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To evaluate the role of Eosinophil to Lymphocyte ratio (ELR) in the Acute Exacerbation of Bronchial Asthma.

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Abstract

Objective: To study the significance of Eosinophil to Lymphocyte ratio (ELR) in the Acute Exacerbation of Bronchial Asthma.

Method: This was observational cross-sectional study conducted in the Department of Paediatric from August 2021 to August 2022 on the patients visiting emergency department. This study included all the children aged 5 to 15 years with bronchial asthma fulfilling the inclusion criteria, and also the equal number of age and sex-matched controls. ELR of the patients and controls were compared.

Results: This study included 120 cases and equal number of controls, age and sex are matched. The ELR of cases having acute exacerbation of asthma was significantly higher than controls with a mean of 0.16±0.11 for cases and 0.05±0.03 for the controls (p value-0.0001). The mean ELR of cases after 3 months of follow up significantly declined (0.09±0.03). On ROC analysis the best cut off value for ELR to indicate acute exacerbation of asthma was 0.077 with maximum sensitivity of 77.90%, maximum specificity of 79.50%, and a diagnostic accuracy of 85.5%.

Conclusion: The ELR increased significantly during the episode of Acute exacerbation of Bronchial asthma and showed significant decline after 3 months of follow up. This test being simple, easily and widely available will be very helpful in the management of the Bronchial Asthma.

Keywords: ELR, Eosinophils, Lymphocytes

Introduction

Asthma is a most common heterogeneous disease characterized by chronic inflammation of the airways and bronchial hyperreactivity. It is defined by a variable airflow obstruction as well as variation of respiratory symptoms over time and in intensity, such as wheezing, shortness of breath, chest tightness, and cough (1). According to the World Health Organization, India has around 15-20 million asthmatics, with 10%-15% of these being children. (2)

The pathophysiology of asthma involved the inflammatory cells infiltration (neutrophils, eosinophils,

lymphocytes, macrophages) in the airway, with mast cell activation and epithelial cell damage. (3) This inflammation leads to airway swelling, mucus overproduction, dysfunction of bronchial muscles which limits airway flow and is responsible for the symptoms of asthma. (4) Eosinophils are involved in the pathophysiology of various diseases, including parasitic and allergic diseases. Eosinophils move from the blood to inflammatory sites and perform various functions by controlling cytokines and inflammatory responses, and act as antigen-presenting cells in inflammatory responses. the correlation between blood and sputum eosinophilia in patients with asthma generally tends to be positive. (5-7). other than eosinophilic and neutrophilic asthma, there are also patients included in the mixed phenotype, which includes both groups. This phenotype consists of patients with eosinophil level >3% and neutrophil level >60% in induced sputum (8-10). According to Global Initiative for Asthma (GINA), blood eosinophil count is not used for the diagnosis of asthma. However, it can be used as prognostic biomarker, predict response to therapeutics, and considered as a diagnostic biomarker for defining asthma phenotype. Eosinophilia can be related to the severity of the disease [1, 11]. It is known to be an independent risk factor for asthma exacerbations, emergency department visits, and hospitalization due to asthma [12, 13]

Methods

The present study was a hospital-based observational cross-sectional study conducted in the Department of Pediatrics of Sardar Patel Medical College and P.B.M. Hospital, Bikaner for the total duration of 12 months, from August 2021 to August 2022. The sampling method used was simple random sampling. The calculated sample size was 120, calculated based on the previous reported prevalence of acute exacerbation of bronchial asthma in Indian children, which varies from 45% to 63% (14).

Sample calculation was done by using the formula.

$n=Z2p(1-p)/d2$, Z is confidence interval taken 95%

p is prevalence we have taken 45% lower range to have the larger sample size and d = 9 (permissive allowable error 20% of prevalence)

Inclusion criteria for the study included children aged 5-15 years with asthma, all asthma patients fulfilling diagnostic criteria of the Global Asthma Prevention and Control Initiative (GINA 2022 version) (1), and only cases with acute exacerbation of asthma at baseline. Exclusion criteria included patients with pulmonary embolism, chronic bronchitis, tuberculosis, chronic obstructive pulmonary disease, and blood system diseases, patients with other system diseases such as liver, kidney, cardiovascular disease, diabetes, and cancer, patients taking hormone drugs in the past month and guardian not giving consent. The cases with acute exacerbation of bronchial asthma at baseline were followed up after 3 months to compare ELR. The study was commenced after obtaining clearance from the institutional ethical committee. Written consent was taken from the parents for the study and those not willing were excluded from the study. Hemoglobin, platelet, leucocyte, neutrophil, and lymphocyte count measurements were performed within approximately 60 min after blood sampling with KX-21 hematology analyzer. ELR was calculated from the laboratory values and compared between cases and controls. Statistical Package for Social Sciences (SPSS 23.0 for Windows 15.0, Chicago, USA) programmes was used to analyses the data. Results were given as either mean ± standard deviation (SD) or as mean ± standard deviation (median) according to the distribution. Student's t-test was used for the comparison of normally distributed variables. Chi-

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square was used for non-normally distributed variables. Single-factor analysis of variance (one-way ANOVA test) was used to compare measurement data between groups, and Pearson's correlation test was used for the correlation analyses of continuous variables. $p < 0.05$ was considered significant. The receiver operating curve (ROC curve) was used to evaluate the absolute value of neutrophils. The diagnostic value of the absolute value of lymphocytes, PLR and NLR in the different severity of asthma acute attacks and calculate the optimal cut-off value and area under the curve respectively, compare the sensitivity and specificity of asthma diagnosis.

Results

Our study included 120 cases and equal number of age and sex matched controls. The majority of cases were in the age group 5-7 years (59.0%) ,8-10 (27.9%) and >10 years (13.1%). There were 51.6% female and 48.4% male cases, with male to female ratio 0.9:1. Abnormalities on chest skiagram were observed in 82.8% cases at presentation, hyperinflation (71%) was most common, followed by prominent bronchial markings in 9%, with remaining 1.6% had bilateral infiltration in the lungs, 0.8% had haziness.

The Total leucocyte count of cases was significantly higher than the controls, the mean TLC was 12,313.3±4,510.1/mm3 for cases and 9,511.0±3,740.1/mm3 for controls(p value-0.031).The mean Lymphocyte count was significantly lower in cases (20.6±11.2)as compared to control (41.7±10.1) (p value -0.0001).The mean neutrophil count of cases (70.1±14.0) was significantly higher than controls (50.5±11.4) (p value-0.002)(Table 1).The ELR of cases having acute exacerbation of asthma was significantly higher than controls with a mean of 0.16±0.11 for cases and 0.05±0.03 for the controls (p value-0.0001)(Table 1). The mean ELR of cases after 3 months of follow up significantly declined (0.09±0.03) (p value 0.001) (Table 2). On ROC analysis The best cut off value for ELR to indicate acute exacerbation of asthma was 0.077 with maximum sensitivity of 77.90%, maximum specificity of 79.50%, and a diagnostic accuracy of 85.5%(Fig 1).

Discussion

Asthma is a common chronic condition among children, and also the most common cause for hospitalization in children with episode of acute exacerbations. Additionally, children with asthma who are treated in the emergency department are at a higher risk for future exacerbations and a single severe episode can progress to life-threatening respiratory failure.

Our study found that a majority of cases were between 5-7 years old, with 59.0% cases and 36.9% controls, followed by 8-10 years with 27.9% cases, and 36.9% controls. Dondi et al.'s study also reported that the majority of their study population was young, with a median age of 3.1 years and 59% of patients being younger than 6 years. (15) Similar observations of age distribution were also made by Nordrum et al.and Nelson et al. (16,17). Our study also found that majority of cases had hyperinflation with 71% cases, followed by prominent bronchial markings in 9%, with remaining 1.6% had bilateral infiltration in the lungs, 0.8% had haziness, and 17.2% had no abnormality on chest radiography. Similar findings were also reported by Nordrum et al. (16).

Additional causes for these differences in blood cell counts in children with acute exacerbation of asthma may include increased production of inflammatory mediators such as leukotrienes and prostaglandins, activation of the immune system, and changes in blood flow to the lungs. In our study we also found that anemia was more prevalent in acute asthmatics than controls, lower hemoglobin levels were associated with more allergic

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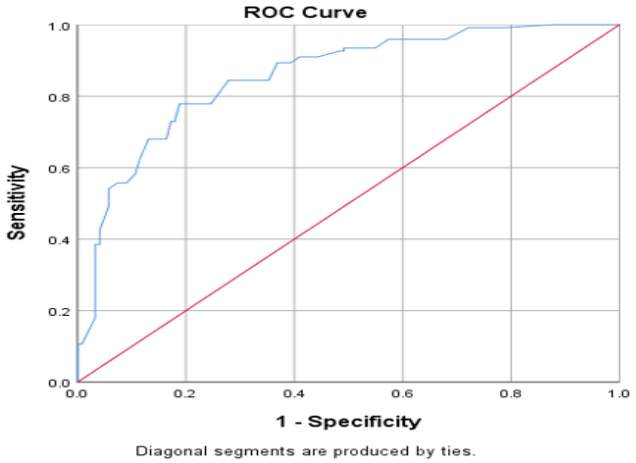
disease. (18) Additionally, the higher WBC counts may be a result of increased recruitment of white blood cells to the lungs in response to inflammation. The lower lymphocyte counts and higher neutrophil counts may be due to the shift of these cells from the circulation to the lungs in response to the inflammation. (19,20). Our study also found that the eosinophil/lymphocyte ratio (ELR) of children with acute exacerbation of asthma was significantly higher compared to controls (p value 0.0001) . The ROC analysis for ELR revealed that the best cut-off value to indicate acute exacerbation of asthma from stable asthma was 0.077 with a maximum sensitivity of 77.90%, maximum specificity of 79.50%, and an accuracy of 85.50%. Additionally, the ELR level of cases at baseline when they had acute exacerbation of asthma was significantly higher than the ELR levels at 3 months of follow-up (p value 0.001). These findings are consistent with previous research on ELR as a marker for asthma. For example, in 2022, Bedolla-Barajas et al conducted a study that found ELR to be significantly higher in patients with asthma compared to healthy controls. (21) Similarly, in 2020, Branicka et al found that ELR values were raised in asthmatics and significantly associated with disease severity and progression. (22)



	Cases	Controls	P value
	Mean±SD		
WBC count	12,313.3±4,510.1	9,511±3,740.1	0.031
Haemoglobin status	11.1±1.6	11.2±1.5	0.040
Lymphocyte counts	20.6±11.2	41.7±10.1	0.0001
Neutrophil counts	70.1±14.0	50.5±11.4	0.002
Absolute Eosinophil count	303.0±129.9	176.8±85.8	0.0001
ELR	0.16±0.11	0.05±0.03	0.0001

Table 1. Comparison between the inflammatory markers between the cases and controls

ELR	Range	Mean	SD	P value
Cases on presentation having acute exacerbation	0.02-0.70	0.16	0.11	0.001
Cases at 3-Month Follow-up	0.070-0.30	0.09	0.03	

Table 2. Comparison of ELR between cases having acute exacerbation on presentation and at 3 months follow up

Conclusion

The ELR increased significantly during the episode of Acute exacerbation of Bronchial asthma and showed significant decline after 3 months of follow up. This test being simple, easily and widely available will be very helpful in the management of the Bronchial Asthma.

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