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COMPARATIVE CROSS-SECTIONAL STUDY OF SPIROMETRY WITH FRACTIONAL EXHALED NITRIC OXIDE (FENO) IN BRONCHIAL ASTHMA PATIENTS AT A TERTIARY CARE CENTRE

Ayisha Thasneem[1], V. Karthik[2*], Sravan Kumar.G[3], Pratima Dhurka[4], Samreen Farooqui[5], T. Pramod Kumar[6]

[1]Senior resident, Department of Pulmonary Medicine, Government General Chest Hospital affiliated to Osmania Medical College, Hyderabad, Telangana, India, Email: ayishathellassery@gmail.com
[2*]Associate Professor Department of Pulmonary Medicine, Government General Chest Hospital affiliated to Osmania Medical College, Hyderabad, Telangana, India, Email: Vkarthikrao19@gmail.com ORCID ID : 0000-0002-8335-356X
[3]Associate Professor, Department of Pulmonary Medicine, Government General Chest Hospital affiliated to Osmania Medical College, Hyderabad, Telangana, India, Email: sravanghanathe@gmail.com
[4]Senior resident, Department of Pulmonary Medicine, Government General Chest Hospital affiliated to Osmania Medical College, Hyderabad, Telangana, India, Email: pratimadhurka2013@gmail.com
[5]Senior resident, Department of Pulmonary Medicine, Government General Chest Hospital affiliated to Osmania Medical College, Hyderabad, Telangana, India Email: farooquisamreen791@gmail.com
[6]Professor, Department of Pulmonary Medicine, Government General Chest Hospital affiliated to Osmania Medical College, Hyderabad, Telangana, India Email: mdrtbchest8@gmail.com

ABSTRACT

Background: Bronchial asthma is a heterogeneous inflammatory airway disease requiring accurate phenotyping for optimal management. While spirometry remains the gold standard for assessing airflow limitation, fractional exhaled nitric oxide (FeNO) provides complementary information on eosinophilic airway inflammation. Limited data exist on the correlation between these modalities in Indian tertiary care settings.

Objective: To evaluate the correlation between spirometric parameters and FeNO levels in bronchial asthma patients and to assess their combined utility in asthma phenotyping and severity assessment.

Methods: This comparative cross-sectional observational study was conducted at Government General and Chest Hospital, Erragadda, Hyderabad, India, over 18 months (2022-2025). One hundred (100) bronchial asthma patients diagnosed according to GINA 2024 criteria underwent comprehensive evaluation including demographic assessment, pre- and post-bronchodilator spirometry, FeNO measurement, and blood biomarker analysis (absolute eosinophil count, neutrophil-lymphocyte ratio). Chi-square test and Pearson correlation analysis were performed to assess associations.

Results: The study population (mean age 36.85±11.89 years, 64% female) demonstrated predominantly moderate-to-severe airflow obstruction (85%). FeNO levels were low (<25 ppb) in 17%, intermediate (25-50 ppb) in 35%, and high (>50 ppb) in 48% of patients. A highly significant association was observed between spirometric obstruction severity and FeNO levels (χ^2=40.86, p<0.00001). Patients with severe obstruction predominantly exhibited high FeNO levels. Peripheral eosinophilia (AEC >300/μL) was present in 49% and showed strong correlation with elevated FeNO (p<0.00001). Overweight/obesity (BMI >25) was present in 38% and associated with severe obstruction in 66% of cases.

Conclusion: FeNO demonstrates strong positive correlation with spirometric obstruction severity in bronchial asthma patients. The combined assessment of spirometry and FeNO provides complementary information for asthma phenotyping, particularly in identifying eosinophilic inflammation. This integrated approach supports precision medicine strategies and targeted biologic therapy selection in Indian tertiary care settings.

KEYWORDS: Bronchial asthma, Fractional exhaled nitric oxide, Spirometry, Eosinophilic inflammation, Asthma phenotyping, Biomarkers, Precision medicine

INTRODUCTION

1.1 Establishing the Territory

Bronchial asthma represents a major global health challenge, affecting over 300 million individuals worldwide and accounting for substantial morbidity, mortality, and healthcare expenditure [1]. In India alone, more than 35 million people suffer from asthma, contributing to nearly half of global asthma-related deaths [2]. The disease is characterized by chronic airway inflammation, variable respiratory symptoms, and reversible airflow limitation, with considerable heterogeneity in clinical presentation, pathophysiology, and treatment response [3].

The Global Initiative for Asthma (GINA) 2024 guidelines emphasize the importance of objective assessment tools for accurate diagnosis, severity classification, and monitoring of asthma control [3]. Spirometry remains the gold standard for quantifying airflow limitation and assessing bronchodilator reversibility, providing essential information on forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and their ratio [4]. However, spirometry primarily

reflects airway caliber and mechanical obstruction rather than the underlying inflammatory processes driving asthma pathogenesis [5].

1.2 Establishing the Niche

Recent advances in asthma management have shifted toward precision medicine approaches that recognize distinct inflammatory phenotypes and endotypes [6]. Type 2 (T2) inflammation, characterized by eosinophilic airway infiltration and mediated by interleukin-4 (IL-4), IL-5, and IL-13, represents the predominant phenotype in approximately 50-70% of asthma patients [7]. Accurate identification of eosinophilic inflammation is crucial for optimizing corticosteroid therapy and selecting appropriate biologic agents targeting T2 pathways [8].

Fractional exhaled nitric oxide (FeNO) has emerged as a non-invasive, point-of-care biomarker that reflects eosinophilic airway inflammation [9]. Nitric oxide is produced by airway epithelial cells through the action of inducible nitric oxide synthase (iNOS), with expression upregulated by T2 cytokines [10]. The American Thoracic Society (ATS) and European Respiratory Society (ERS) recommend FeNO measurement for asthma diagnosis, phenotyping, predicting corticosteroid responsiveness, and monitoring treatment adherence [11]. FeNO values are interpreted as low (<25 ppb), intermediate (25-50 ppb), or high (>50 ppb), with elevated levels indicating active eosinophilic inflammation [11].

Despite the established utility of both spirometry and FeNO in asthma assessment, their correlation and complementary roles remain incompletely characterized, particularly in diverse populations [12]. Several international studies have reported variable associations between FeNO levels and spirometric parameters, with some demonstrating inverse correlations between FeNO and FEV_1 [13], [14], while others found no significant relationship [15]. These discrepancies may reflect differences in study populations, asthma severity, treatment status, and confounding factors such as smoking and obesity [16].

1.3 Occupying the Niche

In the Indian context, comprehensive data on the correlation between spirometry and FeNO in bronchial asthma patients remain limited. Most existing studies have focused on either spirometry or FeNO independently, with few investigating their integrated assessment in tertiary care settings serving diverse patient populations [17]. Furthermore, the relationship between these objective measures and peripheral blood biomarkers such as absolute eosinophil count (AEC) and neutrophil-lymphocyte ratio (NLR) requires further elucidation in Indian cohorts [18].

The present study addresses this knowledge gap by comprehensively evaluating the correlation between spirometric parameters and FeNO levels in a well-characterized cohort of bronchial asthma patients at a major tertiary care center in Hyderabad, India. By integrating clinical, spirometric, and biomarker data, this investigation aims to provide evidence-based insights into asthma phenotyping and support the implementation of precision medicine approaches in resource-constrained settings.

Study Objectives: 1. To assess the correlation between spirometric obstruction severity and FeNO levels in bronchial asthma patients 2. To evaluate the association between peripheral blood eosinophilia and FeNO measurements 3. To characterize the demographic, clinical, and biomarker profiles of asthma patients in a tertiary care setting 4. To determine the clinical utility of combined spirometry-FeNO assessment for asthma phenotyping

2. MATERIALS AND METHODS

2.1 Study Design And Setting

This comparative cross-sectional observational study was conducted in the Department of Pulmonary Medicine, Government General and Chest Hospital, Erragadda, Hyderabad, India, affiliated with Osmania Medical College. The study was approved by the Institutional Ethics Committee of Osmania Medical College (approval obtained prior to study commencement) and conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study duration was 18 months, from the date of ethical approval through 2022-2025.

2.2 Study Population

2.2.1 Sample Size

A total of 100 bronchial asthma patients were enrolled from both outpatient and inpatient departments.

2.2.2 Inclusion Criteria

Patients diagnosed with bronchial asthma based on clinical manifestations and spirometry according to GINA 2024 guidelines [3]

Age >12 years

Provision of written informed consent

2.2.3 Exclusion Criteria

Patients experiencing acute exacerbation at the time of assessment

Current use of oral corticosteroids

Previous history of tuberculosis or other chronic respiratory illnesses (chronic obstructive pulmonary disease, interstitial lung disease, bronchiectasis)

Patients unwilling to participate or unable to perform spirometry or FeNO measurement

2.3 Data Collection

2.3.1 Clinical Assessment
After obtaining written informed consent, detailed clinical history was recorded using a standardized case proforma, including: - Demographic data (age, sex, occupation) - Presenting symptoms (cough, sputum production, shortness of breath, wheeze) - Duration of asthma - Exposure history (dust, smoke, occupational allergens) - Smoking history - Comorbidities (diabetes mellitus, systemic hypertension, thyroid disorders, gastroesophageal reflux disease, upper airway disorders)
Physical examination included measurement of height and weight for body mass index (BMI) calculation, vital signs assessment, and comprehensive respiratory system examination including upper airway evaluation.

2.3.2 Laboratory Investigations
Complete blood count with differential was performed for all patients, with calculation of: - Absolute eosinophil count (AEC): Eosinophilia defined as AEC >300 cells/µL - Neutrophil-lymphocyte ratio (NLR): Categorized as <2, 2-4, or >4 - Hemoglobin levels: Anemia defined as <12 g/dL

2.3.3 Spirometry
Pre- and post-bronchodilator spirometry was performed using an NDD spirometer (Easy on PC, Serial number 252223) according to ATS/ERS standardized guidelines [4]. The procedure included:
Preparation: - Patient identification confirmation - Measurement of height and weight without shoes - Instruction and demonstration of the maneuver
Procedure: - Patient assumed upright posture - Nose clip applied - Normal breathing followed by maximal inspiration with pause <2 seconds at total lung capacity - Maximal forced expiration until no more air could be expelled - Maximal inspiration back to full lung capacity - Minimum of three acceptable maneuvers performed
Parameters Measured: - Forced expiratory volume in 1 second (FEV_1) - Forced vital capacity (FVC) - FEV_1/FVC ratio.
Bronchodilator Response: Post-bronchodilator spirometry was performed 15 minutes after administration of 400 µg salbutamol via metered-dose inhaler with spacer.
Severity Classification: Degree of obstruction was classified based on FEV_1 % predicted [4]: - Mild: FEV_1 ≥70% predicted - Moderate: FEV_1 50-69% predicted - Severe: FEV_1 <50% predicted
2.3.4 Fractional Exhaled Nitric Oxide (FeNO) Measurement
FeNO was measured using the NObreath® device (Bedfont Scientific Ltd., UK), which conforms to ATS/ERS guidelines and is recommended by the National Institute for Health and Care Excellence (NICE) [11].
Procedure: - Patient instructed to take a maximal inspiration - Gentle exhalation through filtered mouthpiece at constant flow rate (50 mL/s) for approximately 10 seconds - Real-time display of FeNO value on device screen - Measurement repeated if necessary to ensure reproducibility
Interpretation: FeNO levels were categorized according to ATS guidelines [11]: - Low: <25 ppb - Intermediate: 25-50 ppb - High: >50 ppb

2.4 Statistical Analysis
Data were entered in Microsoft Excel and analyzed using SPSS version 26.0. Descriptive statistics were calculated for all variables. Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data and median with interquartile range (IQR) for skewed data. Categorical variables were presented as frequencies and percentages.
Chi-square test (or Fisher's exact test when appropriate) was used to assess associations between categorical variables, including spirometric obstruction severity and FeNO categories, AEC levels and FeNO categories, and BMI categories and obstruction severity. Independent sample t-test was used for comparing means between two groups. A p-value <0.05 was considered statistically significant.

2.5 Ethical Considerations
The study was conducted in accordance with ethical principles for medical research involving human subjects. Written informed consent was obtained from all participants in their preferred language (English, Hindi, or Telugu). Patient confidentiality was maintained throughout the study. No additional costs were incurred by participants, and the study did not interfere with standard clinical care.

3. RESULTS
3.1 Demographic Characteristics
The study enrolled 100 bronchial asthma patients with a mean age of 36.85±11.89 years (range: <20 to >70 years). The age distribution showed peak prevalence in the 41-50 years group (28%), followed by 21-30 years (27%) and 31-40 years (27%), indicating predominant involvement of young to middle-aged adults. Female patients constituted 64% of the study population, while males comprised 36%, demonstrating a clear female predominance.
Body mass index (BMI) analysis revealed that 56% of patients had normal BMI (18.5-24.9 kg/m²), while 38% were overweight or obese (BMI ≥25 kg/m²), including 29% overweight (BMI 25-29.9) and 9% obese (BMI ≥30). Only 6% were underweight (BMI <18.5). Among patients with elevated BMI (>25 kg/m², n=38), the majority (66%) exhibited severe airflow obstruction, 26% had moderate obstruction, and only 8% had mild obstruction, suggesting a strong association between higher BMI and worsened pulmonary function. Figure-3

3.2 Clinical Presentation

Shortness of breath was the most prevalent symptom, reported by 84% of patients, followed by wheeze (70%), cough (67%), and sputum production (38%). This symptom profile aligns with classical asthma presentations as defined by GINA guidelines.

Comorbidity analysis revealed that upper airway disorders (allergic rhinitis, sinusitis) were present in 20% of patients, gastroesophageal reflux disease (GERD) in 15%, thyroid disorders (hypo/hyperthyroidism) in 7%, and diabetes mellitus type 2 and systemic hypertension each in 5% of patients. No patients had documented cardiovascular disease.

Regarding exposure history, only 16% of patients reported significant environmental or occupational exposures (dust, smoke, chemical irritants), while 84% denied such exposures. Active smoking was reported by 8% of patients, with 92% being non-smokers. Among the 8 smokers, all demonstrated moderate-to-severe obstruction, with 62.5% (5/8) showing severe obstruction.

3.3 Hematological Biomarkers

Hemoglobin analysis showed that 38% of patients had anemia (Hb <12 g/dL), including 8% with severe anemia (Hb <10 g/dL) and 30% with mild-to-moderate anemia (Hb 10-12 g/dL). The remaining 62% had normal hemoglobin levels (>12 g/dL).

Neutrophil-lymphocyte ratio (NLR) distribution demonstrated that 33% of patients had NLR <2, 47% had NLR 2-4, and 20% had elevated NLR >4, suggesting varying degrees of systemic inflammation with a subset exhibiting neutrophilic predominance.

Absolute eosinophil count (AEC) revealed that 49% of patients had peripheral eosinophilia (AEC >300 cells/μL), while 51% had AEC <300 cells/μL, indicating that approximately half the population exhibited eosinophilic inflammation.

3.4 Spirometric Findings

Pre-bronchodilator spirometry demonstrated that only 15% of patients had mild obstruction (FEV_1 ≥70% predicted), while 39% had moderate obstruction (FEV_1 50-69% predicted) and 46% had severe obstruction (FEV_1 <50% predicted). Thus, 85% of the study population exhibited moderate-to-severe airflow limitation, indicating predominantly advanced disease or suboptimal control.

3.5 FeNO Measurements

FeNO level distribution showed that 17% of patients had low FeNO (<25 ppb), 35% had intermediate FeNO (25-50 ppb), and 48% had high FeNO (>50 ppb). Nearly half the population demonstrated elevated FeNO levels indicative of significant eosinophilic airway inflammation. Figure-1.

3.6 Correlation Between Spirometric Obstruction Severity and FeNO Levels

Chi-square analysis revealed a highly significant association between degree of spirometric obstruction and FeNO categories (χ^2=40.86, p<0.00001). Among patients with mild obstruction (n=15), 67% (10/15) had low FeNO, 20% (3/15) had intermediate FeNO, and 13% (2/15) had high FeNO. In contrast, among patients with moderate obstruction (n=39), only 13% (5/39) had low FeNO, 51% (20/39) had intermediate FeNO, and 36% (14/39) had high FeNO. Most strikingly, among patients with severe obstruction (n=46), only 4% (2/46) had low FeNO, 26% (12/46) had intermediate FeNO, and 70% (32/46) had high FeNO.

This gradient demonstrates that as spirometric obstruction severity increases, FeNO levels tend to be progressively higher, with the highest deviations from expected values observed in the low FeNO-mild obstruction and high FeNO-severe obstruction groups.

3.7 Association Between Absolute Eosinophil Count and FeNO Levels

A highly significant association was observed between peripheral eosinophilia and FeNO levels (p<0.00001). Among patients with AEC <300 cells/μL (n=51), 33% (17/51) had low FeNO, 43% (22/51) had intermediate FeNO, and 24% (12/51) had high FeNO. In contrast, among patients with AEC >300 cells/μL (n=49), none had low FeNO, 27% (13/49) had intermediate FeNO, and 73% (36/49) had high FeNO.Figure-2

This strong correlation indicates that peripheral eosinophilia reliably predicts elevated FeNO levels and eosinophilic airway inflammation.

3.8 Association Between Absolute Eosinophil Count and Spirometric Obstruction

Among patients with AEC <300 cells/μL (n=51), 22% (11/51) had mild obstruction, 47% (24/51) had moderate obstruction, and 31% (16/51) had severe obstruction. Among patients with AEC >300 cells/μL (n=49), none had mild obstruction, 24% (12/49) had moderate obstruction, and 76% (37/49) had severe obstruction. While obstruction severity tended to increase with rising AEC, this association did not reach statistical significance (p=0.125).

4. DISCUSSION

4.1 Principal Findings

This comparative cross-sectional study demonstrates a highly significant positive correlation between spirometric obstruction severity and FeNO levels in bronchial asthma patients ($p<0.00001$). Patients with severe airflow limitation predominantly exhibited elevated FeNO, indicating active eosinophilic inflammation. Furthermore, peripheral eosinophilia (AEC >300 cells/μL) showed strong correlation with high FeNO levels ($p<0.00001$), supporting the utility of combined biomarker assessment for asthma phenotyping. These findings underscore the complementary roles of spirometry and FeNO in comprehensive asthma evaluation and have important implications for precision medicine approaches in tertiary care settings.

4.2 Demographic Profile and Clinical Characteristics

The mean age of 36.85±11.89 years in our cohort, with peak prevalence in the 41-50 years age group, aligns with recent epidemiological trends showing increasing adult-onset asthma in India [2]. This age distribution is consistent with international studies reporting mean ages of 40-43 years [13], [14], [19]. The shifting burden from pediatric to adult populations reflects urbanization, lifestyle changes, and increasing environmental pollutant exposure [2].

The observed female predominance (64%) corroborates global trends and previous Indian studies [13], [14], [20]. While childhood asthma is more common in males, adult-onset asthma disproportionately affects females due to hormonal influences, smaller airway caliber, and greater susceptibility to eosinophilic inflammation post-puberty [2], [21]. Endogenous estrogen and progesterone modulate airway responsiveness and inflammatory responses, contributing to sex-based differences in asthma prevalence and severity [21].

The finding that 38% of patients were overweight or obese (BMI ≥25) is clinically significant, as obesity is increasingly recognized as an important asthma phenotype modifier [22]. Among patients with elevated BMI, 66% exhibited severe obstruction, suggesting a dose-response relationship between body weight and airway impairment. Obesity promotes asthma through multiple mechanisms including mechanical effects on lung function, systemic inflammation mediated by adipokines (leptin, IL-6), and comorbidities such as GERD and obstructive sleep apnea [22], [23]. Obese asthmatics often exhibit a non-eosinophilic, corticosteroid-insensitive phenotype with reduced response to standard therapy [23].

4.3 Symptom Profile and Comorbidities

The predominance of shortness of breath (84%) and wheeze (70%) as cardinal symptoms aligns with GINA 2024 diagnostic criteria [3] and previous studies [14], [19], [20]. The relatively lower prevalence of sputum production (38%) suggests predominantly non-productive cough, characteristic of eosinophilic or allergic asthma phenotypes rather than neutrophilic inflammation or coexisting chronic bronchitis [24].

Upper airway disorders were present in 20% of patients, supporting the "unified airway" hypothesis that upper and lower airways function as a single immunological entity [25]. Allergic rhinitis and sinusitis can trigger and exacerbate lower airway dysfunction, with studies demonstrating that patients with allergic rhinitis have elevated FeNO levels and increased risk of asthma development [25]. GERD, identified in 15% of our cohort, represents an important comorbidity that can worsen asthma through microaspiration and vagal-mediated bronchoconstriction [26]. The bidirectional relationship between GERD and asthma is well-established, with asthma medications (beta-agonists, theophylline) potentially promoting reflux by reducing lower esophageal sphincter tone [26].

4.4 Spirometric Findings and Disease Severity

The finding that 85% of patients had moderate-to-severe obstruction (FEV_1 <70% predicted) indicates predominantly advanced disease or suboptimal control in our tertiary care population. This high proportion of severe cases likely reflects referral bias, as tertiary centers typically receive patients with more severe or difficult-to-control asthma. Previous studies have reported variable distributions, with some showing lower proportions of severe obstruction [19], [20], possibly reflecting differences in study settings, patient selection, and treatment access.

The predominance of moderate-to-severe obstruction underscores the need for comprehensive phenotyping and optimization of anti-inflammatory therapy in this population. Spirometry provides essential information on airflow limitation but does not directly assess underlying inflammatory processes, highlighting the complementary role of biomarkers such as FeNO [5].

4.5 FeNO Levels and Eosinophilic Inflammation

The distribution of FeNO levels in our study—with 48% of patients exhibiting high FeNO (>50 ppb)—indicates substantial eosinophilic airway inflammation in nearly half the population. This finding has important therapeutic implications, as patients with elevated FeNO typically demonstrate good response to inhaled corticosteroids (ICS) and may be candidates for biologic therapies targeting T2 inflammation [7], [8].

The 17% of patients with low FeNO (<25 ppb) may represent non-eosinophilic phenotypes, including neutrophilic or paucigranulocytic asthma, which often exhibit reduced corticosteroid responsiveness [24]. These patients may benefit from alternative therapeutic approaches, including long-acting bronchodilators, leukotriene modifiers, or macrolide antibiotics [24].

4.6 Correlation Between Spirometry and FeNO

The highly significant association between spirometric obstruction severity and FeNO levels ($\chi^2=40.86$, $p<0.00001$) represents a key finding of this study. Patients with severe obstruction (FEV_1 <50% predicted) predominantly exhibited high FeNO (70%), while those with mild obstruction (FEV_1 ≥70% predicted) predominantly had low FeNO (67%). This gradient suggests that worsening airflow limitation is associated with increasing eosinophilic inflammation.

Our findings align with several international studies demonstrating inverse correlations between FeNO and FEV_1 [13], [14], [27]. Al Ghobain et al. reported a significant negative correlation between FeNO and FEV_1% predicted (r=-0.18, p=0.027) in Saudi Arabian asthma patients [13]. Similarly, Nguyen et al. found inverse correlations between FeNO and multiple spirometric parameters (FEV_1, FEV_1/FVC, PEF) in Vietnamese patients [14]. Michils et al. demonstrated that airway caliber is an independent determinant of FeNO, with a negative FeNO-FEV_1 relationship requiring correction factors for accurate interpretation [27].

However, some studies have reported no significant correlation between FeNO and spirometric parameters [15], [28]. Nakwan et al. found no correlation between FeNO and lung function in well-controlled asthma patients [15], suggesting that the FeNO-spirometry relationship may be influenced by disease control status and treatment. These discrepancies likely reflect differences in study populations, asthma severity, treatment regimens, and confounding factors such as smoking and obesity [16].

The mechanistic basis for the FeNO-spirometry correlation involves the relationship between eosinophilic inflammation and airway remodeling. Chronic eosinophilic inflammation promotes structural changes including subepithelial fibrosis, smooth muscle hypertrophy, and mucus gland hyperplasia, leading to fixed airflow obstruction [29]. Additionally, eosinophil-derived mediators such as major basic protein and eosinophil cationic protein cause epithelial damage and airway hyperresponsiveness [29].

4.7 Correlation Between Peripheral Eosinophilia and FeNO

The strong association between AEC >300 cells/μL and elevated FeNO ($p<0.00001$) demonstrates that peripheral eosinophilia reliably predicts eosinophilic airway inflammation. Among patients with eosinophilia, 73% had high FeNO, while none had low FeNO. This finding supports the use of blood eosinophil count as an accessible surrogate marker for airway eosinophilia [30].

Our results corroborate multiple studies demonstrating positive correlations between blood eosinophils and FeNO [13], [14], [15], [30]. Al Ghobain et al. reported a significant correlation ($r=0.42$, $p<0.0001$) between FeNO and blood eosinophil count [13]. Nakwan et al. found a positive correlation ($r=0.310$, $p=0.004$) even in well-controlled asthma [15]. A recent systematic review confirmed that blood eosinophilia is a reliable predictor of bronchial eosinophilia, superior to FeNO and IgE for discriminating inflammatory phenotypes [30].

The clinical utility of combined AEC and FeNO assessment is particularly relevant for biologic therapy selection. Current guidelines recommend blood eosinophil thresholds (typically ≥150-300 cells/μL) for initiating anti-IL-5/IL-5R biologics (mepolizumab, benralizumab, reslizumab) in severe asthma [7], [8]. Elevated FeNO provides additional evidence of T2 inflammation and may predict treatment response [31]. Porsbjerg et al. demonstrated that pre-treatment combinations of T2 biomarkers (FeNO, blood eosinophils, IgE) improve prediction of biologic therapy outcomes [31].

4.8 Clinical Implications for Precision Medicine

The integration of spirometry, FeNO, and blood biomarkers enables comprehensive asthma phenotyping that informs personalized treatment strategies [6], [7]. Our findings support a precision medicine approach incorporating:

Spirometry for quantifying airflow limitation, assessing severity, and monitoring treatment response

FeNO measurement for identifying eosinophilic inflammation, predicting corticosteroid responsiveness, and monitoring adherence

Blood eosinophil count as an accessible surrogate for airway eosinophilia and biologic therapy selection

Clinical assessment including symptom burden, exacerbation history, and comorbidities

Patients with high FeNO and elevated blood eosinophils represent the T2-high phenotype most likely to benefit from ICS optimization and biologic therapies [7], [8]. Conversely, patients with low FeNO and normal eosinophils may have T2-low asthma requiring alternative approaches [24]. The 35% of patients with intermediate FeNO in our study represent a heterogeneous group requiring individualized assessment and potential longitudinal monitoring [11].

4.9 Strengths and Limitations

Strengths: 1. Comprehensive assessment integrating spirometry, FeNO, and blood biomarkers 2. Standardized methodology following GINA 2024 and ATS/ERS guidelines 3. Well-characterized tertiary care population representative of severe asthma 4. Rigorous statistical analysis with appropriate tests 5. First comprehensive study from Hyderabad combining these modalities

Limitations: 1. Cross-sectional design precludes assessment of longitudinal relationships and treatment response 2. Single-center study may limit generalizability to other settings 3. Lack of sputum eosinophil analysis, the gold standard for airway inflammation assessment 4. No assessment of asthma control status using validated questionnaires (ACT, ACQ) 5. Potential confounding by treatment status, as medication use was not systematically analyzed 6. Small sample size (n=100) may limit subgroup analyses 7. Referral bias inherent to tertiary care setting, with overrepresentation of severe cases 8. No assessment of IgE levels or atopic status 9. Limited data on exacerbation history and healthcare utilization

Future prospective studies should address these limitations by incorporating longitudinal follow-up, treatment response assessment, sputum analysis, and validation in diverse populations including primary care settings.

4.10 Implications for Clinical Practice and Research

This study provides evidence supporting the integration of FeNO measurement into routine asthma assessment in Indian tertiary care centers. The strong correlation between FeNO and spirometric obstruction, combined with the association

between peripheral eosinophilia and elevated FeNO, validates the clinical utility of these complementary biomarkers for phenotyping and treatment guidance.
Healthcare systems should consider implementing FeNO measurement as a point-of-care tool to complement spirometry, particularly in centers managing severe asthma and considering biologic therapies. The relatively low cost and ease of FeNO measurement make it feasible even in resource-constrained settings [9], [11].
Future research directions include: 1. Prospective studies evaluating FeNO-guided treatment algorithms in Indian populations 2. Assessment of FeNO and spirometry changes with biologic therapy initiation 3. Investigation of FeNO-spirometry relationships in specific phenotypes (obesity-related asthma, asthma-COPD overlap) 4. Development of population-specific FeNO reference values for Indian adults 5. Cost-effectiveness analyses of FeNO-guided management strategies

5. CONCLUSION

This comparative cross-sectional study demonstrates a highly significant positive correlation between spirometric obstruction severity and FeNO levels in bronchial asthma patients at a tertiary care center in Hyderabad, India. Patients with severe airflow limitation predominantly exhibited elevated FeNO, indicating active eosinophilic inflammation. Peripheral eosinophilia (AEC >300 cells/μL) showed strong correlation with high FeNO levels, supporting the utility of blood eosinophils as an accessible surrogate marker for airway inflammation.
The combined assessment of spirometry and FeNO provides complementary information that enhances asthma phenotyping beyond either modality alone. Spirometry quantifies airflow limitation and severity, while FeNO identifies eosinophilic inflammation and predicts corticosteroid responsiveness. This integrated approach supports precision medicine strategies, enabling clinicians to optimize anti-inflammatory therapy and select appropriate biologic agents for patients with T2-high asthma.
The high prevalence of moderate-to-severe obstruction (85%) and elevated FeNO (48%) in our tertiary care population underscores the substantial burden of uncontrolled eosinophilic asthma and the need for comprehensive phenotyping and treatment optimization. The association between obesity and severe obstruction highlights the importance of addressing metabolic comorbidities in asthma management.
These findings have important implications for clinical practice in Indian tertiary care settings, supporting the implementation of FeNO measurement as a routine adjunct to spirometry for asthma assessment. Future prospective studies should evaluate FeNO-guided treatment algorithms and assess the impact of integrated phenotyping on clinical outcomes, healthcare utilization, and quality of life in diverse Indian populations.

Acknowledgments
The authors express sincere gratitude to all patients who participated in this study. We acknowledge the technical staff of the Pulmonary Function Laboratory and the nursing staff of the Department of Pulmonary Medicine, Government General and Chest Hospital, Erragadda, Hyderabad, for their assistance in data collection. We thank the Institutional Ethics Committee of Osmania Medical College for approving this study.

Author Contributions
All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Ethics Approval And Informed Consent
This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of Osmania Medical College, Hyderabad, India. Written informed consent was obtained from all participants prior to enrollment. Patient confidentiality was maintained throughout the study, and all data were anonymized for analysis.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict Of Interest
The authors declare that they have no competing interests related to this work.

Data Availability Statement
The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request, subject to institutional ethical approval and patient privacy considerations.

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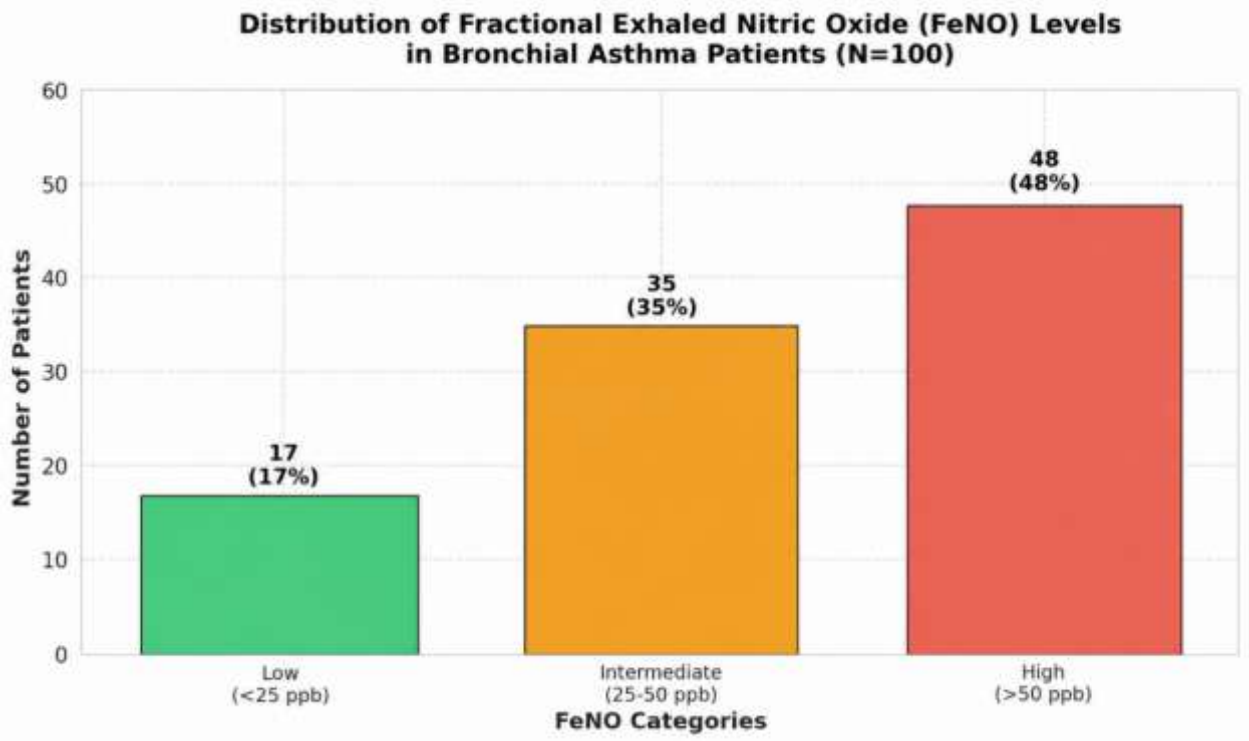

Figure-1

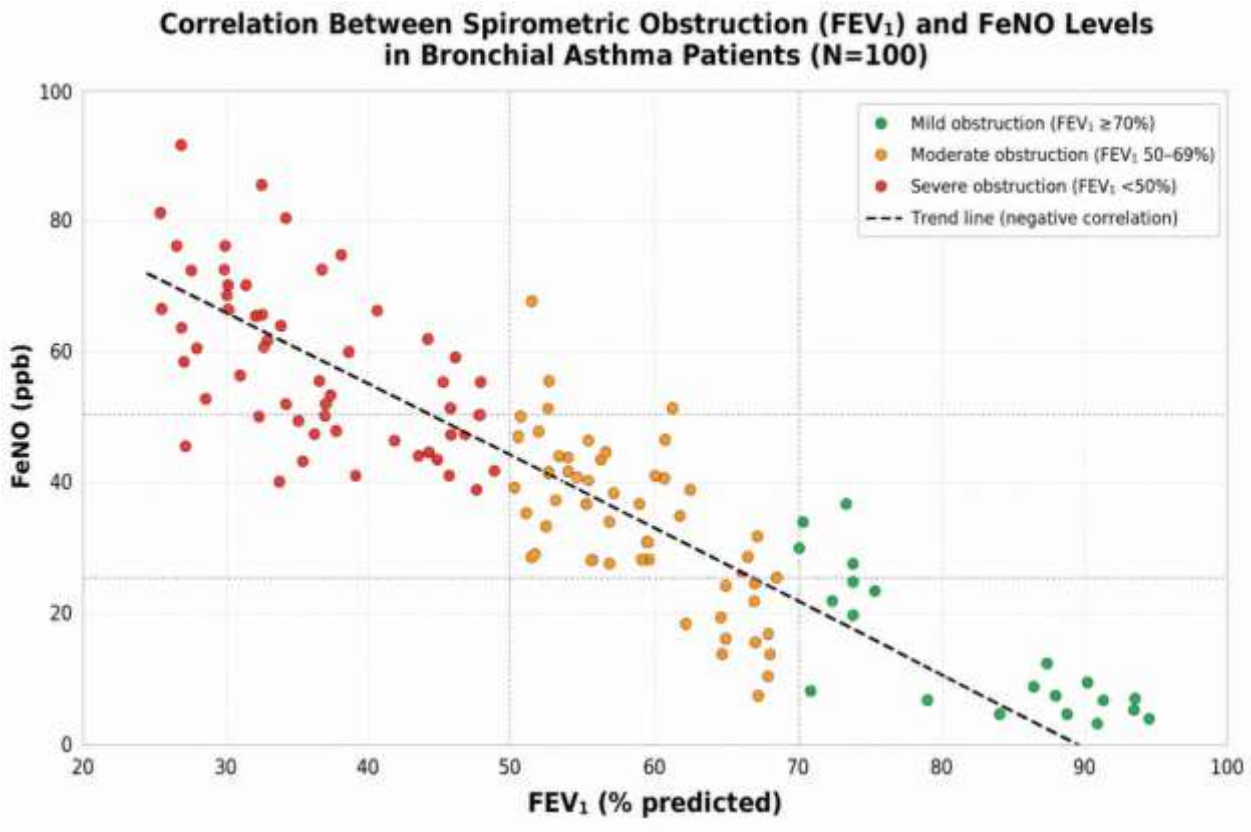

Figure-2

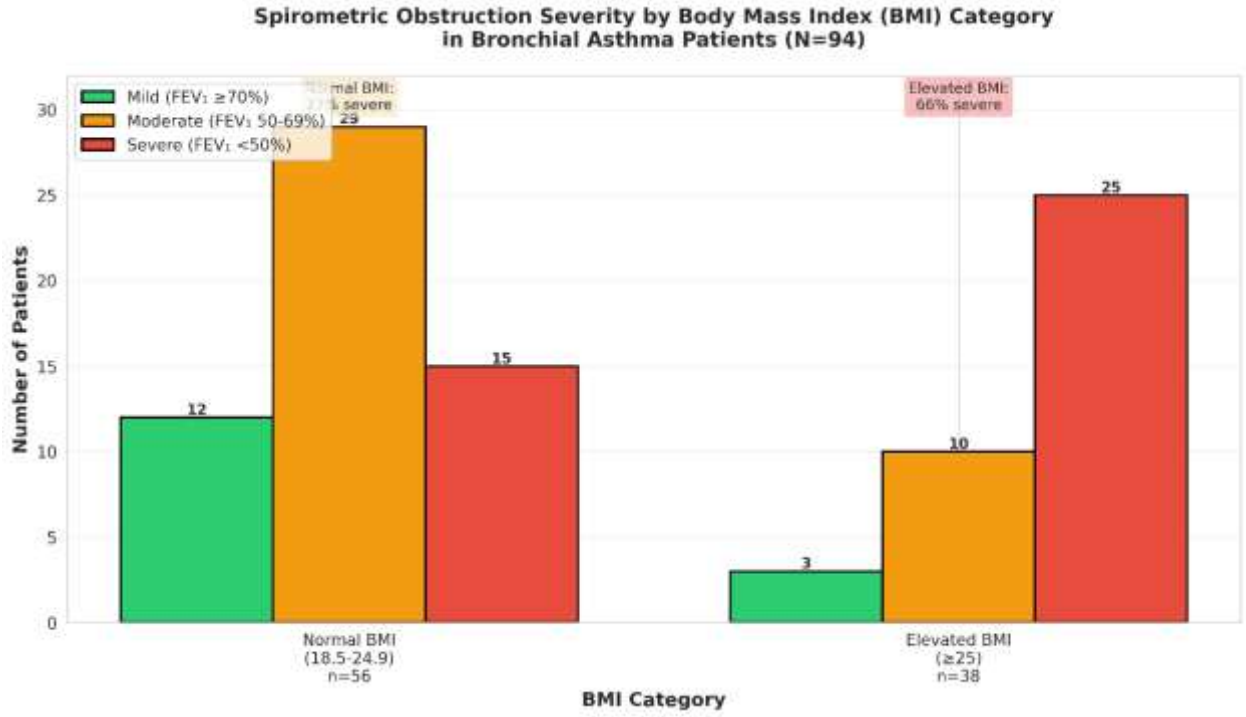
Spirometric Obstruction Severity by Body Mass Index (BMI) Category
in Bronchial Asthma Patients (N=94)
Mild (FEV₁ ≥70%)
Moderate (FEV₁ 50-69%)
Severe (FEV₁ <50%)
Elevated BMI:
66% severe
Number of Patients
0
5
10
15
20
25
30
12
29
15
3
10
25
Normal BMI
(18.5-24.9)
n=56
Elevated BMI
(≥25)
n=38
BMI Category

Figure-3