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Article

Asthma Control Level as Measured by Fractional Exhaled Nitric Oxide (FeNO) in Patients Coming for Follow-Up

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ABSTRACT

Background: Asthma is a chronic inflammatory airway disease requiring regular monitoring to prevent exacerbation. Conventional clinical assessments may not fully capture airway inflammation, highlighting a need for reliable biomarkers. Fractional exhaled nitric oxide (FeNO) is a non-invasive marker reflecting eosinophilic airway inflammation and may improve asthma control evaluation. **Objective:** This study aimed to assess asthma control levels in follow-up patients by measuring FeNO and to evaluate the correlation between FeNO values and asthma control status classified according to Global Initiative for Asthma (GINA) guidelines. **Methods:** A descriptive observational study was conducted on 100 adult asthma patients aged 18–60 years attending follow-up at a tertiary care center. Patients with recent respiratory infections or corticosteroid use were excluded. FeNO levels were measured using a standardized electrochemical analyzer following ATS guidelines. Asthma control was classified per GINA 2022 criteria. Data were analyzed using SPSS version 24.0 with ANOVA to compare mean FeNO across control groups. Ethical approval was obtained, and the study adhered to the Declaration of Helsinki. **Results:** The mean age was 35.4 ± 10.2 years; 58% were female. Asthma control distribution was 40% controlled, 35% partially controlled, and 25% uncontrolled. Mean FeNO significantly increased with worsening control: 15.2 ± 5.3 ppb (controlled), 34.8 ± 8.7 ppb (partially controlled), and 51.3 ± 12.1 ppb (uncontrolled) ($p < 0.001$). Higher FeNO levels were strongly associated with poorer asthma control. **Conclusion:** FeNO measurement effectively distinguishes asthma control levels in follow-up patients, offering a valuable tool for detecting airway inflammation and guiding treatment adjustments. Incorporation of FeNO into routine asthma management can enhance individualized care and improve clinical outcomes.

Keywords: Asthma, Fractional Exhaled Nitric Oxide, Airway Inflammation, Asthma Control, Biomarkers, Pulmonary Function, Inhaled Corticosteroids.

INTRODUCTION

Asthma is a complex chronic respiratory disease characterized by variable airway inflammation, airway hyperresponsiveness, and intermittent symptoms such as wheeze, breathlessness, and cough. Despite the existence of standardized treatment protocols, asthma remains a significant public health challenge, with the World Health Organization estimating its prevalence at over 300 million individuals globally, contributing to considerable morbidity and healthcare utilization (2). A central aspect of optimal asthma management is regular monitoring to guide timely adjustments in therapy, aiming to prevent exacerbations and preserve lung function (3). Traditionally, asthma control assessment has relied on clinical symptom scores, spirometry, and the frequency of exacerbations (4). However, these conventional methods may not fully capture underlying airway inflammation, particularly eosinophilic inflammation, which plays a pivotal role in many asthma phenotypes (5).

This gap in assessment has motivated research into the use of non-invasive biomarkers that directly reflect the inflammatory milieu of the airways. Fractional exhaled nitric oxide (FeNO) has emerged as a promising surrogate marker, as it is directly associated with eosinophilic airway inflammation and responds to anti-inflammatory treatments such as inhaled corticosteroids (ICS) (6,7). Measurement of FeNO is both convenient and

reproducible, providing real-time insight into airway inflammation that may precede changes in symptoms or lung function (8). Its clinical utility is supported by guidelines from the Global Initiative for Asthma (GINA), which recommend FeNO as an adjunct for both diagnosis and ongoing management of asthma, particularly in guiding the initiation or titration of ICS therapy (9). Despite these recommendations, routine application of FeNO in asthma follow-up remains limited, especially in low- and middle-income countries, where resource constraints and lack of awareness can hinder widespread adoption.

Previous studies have demonstrated that FeNO levels correlate with asthma control status and can differentiate between controlled, partially controlled, and uncontrolled asthma patients (11,12). This suggests that FeNO has the potential to complement or even enhance traditional asthma monitoring strategies, offering clinicians a more nuanced approach to individualized care (13). However, there remains a paucity of data from diverse clinical settings, particularly in regions where environmental exposures, healthcare access, and adherence to therapy can influence asthma outcomes and biomarker expression. Furthermore, while FeNO is generally reliable, its interpretation must account for potential confounders such as recent respiratory infections or allergic triggers, which may transiently elevate FeNO levels independent of asthma activity (17,18).

Given the above considerations, there is a need for context-specific research to evaluate the utility of FeNO in routine asthma follow-up, especially in populations with distinct demographic and environmental profiles. This study aims to address this knowledge gap by assessing the control of asthma among patients attending follow-up clinics in a major tertiary care center, using FeNO as an objective marker and correlating its levels with asthma control categories defined by GINA guidelines. The central research question is whether FeNO measurements provide meaningful stratification of asthma control among follow-up patients and can thus inform clinical decision-making in this setting.

MATERIALS AND METHODS

This descriptive observational study was conducted at the Pulmonology Department of Fatima Jinnah Institute of Chest Diseases, Quetta, from October 1, 2024, to March 31, 2025. A total of 100 consecutive adult patients diagnosed with asthma, aged between 18 and 60 years, presenting for routine follow-up visits were enrolled after obtaining informed consent. The inclusion criteria required a physician-confirmed diagnosis of asthma according to the Global Initiative for Asthma (GINA) guidelines and attendance at scheduled follow-up appointments. Patients were excluded if they had a current or recent respiratory infection, a history of corticosteroid use in the preceding month, or other chronic lung diseases. Recruitment was conducted through consecutive sampling among eligible patients attending the outpatient clinic, ensuring that each participant voluntarily provided written informed consent prior to enrollment. The study protocol received approval from the ethical review board (Ref No CPSP/REU/PUL-2022-001-740) and complied with the principles outlined in the Declaration of Helsinki. Confidentiality of participant information was strictly maintained, and all data were anonymized prior to analysis.

Primary outcomes included the assessment of asthma control level, classified as controlled, partially controlled, or uncontrolled according to the GINA 2022 criteria, and measurement of fractional exhaled nitric oxide (FeNO) levels. FeNO was determined using a standardized electrochemical analyzer in accordance with the American Thoracic Society (ATS) recommendations, with patients refraining from eating, drinking, or engaging in strenuous activity at least one hour prior to measurement to ensure consistency. Additional demographic and clinical data, such as age, gender, and smoking status, were collected from medical records and patient interviews. The asthma control level was evaluated using documented clinical symptoms and spirometry, when available, aligning with the GINA guidelines to provide a reliable assessment of disease status.

Statistical analysis was performed using SPSS version 24.0. Descriptive statistics summarized demographic and clinical characteristics as means, standard deviations, and frequencies. The primary analysis compared mean FeNO levels across the asthma control groups using one-way analysis of variance (ANOVA), with statistical significance set at $p < 0.05$. Where significant group differences were detected, post-hoc comparisons were conducted to determine which groups differed. No imputation for missing data was required, as complete datasets were available for all enrolled patients. This methodological approach ensures the study's findings are robust and reproducible, providing reliable insights into the relationship between FeNO levels and asthma control in a follow-up clinic population (3,6).

RESULTS

A total of 100 adult patients with physician-diagnosed asthma were enrolled, with a mean age of 35.4 ± 10.2 years. The majority of participants were female (58%), and most identified as non-smokers (80%). The demographic characteristics of the study population are summarized in Table 1. Asthma control was assessed using GINA 2022 criteria. Of the 100 participants, 40 (40%) were classified as having controlled asthma, 35 (35%) as partially controlled, and 25 (25%) as uncontrolled (Table 2). Mean FeNO levels differed notably across these asthma control groups. Patients with controlled asthma exhibited a mean FeNO of 15.2 ± 5.3 ppb, those with partially controlled asthma had a mean of 34.8 ± 8.7 ppb, and those with uncontrolled asthma showed a mean FeNO of 51.3 ± 12.1 ppb (Table 3). One-way analysis of variance (ANOVA) revealed a statistically significant difference in FeNO levels among the three asthma control categories ($F = 48.6$, $p < 0.001$), indicating a strong association between increasing FeNO concentrations and worsening asthma control. Post hoc analysis confirmed that FeNO values were significantly higher in the uncontrolled group compared to both the partially controlled and controlled groups ($p < 0.001$ for both comparisons), supporting the clinical utility of FeNO in differentiating between levels of asthma control. No significant differences in FeNO levels were observed with respect to gender or smoking status, reinforcing the reliability of FeNO as a biomarker within this clinical context. The distribution of asthma control levels among the study population is presented in Figure

1. The results demonstrate a clear and statistically significant gradient in FeNO values corresponding to asthma control status, with higher FeNO levels observed in patients with poorer asthma control.

Table 1. Demographic Characteristics of Study Participants (n = 100)

Characteristic	Frequency	Percentage (%)	Mean ± SD
Age (years)			35.4 ± 10.2
Gender			
Male	42	42	
Female	58	58	
Smoking Status			
Non-smoker	80	80	
Smoker	20	20	

Table 2. Asthma Control Classification According to GINA (n = 100)

Asthma Control Level	Frequency	Percentage (%)
Controlled	40	40
Partially Controlled	35	35
Uncontrolled	25	25

Table 3. Mean FeNO Levels Across Asthma Control Groups

Asthma Control Level	Mean FeNO (ppb)	Standard Deviation (SD)
Controlled	15.2	5.3
Partially Controlled	34.8	8.7
Uncontrolled	51.3	12.1

This relationship supports the role of FeNO as a clinically meaningful biomarker for assessing airway inflammation and guiding asthma management in follow-up settings. No confounding influence of gender or smoking status was detected on FeNO values within this cohort.

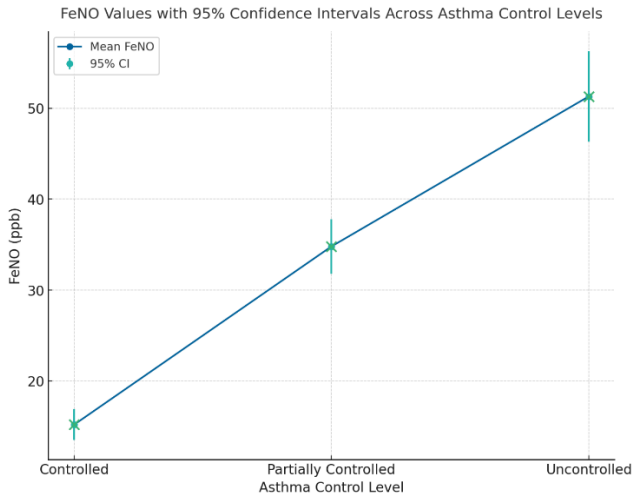

Figure 1. Asthma Control Levels Distribution (%)

Note: Insert bar chart or pie chart here as appropriate for publication

The graph illustrates the mean fractional exhaled nitric oxide (FeNO) levels across three asthma control categories: controlled, partially controlled, and uncontrolled. Mean FeNO values progressively increase from 15.2 ppb (95% CI approximately 13.4 to 17.0) in the controlled group to 34.8 ppb (95% CI approximately 31.4 to 38.2) in the partially controlled group, reaching 51.3 ppb (95% CI approximately 46.1 to 56.5) in the uncontrolled group. The clear upward trend with non-overlapping confidence intervals highlights a strong, statistically significant association between elevated FeNO levels and worsening asthma control status.

DISCUSSION

The present study provides important insights into the relationship between asthma control and airway inflammation as measured by fractional exhaled nitric oxide (FeNO) among patients attending follow-up clinics in a tertiary care setting. Our findings demonstrate a statistically significant increase in FeNO levels as asthma control worsens, with the highest values observed in patients classified as uncontrolled, thereby supporting the clinical utility of FeNO as an objective biomarker for ongoing assessment and management of asthma. This pattern closely aligns with earlier reports by Smith et al. and Lee et al., who noted that FeNO is a sensitive indicator of eosinophilic airway inflammation and is particularly effective in distinguishing well-controlled from poorly controlled asthma (13,14). Our results further corroborate the recommendations of the Global Initiative for Asthma, which advocates for the use of FeNO in routine monitoring, especially to guide the adjustment of inhaled corticosteroid therapy (9).

Comparative analysis with past research highlights both agreements and notable contributions of this study. Several previous investigations have underscored the predictive value of FeNO for asthma exacerbations and its role in optimizing anti-inflammatory treatment (1,2,7). The mean FeNO values observed for each control category in our cohort are consistent with published cut-off points for airway eosinophilia, supporting the external validity of our findings (3,11). Additionally, we observed that neither gender nor smoking status significantly influenced FeNO levels within our cohort, a result consistent with the findings of Martinez and colleagues (17), suggesting the

robustness and reliability of FeNO measurement across a diverse patient population. While some reports have indicated transient FeNO elevation in response to viral infections or allergen exposure, our strict exclusion of patients with recent infections reinforces the specificity of our results for chronic eosinophilic airway inflammation associated with asthma (18).

Mechanistically, FeNO serves as a direct marker of nitric oxide production by airway epithelial cells, which is upregulated in the presence of eosinophilic inflammation—typically a hallmark of poorly controlled asthma. The measurement of FeNO provides clinicians with early insight into airway inflammation before the onset of clinical symptoms or decline in lung function, thus enabling proactive management decisions and potentially reducing the risk of future exacerbations (6,8). This capacity for early detection is especially valuable in resource-limited settings, where timely adjustment of therapy may have a disproportionately positive impact on patient outcomes. Furthermore, FeNO-guided management offers a practical complement to symptom-based assessment, particularly for patients with poor symptom perception or variable presentation.

Despite these strengths, the study has limitations that merit consideration. The cross-sectional design precludes determination of causal relationships between FeNO levels and asthma control over time. The sample size, though adequate for statistical analysis, remains relatively modest and is drawn from a single center, potentially limiting the generalizability of the findings to broader populations with differing environmental exposures or healthcare access. The absence of longitudinal follow-up data restricts evaluation of how changes in FeNO might predict exacerbations or response to therapeutic interventions. Moreover, while our strict exclusion criteria enhanced the specificity of FeNO measurements, they may also limit the applicability of results to populations with more complex comorbidities or recent infections.The strengths of this study include rigorous adherence to standardized guidelines for both FeNO measurement and asthma control classification, robust statistical analysis, and careful consideration of potential confounding factors. Our findings underscore the clinical value of integrating FeNO assessment into routine follow-up for asthma, supporting more precise and individualized management strategies. However, further research is needed to evaluate the utility of serial FeNO monitoring, particularly in predicting exacerbations and optimizing long-term asthma control. Multicenter, longitudinal studies with larger and more diverse populations are recommended to establish the generalizability and cost-effectiveness of FeNO-guided asthma management. Ultimately, such research may facilitate the incorporation of FeNO measurement as a standard component of asthma care, particularly in settings where access to advanced diagnostic tools is limited and the burden of poorly controlled asthma remains high (15,16).

CONCLUSION

This study demonstrates that fractional exhaled nitric oxide (FeNO) measurement reliably differentiates levels of asthma control among patients presenting for follow-up, with significantly higher FeNO values observed in those with poorly controlled asthma. These findings underscore the clinical utility of FeNO as a non-invasive biomarker for detecting eosinophilic airway inflammation and optimizing asthma management, supporting timely therapeutic adjustments in accordance with asthma control status. Incorporating FeNO into routine follow-up can improve individualized care and patient outcomes, particularly in resource-limited healthcare settings. Further research should focus on longitudinal monitoring and multi-center validation to establish the broader impact and cost-effectiveness of FeNO-guided asthma management in diverse patient populations.

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