable to complete spirometry and FeNO test as it induces her panic attacks.

### Case Report

These three cases represent the diagnostic and treatment challenges in asthma and psychiatric disorders. Symptoms of an asthma attack often overlap with somatic symptoms of a panic attack, making clinical assessment difficult in patients with mood disorders. Psychiatric conditions can obscure the interpretation of FeNO and ACT scores, influence medication adherence, and even prevent testing. Risk factors like family history, smoking, and early anxiety predispose patients to this dual burden. FeNO-guided treatment likely reduces asthma exacerbations and may slightly improve control, with minimal impact on severe exacerbations, lung function, quality of life, or treatment dosage (4). The Malaysian Clinical Practice Guidelines recommend FeNO to assess type 2 inflammation and guide corticosteroid therapy. FeNO levels <25 parts per billion suggest minimal eosinophilic activity, levels >50 indicate active inflammation and likely steroid response, while values between 25 and 50 require clinical correlation with history, spirometry, and symptoms. High FeNO level of >50 ppb predicts a better response to corticosteroid therapy than a low level (5,6).

FeNO is produced in elevated amounts from the bronchial epithelium through the activity of inducible nitric oxide synthase (iNOS). Elevated levels of cytokines such as interleukin-4 (IL-4) and interleukin-13 (IL-13) during type 2 inflammatory responses activate the STAT6 signalling pathway, leading to the overexpression of iNOS and subsequent overproduction of NO and contribute to bronchial hyperreactivity, mucus hypersecretion, impaired ciliary function, oxidative stress, and airway tissue damage. Elevated FeNO in **Case 1** supports the presence of active allergic inflammation regardless of subjective symptom confusion.

The Global Initiative for Asthma (GINA) 2024 report recommends FeNO as an adjunct in patients with poor symptom perception or variable control (5). However, interpretation must be cautious in psychiatric populations, where emotional distress may hinder testing as in **Case 3**, where panic

attacks prevent objective assessment, questioning the feasibility in mental health settings. Psychological factors can also modulate FeNO levels independently of airway inflammation. Acute emotional states like anxiety or panic may elevate FeNO through transient immune activation, while chronic stress or depression may lower levels due to hypothalamic-pituitary-adrenal (HPA) axis suppression or corticosteroid effects (3). These cases demonstrate the relationship between asthma control, airway inflammation biomarker (FeNO), and coexisting psychiatric conditions. It emphasises the importance of understanding both immunological and psychosocial influences to evaluate the accuracy of clinical assessments carefully (ACT score) and the interpretation of inflammatory biomarkers (FeNO), thus a multidisciplinary approach is crucial.

**Table 1.** Summary of the cases and investigations

| Case (Age)  | Psychiatric Diagnosis     | ACT Score Range | FEV1/FVC (%) | FEV1 (%predicted) | FVC      | FeNO (ppb) |
|-------------|---------------------------|-----------------|--------------|-------------------|----------|------------|
| Case 1 (23) | Bipolar Disorder          | 14 → 16         | ≥70          | >80               | Normal   | 71         |
| Case 2 (21) | Major Depressive Disorder | 21 → 14         | 88           | >80               | Normal   | Not done   |
| Case 3 (17) | Major Depressive Disorder | 13 → 15         | Not done     | Not done          | Not done | Not done   |

**Keywords:** Asthma, bipolar disorder, FeNO, major depressive disorder, panic attack

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