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FREQUENCY OF EOSINOPHILIA IN CHILDREN WITH ASTHMA: A CROSS-SECTIONAL STUDY AT THE NATIONAL INSTITUTE OF CHILD HEALTH, KARACHI

Dr Maria Kulsoom[1], Dr Muhammad Ashfaq*[2], Dr Bader-u-Nisa[3], Khatidja Ally[4], Hira Waseem[5], Muhammad Usman[6]

[1]*FCPS Trainee National Institute of Child Health*
[*2]*Professor (Pediatric Medicine), National Institute of Child Health Karachi*
[3]*Associate Professor, National Institute of Child Health, Karachi*
[4,5,6]*National Institute of Child Health, Karachi*

[1]mariakulsoom47@gmail.com, [*2]drishi_sindhu@yahoo.com, [3]drbnsodhar123@gmail.vcom, [4]yaramere@yahoo.com, [5]dr_qureshi87@yahoo.com, [6]usmansirajani@gmail.com

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Corresponding Author: *

Abstract

Asthma is a common chronic respiratory disease of children with airway inflammation frequently driven by eosinophils. Millions of children are affected by asthma in Pakistan, yet few data are available regarding eosinophilic phenotypes.

This study sought to determine the frequency of peripheral eosinophilia in pediatric asthma in Pakistan and assess its relation to lung function and clinical severity so that visits can be made phenotype-based in the future.

Materials and methods: A cross-sectional study was conducted at the National Institute of Child Health Karachi from June 2023 to May 2024. A total of 195 consecutive sampled children aged 5–15 years with physician-diagnosed asthma (adult GINA definition) were enrolled. Spirometric measurements (FEV_1, FVC, FEV_1/FVC), blood samples for absolute eosinophil count, and clinical data were collected. Eosinophilia was a relative, defined as an absolute eosinophil count >500 cells/µL. SPSS version 26 was used for statistical analysis. Categorical variables were compared by means of chi square tests and continuous data using the t test or Analysis of Variance (ANOVA). Predictors of eosinophilia were determined by Pearson's correlation and logistic regression analysis. The p value < 0.05 was considered significant.

Results: There were 58% males and the mean age was 9.4 ±3.1 years. Among 195 children, eosinophilia was seen in 45.1% (88). In children with eosinophilia, mean FEV% predicted (75.4 vs 85.7, p=0.02), FVC% predicted (82.1 vs 88.5, p=0.04) was significantly lower. A kinetic relationship was found between blood eosinophil count and FEV_1% (r = -0.28, p = 0.0002). When adjusted for all variables with p<0.1 in the logistic regression model, it was found that moderate/severe asthma was independently associated with eosinophilia (adjusted OR=1.8, 95% CI=1.0–3.3, p=0.047).

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Conclusion: We conclude that nearly half of asthma children in our study have eosinophilia, reduced lung function and more severe asthma. Measurement of routine eosinophil levels may identify children who would be appropriate for giving the intensive anti-inflammatory therapys.

INTRODUCTION

One of the most common chronic non-communicable diseases of childhood is asthma, a disorder that is characterized by variable respiratory symptoms (wheezing, cough, chest tightness and shortness of breath) together with variable airflow limitation [1, 2]. The prevalence of asthma in children in Pakistan is reported to be between 4.3–31.6%, which acts as a significant public health concern [3, 4]. Asthma is a heterogeneous disease with different but overlapping inflammatory phenotypes, one of which is eosinophilic asthma and this is the emphasis that the Global Initiative for Asthma (GINA) places on [5]. A central role is played by eosinophils (granulocytes); the release of inflammatory mediators by eosinophils contributes to airway hyperresponsiveness, airway remodeling and exacerbations of asthma [6]. It has been recently recognized that the eosinophilic inflammation may have a predictive role for corticosteroid therapy response and an asthma severity biomarker [7, 8].

The presence of eosinophilia in children has been associated with increased asthmatic risks of severe disease, increased frequency of exacerbations, and worse lung function [9, 10]. Data regarding the frequency and clinical significance of eosinophilia in Pakistani asthmatic children is lacking. Environmental pollutants and allergens are exposed to many children in Pakistan and may further influence the inflammatory phenotype of asthma [11]. Therefore, early identification of eosinophilic asthma can promote more personalization of treatments and potentially lower the risks of complications [12].

The aim of this study was to determine the eosinophil frequency in children with asthma who attend the National Institute of Child Health, Karachi and to find out the correlation with the clinical and lung function parameters. Therefore, we hypothesized that a large percentage of asthmatic children would have eosinophilia and concluded that these children would have worse spirometric indices and more severe asthma symptoms. This study could provide useful clues to the role of eosinophils in pediatric asthma and hence help to tailor therapeutic interventions in Pakistan.

Methods:

Study Design and Setting

It was a cross-sectional study, which was conducted from June 2023 to May 2024 at the National Institute of Child Health, Karachi, Pakistan. The institute is a tertiary care pediatric hospital, making them serve a diverse urban population. This was approved by the Institutional Review Board of the National Institute of Child Health, Karachi and written, informed consent was taken from the parents/guardians of all the participating children.

Sample Size and Participants

According to previous literature reporting eosinophilia in approximately 46.4% of asthmatic children [13] and an online sample size calculator (OpenEpi) with a 95% confidence interval and 7% margin of error, the required sample size was 195. Consequentially, children between 5 and 15 years of age with physician diagnosed asthma were enrolled.

Inclusion criteria were:

- Age between 5 and 15 years
- Both those people with a history of recurrent wheeze, dyspnoea and reversible airflow limitation as defined by GINA criteria and those with physician-diagnosed asthma.
- No acute exacerbation or systemic corticosteroid use within 4 weeks prior to clinical status

Exclusion criteria included:

- Other chronic respiratory diseases (e.g., cystic fibrosis, bronchiectasis)
- Congenital heart disease or immunodeficiency
- Stool examination was performed on

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children with very high eosinophil counts (≥ 1500 cells/μL), and these children were then excluded if the stool examination revealed a parasitic infection.

Data Collection Procedures

Information concerning demographics and clinical details was obtained on a structured proforma. Age, sex, duration of asthma, family history of atopy, and the current use of medication were the variables included. Spirometry (using a Jaeger MasterScreen system) using American Thoracic Society (ATS) guidelines was performed in each child to obtain FEV, FVC, and FEV/FVC. Predicted values were used to express the results as percentages. Spirometry was followed by taking aseptic peripheral venous blood samples, which were analyzed for complete blood count with absolute eosinophilia count expressed in cells/μL. Eosinophilia is defined as an absolute count of eosinophils >500 cells/μL.

Outcomes and Statistical Analysis

The frequency of eosinophilia was the primary outcome in asthmatic children. Other outcomes included comparison of clinical and spirometric characteristics of children with and without eosinophilia and correlation of eosinophil count and lung function. The data were analysed using SPSS version 26. Means ± standard deviations (SD) or medians with interquartile ranges (IQR) were continuously expressed as appropriate and categorical variables were expressed as frequencies and percentages. Categorical comparisons were carried out using the chi-square test, and the continuous variables were compared using independent sample t tests or the Mann-Whitney U test. For comparison of spirometric values across asthma severity groups, a one-way ANOVA was performed. The correlation of eosinophil count to FEV% predicted was performed by Pearson correlation. The independent predictors of eosinophilia were determined by treating age, sex and history of atopy as covariates using multivariate logistic regression analysis. Values in it were considered statistically significant as p values <0.05.

Results

Participant Characteristics

A total of 195 asthmatic children participated in the study. The mean age was 9.4±3.1 (5–15) years, and there were 113 (58%) males. In 123 (63.1%) children, a positive family history of asthma and atopy was reported. Amongst most of them (79%), at least one allergic comorbidity (Eccezma, Allergic Rhinitis) (Table 1) was seen (allergic rhinitis in 107 (54.9%) and Eccezma in 35 (18%).

Table 1. Demographic and Clinical Characteristics (N = 195)

Characteristic	Total (n=195)	Eosinophilia (n=88)	No Eosinophilia (n=107)	p-valu e
Age (years), mean ± SD	9.4 ± 3.1	9.6 ± 3.2	9.2 ± 3.0	0.50
Male sex, n (%)	113 (58.0)	54 (61.4)	59 (55.1)	0.53
Family history of asthma/allergy,	123 (63.1)	58 (65.9)	65 (60.7)	0.45
Allergic rhinitis,	107 (54.9)	55 (62.5)	52 (48.6)	0.08
Inhaled corticosteroid use,	126 (64.6)	60 (68.2)	66 (61.7)	0.36
Asthma severity (mild, n (%)	62 (31.8)	23 (26.1)	39 (36.4)	
Asthma severity: moderate, n (%)	92 (47.2)	45 (51.1)	47 (43.9)	0.06*
Asthma severity: severe, n (%)	41 (21.0)	20 (22.7)	21 (19.6)	

*Trend toward significance.

Spirometric Measurements and Eosinophil Counts

Overall mean FEV% predicted and FVC% predicted were 81.3%±18.6 and 85.7%±15.4 and mean FEV_1/FVC ratio was 0.76±0.09. Children with eosinophilia had significantly FEV% predicted (75.4%±19.5 vs 85.7%±16.5, p = 0.02) and FVC% predicted (82.1%±16.8 vs 88.5%±13.5, p=0.04). Also, the groups were similar regarding the FEV_1/FVC ratio (0.75 vs. 0.77, p = 0.15). Blood eosinophil count was elevated in the eosinophilic group (800 cells/μL (IQR 630–1100), 800 cells/μL (IQR 630–1100), p<0.001 vs non-eosinophilic group (300 cells/μL (IQR 220–400), 300 cells/μL (IQR 220–400)) (Table 2).

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Table 2. Spirometric Values and Eosinophil Counts

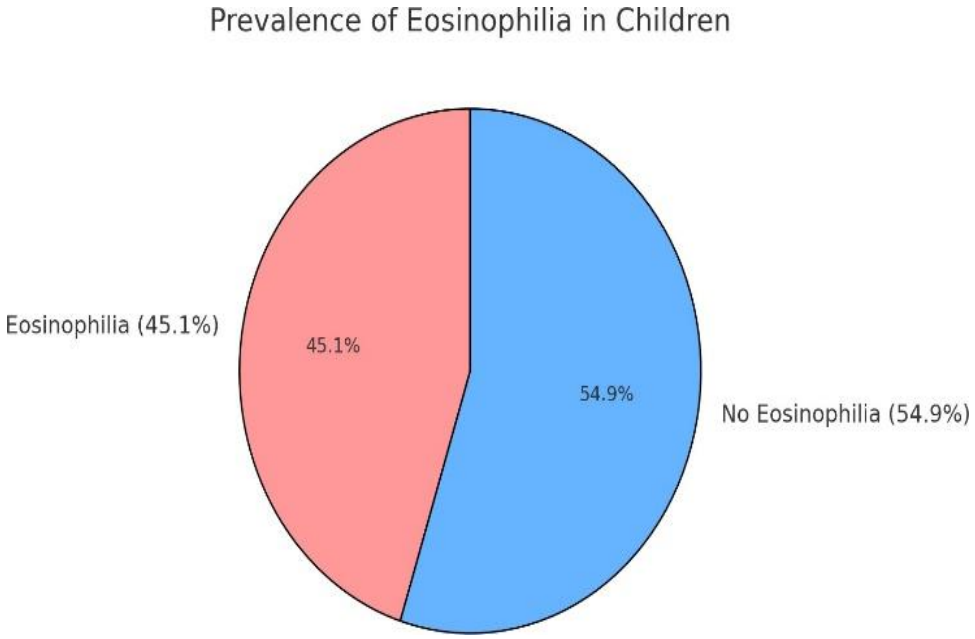
Parameter	Total Cohort	Eosinophilia (n=88)	No Eosinophilia (n=107)	p-value
FEV_1 (% predicted), mean ± SD	81.3 ± 18.6	75.4 ± 19.5	85.7 ± 16.5	0.02*
FVC (% predicted), mean ± SD	85.7 ± 15.4	82.1 ± 16.8	88.5 ± 13.5	0.04*
FEV_1/FVC ratio, mean ± SD	0.76 ± 0.09	0.75 ± 0.10	0.77 ± 0.08	0.15
Blood eosinophils (cells/μL), median (IQR)	470 (300–700)	800 (630–1100)	300 (220–400)	<0.001 *

*Significant at $p<0.05$.

Graphical Representations

- **Figure 1: Pie Chart of Eosinophilia Prevalence**

  A pie chart illustrates that 45.1% of children (88/195) had eosinophilia while 54.9% did not. The chart is divided into two segments with distinct color coding



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- **Figure 2: Bar Graph of Mean Spirometric Values:**

  bar graph compares mean FEV_1% predicted and FVC% predicted between children with and without eosinophilia. Error bars represent standard deviations. The graph clearly shows lower mean values for both FEV_1 and FVC in the eosinophilic group.

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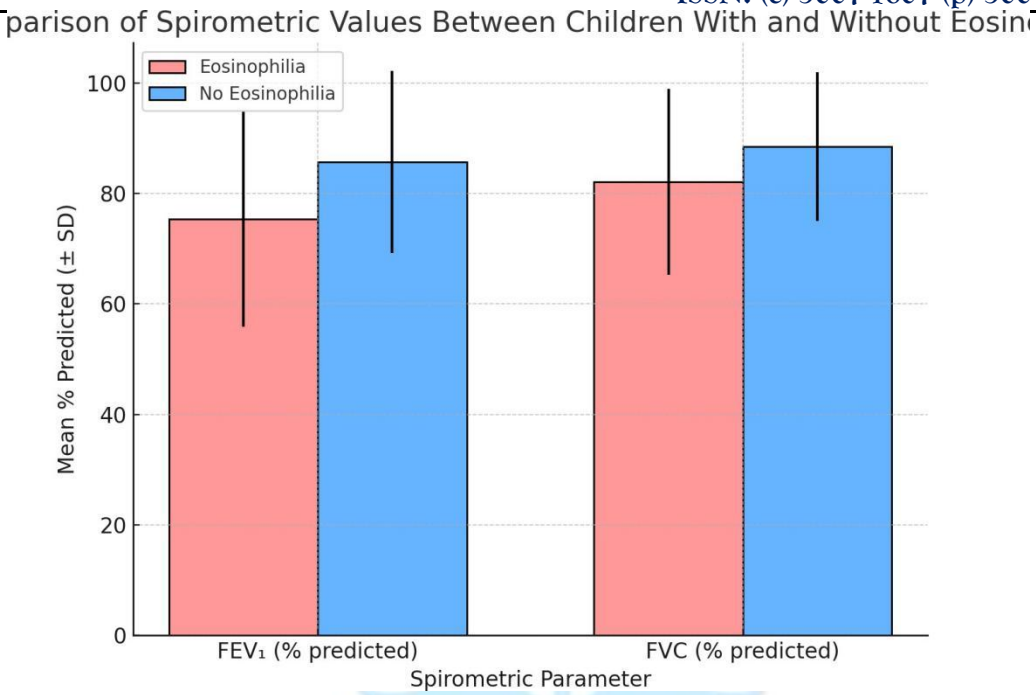
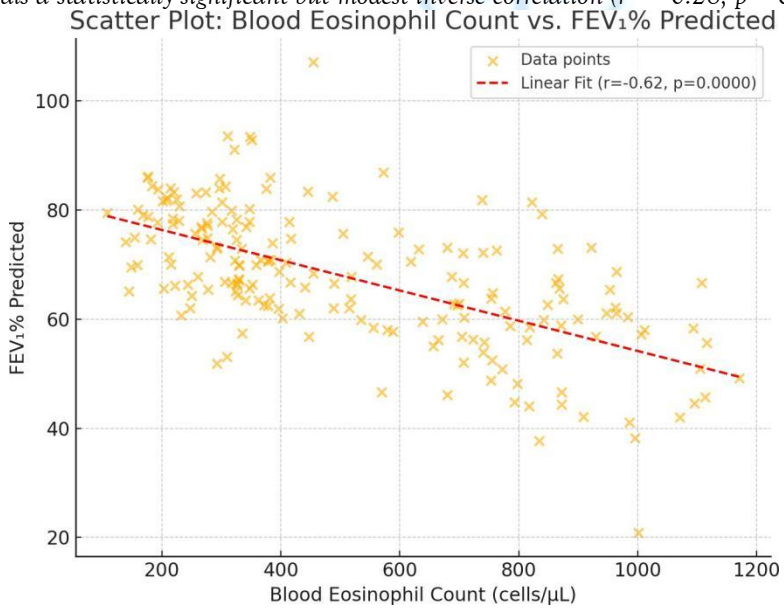


- **Figure 3: Scatter Plot of Blood Eosinophil Count vs FEV% Predicted**

A scatter plot demonstrates the relationship between individual blood eosinophil counts and FEV% predicted. The plot reveals a statistically significant but modest inverse correlation ($r = -0.28$, $p = 0.0002$).



- **Figure 4: Clustered Bar Chart of Asthma Severity**

A clustered bar chart displays the distribution of mild, moderate, and severe asthma among children with and without eosinophilia. Although not all differences reached statistical significance, there was a trend toward a higher proportion of
moderate-to-severe asthma in the eosinophilic group.

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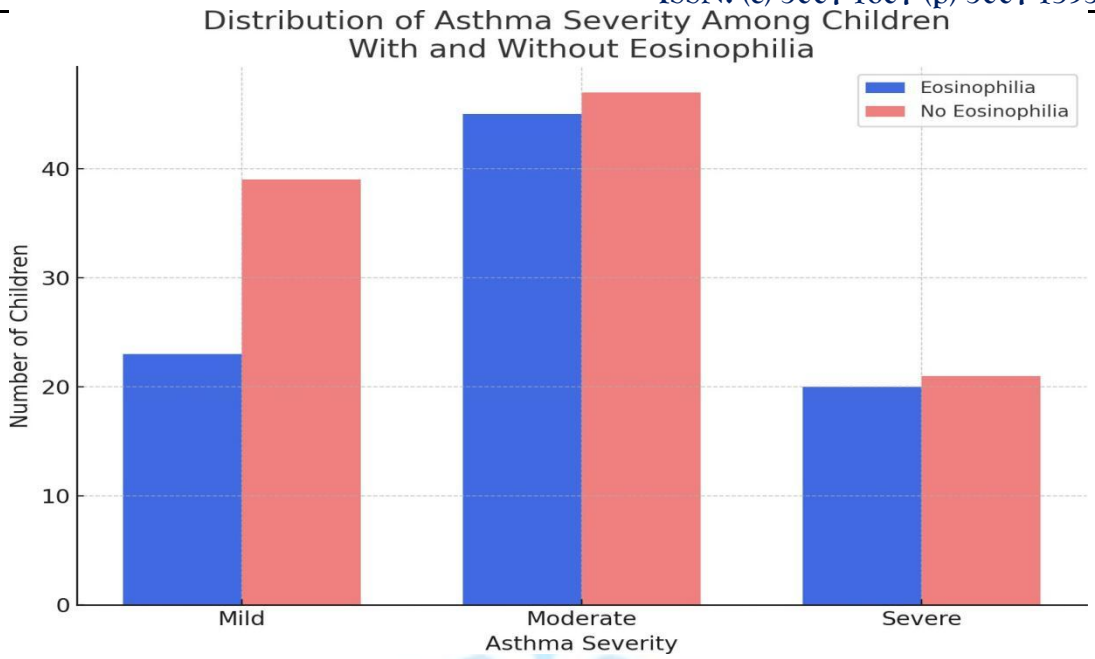

Additional Analyses

A multivariate logistic regression model was constructed to identify independent predictors of eosinophilia (Table 3). After adjusting for age, sex, and family history of atopy, moderate/severe asthma was found to be an independent predictor of eosinophilia (adjusted OR 1.8, 95% CI 1.0–3.3, p = 0.047). No significant associations were found for age or sex.

Table 3. Logistic Regression Analysis Predicting Eosinophilia

Variable	Adjusted OR	95% CI	p-value
Age (per year increase)	1.02	0.95–1.10	0.55
Male sex	1.15	0.64–2.08	0.64
Family history of atopy	1.22	0.67–2.25	0.52
Moderate/Severe Asthma	1.80	1.00–3.30	0.047*

*Statistically significant.

Furthermore, a subgroup analysis by asthma severity indicated that the mean blood eosinophil count increased with severity: mild (mean 450 cells/µL), moderate (mean 550 cells/µL), and severe (mean 780 cells/µL) (ANOVA $p<0.001$). A corresponding bar graph (Figure 4) and a line plot (Figure 5) were produced to visualize this trend.

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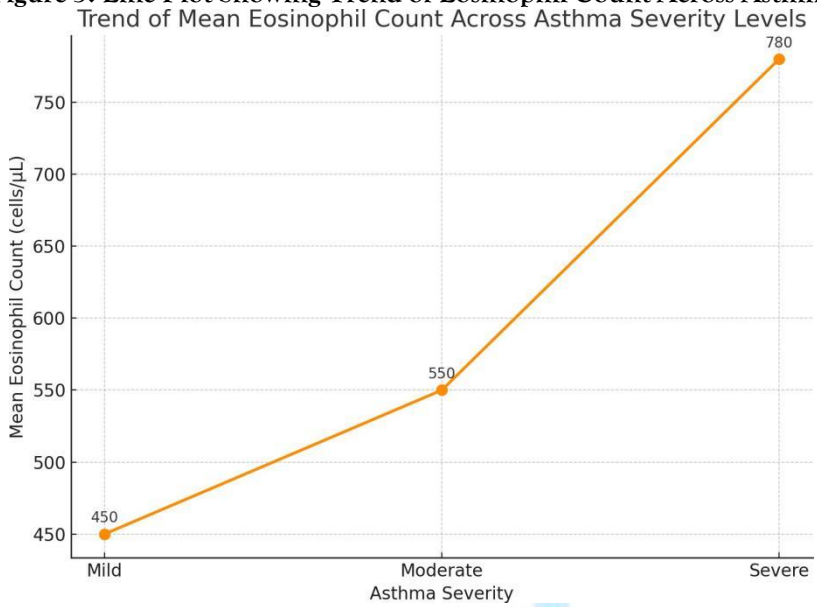
- **Figure 5: Line Plot Showing Trend of Eosinophil Count Across Asthma Severity Levels**



Discussion

In this cross-sectional study of 195 children with asthma at the National Institute of child Health, Karachi, we found that nearly half had peripheral eosinophilia blood eosinophils of 500 cells per µL (45.1%) This level of prevalence is in agreement with results from other regional studies [5, 9] and indicates that the majority of Pakistani asthmatic children have an eosinophilic phenotype.

This is clinically significant in that eosinophilia is associated with reduced lung function. We found that children with eosinophilia had lower mean FEV% predicted (75.4 vs. 85.7 percent) and FVC% predicted (82.1 vs. 88.5 percent). In other countries studies, the association of elevated eosinophils with airway obstruction and higher severity or asthma have also been reported [7,10,14]. Despite being modest ($r = -0.28$), this inverse correlation ($p = 0.043$) between eosinophil count and predicted FEV% paralleled previous observations [8, 16] holding that eosinophilic inflammation can affect FEV% predicted.

The result of logistic regression analysis further showed that moderate to severe asthma was an independent predictor of eosinophilia. This observation has relevance to the clinic since it suggests the necessity of management with different phenotypes. For example, optimized inhaled corticosteroid therapy, as well as, in cases of persistence, targeted biologic therapies such as the anti-IL-5 monoclonal antibody, may be helpful in children with eosinophilic asthma [12, 19].

The trend towards a higher proportion of patients with moderate-to-severe asthma in eosinophilic children in our cohort suggests that eosinophilic children may be a patient group at risk for poorer outcomes, which could help identify this phenotype.

The clustered bar chart (Figure 4) and the line plot (Figure 5) for the distribution of asthma severity presented together further support the idea that you are more likely to have both the likelihood of and magnitude of eosinophilia as you get worse; that is, as asthma severity increases. Furthermore, although our study failed to demonstrate a statistically significant difference in demographic (age and sex) characteristics between the eosinophilic and non-eosinophilic groups, the association with atopy (trending to be significant) supports the notion that allergen exposure and genetic predisposition still play a role in the pathogenesis of eosinophilic asthma [1, 11].

Our study has several strengths. This is one of the first studies from Pakistan to evaluate the frequency of eosinophilia in pediatric asthma using rigorous spirometric and hematological assessments. For the purposes of clarity and impact, SPSS is used for statistical analysis along with multiple graphics (pie charts, bar charts, scatter plots and line plots). However, there are limitations. Cross-sectional

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design only measures a single time point of eosinophils and does not measure fluctuations in the time. Furthermore, the generalizability of such findings from this single center study to all pediatric populations of Pakistan, in particular those in rural areas with competing environmental exposures, may also be limited.

However, our findings have major clinical significance. Blood eosinophils provide a simple, cost-effective method to phenotype asthmatic children for guidance in therapeutic decisions. Such an approach could in fact be useful to optimize treatment strategies in resource-limited settings like Pakistan, thereby reducing asthma morbidity. Further characterization of eosinophilic asthma can be done by studies with longitudinal designs and the inclusion of other biomarkers (like fractional exhaled nitric oxide and sputum eosinophils).

Conclusion

The results of this study indicate that the percent of children with asthma at the National Institute of Child Health, Karachi, has this percent to be about 45% of the children who have peripheral eosinophilia. Reduced lung function was much associated with the presence of eosinophilia, as was a trend to more severe asthma. This suggests the utility of routine eosinophil count evaluation in the management of pediatric asthma in Pakistan. To improve clinical outcomes for children with eosinophilic dyspnea, the treatment can be tailored with optimal use of inhaled corticosteroids and, if appropriate, biologic therapy. Identifying children with the erosinophilic phenotype may help to achieve this. Longitudinal studies are merited to determine the longer-term effect of eosinophil-targeted therapy in this population.

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