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Correlation of Fractional Exhaled Nitric Oxide [Feno], Spirometry, and Symptom Control in Childhood Asthma, A Cross-Sectional Study

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KEYWORDS
Childhood asthma, FeNO, FEV1%, spirometry, symptom control

ABSTRACT:

Introduction:

Childhood asthma is a common respiratory condition, with a challenging symptom management. Fractional exhaled nitric oxide [FeNO] and spirometry are key tools for assessing airway inflammation and lung function, contributing to personalized treatment strategies in pediatric patients.

Aims and Objectives:

To investigate the correlation between FeNO, spirometry, and symptom control in childhood asthma.

Materials and Methods:

This cross-sectional study was conducted at the pediatric respiratory clinic of CHRI from September 2022 to September 2023, with ethical approval and informed consent obtained. Children were evaluated based on symptom control scores per GINA guidelines, followed by spirometry and FeNO analysis. Statistical analysis was performed using SPSS, and Spearman's rank correlation was used to assess relationships between variables, with $p<0.05$ considered significant.

Results:

Among participants, 13.8% had well-controlled, 70% partly controlled, and 16.3% uncontrolled symptoms. Mean FeNO was 25.2 ± 16.9 ppb, and mean FEV1% was 78.7 ± 13.2%. Significant correlations were observed between FEV1% and symptom control [p=0.0005], FeNO and symptom control [p=0.0005], and FeNO and FEV1% [p=0.005].

Conclusion:

FeNO shows an indirect correlation with symptom control and FEV1%. When spirometry is not feasible, FeNO may provide indirect evidence for asthma management.

Introduction:

Asthma, a heterogeneous disease marked by chronic airway inflammation, affects 1–18% of the global population and approximately 14% of children worldwide, making it the most prevalent chronic respiratory condition in childhood [1, 2]. The disease has significant social and economic impacts, leading to nearly 250,000 premature deaths annually [3]. The prevalence of asthma symptoms has been increasing among children and adolescents, particularly in developing countries, due to factors such as genetic predisposition, environmental exposure to passive smoking, microbial contamination, and air pollution [4]. Urbanization and industrialization have further exacerbated this trend, highlighting the role of air pollution in asthma development.

The primary objective of asthma treatment is to achieve and maintain symptom control. Spirometry is the gold standard pulmonary function test used to objectively evaluate lung function in children with asthma, assessing the extent of airway obstruction and response to treatment [6, 7]. However, many asthmatic children exhibit normal forced expiratory volume at 1 second [FEV1] values, even

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when symptomatic, which raises questions about the utility of spirometry in accurately assessing asthma severity in both the short and long term [8, 9].

To complement spirometry, inflammatory markers like Fractional Exhaled Nitric Oxide [FeNO] are crucial for monitoring asthma, as they provide a non-invasive method to assess airway inflammation, a key component in asthma pathogenesis [10, 11]. This study aims to investigate the correlation between FeNO, spirometry, and symptom control in childhood asthma, providing a more comprehensive understanding of disease severity and management [12].

Methodology:

The study was conducted after obtaining clearance from the institutional ethics committee and obtaining informed consent. A sample size of 77 was calculated using regression methods-correlation coefficient formula in nMaster software version 2.0 with 5% alpha error and power of 80% and r value of -0.304 taken from Dabbaghzadeh, A et al study [10]. A cross-sectional study was carried out at the paediatric respiratory clinic of a tertiary care hospital in Southern India over a period of one year, from September 2022 to September 2023. The study population included all children aged 7 to 18 years with suspected asthma or those already diagnosed with asthma according to GINA guidelines.

Children with acute exacerbation of asthma, those on inhalational corticosteroids or oral corticosteroid therapy in the last two weeks, those with other pulmonary comorbidities, those unable to perform spirometry and FeNO properly, and those whose parents refused consent were excluded from the study. After obtaining history and conducting a physical examination, the children were categorised according to the GINA guidelines symptom control score into well-controlled, partly controlled, and uncontrolled asthma. The presence of the following symptoms [daytime symptoms >twice a week, night awakenings due to asthma, use of SABA-reliever medications >twice a week, activity limitation] in the previous four weeks was evaluated. Patients scoring 0 were categorised as well-controlled asthma, those with 1–2 symptoms as partly controlled, and those with 3–4 symptoms as uncontrolled asthma.

FeNO was measured according to the American Thoracic Society guidelines using a portable analyser [Niox VERO] controlled by an acoustic emission signal to maintain an expiratory flow rate of 50 ml/sec. FeNO values were categorised as low, high, or indeterminate: <20 ppb as low FeNO, >35 ppb as high FeNO, and 20–35 ppb as indeterminate FeNO.

Spirometry was performed by a qualified practitioner according to American Thoracic Society guidelines. FEV1% was categorised as follows: FEV1 80–100% as mild airway obstruction, 50–80% as moderate airway obstruction, 30–50% as severe airway obstruction, and <30% as very severe airway obstruction.

Each child underwent both spirometry and FeNO testing. Additionally, anthropometric data [such as age and gender] and general physical examination findings were collected at the time of assessment.

Statistical analysis was conducted using SPSS software v 29. Percentage and frequency analysis were used for categorical variables, while mean and standard deviation were employed for continuous variables. Spearman's rank correlation was utilised to assess the relationship between variables, with a p-value of 0.05 considered statistically significant.

Results:

A total of 80 children aged 7 to 18 years were included in the study. The majority of participants [52.4%] were between 7 and 10 years old, followed by 33.8% aged 11 to 14 years, and 13.8% aged 15 to 18 years. There was a male predominance in the study, with 63% of participants being male and 37% female [Table 1].

Based on the GINA guidelines, 13.8% of the participants had well-controlled asthma, 70% had partly controlled asthma, and 16.2% had uncontrolled asthma [Table 2].

The study found significant correlations between FeNO levels, symptom severity, and FEV1%. Children with well-controlled asthma had a mean FEV1% of 88.5 ± 3.7, while those with partly controlled and uncontrolled asthma had mean FEV1% values of 80.3 ± 11.8 and 63.2 ± 11.9, respectively [p = 0.0005]. Similarly, FeNO levels were significantly different across the symptom control groups, with mean values of 9.8 ± 4.5 ppb for well-controlled, 22.7 ± 12.0 ppb for partly controlled, and 48.7 ± 19.2 ppb for uncontrolled asthma [p = 0.0005] [Table 3].

The analysis demonstrated a strong inverse correlation between FeNO and FEV1% [r = -0.524, p = 0.0005] [Figure1], and a positive correlation between FeNO and symptom severity [r = 0.669, p = 0.0005]. Additionally,

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symptom severity negatively correlated with FEV1% [r = -0.599, p = 0.0005] [Table 5].

Post-hoc Tukey HSD analysis revealed significant differences in FEV1% between the uncontrolled asthma group and both the well-controlled and partly controlled groups [p = 0.005]. Similarly, FeNO values were significantly different across all symptom control groups, confirming the distinctiveness of FeNO as an indicator of asthma severity [Table 4].

Table 1: Characteristics of the study population

Characteristics	Number [80]	Percentage [%]
Age		
7 to 10 years	42	52.4
11 to 14 years	27	33.8
15 to 18 years	11	13.8
Gender		
Male	50	63
Female	30	37

Table 2: Symptom control [GINA guidelines]

Characteristics	Number [80]	Percentage [%]
Well controlled	11	13.8
Partly controlled	56	70
Uncontrolled	13	16.2

Table 3: Correlation between FeNO, symptom severity and FEV1

Variable	Symptom severity score	N	Mean [SD]	F-value	*p*-value
FEV1%	Well controlled	11	88.5 +- [3.7]	17.560	0.0005*
	Partly controlled	56	80.3 +-[11.8]		
	Uncontrolled	13	63.2 +-[11.9]		
FeNO	Well controlled	11	9.8 +- [4.5]	31.101	0.0005*
	Partly controlled	56	22.7 +- [12.0]		
	Uncontrolled	13	48.7 +-[19.2]		

*p<0.05 – statistically significant

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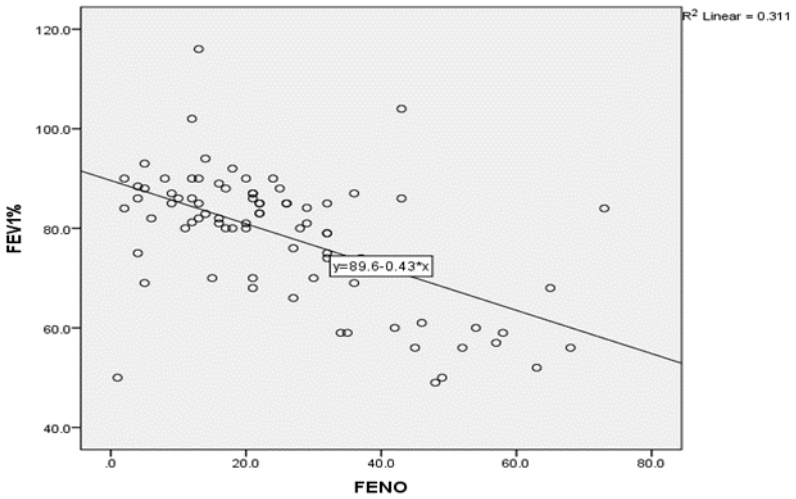

Figure 1: Relationship between FeNO vs FEV1%

Table 4: Post-hoc Tukey HSD multiple comparison analysis between FeNO, symptom severity and FEV1

Dependent Variable			MD [I-J]	Std. Error	p-value	95% CI	
						LB	UB
FEV1%	Well controlled	Partly controlled	8.1838	3.6534	0.071	-0.54	16.91
		Uncontrolled	25.260	4.5383	0.005*	14.41	36.10
	Partly controlled	Uncontrolled	17.076	3.4104	0.005*	8.92	25.22
FeNo	Well controlled	Partly controlled	-12.9140	4.2063	0.008 *	-22.96	-2.86
		Uncontrolled	-38.8741	5.2250	0.005 *	-51.36	-26.38
	Partly controlled	Uncontrolled	-25.9602	3.9265	0.005 *	-35.34	-16.57

*p<0.05 – statistically significant

Table 5: Comparison of symptom severity, FeNO and FEV1%

Variable	Correlation coefficient	p-value
Symptom severity and FeNO	0.669	0.0005*
Symptom severity and FEV1%	-0.599	0.0005*
FeNO and FEV1%	-0.524	0.0005*

*p<0.05 – statistically significant

Discussion:

The findings from our study provide important insights into the correlation between Fractional Exhaled Nitric Oxide [FeNO], spirometry [specifically FEV1%], and symptom control in children with asthma. The mean age of participants was 10.7 years, with the majority in the 7–10-year age group, consistent with similar studies by Dabbaghzadeh et al. [10] and Salviano et al. [16], which suggest that childhood asthma predominantly affects younger children. The male predominance observed in our study [63%] aligns with these studies, indicating a higher

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prevalence of asthma among boys during childhood [10, 16].

Our study demonstrated a significant inverse relationship between FeNO levels and FEV1%, as well as a positive relationship between FeNO levels and asthma symptom severity. These results are in line with the findings of Salviano et al. [16] and Dabbaghzadeh et al. [10], who also reported that higher FeNO levels are associated with poorer asthma control. While the mean FEV1% in our study indicated mild obstruction, other studies, such as those by Salviano et al. [16] and Kumar et al. [17], have reported more severe obstruction in children with poorly controlled asthma. This variation could be due to differences in the study populations or methodologies, including the inclusion of patients with varying degrees of asthma severity.

The strong correlation between symptom control and both FeNO and FEV1% in our study highlights the potential of FeNO as a complementary tool to spirometry in asthma management. Although spirometry remains the gold standard for assessing lung function, its limitations—particularly in children who may exhibit normal FEV1% values despite being symptomatic—necessitate the use of additional markers like FeNO. Our findings support existing evidence that FeNO, as a non-invasive and easy-to-administer test, provides valuable information on airway inflammation and can assist in guiding asthma management, especially in settings where spirometry may not be feasible [10, 11].

However, this study has certain limitations. The relatively small sample size and cross-sectional design restrict the generalizability of our findings. Larger, longitudinal studies are necessary to confirm these results and further explore the long-term relationship between FeNO, FEV1%, and asthma control. Additionally, our study did not account for various asthma comorbidities that could have influenced the outcomes. Future research should include a more comprehensive assessment of these factors.

Conclusion:

This study underscores the importance of FeNO as a non-invasive and practical tool for assessing airway inflammation in pediatric asthma. The significant correlations between FeNO, FEV1%, and symptom control emphasize its potential role in complementing spirometry in asthma management. Given its ease of use, FeNO is particularly useful in outpatient settings, providing clinicians with an additional objective measure to assess disease severity and tailor treatment strategies.

In conclusion, incorporating FeNO measurements into routine asthma management could enhance the accuracy of asthma control assessments and improve outcomes for pediatric patients. Further studies with larger sample sizes and longitudinal follow-up are needed to validate these findings and explore the potential of FeNO in guiding long-term asthma management.

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