Original Article

Identifying the predictive value of fractional exhaled nitric oxide (FeNO) for uncontrolled asthma in 3–7-year-old Thai children

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Background: Fractional exhaled nitric oxide (FeNO) is the method for monitoring airway inflammation. However, a singular FeNO value cutoff may not adequately represent the control status across different ages and demographics. This study aimed to evaluate the correlation between FeNO values and asthma control levels, identifying an optimal cutoff point for children aged 3 to 7 years.

Methods: This cross-sectional study was conducted at Naresuan University Hospital from April 1, 2023 to July 31, 2023. Inclusion criteria were asthmatic patients aged 3 to 7 years who were capable of following commands. Exclusion criteria included children who had a coronavirus disease 2019 (COVID-19) infection, those experiencing difficulty breathing, or unable to perform the FeNO measurement. Eligible patients were classified according to their level of asthma control and underwent FeNO testing.

Results: Out of 108 participants who successfully completed FeNO measurements, a significant difference in FeNO values was observed across controlled, partially controlled, and uncontrolled asthma groups, with uncontrolled asthma presenting significantly higher values. The optimal FeNO cutoff point for predicting uncontrolled asthma was identified as ≥15 ppb with a sensitivity 46.7%, specificity 86.0%, positive predictive value (PPV) 35.0%, negative predictive value (NPV) 90.9%.

Conclusions: This study established a significant correlation between FeNO levels and uncontrolled asthma, FeNO cutoff point ≥15 ppb as the optimal value in predicting uncontrolled asthma in Thai children aged 3–7 years. Factors such as uncontrolled allergic rhinitis, symptoms at onset, smoking exposure, treatment compliance, and inhaled corticosteroid (ICS) usage were associated with FeNO values. The application of FeNO measurement should be integrated with clinical assessments and consideration of these associated factors.

Keywords: Children; fractional exhaled nitric oxide (FeNO); nitric oxide (NO); uncontrolled asthma; prediction

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Introduction

Asthma, a chronic inflammatory disorder of the airways, poses substantial impact on patients' quality of life, necessitating effective control as a principal objective in its management. The Global Initiative for Asthma (GINA) 2022 guidelines (1) underscore the importance of evaluating control levels through clinical and spirometry data to assess airway obstruction. However, spirometry presents challenges

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in young children, particularly those under 6 years of age.

Nitric oxide (NO), produced from the respiratory epithelium as a byproduct of eosinophilia inflammation and L-arginine oxidation, serves as a biological mediator implicated in airway inflammation (2-4). The measurement of fractional exhaled nitric oxide (FeNO) has emerged as a novel tool for monitoring NO in exhaled breath. It is useful assessing airway inflammation and, when combined with clinical assessments, predicting future risk (5,6). Elevated FeNO values are predominantly associated with eosinophilic airway inflammation and type 2 asthma inflammation (7,8). This non-invasive, simple tool is particularly advantageous for use in children as young as 3 to 4 years old (9).

The American Thoracic Society (ATS) (3) and the European Respiratory Society (ERS) (10), in 2005 recommended reference FeNO values for both children and adults. However, FeNO values are influenced by various factors such as age, gender, race, height, and atopy (11). Research in Thailand conducted by Suksawat *et al.* on healthy children indicated that mean FeNO values in the 6–10 years age group are lower than in older children and lower than the values reported in other countries (12). Consequently, a single FeNO cutoff value may not accurately identify uncontrolled asthma across diverse populations. Uncontrolled asthma is associated with increased exacerbations and a higher degree of airway inflammation. Identifying a correlation between uncontrolled asthma and FeNO values could enhance management strategies. Therefore, this study aims to evaluate FeNO values in relation to asthma control levels in Thai children aged 3 to 7 years, aiming to identify an optimal cutoff point and associated factors influencing FeNO levels, thereby contributing to tailored management approaches. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-383/rc).

Highlight box

Key findings

- A fractional exhaled nitric oxide (FeNO) cutoff point of ≥15 ppb was found to predict uncontrolled asthma in Thai children 3–7 years (sensitivity 46.7%, specificity 86%).

What is known and what is new?

- Previous studies have shown that various factors, including age, gender, race, height, and atopy can affect FeNO values. Additionally, a single FeNO cutoff value may not accurately identify uncontrolled asthma across diverse populations.
- This study highlights that younger children exhibit lower FeNO values. Differences in age and ethnicity showed varying FeNO values for predicting uncontrolled asthma.

What is the implication, and what should change now?

- FeNO values should be interpreted in conjunction with clinical symptoms to guide asthma treatment decisions. In Thai children aged 3–7 years with symptomatic asthma, a FeNO value ≥15 ppb may warrant an increase inhaled corticosteroid.

Methods

Study design

A cross-sectional study was conducted at the pediatric tertiary care center of the Naresuan University Hospital in Phitsanulok, Thailand, from April 1, 2023 to July 31, 2023. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Naresuan University Institutional Review Board (No. P3-0001/2566). Informed consent was obtained from all participants and their parents.

Subjects

This study was conducted on asthmatic Thai children who visited the outpatient and inpatient departments at Naresuan University Hospital. Inclusion criteria were asthmatic patients aged 3 to 7 years, capable of following FeNO measurement instructions. Children diagnosed with coronavirus disease 2019 (COVID-19) infection, those experiencing difficulty breathing, or those unable to perform the FeNO measurement were excluded from the study. A minimal sample size for estimating population mean was 44 subjects.

Study procedure

All participants underwent comprehensive history taking, including underlying diseases, respiratory symptoms, and current medication use. Screening for COVID-19 infection was conducted for those suspected of having the infection. The patients were categorized according to the level of asthma control as outlined in the GINA 2022 guidelines (1)—well controlled, partly controlled, and uncontrolled—based on symptoms experienced in the preceding four weeks according to the following criteria: (I) daytime asthma symptoms more than twice per week; (II) nocturnal awakenings due to asthma; (III) use of short-

acting beta-agonist (SABA) relievers for symptoms more than twice per week; and (IV) any activity limitation due to asthma. Absence of these symptoms indicated well-controlled asthma, the presence of 1–2 symptoms indicated partly controlled asthma, and 3–4 symptoms indicated uncontrolled asthma.

Demographic and anthropometric data were collected from each participant. The FeNO level was measured using electrochemical sensor of the NObreath® device. A single technician, who explained and supervised the procedure, conducted the FeNO test. Participants were instructed to exhale into the mouthpiece for 10 seconds. The test was terminated if the participant failed to complete it more than 10 times, experienced difficulty breathing, or refused to continue. Healthcare providers closely monitored the patients during and after the FeNO test.

Statistical analysis

Quantitative variables were expressed as mean and standard deviation (SD), while qualitative variables were presented as percentages. Comparisons among variables and levels of asthma control were conducted using the Chi-squared test and analysis of variance (ANOVA). The FeNO levels across different groups were compared using the Kruskal-Wallis test. The association between factors and FeNO levels was analyzed using a generalized linear mixed model. The diagnostic capability of FeNO levels for identifying uncontrolled asthma was assessed through receiver operating characteristic (ROC) curve analysis, with the optimal FeNO level cutoff determined by the Youden index. A P value of less than 0.05 was considered statistically significant for all tests. Data analyses were carried out using STATA software, version 12.0 (StataCorp., College Station, TX, USA).

Results

A total of 130 participants underwent FeNO measurement at Naresuan University Hospital, of which 22 were excluded due to inability to perform the test. Consequently, 108 participants successfully completed the FeNO measurement, comprising 72 males (66.7%) and 72 individuals (66.7%) with underlying diseases. According to the GINA 2022 guideline, asthma control was categorized as follows: 59 participants (54.6%) were well controlled, 34 (31.5%) were partly controlled, and 15 (13.9%) were uncontrolled. The mean ages for each group were 6.1±1.1, 5.8±1.2, and 6.4±1.4 years for the well-controlled, partly controlled, and uncontrolled group, respectively. Most of the patients had a normal nutritional status, as shown in *Table 1*.

Allergic rhinitis emerged as the most common underlying disease, predominantly presenting as an uncontrolled symptom in an uncontrolled group. The well controlled asthma group exhibited a higher rate of asymptomatic individuals compared to the others. Clinically significant respiratory symptoms were observed in the partly controlled and uncontrolled groups, with a statistically significant difference (P<0.001). Inhaled corticosteroid (ICS), either alone in varying doses or combined with long-acting beta agonists, were commonly used in the well-controlled and partly controlled groups than in the uncontrolled group (P<0.001).

The mean FeNO values for the well-controlled, partly, and uncontrolled asthma groups were 8.8±7.9, 8.6±6.6, and 14.7±10.8 ppb, respectively, with the uncontrolled group showing significantly higher values than the other groups (P=0.03). Excluding factors that might affect the FeNO values, such as uncontrolled allergic rhinitis, resulted in a decrease in the mean FeNO value for the well-controlled asthma group and an increase for the partly controlled asthma group, although these changes were not statistically significant (P=0.053). In terms of ICS usage, the mean FeNO values for the well-controlled, partly controlled, and uncontrolled asthma groups were 8.5±7.8, 8.6±6.7, and 19.2±12.1 ppb, respectively, with a statistical significance (P=0.01), as shown in *Table 2*.

The area under the ROC curve for FeNO levels in detecting uncontrolled asthma was 0.672 (95% CI: 0.518–0.826), as illustrated in *Figure 1*. The optimal cutoff point for FeNO values was identified as equal to greater than 15 ppb, yielding a sensitivity of 46.7%, specificity of 86.0%, positive predictive value (PPV) of 35.0%, negative predictive value (NPV) of 90.9%, and an accuracy of 80.6% (*Table 3*). The low FeNO values ranged from 1 to 7 ppb, whereas high FeNO values were ≥15 ppb, showing a significant distinction (P=0.01), as shown in *Table 4*.

Factors associated with an increase in FeNO levels included uncontrolled allergic rhinitis [incident rate ratio (IRR) 1.29, P=0.002], compliance below 80% (IRR 1.31, P=0.04), symptoms at the time of measurement (IRR 1.13, P=0.046), and uncontrolled asthma (IRR 1.67, P<0.001), all of which were statistically significant. Conversely, second-hand smoking exposure (IRR 0.78, P=0.001), use of corticosteroids (IRR 0.87, P=0.045), and use of ICS with long-acting beta agonists (IRR 0.82, P=0.003) were

Table 1 Demographic data of asthmatic children categorized by level of asthma control

Characteristics	Total (n=108)	Well-controlled (n=59)	Partly controlled (n=34)	Uncontrolled (n=15)	P value
Gender					0.39
Male	72 (66.7)	36 (61.0)	25 (73.5)	11 (73.3)	
Female	36 (33.3)	23 (39.0)	9 (26.5)	4 (26.7)	
Age (years)	6.1±1.2	6.1±1.1	5.8±1.2	6.4±1.4	0.34
Body weight (kg)	25.0±9.4	24.8±8.9	25.9±10.8	23.8±8.4	0.76
Height (cm)	116.9±10.0	116.7±9.5	116.2±11.0	118.1±10.4	0.89
Nutritional status					0.39
Normal	80 (74.1)	42 (71.2)	26 (76.5)	12 (80.0)	
Obesity	13 (12.0)	6 (10.2)	6 (17.6)	1 (6.7)	
Failure to thrive	15 (13.9)	11 (18.6)	2 (5.9)	2 (13.3)	
Co-morbidity	72 (66.7)	40 (67.8)	24 (70.6)	8 (53.3)	0.48
Allergic rhinitis	67 (62.0)	38 (64.4)	24 (70.6)	5 (33.3)	0.04*
Controlled	52 (77.6)	30 (78.9)	20 (83.3)	2 (40.0)	0.10
Uncontrolled	15 (22.4)	8 (21.1)	4 (16.7)	3 (60.0)	0.10
OSA	4 (3.7)	1 (1.7)	2 (5.9)	1 (6.7)	0.47
Snoring	1 (0.9)	1 (1.7)	0 (0.0)	0 (0.0)	0.66
Atopic dermatitis	1 (0.9)	1 (1.7)	0 (0.0)	0 (0.0)	0.66
Mild pulmonary valve stenosis	1 (0.9)	0 (0.0)	1 (2.9)	0 (0.0)	0.33
Bronchopulmonary dysplasia	1 (0.9)	1 (1.7)	0 (0.0)	0 (0.0)	0.66
Homozygous E thalassemia	2 (1.9)	0 (0.0)	1 (2.9)	1 (6.7)	0.20
Current symptoms					
No symptoms	52 (48.1)	42 (71.2)	12 (35.3)	2 (13.3)	<0.001*
Cough	42 (38.9)	8 (13.6)	21 (61.8)	13 (86.7)	<0.001*
Rhinorrhea	30 (27.8)	12 (20.3)	9 (26.5)	9 (60.0)	0.01*
Nasal congestion	4 (3.7)	0 (0.0)	1 (2.9)	3 (20.0)	0.001*
Dyspnea	6 (5.6)	1 (1.7)	1 (2.9)	4 (26.7)	<0.001*
Compliance					0.001*
≥80%	79 (73.1)	45 (76.3)	30 (88.2)	4 (26.7)	
<80%	6 (5.6)	2 (3.4)	3 (8.8)	1 (6.7)	
Medication					
Non-use ICS	26 (24.1)	15 (25.4)	1 (2.9)	10 (66.7)	<0.001*
Use ICS	82 (75.9)	44 (74.6)	33 (97.1)	5 (33.3)	<0.001
ICS usage	43 (39.8)	23 (39.0)	18 (52.9)	2 (13.3)	0.03*
Low dose	17 (15.7)	11 (18.6)	5 (14.7)	1 (6.7)	0.51
Moderate dose	17 (15.7)	10 (16.9)	7 (20.6)	0 (0.0)	0.18
High dose	8 (7.4)	2 (3.4)	5 (14.7)	1 (6.7)	0.13

Table 1 *(continued)*

Table 1 *(continued)*

Characteristics	Total (n=108)	Well-controlled (n=59)	Partly controlled (n=34)	Uncontrolled (n=15)	P value
Inhaled corticosteroid with long-acting beta agonists	40 (37.0)	21 (35.6)	16 (47.1)	3 (20.0)	0.18
Leukotriene antagonist	14 (13.0)	8 (13.6)	5 (14.7)	1 (6.7)	0.73
INS	39 (36.1)	23 (39.0)	14 (41.2)	2 (13.3)	0.14
Antihistamine	34 (31.5)	18 (30.5)	14 (41.2)	2 (13.3)	0.15
Systemic steroid	4 (3.7)	0 (0.0)	1 (2.9)	3 (20.0)	0.001*
Risk factor					
Pet exposure	42 (38.9)	22 (37.3)	14 (41.2)	6 (40.0)	0.93
Secondhand smoking	33 (30.6)	18 (30.5)	10 (29.4)	5 (33.3)	0.96
Environment[†]	47 (43.5)	23 (39.0)	17 (50.0)	7 (46.7)	0.57
Family history of asthma					0.53
Yes	18 (16.7)	11 (18.6)	6 (17.6)	1 (6.7)	
No	90 (83.3)	48 (81.4)	28 (82.4)	14 (93.3)	

Data are presented as n (%) or mean ± SD. [†]Environment, including the pollen, particulate matter, air pollution; *, statistically significant. OSA, obstructive sleep apnea; ICS, inhaled corticosteroid; INS, intranasal corticosteroid; SD, standard deviation.

Table 2 FeNO values across all asthma control groups

FeNO values	Well-controlled	Partly controlled	Uncontrolled	P value
All	59	34	15	
FeNO level (ppb)	8.8±7.9	8.6±6.6	14.7±10.8	0.03*
Exclude uncontrolled allergic rhinitis	51	30	12	
FeNO level (ppb)	8.2±6.7	8.8±6.9	14.1±11.6	0.053
Use ICS	44	33	5	
FeNO level (ppb)	8.5±7.8	8.6±6.7	19.2±12.1	0.01*
No use ICS	15	1	10	
FeNO level (ppb)	9.5±8.5	8.0	12.4±9.9	0.72

Data are presented as mean ± SD or n. *, statistically significant. FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroid; SD, standard deviation.

factors that significantly reduced FeNO values. Whereas pet exposure, family history of asthma and environment did not show correlation with FeNO value. Multivariate analysis revealed that uncontrolled allergic rhinitis, poor compliance, and uncontrolled asthma had a stronger correlation with increased FeNO values, as shown in *Table 5*.

Discussion

The FeNO test has recently become more widely used in assessing asthma control. Evaluating the level of asthma control is crucial for adjusting future risk management strategies. Our study demonstrated a significant correlation between uncontrolled asthma and higher FeNO levels, aligning with the findings of Songnuy *et al.* (13), while showing discordance with other previous studies (11,14,15). However, our results indicated that FeNO values were not effective in distinguishing between partly controlled and well controlled asthma, showing no significant difference in mean FeNO values. This could be attributed to factors

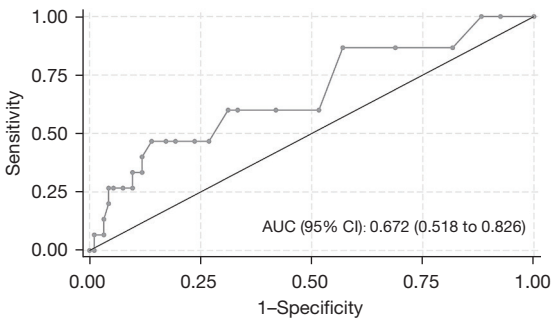

Figure 1 Area under the ROC curve for FeNO levels in detecting GINA-defined uncontrolled asthma. AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; FeNO, fractional exhaled nitric oxide; GINA, Global Initiative for Asthma.

such as uncontrolled allergic rhinitis observed in the well-controlled asthma group. After excluding this factor, FeNO values appeared slightly lower in well controlled compared to partly controlled and uncontrolled asthma, albeit not significantly. Nevertheless, FeNO testing can be useful in evaluating uncontrolled asthma.

Several studies in Asia (16-18) reported higher FeNO values across well-controlled asthma groups than those found in our study. Similar findings were observed in previous research on Thai children over 7 years old (19), suggesting that differences in age and ethnicity may influence FeNO values, with younger children exhibiting lower FeNO values due to different expiratory flow rates and reduced NO synthase activity (20,21). In this study, we were unable to compare mean FeNO values between children receiving ICS and those not receiving ICS due to the small sample size of the non-ICS group, which precluded a clear distinction of FeNO values.

The ATS recommends using FeNO cutoff points in clinical management rather than relying solely on reference values (3). However, these cutoff points vary across different guidelines (6). Our study investigated a FeNO cutoff point of ≥15 ppb for predicting uncontrolled asthma in children aged 3–7, showing high specificity (86.0%) and accuracy (80.6%) but low sensitivity (ROC =0.67). Similarly, another study in children aged 6–11 years identified an optimal FeNO cutoff point of 19 ppb (sensitivity 69%, specificity 59%; ROC =0.58) (22). These findings, along with a previous study in Thailand reporting a higher optimal cutoff point of 31 ppb in children over 7 years old (23), highlight the potential benefit of age-specific FeNO cutoff points for asthma management in children.

Our study supports the use of a FeNO cutoff point to reliably rule out well-controlled asthma. Conversely, low FeNO values (1–7 ppb) may indicate good asthma control. However, FeNO measurements should always be interpreted in conjunction with clinical symptoms to guide asthma treatment decisions. For instance, symptomatic asthma with high FeNO levels might suggest the need for increased ICS dosage, whereas low FeNO values in asymptomatic patients could potentially warrant ICS dose reduction (3,8,24).

FeNO levels are influenced by various factors (17,25). Our study found correlations between FeNO values and uncontrolled allergic rhinitis, symptoms at onset, smoking exposure, compliance, and the use of ICS. Matsunaga *et al.* also demonstrated the effect of allergic rhinitis, showing higher FeNO values in patients with both asthma and rhinitis compared to those with asthma alone (20), due to the eosinophilic airway inflammation in uncontrolled allergic rhinitis leading to increase NO synthesis (26). In contrast, second-hand smoke exposure was associated with lower FeNO values, consistent with previous studies (20,27), as smoking may downregulate NO synthase and reduce exhaled NO levels (27,28). Our findings also corroborate the correlation of FeNO values with the use of corticosteroids, especially ICS combined with long-acting beta-agonists (LABA) and good compliance, similar to Yin *et al.*'s study (29). However, the effect of varying ICS doses on FeNO values was not established. Utilizing FeNO testing can aid in optimizing management by interpreting the response to corticosteroids and adherence (30), suggesting the importance of considering these factors before interpreting FeNO values.

Limitation

This study has limitations, including a small sample size of children with uncontrolled asthma and the absence of symptom duration recording before FeNO measurement. The accuracy of FeNO testing should ideally be assessed before initiating systemic steroid treatment or new treatments, although pre-test restrictions were not feasible. For future research, we recommend longitudinal FeNO measurements before and after treatment to accurately evaluate FeNO's utility in adjusting management strategies.

Conclusions

This study has demonstrated a significant correlation

Table 3 ROC analysis of FeNO levels between uncontrolled and well controlled with partly controlled groups

Cutoff ≥ FeNO level	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
2	100.0	7.5	14.9	100.0	20.4
3	100.0	11.8	15.5	100.0	24.1
4	86.7	18.3	14.6	89.5	27.8
5	86.7	31.2	16.9	93.5	38.9
6	86.7	43.0	19.7	95.2	49.1
7	60.0	48.4	15.8	88.2	50.0
8	60.0	58.1	18.8	90.0	58.3
9	60.0	66.7	22.5	91.2	65.7
10	60.0	68.8	23.7	91.4	67.6
11	46.7	73.1	21.9	89.5	69.4
12	46.7	76.3	24.1	89.9	72.2
13	46.7	80.6	28.0	90.4	75.9
14	46.7	82.8	30.4	90.6	77.8
*15	46.7	86.0	35.0	90.9	80.6
16	40.0	88.2	35.3	90.1	81.5
17	33.3	88.2	31.3	89.1	80.6
19	33.3	90.3	35.7	89.4	82.4
20	26.7	90.3	30.8	88.4	81.5
22	26.7	92.5	36.4	88.7	83.3
24	26.7	94.6	44.4	88.9	85.2
25	26.7	95.7	50.0	89.0	86.1
27	20.0	95.7	42.9	88.1	85.2
29	13.3	96.8	40.0	87.4	85.2
31	6.7	96.8	25.0	86.5	84.3
34	6.7	98.9	50.0	86.8	86.1
38	0.0	98.9	0.0	86.0	85.2
41	0.0	100.0	N/A	86.1	86.1

*, optimal cutoff point. ROC, receiver operating characteristic; FeNO, fractional exhaled nitric oxide; PPV, positive predictive value; NPV, negative predictive value.

Table 4 The range of FeNO values in distinguishing level of control

Range of FeNO values	Controlled and partly controlled	Uncontrolled	P value
Low FeNO (1–7 ppb)	54 (58.1)	6 (40.0)	0.01*
Intermediate FeNO (8–14 ppb)	26 (28.0)	2 (13.3)	
High FeNO (≥15 ppb)	13 (14.0)	7 (46.7)	

Data are presented as n (%). *, statistically significant. FeNO, fractional exhaled nitric oxide.

Table 5 Factors associated with FeNO levels: generalized linear mixed model analysis

Factors	Univariate		Multivariate	
	IRR (95% CI)	P value	Adjusted IRR (95% CI)	P value
Uncontrolled AR	1.29 (1.1, 1.52)	0.002*	1.29 (1.08, 1.54)	0.005*
Second hand smoking	0.78 (0.68, 0.9)	0.001*	0.74 (0.64, 0.85)	<0.001*
Pet exposure	0.96 (0.85, 1.13)	0.53	–	–
Environment	1.05 (0.93, 1.18)	0.46	–	–
Family history of asthma	1.08 (0.92,1.26)	0.37	–	–
Symptom at onset	1.13 (1, 1.28)	0.046*	0.9 (0.78, 1.05)	0.18
Controlled medication				
Use corticosteroid	0.87 (0.76, 0.99)	0.045*	0.82 (0.66, 1.01)	0.06
ICS	1.06 (0.93, 1.2)	0.38	0.87 (0.35, 2.18)	0.77
ICS with LABA	0.82 (0.72, 0.94)	0.003*	0.73 (0.29, 1.84)	0.51
Leukotriene antagonist	0.83 (0.68, 1.01)	0.06	0.88 (0.72, 1.08)	0.21
Compliance				
≥80%	0.9 (0.78, 1.04)	0.16	1.5 (1.19, 1.89)	0.001*
<80%	1.31 (1.01, 1.68)	0.04*	1.97 (1.46, 2.64)	<0.001*
Group				
Partially controlled	0.98 (0.85, 1.13)	0.75	0.98 (0.84, 1.14)	0.77
Uncontrolled	1.67 (1.43, 1.96)	<0.001*	1.97 (1.62, 2.39)	<0.001*

*, statistically significant. Use corticosteroid: including the systemic corticosteroid, inhaled corticosteroid and inhale corticosteroid with long-acting beta agonist. FeNO, fractional exhaled nitric oxide; AR, allergic rhinitis; ICS, inhaled corticosteroid; LABA, long-acting beta agonist; IRR, incident rate ratio; CI, confidence interval.

between FeNO values and uncontrolled asthma. A cutoff point of FeNO equal to greater than 15 ppb was identified as optimal for predicting uncontrolled asthma in Thai children aged 3 to 7 years. Factors associated with FeNO values included uncontrolled allergic rhinitis, symptoms at onset, exposure to smoking, adherence to treatment, and the use of ICS. The application of FeNO testing should be combined with the assessment of clinical symptoms and consideration of these associated factors for a comprehensive evaluation.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Naresuan University Institutional Review Board (No. P3-0001/2566). Informed consent was obtained from all participants and their parents.

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