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Correlation of Serum Ige and Absolute Eosinophil Count in Determining the Severity of Bronchiolitis in Children Aged 2 Month to 2 Years

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KEYWORDS

Bronchiolitis, Immunoglobulin E, Absolute Eosinophil Count, Atopy, Pediatric Respiratory Infection, Severity Scoring, Prognostic Biomarkers

ABSTRACT:

Background:

Bronchiolitis is a leading cause of hospitalization in infants, with disease severity influenced by individual immune responses. In resource-limited settings, identifying cost-effective biomarkers to predict clinical outcomes is essential for early risk stratification and management.

Objective:

To assess the correlation between serum Immunoglobulin E (IgE) levels, absolute eosinophil count (AEC), and clinical severity in children aged 2 months to 2 years with bronchiolitis.

Methods:

A cross-sectional analytical study was conducted over 12 months at a tertiary care hospital in Tamil Nadu, India, involving 118 children experiencing their first episode of bronchiolitis. Serum IgE and AEC were measured and compared with clinical severity scores using standardized criteria. Statistical tests included Spearman's correlation, Chi-square, and Mann–Whitney U tests.

Results:

Elevated serum IgE levels were significantly associated with longer duration of fever, cough, and rhinorrhoea ($p < 0.05$), while AEC showed only a weak correlation with fever duration. No statistically significant association was observed between AEC and serum IgE levels ($p = 0.183$). Neither marker was independently associated with acute wheeze or a family history of atopy.

Conclusion:

Serum IgE levels demonstrated a stronger association with symptom duration than AEC, suggesting their potential utility in identifying children at risk of prolonged illness. These findings highlight the prognostic relevance of IgE in bronchiolitis and support the need for further longitudinal studies to explore its role in predicting disease severity and long-term respiratory outcomes.

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INTRODUCTION

Bronchiolitis is the most frequent lower respiratory tract infection among infants and young children under two years of age, with respiratory syncytial virus (RSV) as the predominant etiological agent [1]. The condition commonly presents with symptoms such as a runny nose, coughing, wheezing, and difficulty breathing. While most cases are mild and self-limiting, a subset of patients experience severe symptoms necessitating hospitalization and respiratory support [2]. Given the unpredictable disease course and the absence of specific antiviral treatment, early identification of infants at risk of severe illness is critical for optimizing care and reducing morbidity.

The immunopathogenesis of bronchiolitis is complex, involving both innate and adaptive immune responses. While viral replication initiates the disease, it is the host inflammatory response that largely determines disease severity. Increasing attention has been given to the role of immune markers such as IgE and AEC in modulating the clinical course of bronchiolitis [3]. These markers, traditionally associated with allergic disorders, may offer insight into individual susceptibility and disease progression, potentially distinguishing phenotypes with an atopic predisposition.

Immunoglobulin E is central to type I hypersensitivity reactions and plays a key role in the pathophysiology of allergic diseases like asthma and allergic rhinitis [4]. It is produced in response to allergen exposure and facilitates the release of inflammatory mediators from mast cells and basophils. Elevated serum IgE levels have been linked to increased airway reactivity and a heightened inflammatory response, both of which are pertinent to the pathogenesis of bronchiolitis [5]. Similarly, eosinophils granulocytic leukocytes involved in parasitic defense and allergic inflammation contribute to airway epithelial damage and mucus hypersecretion when activated [6].

Several studies have investigated the association between elevated serum IgE and AEC levels with the severity of bronchiolitis. Infants diagnosed with bronchiolitis who exhibited elevated serum IgE levels were found to have a greater likelihood of developing recurrent wheezing and experienced longer durations of hospitalization [7]. Polymorphisms in the IL-4 gene, known for its role in regulating IgE synthesis, have been linked to severe cases of RSV bronchiolitis in prospective research, indicating that an atopic predisposition may contribute to increased disease severity [8]. Infants presenting with elevated eosinophil counts during the acute phase of bronchiolitis have been observed to face a higher risk of developing wheeze-associated respiratory conditions within the following three years [9].

However, existing research presents conflicting findings. While some studies support a link between elevated serum IgE or eosinophil counts and disease severity, others have found no significant differences in eosinophil levels between children requiring hospitalization and those managed as outpatients, raising doubts about the reliability of AEC as a prognostic indicator [3]. The heterogeneity in study populations, viral etiologies, and timing of sample collection may contribute to the inconsistent findings.

Despite these inconsistencies, the idea that bronchiolitis may consist of distinct immunophenotypic subtypes-such as atopic and non-atopic remains persuasive. Evidence suggests that children with an atopic background may exhibit an exaggerated Th2 immune response to viral infections, making them more susceptible to severe acute illness and an increased risk of developing asthma later in life [10]. Supporting this concept, elevated IgE levels during infancy have been linked to both more severe viral respiratory infections and a higher likelihood of persistent wheezing by the age of five [11].

In resource-limited settings such as India, where pediatric respiratory infections pose a significant burden on healthcare systems, there is a critical need for low-cost, widely available prognostic tools. Complete blood count (CBC) with differential, which includes eosinophil count, and total serum IgE estimation are accessible in most tertiary care centers. If validated, these markers could facilitate early risk stratification and guide decisions regarding hospitalization, intensive care needs, and follow-up [12].

Yet, Indian data on the correlation between these markers and bronchiolitis severity are limited. Most regional studies have focused on viral epidemiology and clinical risk factors such as prematurity, low birth weight, and passive smoking exposure [13]. Very few have explored

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the role of immune biomarkers in predicting outcomes. This lack of localized evidence hinders the formulation of region-specific clinical guidelines, especially in high-risk subpopulations.

Bronchiolitis, commonly perceived as a self-limiting viral illness in infants, is now increasingly understood to be influenced by the host's immune response. Immune markers such as IgE and AEC, both associated with allergic inflammation, have been linked to greater disease severity, particularly in infants with atopic tendencies [14]. Their elevation may reflect distinct immunophenotypes, such as atopic versus non-atopic bronchiolitis, which could shape both the acute clinical course and long-term respiratory outcomes. Although these markers are affordable and easily measured, they remain underused in routine prognostic evaluation. In countries like India, where pediatric respiratory infections place a significant burden on healthcare systems, the use of IgE and AEC as predictive tools could support early risk assessment, guide clinical decisions, and help identify children at higher risk of recurrent wheezing or asthma.

MATERIALS AND METHODS

Study Design and Duration

This was a cross-sectional analytical study conducted over a 12-month period, from July 2023 to June 2024, at the Department of Paediatrics, Chettinad Hospital and Research Institute, Kelambakkam, Tamil Nadu, India. The cross-sectional design was chosen to evaluate the association between IgE levels, AEC, and clinical severity of bronchiolitis at a single point in time, thereby facilitating an efficient, snapshot-based assessment of correlations between immunological markers and disease severity.

Study Population

A total of 118 children aged 2 months to 2 years, presenting to the outpatient and inpatient departments with symptoms suggestive of acute bronchiolitis, were enrolled in the study.

Inclusion Criteria:

- First episode of wheezing.
- Clinical signs of lower respiratory tract infection, including fever, cough, tachypnea, and/or chest retractions.
- Parental or guardian consent for participation.

Exclusion Criteria:

- Prior diagnosis of bronchial asthma or recurrent wheezing.
- Known congenital heart diseases.
- Primary or secondary immunodeficiency disorders.
- Chronic respiratory illnesses (e.g., bronchopulmonary dysplasia, cystic fibrosis).
- Recent administration (within the past 2 weeks) of systemic corticosteroids or immunoglobulin therapy.

A detailed clinical history was obtained, and physical examination was conducted to assess eligibility. Children fulfilling inclusion criteria were consecutively recruited after obtaining informed written consent from parents or legal guardians.

Ethical Clearance

The study protocol was approved by the Institutional Human Ethics Committee (Approval No: IHEC-I/2004/23) of Chettinad Hospital and Research Institute. The study adhered strictly to ethical principles outlined in the Declaration of Helsinki. All information obtained was kept confidential, and participants were assured of the right to withdraw at any stage without affecting their standard medical care.

Clinical Evaluation and Severity Scoring

Each child underwent a thorough clinical examination upon presentation. Severity of bronchiolitis was objectively assessed using a validated clinical scoring system comprising five parameters:

1. Respiratory rate (age-adjusted thresholds).

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2. Presence and character of wheeze (audibility and timing).
3. Cyanosis (at rest or on exertion).
4. Use of accessory muscles (including intercostal/subcostal retractions, nasal flaring, head bobbing).
5. General appearance (alertness, feeding, and irritability).

Each parameter was scored from 0 (normal) to 2 (severe). The total score (maximum of 10) was used to classify bronchiolitis severity as [15]:

- Mild (0–3),
- Moderate (4–6),
- Severe (7–10).

This systematic scoring helped standardize the evaluation and categorize disease burden for correlation with biochemical markers.

Sample Collection and Laboratory Analysis

On the day of presentation, 5 mL of venous blood was collected under strict aseptic precautions using a sterile syringe. The samples were transferred into clot-activator tubes, allowed to clot at room temperature, and then centrifuged at 3000 rpm for 10 minutes to separate the serum.

Laboratory Investigations:

1. AEC: Measured using an automated haematology analyser (Sysmex or equivalent), which provided reliable leukocyte differential counts.
2. IgE: Quantified using a commercially available Enzyme-Linked Immunosorbent Assay (ELISA) kit .The test was performed according to the manufacturer's instructions, including all incubation and wash steps. The results were expressed in international units per millilitre (IU/mL).

All analyses were conducted at the Department of Biochemistry, under standard internal quality control measures and supervision of trained laboratory personnel.

Statistical Analysis

Data were initially compiled in Microsoft Excel 2019 and further analyzed using IBM SPSS Statistics 16.0.

- Continuous variables were summarized as mean ± standard deviation (SD) for normally distributed data, or median and interquartile range (IQR) for skewed data. Categorical variables were expressed as frequencies and percentages.
- The association between IgE levels, AEC, and clinical severity scores was evaluated using Spearman's rank correlation coefficient (ρ), given the non-parametric distribution of data.
- Differences between groups (e.g., normal vs. elevated IgE) were assessed using the Mann–Whitney U test, Student's t-test, or Chi-square test, as appropriate based on data type and distribution.
- A p-value < 0.05 was considered statistically significant throughout.

3. Results

3.1 Descriptive Statistics

A total of 118 children aged between 2 months and 2 years were enrolled in the study. The mean age of the participants was 0.99 years (SD ± 0.72), indicating that a significant proportion of the study population consisted of infants. The gender distribution was nearly equal, with 60 males (50.8%) and 58 females (49.2%).

Most children (72%) had no prior history of hospitalization, and 78% presented with wheeze or stridor. A positive family history of allergy was reported in 43.2% of participants, suggesting a possible atopic background in a notable subset. Only 15.3% of the children exhibited abnormal AEC, while 84.7% had values within the normal range, as determined by age-specific reference values.

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These demographic and clinical characteristics are detailed in Table 1.

Table 1. Demographic and Clinical Characteristics of Study Participants

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	60	50.8
	Female	58	49.2
Recent Hospitalisation	Yes	33	28.0
	No	85	72.0
Prior Hospitalisation	Yes	33	28.0
	No	85	72.0
Wheeze/Stridor	Yes	92	78.0
	No	26	22.0
Family History of Allergy	Yes	51	43.2
	No	67	56.8
Eosinophil Count	Normal	100	84.7
	Abnormal	18	15.3

The average age was 0.99 years (SD = 0.72). The mean duration of illness was 3.18 days (SD = 0.83). Frequencies for symptom durations are shown in **Table 2**.

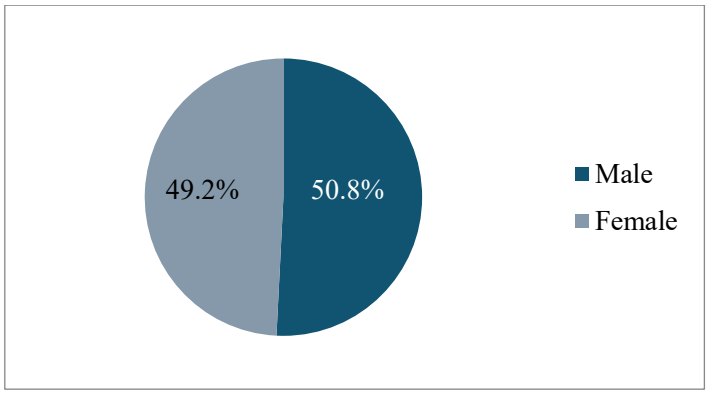

Figure 1: Gender distribution in the study population

Table 2. Duration of Symptoms Among Study Participants

Symptom	Category	Frequency (n)	Percentage (%)
Fever	No	96	81.4
	1 day	2	1.7
	2 days	9	7.6
	3 days	7	5.9
	4 days	2	1.7
Cough	No	14	11.9
	2 days	25	21.2
	3 days	42	35.6
	4 days	27	22.9

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	5 days	6	5.1
	No	51	43.2
	2 days	18	15.3
Rhinorrhoea	3 days	28	23.7
	4 days	14	11.9
	5 days	3	2.5

3.2 Association Between AEC and IgE Levels

The association between absolute eosinophil count (AEC) and serum IgE levels was assessed using the Pearson Chi-square test. The analysis did not reveal a statistically significant relationship between the two variables ($\chi^2 = 1.769$, df = 1, p = 0.183), as shown in **Table 3**.

Table 3. Association Between AEC and IgE Levels

Test	Value	df	*p*-value
Pearson Chi-Square	1.769	1	0.183

3.3 Comparison Between IgE and Eosinophil Count

Using the Mann-Whitney U test, the mean rank for IgE levels (127.79) was significantly different from that of eosinophil count (109.21), with $Z = -2.091$ and $p = 0.037$, as presented in **Table 4**.

Table 4. Mann-Whitney U Test Comparison Between IgE and Eosinophil Count

Group	N	Mean Rank	Z	*p*-value (2-tailed)
IgE Levels	118	127.79	-2.091	0.037*
Absolute Eosinophil Count	118	109.21		

*Significant at $p < 0.05$

3.4 Correlation Between Clinical Features and IgE Levels

Positive correlations were observed between IgE levels and the duration of fever ($r = 0.290$, $p = 0.001$), cough ($r = 0.204$, $p = 0.027$), and rhinorrhea ($r = 0.325$, $p = 0.000$). No significant correlation was found with wheeze/stridor or family history of allergy. Full results are shown in **Table 5**.

Table 5. Correlation Between Clinical Features and IgE Levels

Variable	*r*	*p*-value
Duration of Fever	0.290	0.001*
Duration of Cough	0.204	0.027*
Duration of Rhinorrhea	0.325	0.000*
Wheeze/Stridor	0.142	0.124
Family History of Allergy	0.021	0.824

*Significant at $p < 0.05$

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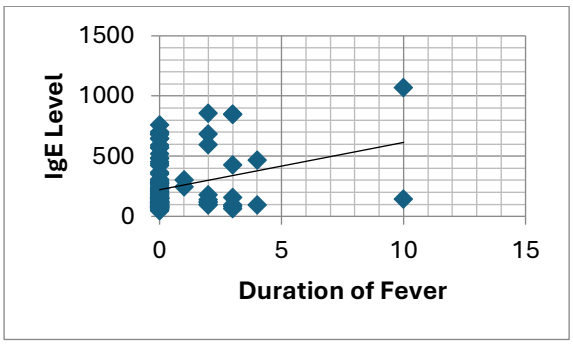

Figure 2: Correlation between duration of fever and IgE

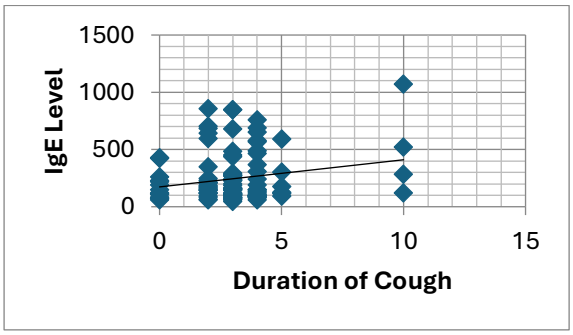

Figure 3: Correlation between duration of cough and IgE

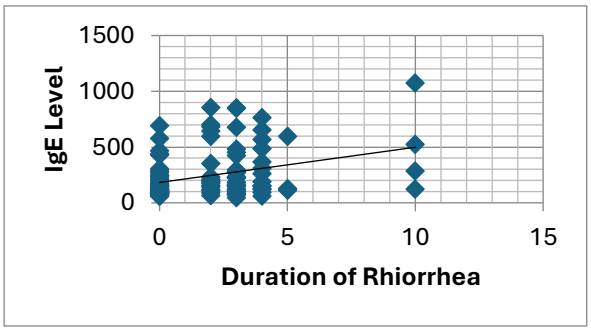

Figure 4: Correlation between rhinorrhoea and IgE

3.5 Correlation Between Clinical Features and Eosinophil Count

Only duration of fever showed a significant correlation with AEC ($r = 0.184$, $p = 0.046$). Other clinical features were not significantly correlated. These are summarized in **Table 6**.

Table 6. Correlation Between Clinical Features and AEC

Variable	*r*	*p*-value
Duration of Fever	0.184	0.046*
Duration of Cough	-0.031	0.740
Duration of Rhinorrhoea	0.004	0.966
Wheeze/Stridor	0.020	0.831
Family History of Allergy	-0.148	0.110

*Significant at $p < 0.05$

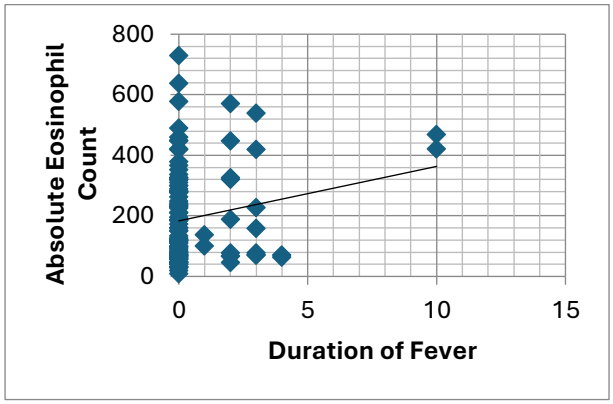

Figure 5: Correlation between duration of fever and AEC

DISCUSSION

This cross-sectional study investigated the relationship between AEC, IgE, and clinical features in children aged 2 months to 2 years diagnosed with acute bronchiolitis. Our findings provide insights into the immunological mechanisms involved in bronchiolitis and their potential clinical relevance.

The study population demographics were consistent with known epidemiological patterns, with the majority being infants under one year and an almost equal gender distribution. The high prevalence of wheezing and stridor observed aligns with the typical presentation of bronchiolitis in young children. Sudy by Øymar, K., Skjerven, H. O., and Mikalsen, I. B. emphasized that bronchiolitis is a leading cause of hospitalization during infancy and contributes significantly to respiratory morbidity [16]. Further supporting our findings, Sung, R. Y. T., Chan, R. C. K., Tam, J. S., Cheng, A. F. B., and Murray, H. G. S. reported that RSV was responsible for

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over 85% of virologically confirmed bronchiolitis cases in hospitalized infants, with a peak incidence in children around 5 months of age and a notable tendency for recurrent wheezing following the initial infection [17]. Elevated serum IgE levels in early life have been associated with persistent wheezing and a higher risk of developing asthma by age six, suggesting an atopic predisposition in a subset of bronchiolitis cases. Approximately 10–15% of infants with bronchiolitis may go on to develop asthma, particularly those with elevated IgE and a family history of atopy [18].

Notably, 15.3% of participants exhibited elevated eosinophil counts; however, no statistically significant association was observed between increased AEC and elevated serum IgE levels. This contrasts with some previous studies suggesting that eosinophilic inflammation and IgE-mediated immune responses jointly contribute to the pathophysiology of bronchiolitis, potentially indicating an atopic predisposition in a subset of children. In our study, significant positive correlations were identified between serum IgE levels and the duration of fever, cough, and rhinorrhoea, indicating that elevated IgE may be associated with prolonged symptomatic illness. This supports the hypothesis that IgE-mediated mechanisms may influence the inflammatory response and clinical course of bronchiolitis. These findings are consistent with those of Lee Chung, H. and Jang, Y. Y who reported that high serum IgE levels in children with RSV bronchiolitis were associated with more severe respiratory symptoms, longer duration of fever, and an increased risk of recurrent wheezing [19]. Similarly, a study by Kumar, R., Pajanivel, R., Koteeswaran, G. and Menon, S highlighted the role of serum IgE as a marker of ongoing airway inflammation in asthmatic patients, further supporting its relevance in airway diseases characterized by Th2-mediated immune responses [20]. However, in our cohort, serum IgE levels did not correlate significantly with the presence of wheeze or stridor, nor with family history of allergy, suggesting that while IgE may influence symptom duration, it may not directly predict acute airway involvement or hereditary atopy. Mitri, E. J., Zheng, D. X., Garg, V., Crifase, C. C., Herrera, N. M., Espinola, J. A., Hasegawa, K. and Camargo, C. A also found that elevated sIgE levels were significantly correlated with prolonged duration of fever, cough, and rhinorrhoea in infants hospitalized for bronchiolitis, while blood eosinophilia was not linked to disease severity or symptom duration- highlighting the independent role of IgE as a biomarker of bronchiolitis severity[3]. Additionally, findings by Everard, M. L., Fox, G., Walls, A. F., Quint, D., Fifield, R., Walters, C., Swarbrick, A., and Milner, A. D. support the possibility of local IgE production in the airways during RSV bronchiolitis, with IgE detected in bronchoalveolar lavage samples and IgE mRNA identified in both upper and lower respiratory tract specimens, suggesting that mucosal IgE responses may contribute to the inflammatory process independently of circulating IgE levels [21].

The lack of a strong correlation between AEC and clinical severity scores suggests that eosinophilic activity represents only one component of the complex immunopathogenesis of bronchiolitis. Viral infections trigger a multifaceted immune response involving various cell types and mediators, including neutrophils, cytokines, and other inflammatory pathways, which likely contribute significantly to clinical severity and outcomes. This aligns with findings by Gambadauro, A., Mollica, S., Rosa, E., Xerra, F., Li Pomi, A., Valenzise, M., Messina, M. F., Vitale, A., Gitto, E., Wasniewska, M., Zirilli, G. and Manti, S., who reported that while elevated eosinophil counts were associated with prolonged hospital stay, other severity outcomes were more strongly linked to broader hematological and inflammatory changes [22]. Notably, Di Lorenzo, G., Pacor, M. L., Morici, G., Drago, A., Esposito-Pellitteri, M., Candore, G., Lo Bianco, C., and Caruso, C. demonstrated that in acute asthma exacerbations, serum levels of eosinophil cationic protein (ECP)- a marker of eosinophil activation- correlated more strongly with bronchoconstriction and bronchodilator responsiveness than eosinophil counts alone [23].

The utility of serum IgE as a prognostic marker in bronchiolitis warrants further investigation, particularly in children who experience recurrent wheezing episodes or are at risk of progressing to asthma. Prior studies, including those by Ahmad Al Obaidi, A. H., Mohamed Al Samarai, A. G., Yahya Al Samarai, A. K., and Al Janabi, J. M., have demonstrated that elevated serum IgE levels in infants with bronchiolitis are associated with an increased likelihood of recurrent wheezing and eventual asthma development [24]. A recent multicentre study by

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Mitri, E. J., Zheng, D. X., Garg, V., Crifase, C. C., and Herrera, N. M., further supports this association, reporting that while blood eosinophilia did not correlate with bronchiolitis severity in hospitalized infants, the presence of sIgE was independently linked to more severe clinical presentations [3]. Complementing these findings, Wen, H., Xia, H., Tao, F., Jin, T., Liu, Z., Dai, H., and Yu, Y. observed that children with atopic constitution bronchiolitis had significantly higher serum total IgE levels than non-atopic and healthy controls, with elevated IgE strongly predicting poor prognosis, including a heightened risk of recurrent wheezing and subsequent asthma [25]. These collective findings reinforce the emerging role of serum IgE- not merely as a marker of allergic sensitization, but as a potential indicator of disease trajectory in pediatric bronchiolitis. While the cross-sectional nature of the present study precludes causal inferences, the significant correlations observed between IgE levels and symptom duration suggest that immune profiling may help stratify disease burden and inform early, personalized management strategies.

CONCLUSION

This study's strengths include the application of a standardized clinical severity scoring system and carefully defined inclusion and exclusion criteria, which helped reduce potential confounding factors. However, certain limitations must be acknowledged. The cross-sectional design limits the ability to assess temporal trends or establish causality between immune markers and clinical outcomes. Furthermore, the single-center setting and relatively modest sample size may restrict the generalizability of the findings. Future longitudinal, multicentre studies with larger, more diverse populations are necessary to validate these associations and explore the temporal evolution of immune responses in bronchiolitis.

In conclusion, while no significant association was found between AEC and serum IgE levels, elevated IgE was significantly correlated with the duration of key symptoms such as fever, cough, and rhinorrhoea. These findings suggest that IgE-mediated pathways may play a more prominent role in influencing the clinical course of bronchiolitis than eosinophilic inflammation alone. Understanding these immunological patterns could contribute to improved prognostication and potentially guide the development of targeted interventions for children at higher risk of prolonged or severe illness.

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