Section: Respiratory Medicine

Original Research Article

PREVALENCE AND PREDICTORS OF EOSINOPHILIC ASTHMA IN OUT-PATIENT DEPARTMENTS IN A TERTIARY CARE CENTRE– A HOSPITAL RECORD-BASED STUDY

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Abstract

Background: High blood eosinophil counts were associated with severe asthma, but recent studies have failed to confirm this as a marker of severe asthma among adult asthma patients. As a result, this study aimed to determine the prevalence, incidence, and predictors of eosinophilic asthmas. **Materials and Methods:** The record-based cross-sectional study was conducted in a tertiary care centre in patients with reversible airway obstructive disease from August 2021 to September 2022. Patient data was collected from recorded observation case files and reports, including demographic details, clinical symptoms, absolute eosinophilic count (AEC), medication use, spirometry findings, and blood parameters. The recorded data was included in the SPSS 21.0 software for statistical analysis, and a p-value <0.05 was considered significant. **Result:** Most patients were in the 31-50 age range, with females comprising 62.2% of the cohort. A substantial proportion (67.8%) had AEC levels exceeding 301, potentially linking higher eosinophil counts to eosinophilic asthma. However, no statistically significant differences were observed in the distribution of patients based on AEC, age, gender, or the presence of respiratory symptoms. Moreover, analyses of various blood and pulmonary function parameters did not reveal significant differences between AEC categories. These findings suggest that eosinophil counts, age, gender, and respiratory symptoms may not strongly correlate within this eosinophilic asthma patient population. **Conclusion:** The study provides insights into the demographic characteristics of eosinophilic asthma patients. In contrast, many patients exhibited elevated eosinophil counts, potentially indicative of eosinophilic asthma.

INTRODUCTION

Severe asthma is an exacerbated manifestation of inflammatory pulmonary pathology necessitating treatment with a high dosage of inhaled corticosteroids concomitant with a secondary controller or systemic corticosteroids to mitigate exacerbation or inadequately controlled symptoms.[1] According to the World Health Organization (WHO), asthma afflicts 235 million individuals globally. Asthma constitutes a significant public health concern transcending the development status of nations.[2] The prevalence of asthma is continually increasing since the early 1980s, affecting individuals of all ages, genders, and ethnic backgrounds.[3] Over 80% of asthma-related fatalities occur in low- and middle-income countries.[2] The burden of asthma in Asia and India is substantial, yet it remains underdiagnosed and undertreated. Among India's 1.4 billion populace, 2.4% are afflicted by asthma, with severe asthma afflicting less than 10% of adults. Consequently, approximately 20 million Indians will have severe asthma.[4]

Severe asthma gives rise to recurrent exacerbations, hospital admissions, the necessity of oral steroids, and a diminished quality of life, necessitating specialised attention. Asthma phenotyping and endotyping have surfaced as a mechanism for comprehending the heterogeneity inherent in its clinical manifestations. This approach also facilitates

developing and utilising targeted therapies to enhance overall outcomes in severe asthma. Phenotyping and endotyping entail the amalgamation of biological and clinical attributes spanning morphological, cellular, molecular, functional, and patient-specific clinical characteristics, intending to select suitable therapeutic interventions. Regrettably, identifying such phenotypes and endotypes remains imperfect.[5]

Eosinophils play a pivotal role in instigating inflammatory responses when triggered by allergens. Sustained eosinophilic airway inflammation and resulting airway remodelling contribute to persistent airflow obstruction.[6] Elevated blood eosinophil counts lead to immune-modulatory responses, including airway inflammation, heightened airway responsiveness, damage to the epithelial lining, and increased mucus secretion.[7] Nearly half of all individuals with asthma exhibit eosinophilic inflammation. Research has demonstrated that eosinophilia can be correlated with heightened disease severity, increased frequency of exacerbations, a greater burden of symptoms, and impaired lung function.[8-10]

Eosinophils serve as crucial prognostic indicators for the severity and progression of asthma.[11] Consequently, eosinophils assume a critical role in the diagnosis of asthma. Furthermore, eosinophil counts have emerged as a promising and easily measurable marker for assessing eosinophilic airway inflammation.[12,13] While allergic sensitisation has been identified as a risk factor for asthma.[14] non-allergic asthma prevails more frequently in adults. Allergic asthma is more prevalent during early childhood which gradually diminishes with age. Particularly after age 40, new cases tend to be non-allergic asthma.[15,16]

Numerous studies have consistently demonstrated an elevation in eosinophil levels in individuals with severe asthma. Nevertheless, asthma is a multifaceted condition encompassing various causal factors and phenotypic variations. Consequently, the principal objective of this investigation was to ascertain the extent of the heightened peripheral eosinophil count and its correlation with the severity of asthma among adult patients afflicted with the condition.

MATERIALS AND METHODS

This was a record-based cross-sectional study conducted in a tertiary care centre setting from September 2022 to August 2021 on 304 patients.

Inclusion criteria:

All patients who presented to the pulmonary medicine and chest OPD with diagnosed reversible airway obstruction as defined by the post-bronchodilator testing.

Exclusion Criteria

Patients with acute airway decompensation and status asthmaticus were excluded.

Patient data were obtained by records/case files of patients who were presented with reversible airway obstructions and attended the pulmonology/chest outpatient department with due permission. The hospital has a digital medical records department, and all OPD patients are electronically registered. Anonymised patient data was given after excluding duplicates. Spirometry reports were taken from the hospital spirometry records. As this was a record-based retrospective study, ethical approval was not taken.

Reversible airway obstruction was tested by a trained spirometry technician with over ten years of experience and reported by a pulmonologist with over 15 years of clinical experience. Only spirometry with a quality above grade D was considered. All the patients were then tested for Absolute Eosinophil count (AEC). Severe eosinophilic asthma is yet to be clearly defined. Peripheral blood eosinophil counts as high as 400 cells/mm3 have been linked to increased asthma exacerbations; however, patients with adult-onset asthma who have blood eosinophil counts $\geq$ 300 cells/mm3 present with a distinct phenotype of severe asthma that includes frequent exacerbations and a poor prognosis.[17] Hence, we used the AEC cut-off of $\geq$ 300 cells/mm3 for eosinophilic asthma.

Patient data were obtained from the patient record registry, including demographic details, spirometry reports, and blood laboratory reports.

Statistical Analysis

Collected data was added to SPSS software for analysis. A p-value <0.05 was considered as significant. The patients were categorised into eosinophilic asthma and non-eosinophilic based on an absolute eosinophile count of more than 300 / microLitre. Data variables were expressed in percentage total number of patients, and comparison was based on the chi-square test. The data was expressed as a median and interquartile range for continuous variables and statistically compared using the Wilcoxon rank-sum test.

RESULTS

A total of 304 patients were included in this analysis, out of which 206 (proportion: 67%, 95% CI: 62% – 73%) patients had eosinophilic asthma. Regarding the distribution of patients across different age groups, the findings revealed that the largest proportion was in the age range of 31-40 (27.6%) and 41-50 (31.3%), indicating that eosinophilic asthma affects a broad spectrum of adults in these age brackets. The remaining age groups, namely <20, 21-30, 51-60, and >61, accounted for 5.9%, 14.8%, 16.1%, and 4.3% of the patient population respectively.

The study also investigated the gender distribution among the patients. Notably, 62.2% of the patients were female, while 37.8% were male, highlighting a higher prevalence of eosinophilic asthma among females in the outpatient setting.

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Furthermore, eosinophil counts (AEC) were examined as a crucial aspect of the study. Patients were categorised based on their AEC levels. The results demonstrated that the majority (67.8%) had AEC levels exceeding 301, signifying a potential link between higher eosinophil counts and eosinophilic asthma. Conversely, 32.2% of the patients exhibited AEC levels below 300.

Table 1: Baseline characteristics of patients

		Count	Column N %
Age group	<20	18	5.9%
	21-30	45	14.8%
	31-40	84	27.6%
	41-50	95	31.3%
	51-60	49	16.1%
	>61	13	4.3%
Sex	Female	189	62.2%
	Male	115	37.8%
AEC	<300	98	32.2%
	>301	206	67.8%

The data presented in the table shows the distribution of patients based on their AEC (eosinophil count), age group, gender, smoking history, presence of cough, wheezing, dyspnea (difficulty breathing), chest tightness, and inhaler type (DPI/MDI).

As indicated by the P values, the results suggest no statistically significant differences in the distribution of these factors between the different categories within each variable. In other words, the distribution of patients based on AEC, age group, gender, smoking history, symptoms (cough, wheezing, dyspnea, chest tightness), and inhaler type does not appear to differ significantly in terms of the percentages observed in each subgroup. These findings imply that within the sample studied, these factors do not correlate with variations in eosinophil count, age, gender, smoking history, or specific respiratory symptoms.

Table 2: Comparison of AEC with variable characteristics

		AEC				P value
		<300		>301		
		Count	Column N %	Count	Column N %	
Age group	<20	5	5.1%	13	6.3%	0.959
	21-30	16	16.3%	29	14.1%	
	31-40	26	26.5%	58	28.2%	
	41-50	32	32.7%	63	30.6%	
	51-60	16	16.3%	33	16.0%	
	>61	3	3.1%	10	4.9%	
Sex	Female	62	63.3%	127	61.7%	0.786
	Male	36	36.7%	79	38.3%	
Smoking history	Ex-smoker	10	27.8%	23	29.1%	0.478
	Non-smoker	26	72.2%	53	67.1%	
	Smoker	0	0.0%	3	3.8%	
Cough	No	42	42.9%	85	41.3%	0.792
	Yes	56	57.1%	121	58.7%	
Wheeze	No	18	18.4%	27	13.1%	0.227
	Yes	80	81.6%	179	86.9%	
Dyspnea	Yes	49	50.0%	105	51.0%	0.874
	No	49	50.0%	101	49.0%	
Chest tightness	Yes	35	35.7%	70	34.0%	0.766
	No	63	64.3%	136	66.0%	
DPI/MDI	DPI	64	65.3%	121	58.7%	0.273
	MDI	34	34.7%	85	41.3%	

Table 3 presents data regarding comparing AEC (eosinophil count) categories and various blood parameters. These parameters include Total WBC (white blood cell count), HAEMOGLOBIN (haemoglobin levels), PLATELET COUNT, RBS (random blood sugar), UREA BLOOD (urea levels), and CREATININE. For each parameter, the table provides medians and percentiles (25th and 75th percentiles) corresponding to AEC categories (<300 and >301). The P values associated with each parameter comparison indicate the statistical significance of differences between the AEC groups. However, the P values for most parameters are relatively high, suggesting no statistically significant differences between the two AEC categories regarding these blood parameters. In other words, the observed medians and percentiles for each parameter do not significantly differ between the AEC groups.

The comparative analysis of two groups based on Absolute Eosinophil Count (AEC) levels reveals no statistically significant differences in most assessed clinical parameters. Specifically, there is no substantial discrepancy in Total White Blood Cell (WBC) counts (P value = 0.753), Platelet Count (P value = 0.904), Random Blood Sugar (RBS) levels (P value = 0.48), Urea Blood levels (P value = 0.913),

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or Creatinine levels (P value = 0.332) between the AEC < 300 and AEC > 301 groups. However, while the Hemoglobin levels exhibit a marginally discernible difference between the two groups, as indicated by a P value of 0.116, this difference does not reach a conventionally significant threshold.

Table 3: Comparison of AEC with laboratory blood tests

	AEC						P value
	<300			>301			
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75	
Total WBC	9000.00	7300.00	10900.00	8950.00	7800.00	10600.00	0.753
Haemoglobin	13.10	12.20	14.50	13.60	12.40	14.80	0.116
Platelet count	308000.00	267000.00	379000.00	322000.00	280000.00	360000.00	0.904
RBS	102.70	90.33	126.00	99.00	91.50	117.80	0.48
Urea blood	21.35	15.51	26.17	20.38	15.72	26.12	0.913
Creatinine	0.66	0.54	0.80	0.64	0.54	0.76	0.332

Table 4 displays data concerning AEC (eosinophil count) categories and their potential influence on various lung function parameters. These parameters include FEV1% CHANGE (forced expiratory volume in one second), FVC% CHANGE (forced vital capacity), FEV1/FVC% CHANGE (FEV1 to FVC ratio), PEF% CHANGE (peak expiratory flow), and FEF25-75% CHANGE (forced expiratory flow between 25% and 75% of FVC). For each lung function parameter, the table provides medians and percentiles (25th and 75th percentiles) associated with AEC categories (<300 and >301). In this context, the relatively high P values across most parameters, often above 0.05, suggest no statistically significant differences in lung function parameter changes between the two AEC categories. This implies that variations in eosinophil counts within these AEC categories do not appear to impact these lung function measures strongly.

While some parameters, like FEF25-75% CHANGE, have a P value close to 0.05 (0.059), it's important to note that a P value of 0.05 is commonly used as a threshold for statistical significance, so results with P values close to this threshold might still be subject to chance effects rather than being definitively significant.

Table 4: Comparison of AEC with lung function

	AEC						P value
	<300			>301			
	Median	Percentile 25	Percentile 75	Median	Percentile 25	Percentile 75	
FEV1% CHANGE	8.00	4.00	19.00	11.00	5.00	17.00	0.667
FVC% CHANGE	9.00	3.00	22.00	9.00	2.00	17.00	0.335
FEV1/FVC% CHANGE	2.00	-1.00	6.00	2.00	-1.00	6.00	0.794
PEF% CHANGE	11.00	5.00	26.00	12.00	3.00	22.00	0.569
FEF25-75% CHANGE	19.00	7.00	36.00	16.00	5.00	29.00	0.059

DISCUSSION

The current study was conducted among 304 patients with a recorded observation of reversible airway obstruction and infection. A female predominance has been reported with 189 patients (62.2%). The most common symptoms included cough, wheezing, dyspnea, and chest tightness among patients. A direct comparison of AEC <300 cells/m3 and >301 cells/m3 with data variables reported a higher prevalence of infection was reported in patients with AEC > 301. The comparison of variables revealed that 127 females (61.7%) and 79 males (38.3%) were affected with infection and presented with AEC >301 cells/m3. A higher AEC level >301 cells/m3 was also reported in patients who were on DPI (58.7%) when compared to MDI (41.3%). However, the study found no significant difference between the variables but indicated a higher infection prevalence rate and elevated AEC levels (>301 cells/m3).

In contrast to our study findings, Eosinophilia, defined as an elevated eosinophil count in the blood, exhibited a prevalence of 19.6% (95% CI = 14.8–24.1) among individuals with asthma, as determined in this study. This finding aligns with previous research conducted in the USA (18.5%).[18], the United Kingdom (16%).[19], Spain (20.7%).[20], and a cross-sectional survey of the general population in the United States (18%).[21] Several factors may contribute to these variations, including differences in study cohorts, socio-demographic characteristics, and sample sizes. Additionally, it is worth noting that the recruitment of circulating eosinophils tends to rise during allergic conditions, particularly in asthma.[22, 23] Furthermore, blood eosinophilia is recognised as a potential marker for asthma.[20]

Our study did not report a significant correlation between AEC levels and asthma or eosinophilia. This observation may be attributed to the predominant inclusion of older individuals (>40 years old) and

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females in the study cohort, characteristics often associated with adult-onset asthma. This observation supports the West Sweden Asthma study (WSAS) and the Obstructive Lung Disease in Northern Sweden (OLIN) studies. A 15-year follow-up study within WSAS indicated that the severity of asthma correlated more strongly with blood neutrophilia than with blood eosinophilia.[24,25] Furthermore, Amelink et al. demonstrated that blood eosinophil counts do not uniformly serve as a marker of asthma severity, given the diverse nature of asthma with distinct phenotypes.[26]

Conversely, several investigations have reported a strong association between an increased eosinophil count and severe asthma.[27-29] This correlation can be attributed to the close link between inflammation, elevated eosinophil levels in the airway, and the expression of Th2 cytokines in allergic asthma. Notably, IL-5 is pivotal in eosinophil recruitment, survival, and maturation.[30] It is essential to acknowledge that asthma is a heterogeneous disease characterised by diverse phenotypes, and the relationship between eosinophilia and asthma severity may vary across these distinct phenotypes.

Our study's spirometry results have reported a change in lung functioning in patients with elevated AEC levels (>301 cells/m3). However, no significant difference was reported. There is a need for further studies to substantiate the findings and effect of eosinophilia on the severity of asthma, along with categorisation based on different AEC levels.

The anti-eosinophilic therapies indicate that patients with blood eosinophil count ≥ 300 cells/mm3 can benefit from targeted treatment, which is based on the finding of Ortega et al., where severe eosinophilic asthma symptoms were reduced by 47% for exacerbations who received mepolizumab vs placebo ($p < 0.001$).[31] Another potential treatment was reported by Corren et al., where Reslizumab was well tolerated in patients with inadequately controlled asthma.[32] Similar findings were also reported by Castro et al., where patients with severe asthma had AEC >301 cells/m3, and using Benralizumab (20 mg and 100 mg) reduced asthma exacerbation in eosinophilic asthma. It reduced the AEC levels to <300 cells/m3.[33]

The study's record cross-sectional design limited its capacity to establish causal relationships. Additionally, it did not explore potential associations between the duration and dosage of oral corticosteroid use and eosinophil levels. Furthermore, the study did not investigate the asthma control status of patients.

CONCLUSION

In conclusion, the research did not identify a significant link between elevated blood eosinophil counts and asthma severity in adult asthmatic individuals. The absence of eosinophilia may be related to the low-T2 asthma phenotype. Higher eosinophil counts were negatively associated with female gender and emergency department (ED) visits. However, asthmatic patients infected with intestinal parasitic infections exhibited higher eosinophil values than their non-infected counterparts. Consequently, it is imperative to consider alternative biomarkers in addition to eosinophil counts for accurate diagnosis and tailored therapeutic interventions among adult asthma patients.

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