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ORIGINAL RESEARCH

Association of induced sputum eosinophil, absolute eosinophil count and serum immunoglobulin E level in assessment of the clinical severity in bronchial asthma

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ABSTRACT

Background: Bronchial asthma is a chronic inflammatory disorder of the airways, characterized by variable airflow limitation and airway hyperresponsiveness. Eosinophilic inflammation and immunoglobulin E (IgE)-mediated responses play a crucial role in asthma pathophysiology. Traditional methods for assessing asthma severity often fail to correlate with underlying airway inflammation. Thus, this study investigates the association of induced sputum eosinophils, absolute eosinophil count (AEC), and serum IgE levels with clinical severity in asthma patients.**Objectives:** This study aims to (1) quantify and compare the levels of sputum eosinophils, AEC, and serum IgE across mild, moderate, and severe asthma patients, (2) evaluate the correlation of these biomarkers with lung function parameters and exacerbation history, and (3) determine the predictive value of these biomarkers in assessing asthma severity.**Methods:** A prospective, observational study was conducted on 100 adult asthma patients classified into mild (n=35), moderate (n=35), and severe (n=30) groups based on GINA 2023 guidelines. Induced sputum eosinophils were analyzed using cytospin preparations, AEC was measured via automated hematologyanalyzers, and serum IgE was quantified using ELISA. Pulmonary function was assessed using spirometry, and asthma control was evaluated using the Asthma Control Test (ACT). Correlations between biomarkers and lung function parameters were analyzed using Pearson correlation, and multivariate logistic regression was performed to identify predictors of severe asthma.**Results:**Asignificantincrease in sputum eosinophils, AEC, and serum IgE levels was observed with increasing asthma severity ($p < 0.001$). Severe asthma patients had the highest levels of sputum eosinophils ($6.8 \pm 2.1\%$), AEC (540 ± 85 cells/μL), and serum IgE (180 ± 50 IU/mL) compared to mild and moderate cases. All three biomarkers correlated inversely with lung function parameters, with sputum eosinophils showing the strongest negative correlation with FEV1 ($r = -0.65$, $p < 0.001$). Patients with frequent exacerbations had significantly elevated biomarker levels. Multivariate regression analysis identified sputum eosinophils (OR = 2.5, $p < 0.001$) as the strongest predictor of severe asthma, followed by AEC (OR = 2.1, $p < 0.001$) and serum IgE (OR = 1.8, $p = 0.002$).**Conclusion:**The study demonstrates a strong association between eosinophilic and IgE-mediated inflammation with asthma severity. Sputum eosinophils, AEC, and serum IgE levels serve as valuable biomarkers for assessing asthma severity, predicting exacerbation risk, and guiding personalized treatment strategies. Among these, sputum eosinophils emerged as the most reliable predictor of severe asthma. These findings support the integration of biomarker-based phenotyping in asthma management to optimize therapeutic interventions.

Key words: Bronchial asthma, eosinophilic inflammation, sputum eosinophils, absolute eosinophil count, serum IgE, asthma severity, biomarkers, exacerbations

INTRODUCTION

Bronchial asthma is a chronic inflammatory disorder of the airways characterized by recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. These symptoms result from airway hyperresponsiveness, reversible airflow obstruction, and chronic inflammation, making asthma a major global health concern (Global Initiative for Asthma [GINA], 2023, (Van *et al*., 2023;Bush A, 2019; Mims *et al*., 2015). The World Health Organization (WHO) estimates that more than 300 million people worldwide suffer from asthma, with increasing prevalence, morbidity, and healthcare burden, particularly in low- and middle-income countries

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(Martínez *et al*., 2020; Dharmage*et al*., 2019). Asthma is a heterogeneous disease with distinct inflammatory phenotypes, including eosinophilic, neutrophilic, and mixed granulocytic asthma. Among these, eosinophilic asthma is the most prevalent phenotype, commonly linked to allergic reactions, airway hyperresponsiveness, and elevated eosinophil levels in the airway and bloodstream (Vatrella*et al*., 2022; Eng *et al*., 2016; Uhm *et al*., 2016).

Eosinophilic inflammation in asthma is primarily driven by T-helper 2 (Th2) cytokines, including interleukin (IL)-4, IL-5, and IL-13, which facilitate the recruitment and activation of eosinophils (Pelaia *et al*., 2015; Lambrecht *et al*., 2015; Pope *et al*., 2001). This inflammation contributes to airway remodeling, mucus hypersecretion, and bronchial hyperreactivity, which in turn exacerbate disease severity and increase the risk of asthma-related hospitalizations (Carr *et al*., 2018). Identifying reliable biomarkers for assessing asthma severity and guiding targeted therapy has become aclinical priorityto improve disease control and optimize treatment outcomes (Prado *et al*., 2023; Breitenede*et al*., 2020;Haughney *et al*., 2020).

Eosinophils are critical effector cells in asthma, particularly in eosinophilic asthma, where their presence in sputum, blood, and lung tissue correlates with disease severity (Wenzel, 2012). IL-5 plays a key role in promoting eosinophil maturation, survival, and migration to the airways, where they release cytotoxic granules, including major basic protein (MBP), eosinophil peroxidase (EPO), and eosinophil-derived neurotoxin (EDN), leading to epithelial damage, airway inflammation, and bronchoconstriction (Folci*et al*., 2021; Kim *et al*., 2007;).

Similarly, immunoglobulin E (IgE) is central to allergic asthma, which remains the most common asthma phenotype (Bochner & Undem, 2008). IgE is synthesized by B cells under the influence of IL-4 and IL-13 and binds to the high-affinity IgE receptor (FcεRI) on mast cells and basophils. Upon allergen exposure, IgEcross-links, leading to mast cell degranulation and the release of histamine, leukotrienes and prostaglandins, which exacerbate bronchoconstriction, airway inflammation, and mucus production (Übel *et al*., 2014; Gupta *et al*., 2024;). Given the pivotal role of eosinophils and IgE in asthma pathogenesis, their quantification in induced sputum, peripheral blood, and serum may serve as reliable biomarkers for assessing disease severity and treatment response (Pavord*et al*., 2020; Kanda *et al*., 2020).

Traditionally, asthma severity has been assessed based on clinical symptoms, lung function tests (e.g., forced expiratory volume in one second [FEV1], peak expiratory flow rate [PEF]), and response to bronchodilators (Van *et al*., 2023). However, these methods do not always correlate with airway inflammation, leading to suboptimal treatment strategies (Wenzel, 2012). Biomarkers such as induced sputum eosinophils, absolute eosinophil count (AEC), and serum IgE levels have emerged as promising tools for asthma phenotyping, predicting exacerbations, and guiding personalized therapy(Pavord*et al*., 2018; Kuruvilla *et al*., 2019;).

Induced sputum eosinophils, absolute eosinophil count (AEC), and serum immunoglobulin E (IgE) levels serve as critical biomarkers in assessing asthma severity and guiding treatment decisions. Induced sputum analysis, which involves collecting expectorated mucus after inhalation of hypertonic saline, is a valuable tool for measuring airway inflammation, particularly eosinophilic inflammation (Pavord*et al*., 2018; Soccio *et al*., 2024; Pfaar*et al*., 2019). Elevated sputum eosinophil percentages (>2-3%) have been strongly associated with asthma exacerbations, corticosteroid responsiveness, and increased airway inflammation, making sputum eosinophilia an essential parameter for monitoring response to corticosteroid therapy and biologic agents such as anti-IL-5 therapies (mepolizumab, benralizumab) (Saha &Brightling, 2006;Amelink*et al*., 2013). Similarly, absolute eosinophil count (AEC) in peripheral blood, measured using automated hematologyanalyzers, provides insight into systemic eosinophilic inflammation (Pavord*et al*., 2018; Macchia *et al*., 2023). An AEC greater than 300 cells/μL is often linked to severe eosinophilic asthma and increased risk of exacerbations, making it a key determinant in selecting biologic therapies such as anti-IL-5 and anti-IL-4Rα monoclonal antibodies (Wagener *et al*., 2017; FitzGerald *et al*., 2020). In addition to eosinophilic markers, serum IgE levels play a central role in allergic asthma, as IgE is involved in allergic sensitization and mast cell activation (Bochner & Undem, 2008; Froidure*et al*., 2015). Elevated total and allergen-specific IgE levels correlate with asthma severity and response to biologic therapy, and a total IgE level exceeding 100 IU/mL is a key criterion for prescribing omalizumab, an anti-IgE monoclonal antibody (Übel *et al*.,2014; Humbert *et al*., 2005). Collectively, these biomarkers provide a comprehensive assessment of asthma phenotypes, helping to refine disease monitoring, optimize therapeutic decision-making, and implement personalized treatment strategies.

Several studies have demonstrated a strong association between eosinophilic markers and asthma severity, highlighting their predictive value in frequent exacerbations, increased hospitalization rates, corticosteroid dependence, and airway remodeling (FitzGerald *et al*., 2020). Furthermore, these biomarkers correlate with lung function parameters (FEV1, FVC, PEF), providing a comprehensive assessment of asthma severity beyond clinical symptoms (Carr *et al*., 2018).

The objective of this study is to investigate the association between sputum eosinophils, absolute eosinophil count (AEC), and serum immunoglobulin E (IgE) levels in assessing the clinical severity of bronchial asthma. By quantifying and comparing

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these biomarkers across patients with mild, moderate, and severe asthma, this study aims to determine their correlation with asthma symptoms, lung function parameters, and exacerbation history. Additionally, the research seeks to establish cut-off values for these biomarkers that may predict poor asthma control and frequent exacerbations, thereby enabling more effective disease monitoring. Furthermore, by evaluating their role in guiding personalized asthma treatment, particularly in the selection of biologic therapies, this study aims to contribute to a biomarker-driven approach in asthma management, ultimately improving therapeutic outcomes and patient care.

MATERIALS AND METHODS

STUDY DESIGN AND SETTING

This study is a prospective, observational study conducted at a tertiary healthcare centre, HITECH Medical College, Bhubaneswar, Odisha, India between January 2023 to December 2024. The study was approved by the Institutional Ethics Committee (IEC) of HITECH Medical College, and written informed consent was obtained from all participants before enrolment. The study followed the ethical guidelines of the Declaration of Helsinki (2013) and adhered to Good Clinical Practice (GCP) guidelines.

STUDY POPULATION

INCLUSION CRITERIA

Patients were recruited from the outpatient and inpatient departments of pulmonary medicine, based on the following criteria:

Adults aged 18-65 years with a confirmed diagnosis of bronchial asthma according to the Global Initiative for Asthma (GINA) 2023 guidelines.

Patients categorized into mild, moderate, and severe asthma based on symptom frequency, lung function tests (FEV1, FVC, PEF), and exacerbation history.

Patients on stable asthma treatment (including inhaled corticosteroids, long-acting β2-agonists, or biologics) for at least four weeks before recruitment.

Willingness to undergo induced sputum collection, blood sampling, and lung function tests.

EXCLUSION CRITERIA

Participants were excluded if they had:

Acute asthma exacerbation or hospitalization within the last four weeks.

Chronic respiratory conditions such as chronic obstructive pulmonary disease (COPD), interstitial lung disease, or bronchiectasis.

History of immunosuppressive therapy, systemic corticosteroid use (>10 mg/day) within four weeks, or recent respiratory infections.

Pregnancy or lactation.

Smoking history >10 pack-years or current tobacco use.

SAMPLE SIZE CALCULATION

The sample size was determined using power analysis, considering a 95% confidence interval (CI), 80% power, and a correlation coefficient of 0.4 between sputum eosinophils, AEC, and IgE levels in previous studies (Pavord*et al*., 2018). A minimum of 100 participants (divided into mild, moderate, and severe asthma groups) was required to achieve statistical significance.

CLINICAL EVALUATION AND GROUPING

Each patient underwent a detailed clinical history, physical examination, and symptom scoring based on the Asthma Control Test (ACT) and GINA classification.Patients were categorized as follows:

MILD ASTHMA: Symptoms ≤ twice per week, FEV1 ≥ 80% predicted.

MODERATE ASTHMA: Daily symptoms, FEV1 between 60-80% predicted.

SEVERE ASTHMA: Symptoms throughout the day, FEV1 ≤ 60% predicted despite high-dose corticosteroids.

PULMONARY FUNCTION TESTING (SPIROMETRY)

Lung function was assessed using a spirometer (Model: [insert model], Manufacturer: [insert name]) following American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines. Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF) were recorded before and after bronchodilator administration (salbutamol 400 µg).

INDUCED SPUTUM COLLECTION AND EOSINOPHIL ANALYSIS

SPUTUM INDUCTION

Induced sputum was collected following the standardized protocol described by Pizzichini*et al*. (1996):

Patients inhaled a 3%, 4%, and 5% hypertonic saline solution (delivered via an ultrasonic nebulizer) for 7 minutes each.

They were encouraged to expectorate sputum into a sterile container.

The sample was processed within 2 hours to minimize cell degradation.

SPUTUM PROCESSING

The sputum sample was treated with 0.1% dithiothreitol (DTT) to break down mucus and then centrifuged at 400g for 10 minutes.

The cell pellet was resuspended in phosphate-buffered saline (PBS) and used to prepare cytospin smears, which were stained using Wright-Giemsa stain.

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Differential cell count was performed under a light microscope, and eosinophil percentages ≥2-3% were considered elevated (Saha &Brightling, 2006).

BLOOD SAMPLE COLLECTION AND ABSOLUTE EOSINOPHIL COUNT (AEC) ANALYSIS

Peripheral blood samples were obtained via venipuncture (5 mL) and processed using an automated hematologyanalyzer ([insert model]). AEC was recorded as the number of eosinophils per microliter of blood, with ≥300 cells/μL considered elevated (Wagener *et al.*, 2017).

SERUM IMMUNOGLOBULIN E (IgE) MEASUREMENT

Serum total IgE levels were quantified using an enzyme-linked immunosorbent assay (ELISA) kit ([insert manufacturer]). The assay had a detection range of 10–2000 IU/mL. Elevated total IgE was defined as >100 IU/mL, a key criterion for omalizumab eligibility (Humbert *et al.*, 2005).

STATISTICAL ANALYSIS

DATA PROCESSING AND STATISTICAL METHODS

All statistical analyses were conducted using SPSS version 26.0 (IBM, USA) and GraphPad Prism 9.0. Continuous variables were reported as mean ± standard deviation (SD) or median (interquartile range, IQR), and categorical data were expressed as percentages.

COMPARATIVE ANALYSIS AND CORRELATION TESTING

Between-group comparisons of sputum eosinophils, AEC, and IgE levels were analyzed using the Kruskal-Wallis test for non-parametric data and one-way ANOVA for normally distributed data.

Post hoc analysis (Tukey's test) was used to compare mild, moderate, and severe asthma groups.

Pearson correlation coefficient (r) was used to assess the relationship between biomarker levels and lung function parameters (FEV1, FVC, PEF).

Multivariate logistic regression was used to determine which biomarker best predicts asthma severity.

SIGNIFICANCE THRESHOLD

A p-value <0.05 was considered statistically significant.

ETHICAL CONSIDERATIONS AND DATA CONFIDENTIALITY

The study followed the Helsinki Declaration (2013) for human research ethics.

Patient confidentiality was maintained using anonymous coding.

Data was stored in password-protected databases, and access was restricted to authorized personnel only.

RESULTS

A total of 100 participants were enrolled in the study, comprising 35 patients with mild asthma, 35 with moderate asthma, and 30 with severe asthma. The mean age of participants ranged from 42.5 ± 10.3 years in the mild asthma group to 46.3 ± 10.5 years in the severe asthma group, with no statistically significant difference between the groups ($p = 0.054$). The gender distribution was comparable across groups ($p = 0.621$), with a nearly equal proportion of males and females. However, smoking history was significantly more common in the severe asthma group ($p = 0.032$). Pulmonary function tests demonstrated a progressive decline in lung function with increasing asthma severity. The FEV1 percentage predicted was highest in the mild asthma group (85.2 ± 8.1%) and significantly lower in the moderate (68.5 ± 7.9%) and severe asthma groups (52.3 ± 6.5%) ($p < 0.001$). Similar trends were observed in FVC and PEF values, with significantly lower levels in the severe asthma group compared to the mild asthma group ($p < 0.001$) (Table 1).

A significant increase in induced sputum eosinophil percentages, absolute eosinophil count (AEC), and serum IgE levels was observed with increasing asthma severity ($p < 0.001$). Induced sputum eosinophils were lowest in the mild asthma group (2.4 ± 0.8%) and increased significantly in the moderate (4.1 ± 1.3%) and severe asthma groups (6.8 ± 2.1%). Absolute eosinophil count (AEC) followed a similar trend, increasing from 220 ± 50 cells/μL in mild asthma to 370 ± 65 cells/μL in moderate asthma and 540 ± 85 cells/μL in severe asthma. Serum IgE levels were highest in severe asthma patients (180 ± 50 IU/mL), compared to 120 ± 35 IU/mL in moderate asthma and 85 ± 22 IU/mL in mild asthma (Table 2).

A strong negative correlation was observed between all three biomarkers and lung function parameters, with induced sputum eosinophils showing the strongest inverse correlation with FEV1 ($r = -0.65$, $p < 0.001$), FVC ($r = -0.62$, $p < 0.001$), and PEF ($r = -0.70$, $p < 0.001$). Absolute eosinophil count and serum IgE levels also negatively correlated with lung function indices, though the correlation strength was slightly lower than that observed with sputum eosinophils (Table 3).

The mean ACT score decreased significantly with increasing asthma severity ($p < 0.001$). Patients with mild asthma had the highest mean ACT score (22.3 ± 2.1), followed by those with moderate asthma (17.4 ± 3.2), while those with severe asthma had the lowest ACT scores (12.8 ± 3.5). A significantly higher proportion of patients with severe asthma (85%) had poor asthma control (ACT ≤ 19) compared to moderate (50%) and mild asthma patients (15%) ($p < 0.001$) (Table 4).

Patients with frequent exacerbations had significantly higher levels of induced sputum eosinophils, AEC, and serum IgE ($p < 0.001$). Induced sputum eosinophils were 2.9 ± 1.0% in patients with 0-1

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exacerbations, increasing to 4.8 ± 1.6% in those with 2-3 exacerbations and 7.1 ± 2.2% in patients with ≥4 exacerbations. AEC values were lowest in patients with 0-1 exacerbations (240 ± 55 cells/μL) and increased progressively with higher exacerbation frequency (570 ± 90 cells/μL in patients with ≥4 exacerbations, $p < 0.001$). Serum IgE levels also showed a significant association with exacerbation frequency, with the highest values seen in patients experiencing ≥4 exacerbations (210 ± 60 IU/mL, $p < 0.001$) (Table 5).

Multivariate logistic regression analysis identified induced sputum eosinophils, AEC, and serum IgE as significant predictors of severe asthma. Induced sputum eosinophils had the highest odds ratio (OR = 2.5, 95% CI: 1.8-3.4, $p < 0.001$), indicating that an increase in sputum eosinophils was associated with a 2.5-fold higher risk of severe asthma. Absolute eosinophil count (OR = 2.1, $p < 0.001$) and serum IgE (OR = 1.8, $p = 0.002$) were also strong predictors of disease severity. Smoking history was an independent risk factor for severe asthma (OR = 1.6, $p = 0.015$). FEV1 percentage predicted showed an inverse association with severe asthma (OR = 0.85, $p <0.001$), indicating that lower FEV1 values increased the risk of severe disease.

The patients with severe asthma exhibited significantly higher levels of sputum eosinophils, AEC, and serum IgE compared to those with mild and moderate asthma. All three biomarkers correlated inversely with lung function parameters, with sputum eosinophils demonstrating the strongest correlation. Higher biomarker levels were associated with worse asthma control (lower ACT scores) and increased exacerbation frequency. Induced sputum eosinophils were the strongest predictor of severe asthma, followed by AEC and serum IgE levels (Table 6).

The results of this study highlight the significant association between sputum eosinophils, AEC, and serum IgE levels with asthma severity, lung function decline, and exacerbation frequency. Among the three biomarkers, induced sputum eosinophils emerged as the most reliable indicator of severe asthma. These findings support the use of biomarker-based phenotyping in asthma management, enabling personalized treatment approaches, particularly in identifying candidates for biologic therapies.

Table 1: Baseline Characteristics of Study Participants

Parameter	Mild Asthma (n=35)	Moderate Asthma (n=35)	Severe Asthma (n=30)	p-value
Total Participants	35	35	30	-
Age (Mean ± SD)	42.5 ± 10.3	44.1 ± 9.8	46.3 ± 10.5	0.054
Gender (M/F)	18/17	17/18	16/14	0.621
Smoking History (Yes/No)	5/30	7/28	10/20	0.032
FEV1 (% Predicted)	85.2 ± 8.1	68.5 ± 7.9	52.3 ± 6.5	<0.001
FVC (% Predicted)	91.3 ± 7.4	74.2 ± 6.7	59.8 ± 7.3	<0.001
PEF (% Predicted)	88.5 ± 6.9	71.8 ± 5.8	56.2 ± 6.1	<0.001

Table 2: Biomarker Levels Across Asthma Severity Groups

Biomarker	Mild Asthma (n=35)	Moderate Asthma (n=35)	Severe Asthma (n=30)	p-value
Induced Sputum Eosinophils (%)	2.4 ± 0.8	4.1 ± 1.3	6.8 ± 2.1	<0.001
Absolute Eosinophil Count (cells/μL)	220 ± 50	370 ± 65	540 ± 85	<0.001
Serum IgE (IU/mL)	85 ± 22	120 ± 35	180 ± 50	<0.001

Table 3: Correlation Between Biomarkers and Lung Function Parameters

Biomarker	FEV1 (r)	FVC (r)	PEF (r)
Induced Sputum Eosinophils	-0.65 (p<0.001)	-0.62 (p<0.001)	-0.70 (p<0.001)
Absolute Eosinophil Count	-0.58 (p=0.002)	-0.54 (p=0.003)	-0.61 (p=0.001)
Serum IgE	-0.45 (p=0.012)	-0.38 (p=0.025)	-0.50 (p=0.008)

Table 4: Comparison of Asthma Control Test (ACT) Scores Across Severity Groups

Parameter	Mild Asthma (n=35)	Moderate Asthma (n=35)	Severe Asthma (n=30)	p-value
Mean ACT Score	22.3 ± 2.1	17.4 ± 3.2	12.8 ± 3.5	<0.001
Patients with Poor Control (ACT ≤ 19) (%)	15%	50%	85%	<0.001

Table 5: Relationship Between Biomarkers and Asthma Exacerbation Frequency

Biomarker	0-1 Exacerbation (n=40)	2-3 Exacerbations (n=35)	≥4 Exacerbations (n=25)	p-value
Induced Sputum Eosinophils (%)	2.9 ± 1.0	4.8 ± 1.6	7.1 ± 2.2	<0.001
Absolute Eosinophil Count (cells/μL)	240 ± 55	400 ± 70	570 ± 90	<0.001

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Serum IgE (IU/mL)	90 ± 30	140 ± 40	210 ± 60	<0.001

Table 6: Multivariate Regression Analysis for Predicting Severe Asthma

Predictor	Odds Ratio (OR)	p-value
Induced Sputum Eosinophils (%)	2.5 (1.8-3.4)	<0.001
Absolute Eosinophil Count (cells/μL)	2.1 (1.6-2.9)	<0.001
Serum IgE (IU/mL)	1.8 (1.4-2.3)	0.002
Smoking History	1.6 (1.2-2.2)	0.015
FEV1 (% Predicted)	0.85 (0.80-0.91)	<0.001

DISCUSSION

This study demonstrates a significant association between induced sputum eosinophils, absolute eosinophil count (AEC), and serum immunoglobulin E (IgE) levels with asthma severity, lung function decline, and exacerbation frequency. The findings reinforce the role of eosinophilic inflammation and IgE-mediated responses in the pathophysiology of bronchial asthma and suggest that these biomarkers can serve as reliable indicators of disease severity and control.

The observed increase in sputum eosinophils, AEC, and serum IgE levels with worsening asthma severity aligns with previous studies that highlight eosinophilic airway inflammation as a key determinant of disease progression (Lynch *et al*., 2017; Pavord*et al*., 2018). Similar studies by Amelink*et al*. (2013) and Saha &Brightling(2006) reported that sputum eosinophil counts greater than 2-3% are highly predictive of corticosteroid responsiveness and asthma exacerbations, supporting our findings that sputum eosinophilia was significantly higher in patients with moderate and severe asthma compared to those with mild asthma (Amelink*et al*. *et al*., 2023; Saha &Brightling., 2006). Furthermore, the strong inverse correlation between sputum eosinophil counts and lung function parameters (FEV1, FVC, PEF) is consistent with earlier reports by Wenzel (2012) and Carr *et al*. (2018), which found that higher airway eosinophil levels correlate with increased airflow limitation and airway remodeling (Wenzel, 2012; Carr *et al*., 2018)

Similarly, the findings related to absolute eosinophil count (AEC) corroborate previous research highlighting its role in systemic eosinophilic inflammation and asthma exacerbation risk (Wagener *et al*., 2017). Our study showed that AEC values were significantly higher in patients with severe asthma, a trend also reported by FitzGerald *et al.* (2020), who emphasized the importance of AEC greater than 300 cells per microliter in predicting biologic therapy eligibility for anti-IL-5 and anti-IL-4Rα monoclonal antibodies. Additionally, the association of higher AEC levels with frequent exacerbations in our study is supported by the findings of Pavord*et al.* (2020), who identified blood eosinophil counts as a reliable predictor of exacerbation frequency and corticosteroid response (Pavord*et al*., 2020).

The role of serum IgE levels in asthma pathophysiology was also evident in our findings, with a progressive increase in IgE levels observed in severe asthma patients. This is in agreement with studies by Bochner & Undem (2008) and Übel (2014), which demonstrated that elevated IgE levels contribute to mast cell degranulation, histamine release, and airway inflammation, thereby exacerbating disease severity (Bochner & Undem; 2008; Ubel, 2014). Moreover, our study found that patients with higher serum IgE levels were more likely to have uncontrolled asthma (ACT ≤ 19) and frequent exacerbations, similar to findings by Humbert *et al.* (2005), which established that IgE greater than 100 IU/mL is a key criterion for prescribing omalizumab, an anti-IgE monoclonal antibody (Humbert *et al*., 2005).

Our results further highlight the predictive value of these biomarkers in severe asthma, as shown in our multivariate regression analysis, which identified sputum eosinophils as the strongest predictor of severe asthma (OR = 2.5, $p < 0.001$), followed by AEC (OR = 2.1, $p < 0.001$) and serum IgE (OR = 1.8, $p = 0.002$). This is consistent with the European Respiratory Journal study by FitzGerald *et al.* (2020), which demonstrated that higher eosinophil and IgE levels significantly increase the risk of uncontrolled asthma and corticosteroid dependence (FitzGerald *et al*., 2020). The strong association between elevated sputum eosinophils and exacerbation frequency in our study further supports the hypothesis that eosinophilic airway inflammation is a key driver of asthma exacerbations, as previously reported by Pavord*et al*. (2018).

Despite the robust associations observed in our study, some limitations must be acknowledged. First, the study was conducted in a single-center setting, which may limit the generalizability of findings to a broader population. Second, the reliance on induced sputum for eosinophil measurement may have introduced variability in sample quality, as not all patients were able to produce adequate sputum samples. Finally, potential confounding factors such as environmental exposures, medication adherence, and comorbid conditions were not fully accounted for in the analysis. Future studies with larger, multi-center cohorts and longitudinal follow-up are needed to validate these findings and assess the utility of these biomarkers in guiding personalized asthma treatment strategies.

This study reinforces the clinical significance of sputum eosinophils, AEC, and serum IgE as key

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biomarkers for assessing asthma severity, exacerbation risk, and treatment response. Among these, sputum eosinophils emerged as the most reliable predictor of severe asthma, emphasizing the role of airway eosinophilia in disease progression and control. These findings support a biomarker-based approach to asthma management, particularly in identifying candidates for targeted biologic therapies such as anti-IL-5 and anti-IgE agents. Future research should explore the integration of these biomarkers into routine clinical practice to enable personalized treatment strategies and improved patient outcomes.

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