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The Role of Nasal Cytology in the Phenotyping and Monitoring of Chronic Rhinitis in Children

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ABSTRACT

Background: Local allergic rhinitis (LAR) is a rhinitis subtype characterised by an IgE-mediated response in the nasal mucosa. Although the nasal provocation test (NPT) is the diagnostic gold standard, it is impractical in many centres. Consequently, patients are often misclassified as having non-allergic rhinitis, delaying appropriate treatment. This study evaluated the role of nasal cytology in the classifying and monitoring paediatric allergic rhinitis (AR), distinguishing probable LAR (pLAR), and guiding treatment.

Methods: This retrospective study analysed data from 255 patients diagnosed with chronic rhinitis between March and June 2024. After applying exclusion criteria (recent allergy treatment, nasal deformities, incomplete records), 48 patients were included and grouped as pLAR ($n = 11$) or AR ($n = 37$). Nasal eosinophilia and atopy markers were assessed with clinical symptoms, before and after treatment.

Results: The mean age was 10.5 years (range: 3–17), with 64.6% male. AR was diagnosed in 77% and pLAR in 23%. Asthma was the most common comorbidity (37.5%). Persistent, moderate-severe symptoms were seen in 68.8%, with pollen sensitivity present in 76.3%. After treatment, both VAS scores and nasal eosinophil rates (NEOS%) significantly decreased in both groups ($p < 0.05$). NEOS% was higher in patients with atopic dermatitis and lower in those with adenoidal hypertrophy. AEC and NEOS% were positively correlated ($p < 0.001$), suggesting a link between systemic and local eosinophilia.

Conclusions: Patients with pLAR showed clinical and laboratory improvement similar to AR following treatment. Nasal cytology may be a useful diagnostic and monitoring tool in children with chronic rhinitis.

1 | Introduction

Allergic rhinitis (AR), the most prevalent form of chronic rhinitis, increasingly affects quality of life in both children and adults worldwide [1, 2]. Besides systemic AR, confirmed by specific IgE (sIgE) and skin prick test (SPT), local allergic rhinitis (LAR) – characterised by a localised response to allergens in the nasal mucosa, as indicated by nasal sIgE secretion and nasal allergen provocation testing (NPT) – has emerged as a significant research focus [3]. Differentiating LAR from non-allergic rhinitis (NAR) is essential due to their distinct clinical features and treatment approaches [4]. Although NPT is the diagnostic gold standard [5], it is rarely available in routine practice. Therefore, a simple, accessible and non-invasive alternative is urgently needed.

Nasal cytology, utilised for years in both adults and children [6, 7], offers a valuable alternative. As described by Meltzer and Jalowayski in 1988 [8], it helps differentiate allergic, non-allergic and infectious rhinitis, classify cellular responses and monitor

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Summary

- Nasal cytology is a practical and non-invasive tool for evaluating paediatric chronic rhinitis.
- It reflects both symptom severity and response to treatment through the identification of nasal eosinophilia.
- In children without systemic sensitisation, eosinophilic inflammation detected by nasal cytology may suggest a local allergic mechanism.
- In centres without access to nasal provocation testing, cytological evaluation may serve as a surrogate indicator of local allergic rhinitis.
- Incorporating nasal cytology into routine clinical assessment may improve phenotyping and guide individualised treatment strategies in paediatric rhinitis.

disease progression. Sampling involves nose blowing or mucosal scraping, and analysis focuses on inflammatory cells, including eosinophils, basophils, neutrophils and mast cells. Eosinophil counts increase in allergic nasal diseases and are linked to histaminergic symptoms like sneezing, rhinorrhea and itching [9]. Their cytological density correlates with symptom severity and treatment response [10]. The visual analogue scale (VAS), used to measure the intensity of nasal symptoms, is an effective tool for evaluation [11].

Although there is no definitive threshold for defining nasal eosinophilia, studies – primarily involving adult patients – often consider 5% or higher in the distribution of inflammatory cells as indicative of nasal eosinophilia [12]. Values above this threshold are significant for diagnosing AR, NAR and non-allergic rhinitis with eosinophilia (NARES). This study aimed to assess the utility of nasal cytology in diagnosing and managing paediatric AR, examining its relationship with clinical symptoms, sensitisation patterns, VAS scores, serum atopy markers and atopic comorbidities.

2 | Materials and Methods

2.1 | Study Subjects

This study was conducted in accordance with the Declaration of Helsinki and was approved by Dokuz Eylül University Non-Interventional Research Ethics Committee (Approval No: 2024/24-02, Date: 10.07.2024). Access permission was obtained from the hospital archive and statistics unit, and verbal consent was obtained from the patients' parents for the use of their medical data in accordance with the Personal Data Protection Law.

In our paediatric allergy clinic, patients with AR symptoms, elevated total IgE and nasal/peripheral eosinophilia but negative SPT or sIgE are evaluated for other rhinitis causes (infectious rhinitis, vasomotor rhinitis, drug-induced rhinitis, hormonal rhinitis, etc.). If excluded, treatment is initiated according to clinical guidelines [13]. At the first-week follow-up, patients showing significant improvement in VAS scores and nasal eosinophil percentage (NEOS%) are classified as probable local allergic rhinitis (pLAR), as NPT is unavailable. Non-responders are referred to otolaryngology to evaluate anatomical issues or NAR, such as NARES.

Between March and June 2024, 255 children (aged 2–18 years) with chronic rhinitis were screened, and patients with NEOS% > 5% were selected. Patients were excluded if they had recent infections, used corticosteroids, antihistamines or leukotriene receptor antagonists (LTRA) in the past 4 weeks, had nasal deformities, prior nasal surgery or systemic illness ($n = 58$). Additional exclusions were due to incomplete data ($n = 82$) or poor follow-up/treatment adherence ($n = 67$). In total, 37 patients were diagnosed with AR, and 11 were classified as pLAR. The study flow is shown in Figure 1.

2.2 | Methods of Nasal Cytology

In our clinic, nasal swabs (2 × 10 mm, paediatric cotton applicator tip, Puritan) are routinely used for chronic rhinitis evaluation due to their practicality and patient comfort across all paediatric age groups. Samples are gently taken from the middle portion of the inferior turbinate under anterior rhinoscopy, rolled onto glass slides, air-dried and stained using the Wright–Giemsa dip method in the haematology laboratory. Slides are then examined under 1000× magnification with immersion oil by two blinded specialists. At least 50 fields are analysed for epithelial and inflammatory cells – including eosinophils, basophils and mast cells – and bacterial presence using the Meltzer–Jalowayski semi-quantitative method [8]. The eosinophil percentage is calculated by dividing the number of eosinophils by total inflammatory cells. Other cell types were excluded, as the study focused solely on nasal eosinophilia.

2.3 | Clinical Assessment

Demographic data, symptoms, clinical history, examination findings, aeroallergen sensitivities, concomitant diseases and treatments received were analysed. Additionally, the patients' pre-treatment VAS scores (pre-VAS), nasal eosinophil rates, absolute eosinophil counts (AEC) and T. IgE, along with their control levels at the 1st-week and 1st-month follow-ups, were also evaluated (Figure 1b). Nasal eosinophilia was defined as a concentration of 5% or greater (Figure 2), and the presence of more than 400 eosinophils/μL in the complete blood count was considered peripheral eosinophilia. Patients with a history of atopic dermatitis (AD), asthma and adenoid hypertrophy (AHT) diagnosed via nasopharyngeal endoscopy by an otolaryngologist within the past year were also classified as having additional comorbidity.

In our clinic, the VAS is a simple and effective tool to assess AR symptoms. Patients mark a point on a 10 cm line reflecting symptom severity; for children under 10, parents assist. Treatment plans are based on initial VAS scores per ARIA guidelines. Follow-up assessments, including VAS and nasal cytology at weeks 1 and 4, guide treatment adjustments.

In our laboratory, allergen extracts used in SPT were manufactured by Lofarma S.p.A. (Milan, Italy). Allergens include pollens (Poaceae, *Artemisia vulgaris*, *Betula alba*, *Olea europaea*,

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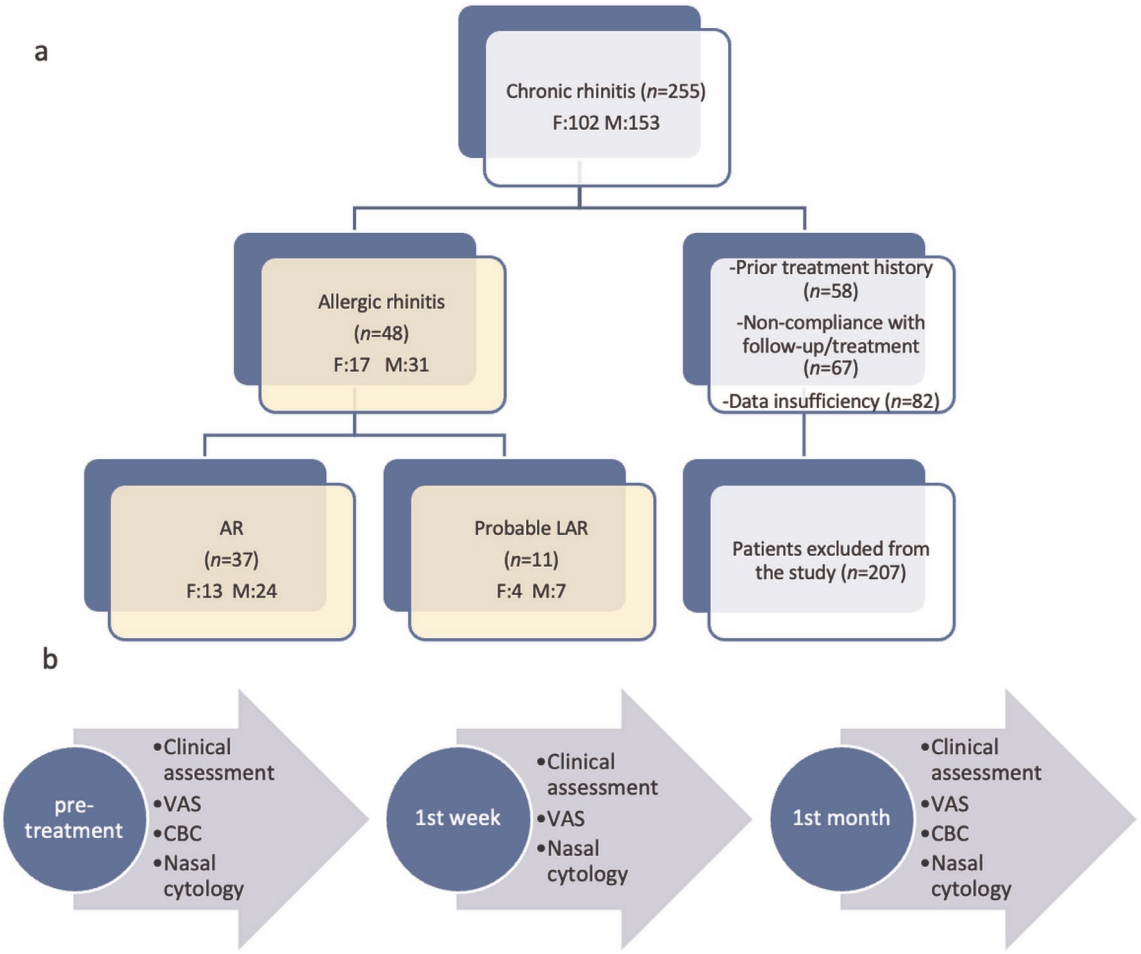


FIGURE 1 | Evaluation process and the flowchart of the study. (a) Inclusion and exclusion process of the patients evaluated in the study. (b) Study flowchart and evaluated clinical/laboratory parameters. AR: allergic rhinitis; CBC: complete blood count; F: female; LAR: local allergic rhinitis; M: male; VAS: visual analogue scale.

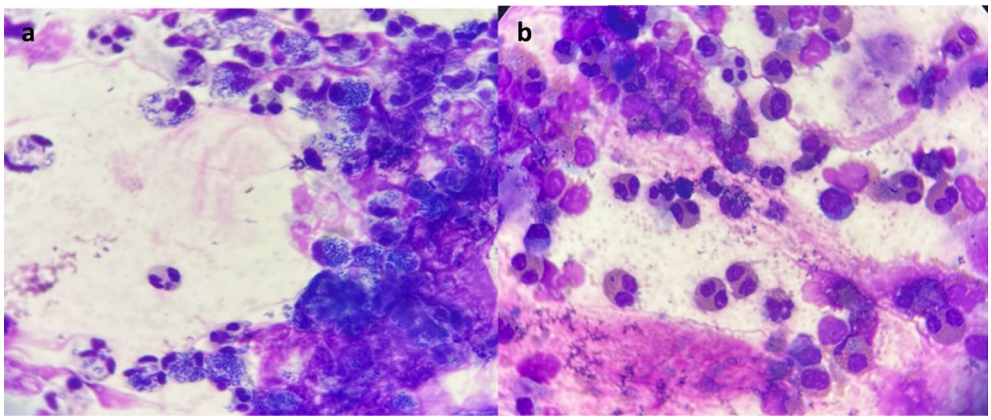


FIGURE 2 | Nasal cytology samples of the cases. (a) Densely granulated neutrophils accompanying eosinophils in the early phase of AR. (b) Eosinophils with distinctly granular, bilobed nuclei as fundamental cells of AR.

Fagus sylvatica, *Alnus glutinosa*, Phleum), house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), animal danders (*Felis domesticus* and *Canis familiaris*) and moulds (*Alternaria alternata* and *Aspergillus fumigatus*). In this test, histamine and saline were used as positive and negative controls, respectively. A wheal ≥3 mm over the negative control is considered positive, and results are interpreted based on correlation with clinical symptoms. Monosensitisation refers to sensitivity to one allergen; multiple sensitivities indicate polysensitisation. NPT could not be performed due to technical limitations, preventing confirmation of LAR or distinction from NARES.

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TABLE 1 | Demographic and clinical characteristics of the cases.

	pLAR ($n=11$)	AR ($n=37$)	p	Total ($n=48$)
Age [mean (min–max)] (years)	8 (3–16)	10 (3–17)	0.154	10.5 (3–17)
	n **(%)**	***n*** **(%)**		***n*** **(%)**
Gender				
F	4 (36.4)	13 (35.1)	0.940	17 (35.4)
M	7 (63.6)	24 (64.9)		31 (64.6)
Comorbidities				
Asthma	3 (27.3)	15 (40.5)	0.425	18 (37.5)
AD	0 (0)	8 (21.6)	0.170	8 (16.7)
AHT	2 (18.2)	3 (8.1)	0.321	5 (10.4)
Symptoms				
Nasal congestion	6 (54.5)	18 (48.6)	0.731	25 (50)
Sneezing	6 (54.5)	23 (62.2)	0.650	29 (60.4)
Rhinorrhea	6 (54.5)	23 (62.2)	0.650	29 (60.4)
Itching	6 (54.5)	22 (59.5)	0.772	28 (58.3)
Ocular	5 (45.5)	20 (54.1)	0.616	25 (52.1)
Duration				
Intermittent	4 (36.4)	11 (29.7)	0.677	15 (31.3)
Persistent	7 (63.6)	26 (70.3)		33 (68.8)
Severity				
Mild	5 (45.5)	10 (27)	0.247	15 (31.3)
Moderate–severe	6 (54.5)	27 (73)		33 (68.8)
Sensitisation				
Monosensitised	—	9 (24.3)	—	9 (18.8)
Polysensitised	—	28 (75.7)		28 (58.3)
Sensitisation group				
Pollen	—	29 (78.4)	—	29 (60.4)
Dander	—	22 (59.5)		22 (45.8)
Dust	—	7 (18.9)		7 (14.6)
Mould	—	6 (16.2)		6 (12.5)
Family history of atopy	7 (63.6)	29 (78.4)	0.322	36 (75)

Abbreviations: AD: atopic dermatitis; AHT: adenoid hypertrophy; AR: allergic rhinitis; F: female; M: male; pLAR: probable local allergic rhinitis.

2.4 | Statistical Analysis

Statistical analyses of the obtained data were conducted using SPSS version 29. The normality of the variables was assessed using histograms, probability plots and the Kolmogorov–Smirnov test. The independent samples *t*-test and ANOVA were applied for normally distributed variables, whereas the Wilcoxon and Mann–Whitney *U* tests were used for non-normally distributed variables. In comparing quantitative data, Pearson correlation analysis was used for normally distributed variables, whilst Spearman correlation analysis was applied otherwise. In descriptive analyses, non-normally distributed data were expressed as median (med) and interquartile range (IQR), whereas normally distributed data were presented as frequency, mean, percentage and minimum–maximum (range) values. Results were evaluated within a 95% confidence interval, with a significance level of $p<0.05$. This study was reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guideline.

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TABLE 2 | Relationship of VAS scores with clinical features.

	pre-VAS med (IQR)	*p*	VAS-1w med (IQR)	*p*	VAS-1m med (IQR)	*p*	1st week VAS% change med (IQR)	*p*	1st month VAS% change med (IQR)	*p*
Comorbidities										
Asthma	6.5 (2)	0.545	4 (1)	0.678	2 (2)	0.680	33 (17)	0.873	61 (35)	0.529
AHT	7 (2)	0.754	4 (2)	0.653	2 (2)	0.770	33 (30)	0.635	66 (27)	0.660
AD	7 (1)	0.407	5 (2)	0.356	3.5 (2)	0.205	30.5 (15)	0.677	48.5 (28)	0.405
Symptoms										
Congestion	6 (3)	***0.002	4 (2)	0.113	2 (3)	0.102	33 (27)	0.918	61 (37)	0.934
Itching	8 (2)	***0.003	5 (2)	0.136	3 (3)	0.394	33 (21)	0.809	62 (39)	0.407
Rhinorrhea	8 (2)	***0.004	5 (2)	**0.007	3 (3)	*0.041	28 (20)	0.117	60 (34)	0.554
Sneezing	7 (2)	0.177	4 (2)	0.880	3 (3)	0.614	33 (21)	0.380	62 (38)	0.440
Ocular	7 (2)	0.254	5 (2)	0.309	3 (3)	0.966	37 (30)	0.950	62 (33)	0.310
Duration										
Intermittent	6 (2)	#0.014	4 (3)	##0.002	2 (3)	0.197	42 (38)	#0.039	60 (43)	0.964
Persistent	7 (2)		5 (2)		3 (2)		33 (15)		62 (34)	
Severity										
Mild	7 (3)	0.505	5 (1)	0.991	3 (2)	0.541	33 (22)	0.867	57 (33)	0.138
Moderate-severe	7 (2)		4 (3)		2 (3)		33 (21)		62 (41)	
Sensitisation										
Monosensitised	7 (2)	0.605	5 (1)	0.206	3 (2)	1	28 (21)	0.055	62 (34)	0.887
Polysensitised	7 (2)		4.5 (1)		3 (2)		37 (22)		59 (34)	

Note: For the statistical data, which is evaluated as present or absent: *$p<0.05$, **$p<0.01$, ***$p<0.001$. For the statistical data, which is evaluated between each group: #$p<0.05$, ##$p<0.01$.
Abbreviations: AHT, adenoid hypertrophy; AD, atopic dermatitis; VAS, visual analogue scale; pre-VAS, pre-treatment VAS scores; VAS-1w, VAS scores in the first week; VAS-1m, VAS scores in the first month.

3 | Results

3.1 | General Population

Amongst the 48 patients (mean age: 10.5 years; 64.9% male), the most common symptoms were sneezing and rhinorrhea (60.4%). Persistent, moderate–severe rhinitis was observed in 68.8% of cases. Sensitisation was detected in 77.1% of patients, with 75.6% polysensitised – mostly to pollen – and 24.3% monosensitised. Pollen-animal dander co-sensitisation was the most frequent pattern (39.2%). Eleven patients (22.9%) without sensitisation were classified as pLAR. Detailed demographic and clinical features are provided in Table 1.

Treatment data revealed 87.5% of patients received NCS, 50% oral antihistamines (OAH) and 25% LTRA. All asthma cases were treated with inhaled corticosteroids, and 22% received LTRA. Due to the high prevalence of pollen sensitivity, persistent symptoms and seasonal exposure, ARIA-based treatment was extended to 1 month following early response.

Baseline symptom scores, treatment-related changes and their association with NEOS% were evaluated. Higher baseline VAS scores were observed in those presenting with nasal congestion, itching and rhinorrhea ($p<0.005$), with rhinorrhea remaining significantly associated with elevated scores at both week 1 and month 1 ($p=0.007$ and $p=0.041$). Patients with persistent rhinitis showed higher VAS scores both at baseline and after 1 week compared to those with intermittent symptoms ($p=0.014$ and $p=0.002$). Additionally, VAS-1w improvement was significantly greater in the pollen-sensitive group compared to others ($p=0.027$) (Table 2).

Total IgE levels were significantly higher in polysensitised patients both before and after treatment ($p=0.031$ and $p=0.016$, respectively), whereas no such association was observed for AEC. On the other hand, a significant correlation was identified between baseline NEOS% and AEC values ($p<0.001$) (Figure 3c).

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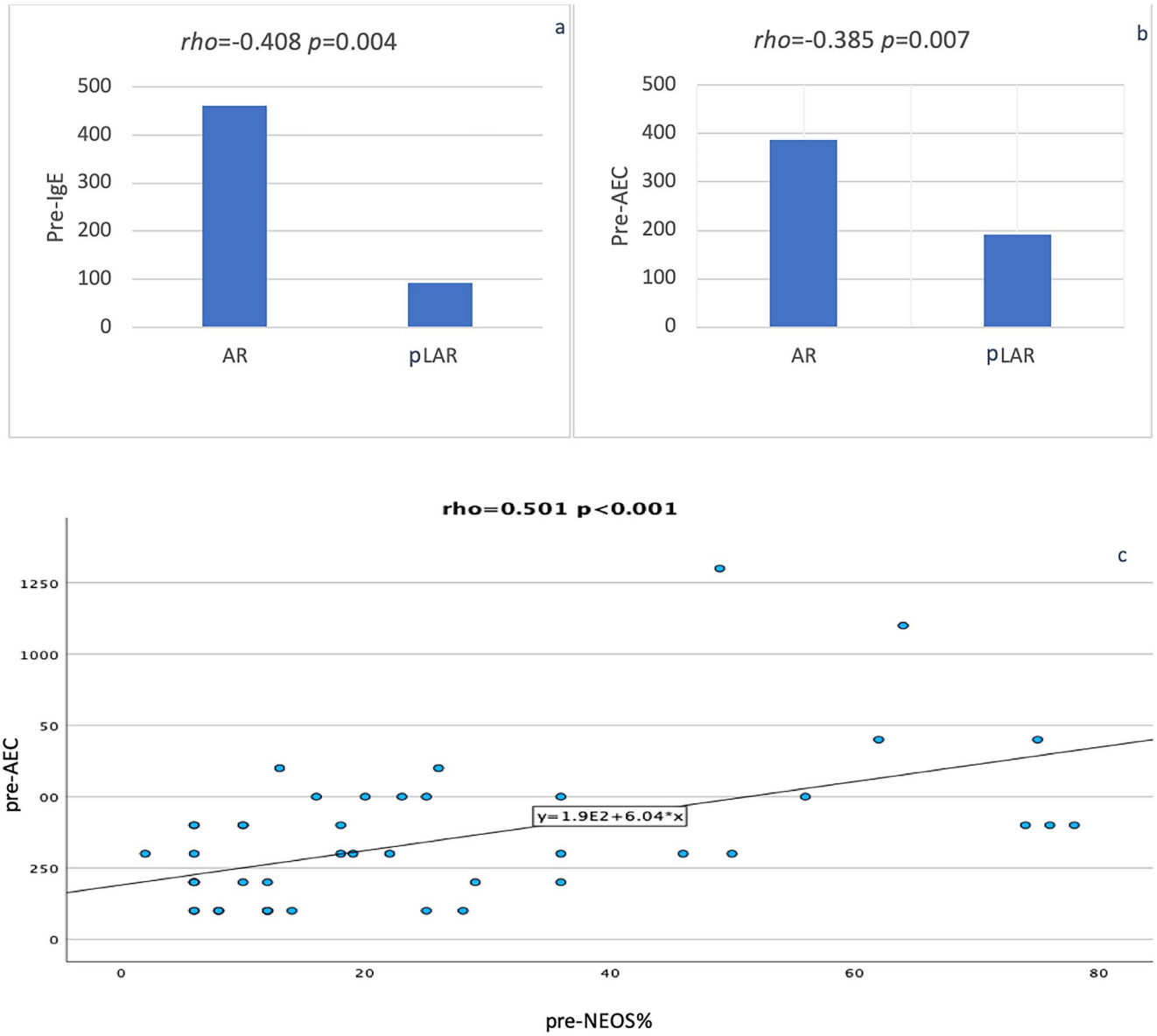


FIGURE 3 | Comparison of pre-IgE levels (a) and pre-NEOS% values (b) between AR and probable LAR groups, and correlation analysis between pre-AEC and pre-NEOS% (c). AR: allergic rhinitis; pLAR: probable local allergic rhinitis; pre-AEC: pre-treatment absolute eosinophil count; pre-IgE: pre-treatment total immunoglobulin E; pre-NEOS%: pre-treatment rate of nasal eosinophilia.

Patients with AD exhibited higher NEOS% values both before and after treatment ($p = 0.040$ and $p = 0.021$, respectively). In contrast, patients with AHT were diagnosed with rhinitis at a younger age and had lower baseline NEOS% values ($p = 0.048$ and $p = 0.042$, respectively).

When comparing the clinical features between the AR and pLAR groups, the AR group exhibited significantly higher baseline total IgE, 1-month IgE levels and AEC ($p = 0.05$, $p < 0.01$ and $p = 0.008$, respectively) (Figure 3a,b).

No statistically significant differences were observed between two groups in terms of age, gender, severity of symptoms, comorbidities or pre-treatment NEOS% values ($p > 0.05$) (Table 3). Furthermore, both groups showed statistically significant reductions in VAS and NEOS% at 1-week and 1-month follow-ups ($p < 0.05$) (Table 3).

4 | Discussion

In this retrospective analysis of children with chronic rhinitis evaluated during the spring season, pollen sensitisation was observed in the majority (60.4%), with sneezing and rhinorrhea being the most frequently reported symptoms. Rhinorrhea, in particular, was associated with greater symptom burden, and most patients exhibited a persistent, moderate-to-severe phenotype.

Significant reductions in both VAS and NEOS% values were observed following ARIA-guided treatment. Furthermore, a significant correlation was found between baseline AEC and NEOS% values, in line with previous studies suggesting a link between systemic eosinophilia and local nasal eosinophilic inflammation [14]. This relationship may support the concurrent use of both systemic and local eosinophil markers in patient stratification and treatment monitoring.

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TABLE 3 | Relationship between rhinitis classification and treatment responses.

	pLAR $n=11$ med (IQR)	AR $n=37$ med (IQR)	p	Total $n=48$ med (IQR)
pre-VAS	6 (3)	7 (2)	0.138	7 (2)
VAS-1w	4 (4)	5 (1)	0.170	4.5 (1)
VAS-1m	2 (2)	3 (2)	0.08	3 (3)
pre-VAS vs. VAS-1w (p)	**0.005	***< 0.001	.	***< 0.001
pre-VAS vs. VAS-1m (p)	*0.03	***< 0.001	.	***< 0.001
VAS-1w vs. VAS-1m (p)	**0.007	***< 0.001	.	***< 0.001
pre-IgE (IU/mL)	95 (126)	261 (597)	*0.049	153 (461)
IgE-1m (IU/mL)	58 (115)	277 (418)	***< 0.001	161 (354)
pre-IgE vs. IgE-1m (p)	0.386	0.307	.	0.205
pre-NEOS%	12 (10)	20 (39)	0.188	17 (28)
NEOS%-1w	4 (5)	8 (15)	0.168	7 (14)
NEOS%-1m	2 (4)	4 (11)	0.175	4 (9)
pre-NEOS% vs. NEOS%-1w (p)	**0.003	*** < 0.001	.	*** < 0.001
pre-NEOS% vs. NEOS%-1m (p)	**0.003	*** < 0.001	.	*** < 0.001
NEOS%-1w vs. NEOS%-1m (p)	*0.011	**0.001	.	*** < 0.001
pre-AEC ($10^3/\mu L$)	200 (200)	400 (300)	***0.008	300 (350)
AEC-1m ($10^3/\mu L$)	200 (300)	300 (400)	0.246	300 (375)
pre-AEC vs AEC-1m	0.129	0.131	.	0.372

Note: p values indicate within-group comparisons. *$p<0.05$, **$p<0.01$, ***$p<0.001$.

Abbreviations: AEC-1m, absolute eosinophil counts in the first month; AR, allergic rhinitis; IgE-1m, IgE in the first month; NEOS%-1m, the rate of nasal eosinophilia in the first month; NEOS%-1w, the rate of nasal eosinophilia in the first week; pre-VAS, pre-treatment VAS scores; pre-AEC, pre-treatment absolute eosinophil counts; pLAR, probable local allergic rhinitis; pre-IgE, pre-treatment IgE; VAS-1w, VAS scores in the first week; VAS-1m, VAS scores in the first month; pre-NEOS%, pre-treatment rate of nasal eosinophilia; VAS, vizual analog scale.

The relationship between AR and AHT has been the focus of numerous studies over the years [15]. Whilst some studies suggest that AR increases the likelihood of AHT [16], others have found no such association [17]. For instance, Cho et al. reported that sIgE to pollens may be absent in serum but present in adenoidal tissue [18]. In our study, patients with AHT were diagnosed with rhinitis earlier and had lower baseline NEOS% values. In this context, we propose that even in the absence of detectable systemic sensitisation in cases with suspected AHT, LAR should be considered, especially in patients presenting with early-onset rhinitis symptoms.

In our study, all patients with a history of AD were included in the AR group, and these patients showed significantly higher nasal eosinophil levels. Similarly, a study that included nasal cytology results from 140 children reported that nasal eosinophilia was detected more frequently in cases of AD, asthma and AR compared to healthy controls [19]. Whilst eosinophil levels are known to correlate with disease activity in AD [20], further studies are needed to elucidate their role within the context of the atopic march.

Although evidence remains limited, existing literature increasingly recognises LAR and AR as distinct phenotypes. LAR is often characterised by moderate-to-severe, persistent symptoms, yet fewer systemic comorbidities such as asthma or rhinosinusitis [21]. In this context, although the AR group exhibited significantly higher baseline and 1-month total IgE levels and AEC values compared to the pLAR group, no significant differences were observed in terms of age, gender, clinical symptom profile or the severity of rhinitis. Moreover, both groups showed reductions not only in VAS scores but also in NEOS% following optimal treatment.

This study has several limitations, including the absence of NPT, the lack of a non-allergic control group and a short follow-up period confined to a single season. The small number of pLAR patients and retrospective design may also have introduced selection bias. Nonetheless, the observed reductions in VAS and NEOS% scores suggest that nasal cytology may offer a practical alternative for diagnosis and monitoring, particularly in settings where NPT is unavailable. Further prospective studies involving larger cohorts are warranted to validate these findings.

Author Contributions

Damla Baysal Bakır: conceptualisation, methodology, writing – original draft. **Özge Atay:** conceptualisation, methodology. **Halime Yağmur:** data collection, investigation. **Gizem Kabadayı:** data collection, investigation. **Dilek Tezcan:** data curation, formal analysis. **Suna Asilsoy:** supervision, review and editing. **Nevin Uzuner:** supervision, review and editing.

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Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee (Approval No: 2024/24-02, Date: 10.07.2024).

Consent

Archive access was granted, and verbal parental consent was obtained in line with the Personal Data Protection Law for the use of anonymised data.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/coa.70040.

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