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Diagnostic accuracy of fractional exhaled nitric oxide in asthma

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Abstract

Background: Asthma, a prevalent condition affecting 350 million individuals worldwide, manifests as airway inflammation and hyperreactivity. Fractional Exhaled Nitric Oxide (FeNO) serves as a quantifiable indicator of nitric oxide concentration in exhaled breath, providing valuable insights into inflammatory processes associated with asthma.

Objectives: To assess the diagnostic accuracy of FeNO in patients with a confirmed diagnosis of asthma.

Methodology: Retrospective data analysis of 811 adult patients at PRS Hospital, India, over an 18-month period. with a verified diagnosis of asthma. Exclusion criteria included individuals under 18 years old.

Results: Of the 811 participants, 61.1% were female (N=496), and 38.8% were male (N=315), with a mean age of 42 +/- 15.41 SD. The age group of 21-30 constituted the highest percentage at 24.78%. Sensitivity (87.7%), specificity (91.2%), positive predictive value (90.5%), negative predictive value (86.8%), and diagnostic efficacy (88.5%) were calculated to determine the diagnostic accuracy of FeNO.

Conclusion: FeNO is an effective add-on tool for the diagnosis of asthma.

Keywords: Diagnostic Accuracy; Feno; Asthma; Sensitivity; Specificity

1. Introduction

Asthma involves excessive and easily triggered contractions of the airway, both spontaneously and in response to various external and internal stimuli. This airway hyperresponsiveness accompanies increased sensory irritability of the airways and heightened mucus secretion [1]. The diverse clinical manifestations of asthma encompass a range of environmental factors interacting with the respiratory passages, leading to both immediate and prolonged inflammation. Additionally, the condition's complexity arises from the varying roles of smooth muscle contraction, edema, and the restructuring of airway elements [2].

In terms of epidemiology, asthma comprises a range of diseases, and it is increasingly apparent that the disease is heterogeneous concerning immunopathology, clinical phenotypes, response to therapies, and natural history [3,4]. Factors associated with asthma include genetic predisposition, specifically family history [1,2,5]. The disease is also linked to exposure to tobacco smoking and other inflammatory gases or particulate matter. Although not fully understood, asthma is recognized as a multi-factorial pathology influenced by both genetics and environmental exposure.

The pathophysiology of asthma involves the acute and fully reversible inflammation of the airways, often triggered by exposure to environmental stimuli. Bronchial hypersensitivity inherent in asthma then induces inflammation in the airway, resulting in increased mucus production and heightened airway resistance, particularly during expiration [1,4].

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Fractional exhaled nitric oxide (FeNO) serves as a measure of the concentration of nitric oxide in a person's exhaled breath. This gas, generated in response to an inflammatory process [7], plays a crucial role in regulating vascular and bronchial tone within the immune system. FeNO serves as a biomarker for asthma offering insights into the extent of inflammation within the lungs [8]. This particulate matter is quantifiable through a breath test, assisting clinicians in delivering more precise care. The testing generates a FeNO score, assigning a numerical value to the degree of inflammation and thus aiding in the diagnostic process for asthma. Notably, NO is released during type 2 allergic inflammation, and even in the mild stages of asthma, patients exhale NO in higher concentrations. Extensive research has explored the diagnostic and monitoring capabilities of FeNO, emphasizing its potential in asthma[9]. Existing research suggests that a threshold value of 50 ppb effectively applies to identify asthma.

Objectives

Tto assess FeNO's diagnostic accuracy in patients with a confirmed asthma diagnosis, validated through a pulmonary function test. The evaluation focussed on determining sensitivity, specificity, positive predictive value, negative predictive value and diagnostic efficacy to ensure accuracy.

2. Materials and methods

This retrospective study was conducted at Pulmonary and Sleep medicine department of PRS Hospital, India. The medical records of all consecutive FeNO tests conducted in PRS Hospital from January 2014 to June 2015 over a period of 18 months were analysed for the study. The study included 811 patients with a confirmed asthma diagnosis, excluding those below the age of 18. Data collection and analysis utilized electronic medical records and hospital medical documentation. A FeNO value of more than 50 ppb was taken as the cut-off point for diagnosis of asthma.

2.1. Statistical analysis

The statistical analysis of the study was done using Epi info 7 software for evaluating sensitivity, specificity, positive predictive value, negative predictive value and, diagnostic efficacy. Data entry was done using Microsoft 365.

3. Results

The study analyzed the medical documentation and Electronic Medical Records of patients who underwent the FeNO test in the Pulmonology department at PRS Hospital, India. In total, 811 patients participated in the study, with females comprising the majority at 61.1% (n=496) compared to males at 38.8% (n=315). The patients' mean age was 42 +/- 15.41 SD years, covering a broad age range from 18 to 86 years, with the majority falling between 21 and 60 years. Notably, the age group of 21-30 accounted for the highest percentage at 24.7%. Among the 811 patients, 18 (2.2%) had Diabetes Mellitus, 23 (2.8%) had hypertension, and 26 (3.2%) had hypothyroidism.

To assess FeNO's diagnostic accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic efficacy were computed. When the diagnostic cut-off point was kept as 50ppb or more in asthma, the findings revealed a sensitivity of 87.7%, specificity of 91.2%, positive predictive value of 90.5%, negative predictive value of 86.8%, and diagnostic efficacy of 88.5%.

Table 1 Baseline characteristics**.**

	Number	**Percentage**
Age (in years)		
18-20	46	5.6
21-30	201	24.7
31-40	159	19.6
41-50	148	18.2
51-60	134	16.5
61-70	96	11.8
71-80	26	3.2

>80	1	0.1
Gender:		
Female	496	61.1
Male	315	38.8
Comorbidities:		
Diabetes mellitus	18	2.2
Hypertension	23	2.8
Hypothyroidism	26	3.2

Table 2 Diagnostic Accuracy

Diagnostic Accuracy	Percentage
Sensitivity	85.7
specificity	91.2
Positive Predictive value	90.5
Negative Predictive value	86.8
Diagnostic efficacy	88.5

4. Discussion

This study, conducted at PRS hospital in India, aimed to assess the diagnostic accuracy of Fractional Exhaled Nitric Oxide in patients with asthma. 811 patients participated in the study. The age distribution, with the highest percentage in the 21-30 age group, sheds light on the prevalence of asthma in specific age brackets. The following calculated parameters, sensitivity (87.7%), specificity (91.2%), positive predictive value (90.5%), negative predictive value (86.8 %), and diagnostic efficacy (88.5%), indicate promising results for FeNO as an effective diagnostic tool for asthma.

According to Antonius Schneider et al, a multi-center diagnostic study involving patients was conducted to assess FeNO measurement and follow after 12 weeks. The study included 308 patients, of whom 186 (60·4%) were female with an average age of 44·7 years. Among the participants, 161 (52·3%) had asthma. Statistical analysis revealed a ssensitivity of 0·24, a specificity of 0·99, positive predictive value of 0·95, and negative predictive value of 0·54 for FeNO> 50ppb [10].

A study conducted by Enrico Hefflerb et al revealed that elevated FeNO values increase the likelihood of the patient being diagnosed with asthma. The data demonstrated a sensitivity of 43 – 88%, a specificity of 60-92% for asthma diagnosis, with Positive Predictive Value and Negative Predictive Values ranging from 54-95% and 65-93% respectively [11].

Christina Kellerer et al, found that FeNO cut off >50 ppb is appropriate for diagnosing asthma (sensitivity 35%, specificity 92%). In cases of allergic rhinitis and wheezing, FeNO would have a higher cut off level of > 33 ppb with a PPV >70% [12].

In a separate study conducted by Ahmed Badar et al, Fractional exhaled nitric oxide (FeNO) emerged as a viable biomarker for airway inflammation. They explored the correlation between FeNO, blood eosinophil levels, IgE, and other inflammatory cytokines. The study revealed a positive correlation between FeNO and blood eosinophils as well as total blood IgE. However, no association was found between FeNO and serum inflammatory cytokines. The study identified a higher predictive ability when FeNO exceeded 50ppb. The cutoff point for blood eosinophils (≥4.0%) and total IgE (≥350) demonstrated sensitivity rates of 66.7% and 66.7%, with specificities of 60.0% and 63.6% respectively [13].

In a study carried out by Lixiu He et al, 265 patients with asthma were studied from October 2014 to June 2015. Positive correlations were observed for gender (r=0.138, P=0.005), atopy (r=0.598, P<0.001) and rhinitis (r=0.485, P <0.001) while negative correlations was found for age (r=−0.220, P<0.001). statistical analysis was done demonstrating sensitivity of 79.9%, specificity of 54.7%, positive predictive value of 77.9%, and negative predictive value 58.1%[14].

As explored in a study by Zhi Guo et al, an analysis of 25 studies involving 3983 subjects was conducted. For the entire group of participants, sensitivity, specificity, and diagnostic odds ratio were reported as 72% (95% CI, 70-74%), 78% (95%CI, 76-80%) and 15.92 (95% CI, 10.70-23.68), respectively[15]

Abbreviation

- FeNO - Fractional Exhaled nitric oxide.
- NO - Nitric oxide.
- SD - Standard Deviation.
- CI - Confidence Interval.
- PPB - Parts per billion.
- IGE - Immunoglobin E.
- PPV - Positive predictive value.
- NPV - Negative predictive value.
- P - Probability.
- r - Correlation coefficient.

5. Conclusion

The high sensitivity and specificity values suggest that FeNO is adept at correctly identifying both positive and negative cases. The positive predictive value signifies a low rate of false positives, which shows its reliability. Similarly, the negative predictive value provides insight to the tool's capability to accurately rule out asthma in non-afflicted individuals. The overall diagnostic efficacy of 88.53% is indicative of FeNO's effectiveness in distinguishing asthma cases within the studied population. In conclusion, this retrospective study supports FeNO as a valuable add-on tool in the diagnosis of asthma.

Compliance with ethical standards

Disclosure of conflict of interest

Conflict of interest: Nil.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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