Evaluation and Correlation of Serum Immunoglobulin E and Vitamin D Levels in Asthma Patients

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Abstract

Background: Asthma is a chronic airway inflammation, often linked with elevated IgE levels and immune dysregulation. Vitamin D, known for its immune-modulatory effects, may influence asthma severity. This study aims to explore the relationship between serum IgE and vitamin D levels in adult asthma patients and their correlation with asthma severity. **Material and Methods:** A one-year, hospital-based observational study was conducted at Medical College & Hospital, Kolkata, on 100 adult asthma patients. Exclusion criteria included recent bronchodilator use, immunocompromised status, or inability to perform spirometry. Data collected included patient history, examination, spirometry, CBC, chest X-ray, and serum IgE and vitamin D levels (via chemiluminescence). Asthma severity was classified according to GINA guidelines. Statistical analysis was performed using SPSS v24 and GraphPad Prism 5, with t-tests, ANOVA, chi-square tests, and Pearson correlation. **Results:** The study involved 100 patients (mean age 34.94 ± 12.96 years; 63% male), with 20% mild, 47% moderate, and 33% severe asthma. Significant associations were found between asthma severity and serum IgE ($P = 0.0004$), vitamin D ($P = 0.00002$), and eosinophil count ($P = 0.0001$). Severe cases had the highest IgE (1436.76 IU/ml) and lowest vitamin D (13.29 ng/ml). A weak negative correlation ($R = -0.42$, $P = 0.000014$) was observed between IgE and vitamin D. **Conclusion:** The study indicates a significant association between serum IgE, vitamin D levels, and asthma severity, suggesting their potential role as biomarkers in asthma management. Further research into vitamin D supplementation as an adjunct therapy is warranted.

Keywords: Asthma, Serum IgE, Vitamin D, Eosinophil Count, Spirometry.

INTRODUCTION

Asthma is a heterogeneous, chronic inflammatory airway disease affecting 235–330 million people worldwide as of 2018.[1,2] A family history of allergy is the strongest risk factor, with additional risk factors including intrauterine exposures, prematurity, diet, obesity, air pollution, antibiotic use, and occupational exposures.[3] Asthma's pathology primarily involves a type 2 immune response leading to airway hyperresponsiveness, inflammation, mucus secretion, and structural airway changes and high total and specific IgE levels.[4,5]

Vitamin D, apart from importance in calcium and phosphate metabolism, also modulates immune responses. Vitamin D receptors (VDRs) are present on immune cells, influencing inflammatory processes. Deficient vitamin D levels (<30 ng/ml) are associated with increased airway hyperresponsiveness, reduced lung function, poor asthma control, and steroid resistance. [6,7]

In this study, estimation of serum IgE and vitamin D levels in cases of asthma has been done to look for any correlation between the two. A significant correlation in this study opens up more avenues of research to see if vitamin D supplementation in cases of asthma can help in reduction of symptoms and morbidity of asthma.

Aims and Objectives

The aim of this study is to investigate the relationship between serum IgE and vitamin D levels in asthmatic patients of varying severity. The study specifically aims to estimate and compare serum IgE and Vitamin D levels across mild, moderate, and severe asthma cases. A key objective is to examine any potential correlation between serum IgE levels and vitamin D levels in asthmatic patients, which could provide insights into their combined impact on asthma severity and management.

MATERIALS AND METHODS

Study setting, design and duration:
After obtaining clearance from Institutional Ethics Committee (Ref No. MC/KOL/IEC/Non-spon/697/12-2017 Dated: 23rd

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December 2017), this hospital based observational descriptive study with cross sectional design was conducted at the Department of Respiratory Medicine, Medical College & Hospital, Kolkata over a period of one year from March 2018 to February 2019.

Inclusion and exclusion criteria:

All patients above 18 years diagnosed as a case of asthma attending the Department of Respiratory Medicine within the time period of study and upon receiving informed written consent were included. Patients unable to perform spirometry, asthmatic patients who have taken bronchodilators within past 24 hours prior to assessment and immunocompromised patients were excluded.

Sample size, sampling technique, and data collection: A total of 100 patients were enrolled through consecutive sampling technique. All patients were subjected to history taking, clinical examination, chest X ray, complete blood counts, serology, computerized spirometry (pre and post bronchodilator), estimation of serum IgE and vitamin D levels. Severity of asthma has been assessed by asthma symptom control questionnaire (GINA assessment of asthma control in adults) computerized spirometry (Spiro Tech, model name: CMSP-01, version1.1.0.27, Clarity Medical Pvt. Ltd., Mohali, India), and the current medications that the patient was using. Six ml of venous blood were drawn from all 100 asthmatic patients, under aseptic conditions by venipuncture using a plastic sterile disposable syringe. The sample collected was distributed in two serum vials and one EDTA vial. Complete blood count was analysed by BECKMAN COULTER DXH 500 cell counters. Absolute eosinophil count was done under a compound microscope in an Improved Neubauer's Chamber. Serum IgE and serum vitamin D was measured by Chemiluminescence immunoassay (SIEMENS CENTAUR XP). A predesigned proforma was filled up with all the above information.

Statistics: Data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS (version 26.0; IBM Corp., Armonk, NY) and GraphPad Prism (version 5). Normality of the data was assessed using the Shapiro-Wilk test. Numerical variables were summarized as mean ± standard deviation, while categorical variables were presented as frequency and percentages. To compare the means between independent (unpaired) normally distributed samples, two-sample t-tests were applied and paired t-tests were used for dependent samples. One-way analysis of variance (ANOVA) was employed to compare the means of three or more groups for normally distributed numerical data, using the F-distribution. The chi-squared test (χ^2) was used for categorical variables to test for statistical significance in the distribution. A p-value of ≤ 0.05 was considered statistically significant. Correlation between variables was evaluated using Pearson's correlation analysis, with the Pearson product-moment correlation coefficient (r) indicating the linear dependence between two variables.

RESULTS

We screened 117 patients for eligibility out of which finally 100 patients were taken for evaluation. Detailed recruitment flowchart is given in [Figure 1].

The age distribution of patients was as follows: ≤20 years (17, 17.0%), 21–29 years (29, 29.0%), 34–38 years (13, 13.0%), 42–50 years (34, 34.0%), and 55–61 years (7, 7.0%). The mean age of patients was 34.94 ± 12.96 years. [Figure 2]

37 (37.0%) patients were female and 63 (63.0%) patients were male. Among them 20 (20.0%) patients had mild asthma, 47 (47.0%) patients had moderate asthma and 33 (33.0%) patients had severe asthma. 28 (28.0%) patients had partly controlled asthma, 35 (35.0%) patients had uncontrolled asthma and 37 (37.0%) patients had well controlled asthma. In mild asthma, the mean age of patients was 38.45 ± 15.96 years. In moderate asthma, the mean age of patients was 35.42 ± 13.06 years. In severe asthma, the mean age of patients was 32.12 ± 10.34 years. Distribution of mean age vs. severity of asthma was however, not statistically significant (P = 0.2145). [Table 1]

The mean absolute eosinophil count of all patients was 527.30 ± 290.82/mm³. For mild asthma, the mean absolute eosinophil count was 328.55 ± 32.56/mm³, while in moderate asthma, it was 407.96 ± 141.03/mm³. In severe asthma, the mean count rose significantly to 817.73 ± 315.97/mm³. The distribution of mean absolute eosinophil count across the severity levels of asthma was statistically significant (P = 0.0004). [Table 1]

The mean pre FEV1/FVC ratio for all patients was 84.94 ± 9.70%. In mild asthma, the pre FEV1/FVC was 80.47 ± 12.26%, in moderate asthma, it was 88.14 ± 8.06%, and in severe asthma, it was 83.08 ± 8.79%. The distribution of pre FEV1/FVC values across asthma severity levels was statistically significant (P = 0.0041). Similarly, the mean post FEV1/FVC ratio for all patients was 87.56 ± 8.91%. In mild asthma, it was 83.34 ± 11.43%, in moderate asthma, it was 90.47 ± 8.36%, and in severe asthma, it was 85.96 ± 6.46%. The distribution of post FEV1/FVC values across asthma severity levels was also statistically significant (P = 0.0043). [Table 1]

The mean pre FEV1 for all patients was 2.04 ± 0.81 L. In mild asthma, it was 2.22 ± 0.79 L, in moderate asthma, it was 1.93 ± 0.98 L, and in severe asthma, it was 2.09 ± 0.51 L. However, the distribution of pre FEV1 values across the different asthma severities was not statistically significant (P = 0.3895). The mean post FEV1 for all patients was 2.25 ± 0.87 L. In mild asthma, it was 2.44 ± 0.82 L, in moderate asthma, it was 2.13 ± 1.09 L, and in severe asthma, it was 2.30 ± 0.46 L. This distribution of post FEV1 values across asthma severities was also not statistically significant (P = 0.3717). [Table 1]

The mean serum total IgE levels for all patients was 696.45 ± 702.23 IU/ml. In mild asthma, the mean was 136.45 ± 106.89 IU/ml, in moderate asthma, it was 414.95 ± 262.64 IU/ml, and in severe asthma, it was 1436.76 ± 736.26 IU/ml. The distribution of serum IgE levels across asthma severity levels was statistically significant (P = 0.0001). [Table 1]

The mean serum vitamin D level for all patients was 17.70 ± 7.11 ng/ml. In mild asthma, it was 22.23 ± 4.05 ng/ml, in moderate asthma, it was 18.86 ± 6.64 ng/ml, and in severe asthma, it was 13.29 ± 6.97 ng/ml. The distribution of serum vitamin D levels across the different severities of asthma was statistically significant (P = 0.00002). [Table 1]
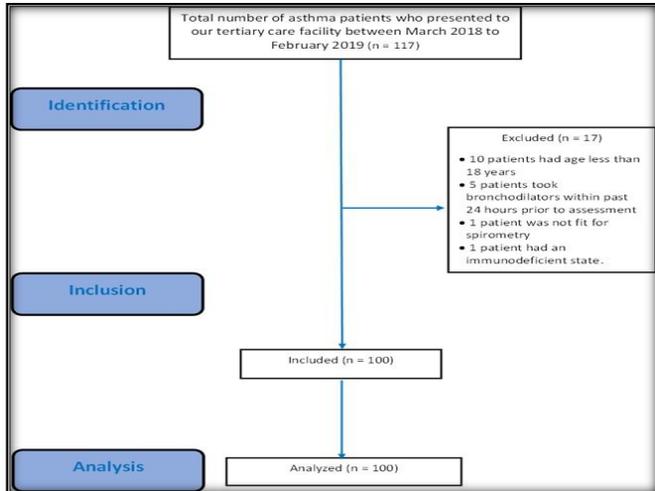
Figure 1: Patient Recruitment Flowchart as per STROBE (Strengthening the Reporting of Observational Studies in Epidemiology)

Figure 2: Distribution of severity of asthma patients based on various age groups (n = 100), (P = 0.0002).

In terms of asthma control, in mild asthma, 3 (15.0%) patients had partly controlled asthma and 17 (85.0%) patients had well-controlled asthma. In moderate asthma, 25 (53.2%) patients had partly controlled asthma, 2 (4.3%) patients had uncontrolled asthma, and 20 (42.6%) patients had well-controlled asthma. In severe asthma, all 33 (100.0%) patients had uncontrolled asthma. The association between asthma control levels and asthma severity was statistically significant (P = 0.0003). [Table 1]

Regarding the distribution of Vitamin D in relation to IgE levels, the correlation was statistically significant (P = 0.000014). The correlation coefficient (R) was -0.42, indicating a weak negative correlation between Vitamin D and IgE values. [Figure 3]
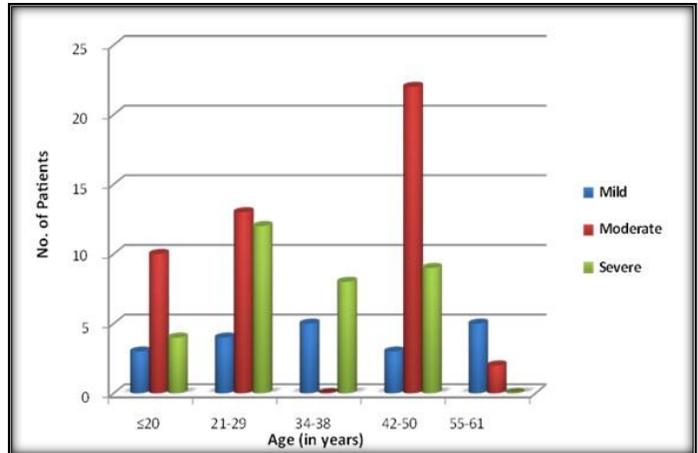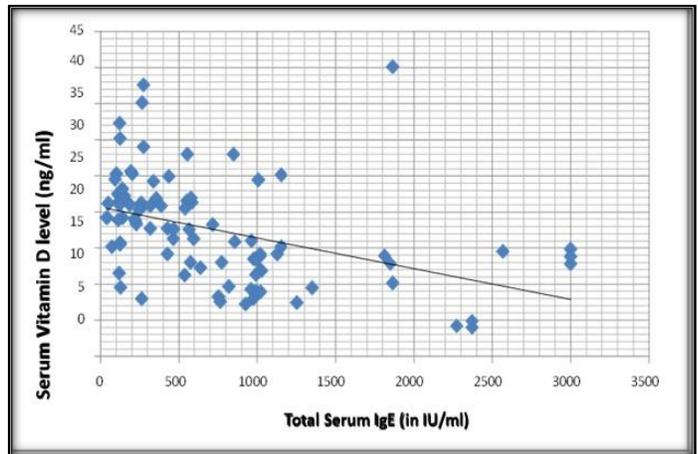

Figure 3: Scatter plot of Total serum IgE vs Serum Vitamin D levels showing moderate negative correlation. Pearson's correlation coefficient = -0.42, p < 0.001. Abbreviations: IgE – Immunoglobulin E, ng/ml – nanograms per milliliter.

Table 1: Descriptive characteristics of asthma patients in the study (n = 100)					
	Asthma Severity			Total	p - value
	Mild (n = 20)	Moderate (n = 47)	Severe (n = 33)		
Continuous Variables (Mean (Standard Deviation))					
Age	38.45 (15.9)	35.42 (13.1)	32.12 (10.3)	34.94 (12.9)	0.214
AEC (cells/mm3)	328.55 (32.6)	407.95 (141.0)	817.72 (315.9)	527.30 (290.8)	0.000*
FEV1/FVC (Pre) (%)	80.46 (12.3)	88.14 (8.1)	83.08 (8.8)	84.93 (9.7)	0.004*
FEV1/FVC (Post) (%)	83.34 (11.4)	90.47 (8.4)	85.96 (6.5)	87.55 (8.9)	0.004*
FEV1 (Pre) (L)	2.22 (0.8)	1.93 (1.0)	2.09 (0.5)	2.04 (0.8)	0.390
FEV1 (Post) (L)	2.44 (0.8)	2.13 (1.1)	2.30 (0.5)	2.25 (0.9)	0.372
Total Serum IgE (IU/ml)	136.44 (106.9)	414.95 (262.6)	1436.76 (736.3)	696.44 (702.2)	0.000*
Serum Vitamin D (ng/ml)	22.23 (4.1)	18.86 (6.6)	13.29 (6.9)	17.69 (7.1)	0.000*
Categorical Variables (n (%))					
Gender					0.113
Male	16 (80.0 %)	30 (63.8 %)	17 (51.5 %)	63 (63.0 %)	
Female	4 (20.0 %)	17 (36.2 %)	16 (48.5 %)	37 (37.0 %)	
Level of Asthma Control					0.000*
Partly controlled	3 (15.0 %)	25 (53.2 %)	0 (0.0 %)	28 (28.0 %)	
Uncontrolled	0 (0.0 %)	2 (4.3 %)	33 (100.0 %)	35 (35.0 %)	
Well controlled	17 (85.0 %)	20 (42.6 %)	0 (0.0 %)	37 (37.0 %)	
*p-value < 0.05 (statistically significant), AEC – Absolute eosinophilic count, L – Liters, FEV1 – Forced expired volume in first second, FVC – Forced vital capacity, IgE – Immunoglobulin E, Pre – Pre-bronchodilator, Post – Post-bronchodilator, IU – International Units, ng – Nanograms, ml – milliliters, mm3 – Cubic Millimeters					

DISCUSSION

The present hospital based observational study with cross sectional design was conducted in the Department of Respiratory Medicine, Medical College and Hospitals, Kolkata. The study period was from March 2018 to February 2019, with an aim to estimate and compare serum IgE, serum vitamin D levels in mild, moderate, and severe asthmatics and to see for any correlation that exists between the two. In the study, a total of hundred patients of asthma who fulfilled all the inclusion and exclusion criteria were included and data was collected according to the proforma.

Demographics: In the present study, 63 (63.0%) patients were male and 37 (37.0%) were female, with a male to female ratio of 1.702. Of the 100 patients, 20 (20%) had mild asthma, 47 (47%) had moderate asthma, and 33 (33%) had severe asthma. In mild asthma, 4 (20.0%) were female and 16 (80.0%) were male; in moderate asthma, 17 (36.2%) were female and 30 (63.8%) were male; and in severe asthma, 16 (48.5%) were female and 17 (51.5%) were male. Age distribution showed that 17 (17.0%) were ≤20 years, 29 (29.0%) were 21-29 years, 13 (13.0%) were 34-38 years, 34 (34.0%) were 42-50 years, and 7 (7.0%) were 55-61 years. The mean age of patients was 34.94 ± 12.96 years. In mild asthma, the mean age was 38.45 ± 15.96 years, in moderate asthma it was 35.43 ± 13.06 years, and in severe asthma, it was 32.12 ± 10.34 years. The distribution of mean age vs. severity of asthma was not statistically significant (P = 0.2145). According to Zein GJ et al.[8] the probability of severe asthma increases with age until 45 years, after which it increases at a slower rate. Asthma duration also influences severity. Older asthmatics (>45) maintain a higher probability of severe asthma, particularly in men. However, the present study did not find a significant correlation with age and severity, possibly due to a smaller sample size and regional differences.

Serum eosinophils: In the current study, the mean absolute eosinophil count was 527.30 ± 290.82/mm³ (normal range: 150-300 cells/mm³). In mild asthma, the count was 328.55 ± 32.56/mm³; in moderate asthma, 407.96 ± 141.03/mm³; and in severe asthma, 817.73 ± 315.97/mm³. The distribution of mean absolute eosinophil count vs. asthma severity was statistically significant (P = 0.0004). This aligns with Roquet A et al.[9] who found higher eosinophil counts in bronchial hyperactivity. Lalrinpuia B et al.[10] also reported a mean eosinophil count of 330 ± 88.64 in asthma patients, concluding that eosinophil count is a key indicator of asthma severity and progression.

Spirometry: Spirometry results showed the mean post FEV1/FVC ratio was 87.55 ± 8.91%. In mild asthma, the mean pre FEV1/FVC was 80.46 ± 12.26%, in moderate asthma, 88.14 ± 8.06%, and in severe asthma, 83.08 ± 8.79%. Distribution of pre FEV1/FVC vs. severity was statistically significant (P = 0.0041). Lambert A et al.[11] studied 1608 participants and found a mean FEV1% predicted of 83% (SD 15). They concluded that reduced FEV1/FVC ratios can support the asthma diagnosis, though they aren't highly specific for diagnostic accuracy.

Serum IgE and Asthma Control: In the current study, in mild asthma, 3 (15.0%) patients had partly controlled asthma and 17 (85.0%) patients had well controlled asthma. In moderate asthma, 25 (53.2%) patients had partly controlled asthma, 2 (4.3%) patients had uncontrolled asthma and 20 (42.6%) patients had well controlled asthma. In severe asthma, 33 (100.0%) patients had uncontrolled asthma. Association of level of asthma control vs. severity of asthma was statistically significant (P = 0.0003). In the present study, the mean serum total IgE of patients was 696.45 ± 702.23 IU/ml. In mild asthma, the mean serum total IgE of patients was 136.44 ± 106.89 IU/ml. In moderate asthma, the mean serum total IgE of patients was 414.95 ± 262.64 IU/ml. In severe asthma, the mean serum total IgE of patients was 1436.76 ± 736.26 IU/ml. Distribution of mean serum total IgE vs. severity of asthma was statistically significant (P = 0.0001). This is in concordance with the findings reported by Sandeep T et al.[12] where they estimated and compared serum IgE levels in mild, moderate, and severe asthmatics and in normal subjects in India. They reported the mean IgE levels in healthy controls and cases were found to be 151.95 IU/L and 756.26 IU/L respectively and statistically significant when the levels were compared between these two groups (P = 0.001). Hence, they concluded serum Immunoglobulin E levels were high in asthmatics as compared to normal subjects. On an average, the levels increased as the severity of asthma increased. The findings of this study are also in agreement with inference of Sunyer J et al.[13] which confirmed the association between asthma and total IgE independent of atopy (i.e. specific IgE).

Serum Vitamin D and asthma control: In the current study the mean serum vitamin D of patients was 17.69 ± 7.11 ng/ml. In mild asthma, the mean serum vitamin D of patients was 22.23 ± 4.05 ng/ml, in moderate asthma, it was 18.86 ± 6.64 ng/ml, whereas in severe asthma, it was 13.29 ± 6.97 ng/ml. Distribution of mean serum vitamin D vs. severity of asthma was statistically significant (P = 0.00002). This is in concordance with the findings of Felicia Montero- Arias et al.[14] where a statistically significant relationship was found between asthma severity and vitamin D sufficiency status: 91.4% of the patients with vitamin D levels below 20 ng/mL and 74.0% of the patients with vitamin D levels between 20 and 30 ng/mL had severe asthma in comparison with 50% of the patients with vitamin D sufficiency (P = 0.02). The result of this study also agrees with the findings of Korn S et al.[15] where they found mean 25(OH)D concentrations were 25.6 (±11.8) ng/ml in asthmatics. Serum levels of 25(OH)D were significantly related to asthma severity (intermittent: 31.1 ± 13.0 ng/ml, mild: 27.3 ± 11.9 ng/ml, moderate: 26.5 ± 12.0 ng/ml, severe: 24.0 ± 11.8 ng/ml, p = 0.046) and asthma control (controlled: 29.5 ± 12.5 ng/ml, partly controlled 25.9 ± 10.8 ng/ml, uncontrolled: 24.2 ± 12.1 ng/ml, P = 0.030).

Correlation between Serum Vitamin D and IgE: The present study found a significant negative correlation between serum IgE levels and serum vitamin D levels (P = 0.000014, R = -0.42). This indicates a statistically significant inverse relationship, suggesting that higher serum IgE levels are associated with lower serum vitamin D levels in patients with asthma. This finding contrasts with some previous studies, such as the study by Korn S et al.[15] which did not observe an association between 25(OH)D and serum IgE levels (P = 0.230). Similarly, the study by Li F et al.[16] also found no significant relationship between

vitamin D status and total IgE (P = 0.50). The differences in the results could be attributed to variations in study design, sample size, and population characteristics. Nevertheless, other studies have shown similar findings to ours; for example, a study by Zeng Y et al.[17] demonstrated that lower vitamin D levels were associated with higher serum IgE levels and asthma severity. Additionally, research by Brehm JM et al.[18] supports our findings by showing a correlation between low vitamin D levels and elevated IgE in pediatric asthma patients. These findings collectively suggest that vitamin D deficiency may play a role in modulating IgE production and asthma severity, though further studies are necessary to understand the underlying mechanisms.

Strengths: This study offers several strengths, including a comprehensive analysis of various biomarkers associated with asthma severity. A key strength of the study is its examination of multiple factors (eosinophil count, FEV1/FVC ratio, serum IgE, and vitamin D levels) across different asthma severity categories, which provides a thorough understanding of the physiological changes in asthma.

Limitations: This study is limited by the small sample size, single-center study population, relatively short duration of the study, which may not capture long-term trends or effects in asthma progression or treatment response and limit the generalizability of the findings to other populations or settings. Additionally, the study's cross-sectional design prevents the establishment of causal relationships between serum IgE levels, vitamin D levels, and asthma severity. Furthermore, the study does not account for some of the potential confounding factors, such as other comorbidities or environmental exposures, that might influence asthma outcomes.

Conclusion

In conclusion, this study demonstrates significant associations between various biomarkers (eosinophil count, FEV1/FVC ratio, serum IgE, and vitamin D levels) and asthma severity. The findings suggest that higher eosinophil counts and serum IgE levels are associated with more severe forms of asthma, while lower serum vitamin D levels correlate with increased asthma severity. However, while the study found a weak negative correlation between serum IgE and vitamin D levels, further research with larger and more diverse samples is necessary to clarify this relationship and determine its clinical significance. Overall, the study highlights the importance of monitoring these biomarkers in the management of asthma and supports the need for personalized treatments based on severity.

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Conflicts of interest
There are no conflicts of interest.

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