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To Assess the Correlation Between the Allergy and the Number of Eosinophils in the Adenoid and Tonsil Tissue

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Abstract: ***Allergic sensitization may contribute to eosinophilic inflammation within adenoid and tonsil tissues in children with adenotonsillar hypertrophy. This study assessed the relationship between allergen sensitization, serum total IgE, and tissue eosinophil counts in 80 children aged 3 to 9 years undergoing adenoidectomy and/or tonsillectomy. Allergy was evaluated through clinical assessment, skin prick testing, and serum total IgE measurement, while eosinophils in adenoid and tonsil tissues were counted by histopathological examination. Of the 80 children, 36 were sensitized and 44 were non-sensitized. Allergic rhinitis symptoms were more common among sensitized children. House dust mites were the leading allergens, and sensitization to more than one allergen was frequent. Sensitized children had higher serum total IgE and markedly greater eosinophil counts in both adenoid and tonsil tissues than non-sensitized children. Adenoid and tonsillar eosinophil counts were independently associated with allergen sensitization and showed good diagnostic performance. Serum total IgE also showed a positive correlation with tissue eosinophilia. The results support the clinical value of examining local eosinophilic inflammation in children with adenotonsillar hypertrophy, particularly when peripheral blood findings do not fully reflect allergic activity. Combining allergy assessment, serum markers, and tissue examination may provide a more complete basis for identifying allergic involvement and guiding patient management.***

Keywords: Adenotonsillar hypertrophy, Allergic sensitization, Tissue eosinophilia, Serum IgE, Allergic rhinitis

1. Introduction

Allergic diseases represent a significant global health burden, affecting millions of individuals worldwide.[1] Eosinophils are key effector cells in allergic inflammation, playing a crucial role in both innate and adaptive immune responses. In allergic rhinitis and asthma, eosinophils infiltrate the nasal mucosa and bronchial epithelium, leading to mucosal oedema, increased mucus production, and airway hyperresponsiveness. The persistence of eosinophils within tissues is mediated by survival promoting cytokines, resulting in prolonged inflammatory responses even in the absence of ongoing allergen exposure.

As a major part of the Waldeyer's ring, adenoids and tonsils play an important role in immune defense. However, this function may be disturbed when they enlarge to cause narrowing of the airway due to chronic stimulation. Adenotonsillar hypertrophy (ATH) is a common disorder in children affecting ~34% of the general pediatric population and 42–70% of the children visiting otolaryngologists.[2]

Higher numbers of eosinophils in adenoid and tonsil tissue strongly suggest an underlying local allergy and help confirm allergic inflammation linked to tissue growth in children.

Peripheral blood eosinophil count is frequently utilized as a biomarker for eosinophilic diseases. Elevated serum eosinophil levels have been reported in patients with allergic rhinitis, asthma, and CRSwNP, often correlating with disease severity and treatment response. A higher eosinophil count in the blood may reflect systemic Th2 inflammation and increased eosinophil trafficking to target tissues. However, serum eosinophilia alone may not always accurately represent local tissue inflammation. Some patients with severe tissue eosinophilia may exhibit normal or only mildly elevated peripheral eosinophil counts.

It is the most common reason for upper airway obstruction in children and can lead to a series of sequelae such as mouth breathing, obstructive sleep apnea, otitis, sinusitis, and craniofacial anomalies. Studies show that children who are allergic or sensitized to aeroallergens have significantly more eosinophils inside their adenoid and tonsil tissues than non-sensitized children.

Although the reasons for ATH remain unelucidated, some studies have suggested allergies as a risk factor. This localized allergic inflammation contributes heavily to the swelling and enlargement of these glands (adenotonsillar hypertrophy), which can cause blocked airways and breathing trouble. Patients exhibiting high tissue eosinophilia despite normal systemic markers might benefit from localized therapies targeting the inflammatory process.

Adenoid tissue eosinophil count and serum Ig-E levels can somewhat predict the presence of clinical features of allergic rhinitis.
Bhandary R[8] et al observed high serum IgE levels reported in 51.0% of allergic individuals compared to 27.5% of nonallergic individuals.

Shabestari MS [3]et al cross sectional study reported family history of asthma and allergic rhinitis, in the patient, positive result of prick test (air allergen, food and mite) and lymphocyte count were significantly higher in patients with allergic adenotonsillar hypertrophy than in patients with non-allergic adenotonsillar hypertrophy. Neutrophil count was significantly higher in patients with non-allergic adenotonsillar hypertrophy than in patients with allergic adenotonsillar hypertrophy. In other variables such as eosinophil count, presence of lipids, gender, age, family history of tonsillitis, smoking in the family, largeness of pharyngeal tonsils, diagnosis method, apnea, persistent night

snoring and continuous mouth breathing, there was no statistically significant difference between the two groups.

Sadeghi-Shabestari et al. [4] found that 70.3% of ATH children tested positive in a skin prick test, while only 10% of the non-ATH children tested positive, and children hypersensitive to dust mites were more susceptible to ATH [5]. In addition, Papatziamos G et al. [6] demonstrated that IgE-positive plasma cells were found in the adenoids of atopic children, while non-atopic adenoids contained none or very few IgE-positive cells. All these reports indicate that there is a close relationship between allergies and ATH. While IgE/AEC aid in identifying allergic predisposition, tissue analysis remains indispensable for personalized therapeutic strategies.

The present study evaluated the correlation between the allergy and the number of eosinophils in the adenoid and tonsil tissue.

2. Materials and Methods

80 patients undergoing adenoidectomy and/or tonsillectomy were investigated for allergic rhinitis by the clinical visit, skin prick test and serum total Ig E at the ENT department. Parents were given written informed consent for including the study. Exclusion criteria were poor cooperation, the presence of immunodeficiency, severe dermatographism, diffuse dermatological conditions, a craniofacial or genetic syndromes. Inclusion criteria were age between 3 and 9 years old children who were undergoing adenoidectomy and/or tonsillectomy. Adenoidectomy indication was adenoid hypertrophy, frequent infection. Skin prick test including antihistamines, antitussives, corticosteroids. Skin prick tests were performed with multitest applicator for thirty most common aeroallergens by the same Allergy and Clinical Immunology specialist. Histamine (10 mg/ml) was used as positive reference and physiological saline was used as negative reference. Skin reactions were evaluated 20 min after the application and at least 3 mm diameter of the induration or larger than that of the negative control was regarded as positive reaction. The patients were divided into 2 groups; sensitized group and nonsensitized group according to the skin prick test results and patients who were positive skin test for at least one of the allergens panel were considered as sensitized. Adenoid and tonsil tissues were examined on the basis of the number of eosinophils with microscopy in hematoxylin-eosin stained sections. Sections were scored under 400× magnification in a blinded fashion. Eosinophils were counted in 10 random sections for all samples. Statistical analysis: Descriptive analyses were presented using median (minimum-maximum) for variables not distributed normally and means ± standard deviations (SD) for normally distributed variables. The Chi-Square test was used for relationship between categorical variables. The kappa coefficient was calculated to investigate the fit between two evaluation criteria in the categorical variables. Roc curve analysis was performed to find the cut off value for adenoid and tonsil tissue eosinophils count to predict the development of atopy. At the same time, Sensitivity, Specificity and Area Under Curve were calculated.

3. Results and Discussion

A total of 80 children undergoing adenoidectomy and/or tonsillectomy were included in the study. Based on allergy testing, 36 (45.0%) children were classified as sensitized and 44 (55.0%) as non- sensitized. The mean age of the study population was 6.8 ± 2.1 years, with no significant difference between sensitized children (7.1 ± 1.9 years) and non-sensitized children (6.5 ± 2.2 years). Similarly, the sex distribution was comparable between the two groups. Males constituted 57.5% (46/80) of the study population, including 61.1% of sensitized and 54.5% of non-sensitized children. With regard to the indication for surgery, adenoid hypertrophy was present in 27.5% (22/80) of children, tonsillar hypertrophy in 22.5% (18/80), and combined adenotonsillar hypertrophy in 50.0% (40/80). Although adenotonsillar hypertrophy was more frequent among sensitized children (58.3%) than non-sensitized children (43.2%), the difference did not reach statistical significance. Likewise, isolated adenoid hypertrophy (22.2% vs. 31.8%) and isolated tonsillar hypertrophy (19.4% vs. 25.0%) were not significantly associated with allergic sensitization. In contrast, allergic rhinitis symptoms were significantly more prevalent among sensitized children. Overall, 38 (47.5%) participants reported symptoms suggestive of allergic rhinitis, with a markedly higher prevalence in the sensitized group (72.2%) compared to the non-sensitized group (27.3%). This difference was highly statistically significant (p & lt; 0.001), indicating a strong association between clinical allergic rhinitis and allergen sensitization. Overall, the baseline demographic characteristics and patterns of hypertrophy were comparable between sensitized and non-sensitized children, whereas the presence of allergic rhinitis symptoms was significantly associated with allergic sensitization. This suggests that differences observed in subsequent tissue eosinophil analyses are less likely to be influenced by baseline demographic factors.

Shah D[7] et al study found mean age was 7.26 ranging from 3 to 18 years of age. 24.24% (16) of the sample population were aged above 10 years with an (SD) of 3.46 and 22 (33%) were female and the remainder 44 (67%) patients were male.

Bhandary R[8] et al cross sectional study observed participants in age group <10years, 24.5% were found to have allergy, in 10- 49 years age group, 30% had allergy, and age group of 50 years and above, 14.3% participants had history of allergy showing no significant association between age and allergy. High serum IgE levels are seen in 27.5% of the patients without allergy and is higher i.e. 51.0% among patients with allergy, which is statistically important and evident that out of 49 participants with history of allergy, 33 participants (67.3%) had high AEC levels, showing statistically significant association between allergy and AEC.

Zou J[9] et al study reported children with eosinophilia exhibited higher total allergen sIgE scores than children without eosinophilia (5.71 ± 5.60 vs. 1.65 ± 3.04), and the percentage of children who were positive for serum sIgE to at least one of the examined allergens was higher in the eosinophilia group compared to the non-eosinophilia group (82.7 vs. 38.9%).

Baugh RF[10] et al observed the role of tonsils in the immunological profile has been well ascertained after thorough research [15], the importance of adenoids amongst the Waldeyer's ring in setting up an immunological response to unknown agents is still a topic of discussion and being vigorously studied off late.

Among the 36 sensitized children, the most frequently identified allergen was Dermatophagoides farinae, with 24 (66.7%) children demonstrating a positive skin prick test, followed by Dermatophagoides pteronyssinus in 21 (58.3%) children. Sensitization to grass pollen mix was observed in 11 (30.6%) children, while animal dander sensitivity was detected in 9 (25.0%). Sensitization to tree pollen, mould mix, and weed pollen was less common, occurring in 16.7%, 13.9%, and 11.1% of participants, respectively. Notably, multiple allergen sensitization (≥2 allergens) was present in 25 (69.4%) children, whereas 11 (30.6%) exhibited sensitization to a single allergen. These findings indicate that house dust mite allergens were the predominant sensitizing agents, and polysensitization was common among allergic children.

Zou J[9] et al study found among the eosinophilia children, 76.9% were sensitized to more than two allergens and levels of IgE specific to D. pteronyssinus, D. farinae, A. alternate, dander, food mix, mugwort, and willow, as well as the total allergen sIgE score were significantly associated with the eosinophil count.

Sadeghi-Shabestari M[4] et al and Papatziamos G et al studies have demonstrated a relationship between allergies and ATH, even suggesting allergies as a risk factor for ATH (3, 5). Although eosinophils and basophils are both important cells involved in allergic reactions, few studies have investigated the relationship between atopy and eosinophils/basophils in ATH children.

Yucel N[11] et al examined skin prick-sensitized children and found that "the number of eosinophils in adenoid and tonsil tissue was significantly higher in sensitized patients".

Bhandary R[8] et al observed tissue eosinophilia was high in 22.5% among patients with no allergy, 51% in patients with allergy and was statistically significant.

Skin Prick Test Positivity Among Sensitized Children. N=36

Allergen	Positive, n (%)
Dermatophagoides farinae	24 (66.7)
Dermatophagoides pteronyssinus	21 (58.3)
Grass pollen mix	11 (30.6)
Tree pollen mix	6 (16.7)
Weed pollen mix	4 (11.1)
Mould mix	5 (13.9)
Animal dander	9 (25.0)
Multiple sensitization (≥2 allergens)	25 (69.4)
Single sensitization	11 (30.6)

Association Between Tissue Eosinophilia and Allergen Sensitization

Variable	Sensitized n (%)	Non-sensitized n (%)
Adenoid eosinophils ≥10 cells/HPF	31 (86.1)	12 (27.3)
Tonsillar eosinophils ≥9 cells/HPF	29 (80.6)	10 (22.7)

Comparison of Serum Total IgE Levels and Tissue Eosinophil Counts

Variable	Sensitized (n = 36)	Non-sensitized (n = 44)
Serum total IgE (IU/mL)	245.8 ± 112.4	64.2 ± 31.8
Adenoid eosinophils (cells/HPF)	18.4 ± 6.2	8.1 ± 3.4
Tonsillar eosinophils (cells/HPF)	15.2 ± 5.1	7.3 ± 2.9

Sensitized children demonstrated significantly higher eosinophil infiltration in both adenoid and tonsillar tissues than non-sensitized children. The mean adenoid eosinophil count was 18.4 ± 6.2 cells/HPF in sensitized children compared with 8.1 ± 3.4 cells/HPF in non-sensitized children, yielding a mean difference of 10.3 cells/HPF (p < 0.001). Similarly, the mean tonsillar eosinophil count was significantly greater in the sensitized group (15.2 ± 5.1 cells/HPF) than in the non-sensitized group (7.3 ± 2.9 cells/HPF), with a mean difference of 7.9 cells/HPF (p < 0.001). These findings suggest a strong association between tissue eosinophilia and allergic sensitization.

Shah D[7] et al study showed among the control group 2 patients out of 30 patients had high eosinophil count in the adenoid tissue on histopathological slide. Whereas, amongst the cases, 14 out of 36 patients had a high eosinophil count. Thus, the number of eosinophils per 10hpf of adenoid tissue slides was significantly higher among the cases with clinical allergic rhinitis.

Marked tissue eosinophilia was strongly associated with allergen sensitization. An adenoid eosinophil count of ≥10 cells/HPF was observed in 86.1% of sensitized children compared with 27.3% of non-sensitized children, corresponding to an odds ratio (OR) of 16.53 (95% CI: 5.10–53.61, p < 0.001). Likewise, tonsillar eosinophil counts ≥9 cells/HPF were identified in 80.6% of sensitized children but only 22.7% of non-sensitized children, resulting in an OR of 14.09 (95% CI: 4.48–44.33, p & lt; 0.001). These results indicate that elevated eosinophil counts in both adenoid and tonsillar tissues are powerful predictors of allergic sensitization.

Fokkens WJ[12] et al. observed "the number of eosinophils in the epithelium and interfollicular space showed a tendency to be higher in number in the allergic group". Evcimik MF[13] et al. studied the association of adenoid hypertrophy with allergic diseases and found that those with allergies had a higher incidence of hypertrophic adenoids, although these patients also had a compounding risk factor of exposure to cigarette smoke in their household.

Shah D[7] et al study showed a statistically significant relationship between allergic rhinitis with total serum Ig-E. The present study found children with allergen sensitization exhibited significantly higher serum total IgE concentrations and tissue eosinophil counts than non-sensitized children. The mean serum total IgE level was 245.8 ± 112.4 IU/mL in sensitized children compared with 64.2 ± 31.8 IU/mL in non-sensitized children (p < 0.001). Similarly, both adenoid eosinophil counts (18.4 ± 6.2 vs. 8.1 ± 3.4 cells/HPF) and tonsillar eosinophil counts (15.2 ± 5.1 vs. 7.3 ± 2.9 cells/HPF) were significantly elevated in the sensitized group (p < 0.001 for both comparisons). These findings demonstrate that allergic sensitization is associated with increased systemic

IgE production as well as enhanced local eosinophilic inflammation. Evcimik MF et al. [13] found that the most common allergen among adenoid hypertrophy children. Dogru M[14] et al. (18) revealed that sensitivity to A. alternata was more frequent in allergic rhinitis patients with adenoid hypertrophy than those without adenoid hypertrophy.

Pagella F[15] et al. assessing the association between adenoid hypertrophy and demographic factors found a significant correlation between adenoid hypertrophy and age.

Multivariable logistic regression analysis identified adenoid eosinophil count, tonsillar eosinophil count, and serum total IgE level as independent predictors of allergen sensitization. Each one-cell increase in adenoid eosinophil count increased the odds of sensitization by approximately 46% (Adjusted OR = 1.46; 95% CI: 1.18–1.81; p < 0.001). Similarly, tonsillar eosinophil count independently increased the likelihood of sensitization (Adjusted OR = 1.25; 95% CI: 1.02–1.53; p = 0.034). Serum total IgE also remained a significant independent predictor (Adjusted OR = 1.02; 95% CI: 1.01–1.04; p = 0.008). In contrast, age and sex were not significantly associated with allergen sensitization after adjustment (p > 0.05). These findings suggest that tissue eosinophilia independently predicts allergic status irrespective of demographic characteristics.

Shah D[7] et al study showed a statistically significant relationship between clinical features of nasal allergy and serum Ig-E levels. A mean value of 285.06 (IU/ml) with an SD of 420.53 (IU/ml) of Ig-E obtained in patients without allergic rhinitis. In comparison to this a mean value of 571.48(IU/ml) with an SD of 659.7 (IU/ml) of serum Ig-E obtained for patients with allergic rhinitis. Kruskal–Wallis rank sum test observed statistical significance between these two groups. Pathologically examined slides of adenoid tissue eosinophil count per 10 random high power fields (hpf) in these patients showed a statistically significant relationship showing a mean value of 0.87/10 hpf with an SD of 2.08/10 hpf in the control group compared to a mean value of 3.75/10 hpf and SD of 4.41/10 hpf among the cases. On further dividing the groups of eosinophil count to determine their significance based on a cut-off of 5 and above, a significant p-value of 0.003248 was achieved by Fisher's exact test for eosinophil count. Adenoid tissue eosinophil count and serum Ig-E levels could somewhat predict the presence of clinical features of allergic rhinitis. Bhandary R[8] et al cross sectional study found Tissue eosinophilia was high overall is 22.5% among patients with no allergy, 51% in patients with allergy, this is statistically significant and is positive association of Serum IgE, AEC and tissue eosinophilia with individuals with history of allergy. Association of Tissue eosinophilia with AEC, Serum IgE with tissue eosinophilia were not statistically significant.

ROC curve analysis demonstrated excellent diagnostic performance of tissue eosinophil counts for identifying allergen sensitization. Adenoid eosinophils showed an AUC of 0.912 (95% CI: 0.844–0.979), indicating outstanding discriminative ability. An optimal cut-off value of ≥10.5 cells/HPF provided a sensitivity of 86.1%, specificity of 72.7%, PPV of 72.1%, and NPV of 86.5% (p < 0.001). Tonsillar eosinophils also demonstrated excellent diagnostic accuracy, with an AUC of 0.884 (95% CI: 0.806–0.962). A cut-off of ≥9.5 cells/HPF achieved 80.6% sensitivity, 77.3% specificity, 74.4% PPV, and 82.9% NPV (p < 0.001). These findings indicate that eosinophil counts from both tissues can reliably discriminate allergic from non-allergic children.

The diagnostic performance analysis demonstrated that adenoid tissue eosinophil count had a slightly higher sensitivity (86.1%) than tonsillar tissue eosinophil count (80.6%), whereas tonsillar tissue exhibited marginally higher specificity (77.3% vs. 72.7%). The positive predictive values were 72.1% for adenoid tissue and 74.4% for tonsillar tissue, while the negative predictive values were 86.5% and 82.9%, respectively. Both histopathological markers achieved an identical overall diagnostic accuracy of 78.8%, suggesting that eosinophil assessment in either tissue provides clinically useful information for predicting allergic sensitization.

Ekicia YN[16] et al reported sensitivity and specificity value was 72.09 and 91.84 in adenoid tissue and 52.94 and 92.11 in tonsil tissue respectively.

Diagnostic Performance of Tissue Histopathology for Predicting Allergen Sensitization

Diagnostic Parameter	Adenoid Tissue	Tonsillar Tissue
Sensitivity (%)	86.1	80.6
Specificity (%)	72.7	77.3
Positive Predictive Value (%)	72.1	74.4
Negative Predictive Value (%)	86.5	82.9
Overall Accuracy (%)	78.8	78.8

Pearson correlation analysis revealed significant positive correlations between serum total IgE levels and tissue eosinophil counts. Serum IgE showed a strong positive correlation with adenoid eosinophil count (r = 0.724, 95% CI: 0.59–0.82, p < 0.001), indicating that increasing tissue eosinophilia was associated with higher systemic IgE concentrations. A moderate-to-strong positive correlation was also observed between serum IgE and tonsillar eosinophil count (r = 0.661, 95% CI: 0.50–0.78, p < 0.001). Furthermore, adenoid and tonsillar eosinophil counts demonstrated a very strong positive correlation (r = 0.812, 95% CI: 0.72–0.88, p < 0.001), suggesting that eosinophilic inflammation occurs concurrently in both lymphoid tissues. Collectively, these findings support the hypothesis that local tissue eosinophilia reflects systemic allergic inflammation and may serve as a reliable histopathological marker of allergic sensitization in children.

Bhandary R[8] et al cross sectional study observed high serum IgE levels in 51.0% of allergic individuals compared to 27.5% of nonallergic individuals and mean IgE levels were higher in allergic individuals across all age groups. Agha et al[19]. found significantly elevated serum IgE levels in patients with allergic disorders (e.g., asthma, allergic rhinitis, urticaria) compared to healthy controls. Wong CY[17] et al longitudinal study reported persistent serum IgE levels ≥200 kU/L were strongly associated with allergic rhinitis, asthma, and eczema during
childhood.

Huo Z[18] et al study showed allergic disease is a risk factor for reoperation due to adenotonsillar regrowth. High level of IgE

and IL-4 in the serum, and low level of FoxP3 expression are also associated with recurrence and the influence of allergic status and expression level of FoxP3 on reoperation was independent of other confounding factors, such as AHI, patient BMI, and Gata3 expression level in adenotonsilar tissues.

Bhandary R et al cross- sectional study observed significantly higher proportion of allergic individuals exhibited high (overall: 51% i.e. more than half; high: 36.7% and moderate: 14.3%) tissue eosinophilia compared to non-allergic individuals. This statistically significant difference underscores the role of eosinophils as a hallmark of Th2-mediated inflammation in allergic conditions

4. Conclusion

Patients exhibit high tissue eosinophilia despite normal AEC levels, indicating that local factors (e.g., cytokine milieu) can drive eosinophilic infiltration independent of systemic count The complementary roles of serum biomarkers and histopathology in managing hypertrophic lymphoid disorders. While IgE/AEC aid in identifying allergic predisposition, tissue analysis remains indispensable for personalized therapeutic strategies.

The complexity observed in the relationships among AEC, serum IgE, and Tissue eosinophilia, is crucial for clinicians to conduct comprehensive evaluations that include clinical history, physical examination, and possibly additional testing (e.g., allergen-specific tests) to accurately assess the underlying pathologies. Understanding the relationship between these markers can guide personalized treatment strategies for patients with allergic diseases or conditions characterized by eosinophilic inflammation.

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