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Aeroallergen Sensitization Patterns in a Lake-Influenced Region of Eastern Anatolia and Their Association with Pediatric Airway Physiology

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Abstract

Objective: To characterize regional aeroallergen sensitization patterns in Eastern Anatolia and assess their association with spirometrically defined airway outcomes among children with asthma from lake-adjacent districts of Van Province and inland districts in other Eastern Anatolian provinces.

Methods: In this retrospective cross-sectional study, 235 children aged 6–18 years were stratified by residence (lake-adjacent districts of Van Province vs inland districts in other Eastern Anatolian provinces). Sensitization burden was defined as the number of positive aeroallergen groups. Spirometry was available for 137 children with physician-diagnosed asthma. Multivariable logistic regression was used to identify independent predictors of airway obstruction (FEV_1/FVC < 0.80), adjusting for age, sex, eosinophilia, and log-transformed IgE.

Results: Sensitization profiles differed by region: house dust mite sensitization was more prevalent in lake-adjacent districts, whereas sensitization to grass and weed pollen was more frequent in inland districts. Among children who underwent spirometry, 22.6% had airway obstruction. Obstruction prevalence increased across sensitization burden categories (0, 1, and ≥2 aeroallergen groups) (8.5%, 20.0%, and 35.0%; p = 0.033). FEV_1/FVC and FEF_{25}-$_{75}$ declined with increasing sensitization burden (p = 0.007 and p = 0.012, respectively). In adjusted analysis, sensitization burden was independently associated with airway obstruction (adjusted OR 1.88, 95% CI 1.24–2.85; p = 0.003). Model discrimination was modest (AUC 0.68, 95% CI 0.59–0.77).

Conclusion: Regional ecological context was associated with distinct patterns of aeroallergen sensitization and clinically relevant differences in airway function. Cumulative sensitization burden was independently associated with spirometrically defined airway obstruction in this pediatric cohort.

Keywords: Aeroallergen; Asthma; Bronchodilator reversibility; Eastern Anatolia; Polysensitization

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Doğu Anadolu'da Göl Etkisindeki Bir Bölgede Aeroalerjen Duyarlanma Paternleri ve Bunların Çocuklarda Havayolu Fizyolojisi ile İlişkisi

Öz

Amaç: Doğu Anadolu'da bölgesel aeroalerjen duyarlanma paternlerini tanımlamak, bu paternlerin Van ilinin göl kıyısındaki ilçelerinde ve diğer Doğu Anadolu illerinin iç kesimlerinde yaşayan astımlı çocuklarda spirometrik olarak tanımlanan havayolu sonuçlarıyla ilişkisini değerlendirmek.

Yöntemler: Bu retrospektif kesitsel çalışmada, 6–18 yaş aralığındaki 235 çocuk ikamet yerine göre (Van ili göl kıyısındaki ilçeler ve diğer Doğu Anadolu illerinin iç kesimleri) sınıflandırıldı. Duyarlanma yükü, pozitif aeroalerjen grup sayısı olarak tanımlandı. Astımı olan 137 çocukta spirometri verisi mevcuttu. Havayolu obstrüksiyonunun ($FEV_1/FVC < 0,80$) bağımsız belirleyicilerini saptamak amacıyla yaş, cinsiyet, eozinofili ve log-dönüştürülmüş IgE için düzeltme yapılarak çok değişkenli lojistik regresyon analizi uygulandı.

Bulgular: Duyarlanma paternleri bölgeye göre farklılık gösterdi: ev tozu akarı duyarlanması göl kıyısındaki ilçelerde daha sık görülürken, çimen ve yabani ot poleni duyarlanması iç kesimlerde daha yaygındı. Spirometri uygulanan çocukların %22,6'sında havayolu obstrüksiyonu saptandı. Obstrüksiyon prevalansı, duyarlanma yükü kategorileri arttıkça yükseldi (%8,5; %20,0; %35,0; p = 0,033). Duyarlanma yükü arttıkça FEV_1/FVC ve FEF_{25-75} değerlerinde azalma gözlendi (sırasıyla p = 0,007 ve p = 0,012). Düzeltilmiş analizde duyarlanma yükü, havayolu obstrüksiyonu ile bağımsız olarak ilişkili bulundu (düzeltilmiş OR 1,88; %95 GA 1,24–2,85; p = 0,003). Modelin ayırt ediciliği orta düzeydeydi (AUC 0,68; %95 GA 0,59–0,77).

Sonuç: Bölgesel ekolojik bağlam, farklı aeroalerjen duyarlanma paternleri ve klinik olarak anlamlı havayolu fonksiyonu farklılıkları ile ilişkili bulundu. Bu pediatrik kohortta kümülatif duyarlanma yükü, spirometri ile tanımlanan havayolu obstrüksiyonu ile bağımsız olarak ilişkiliydi.

Anahtar kelimeler: Aeroalerjen; Astım; Bronkodilatör yanıt; Doğu Anadolu; Polisensitizasyon.

INTRODUCTION

Allergic airway diseases in children, including asthma and allergic rhinitis, are strongly associated with aeroallergen sensitization[1]. Sensitization patterns are influenced by environmental factors such as ambient humidity, vegetation, and altitude, suggesting that ecological context may contribute to variations in disease expression[2,3].

Lake-adjacent environments represent a distinct ecological niche in which relatively high humidity may support humidity-dependent allergens, particularly house dust mites (HDM)4. In contrast, drier inland areas characterized by a predominantly continental climate may exhibit different aeroallergen distributions. Although regional variability in sensitization has been reported, it remains unclear whether these ecological differences are associated with measurable alterations in pediatric airway physiology[2].

Previous studies have often evaluated sensitization burden and lung function separately[2,5,6]. Although some studies have explored the relationship between allergen sensitization and pulmonary outcomes, investigations integrating both sensitization burden and objective lung function parameters within a unified analytical framework remain limited. Moreover, evidence combining regional sensitization patterns with objective spirometric measures within a defined ecological context is still scarce[7–10]. The independent association between cumulative sensitization burden—defined as the number of confirmed aeroallergen sensitivities—and airway obstruction, beyond systemic type 2 inflammatory markers such as eosinophilia and total immunoglobulin E (IgE), has not been clearly established in pediatric populations[11,12]. Differentiating cumulative atopic load from active inflammatory biomarkers may improve clinical risk stratification and the interpretation of spirometric findings[13,14].

The Lake Van region in Eastern Anatolia provides a geographically heterogeneous setting to examine these associations. Districts located along the lakeshore experience a humidity-modified microclimate, whereas surrounding inland districts are characterized by a predominantly continental climate pattern.

The aim of this retrospective study was to characterize regional aeroallergen sensitization patterns in children with asthma and/or allergic rhinitis and to evaluate their associations with spirometric parameters. We hypothesized that children residing in lake-adjacent districts would demonstrate distinct sensitization profiles and that higher cumulative sensitization burden would be independently associated with greater airway obstruction.

METHODS

Study Design and Participants

This retrospective cross-sectional study used routinely collected clinical data from a tertiary pediatric allergy clinic. Data extraction was performed between February and May 2025 and included clinic visits conducted between December 2023 and December 2024.

Medical records of consecutive children aged 6–18 years with physician-diagnosed asthma, allergic rhinitis, or asthma with concomitant allergic rhinitis were reviewed. Diagnoses were established according to the Global Initiative for Asthma (GINA) and Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations[15,16]. Participants were categorized as asthma alone, allergic rhinitis alone, or asthma with concomitant allergic rhinitis.

Exclusion criteria included chronic lung disease other than asthma, congenital heart disease, primary immunodeficiency, acute respiratory infection within 4 weeks before spirometry, and missing key variables required for primary analyses. Analyses were conducted using a complete-case approach. All eligible participants within the study window were included in the analytic cohort (n = 235). Participant flow is presented in Figure 1.

Residence (primary exposure) was defined a priori based on the official residential address recorded at the index visit. Participants were categorized as living in lake-adjacent districts of Van Province or in inland districts in other Eastern Anatolian provinces.

Clinical, Laboratory, and Sensitization Assessment

Demographic and clinical data were extracted from medical records. Absolute eosinophil counts and total serum immunoglobulin E (IgE) were measured using standardized automated laboratory methods. Eosinophilia was defined as ≥500 cells/μL.

Given its right-skewed distribution, total IgE was analyzed as a log-transformed continuous variable and modeled per standard deviation (SD) increase in regression analyses. For descriptive purposes, IgE was categorized into clinically meaningful ranges (≤100, 101–1000, and >1000 IU/mL), reflecting commonly used laboratory reference thresholds and degrees of elevation in pediatric allergy practice. In multivariable models, IgE was analyzed as a log-transformed continuous variable to minimize information loss associated with categorization.

Skin prick testing (SPT) was performed using commercially available standardized aeroallergen extracts (ALK-Abelló, Denmark), including Dermatophagoides pteronyssinus, Dermatophagoides farinae, Ambrosia artemisiifolia, Chenopodiaceae/Amaranthaceae pollen mix, Phleum pratense, Plantago lanceolata, Alternaria alternata, and cat dander, in accordance with established European standards[17]. Histamine and saline served as positive and negative controls, respectively. Tests were read after 15 minutes. Antihistamines were discontinued at least 5 days before testing according to routine clinical protocol. A positive response was defined as a wheal diameter ≥3 mm greater than the negative control.

Aeroallergen sensitization was evaluated at the allergen group level. Patients sensitized to multiple allergens within the same allergen group (e.g., multiple grass pollens) were classified as monosensitized for that group. Aeroallergens were classified into four predefined categories:

(1) HDM sensitization, including Dermatophagoides pteronyssinus and Dermatophagoides farinae;

(2) Grass and weed pollen sensitization, including Ambrosia artemisiifolia, Chenopodiaceae/Amaranthaceae pollen mix, Phleum pratense, and Plantago lanceolata;

(3) Mold sensitization, defined as sensitization to Alternaria alternata, and

(4) Cat dander sensitization.

Sensitization burden was defined as the total number of positive aeroallergen groups (range, 0–4). For descriptive analyses, participants were categorized as follows:

0 groups: no positive sensitization in any of the four aeroallergen groups;

1 group: sensitization to only one aeroallergen group;

≥2 groups: sensitization to two or more aeroallergen groups.

In multivariable regression analyses, sensitization burden was treated as a continuous variable (per additional positive aeroallergen group).

Spirometry and Outcomes

Spirometry was performed according to American Thoracic Society and European Respiratory Society (ATS/ERS) standards in children with physician-diagnosed asthma18.

Measurements were obtained using a computerized spirometer (Jaeger MasterScreen, CareFusion, Germany) during routine outpatient visits when patients were clinically stable and free of acute respiratory symptoms. In routine outpatient clinical practice, spirometry is not performed in children with isolated allergic rhinitis; therefore, lung-function analyses were restricted to participants with asthma.

Of the total cohort (n = 235), 137 children produced acceptable and reproducible spirometry and were included in lung-function analyses.

Measured parameters included forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, peak expiratory flow (PEF), and forced expiratory flow at 25–75% of FVC (FEF_{25-75}), expressed as percentages of predicted values using Global Lung Initiative (GLI) reference equations adjusted for age, sex, and height.

The primary outcome was airway obstruction, defined as FEV_1/FVC < 0.80. In sensitivity analyses, airway obstruction was alternatively defined using the GLI lower limit of normal (LLN) (z-score < −1.64).

Secondary outcomes included continuous FEV_1/FVC, FEF_{25-75} (% predicted), and bronchodilator response (BDR). BDR was primarily defined as an increase in FEV_1 ≥12% from baseline; an absolute increase ≥200 mL was reported as supplementary descriptive information when applicable[19].

Statistical Analysis

Normality of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables are presented as mean ± standard deviation or median (interquartile range), as appropriate. Categorical variables are presented as a number (percentage).

Between-group comparisons were performed using the independent t-test or Mann–Whitney U test for continuous variables and the Pearson chi-square test for categorical variables. Comparisons across sensitization burden categories were conducted using one-way analysis of variance (ANOVA) or the Kruskal–Wallis test, as appropriate. Effect size for continuous variables is reported as eta-squared (η^2).

Multivariable logistic regression analysis was performed to identify independent predictors of airway obstruction among participants with spirometry data (n = 137). Age and sex were included a priori. Eosinophilia, log-transformed IgE (per SD increase), sensitization burden (per allergen increase), and region of residence were included based on clinical relevance. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported.

Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test. Multicollinearity was evaluated using variance inflation factors (VIF). Model discrimination was evaluated using the area under the receiver operating characteristic curve (AUC).

All tests were two-sided, and $p < 0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics (version 29.0). Figures were generated using Python (version 3.12). The study was approved by the local non-interventional clinical research ethics committee (Decision No: GOKAEK; Ref: 2025-01-17; 26 January 2025). Given the retrospective design based on medical record review, the requirement for individual informed consent was waived. All data were anonymized before analysis.

RESULTS

Study Population

Baseline characteristics are summarized (Table I). A total of 235 children were included. The median age was 146 months (IQR 119–181). Male sex was less frequent in lake-adjacent districts compared with inland districts in other Eastern Anatolian provinces (44.5% vs 58.6%; p = 0.042). Urban residence was more common in lake-adjacent districts (83.2% vs 52.6%; p < 0.001).

Table I: Baseline Characteristics According to Province of Residence.

Characteristic	Overall (n=235)	Van (n=119)	Other (n=116)	p-value
Age (months), median (IQR)	146 (119–181)	145 (118–162)	156 (126–201)	**<0.001**
Male sex, n (%)	121 (51.5)	53 (44.5)	68 (58.6)	**0.042**
Urban residence, n (%)	160 (68.1)	99 (83.2)	61 (52.6)	**<0.001**
Clinical phenotype, n (%)				**0.008**
Allergic rhinitis, n (%)	98 (41.7)	42 (35.3)	56 (48.3)	
Asthma, n (%)	71 (30.2)	33 (27.7)	38 (32.8)	
Asthma with allergic rhinitis, n (%)	66 (28.1)	44 (37.0)	22 (19.0)	
Eosinophils ≥500 cells/μL, n (%)	78 (33.2)	41 (34.5)	37 (31.9)	0.781
Total IgE ≤100 IU/mL, n (%)	126 (53.6)	56 (47.1)	70 (60.3)	0.065
Total IgE 101–1000 IU/mL, n (%)	79 (33.6)	43 (36.1)	36 (31.0)	
Total IgE >1000 IU/mL, n (%)	30 (12.8)	20 (16.8)	10 (8.6)	

Baseline demographic and clinical characteristics stratified by province of residence. Province of residence was categorized a priori as Van (lake-adjacent districts) and other Eastern Anatolian provinces (inland districts), reflecting distinct ecological and climatic settings, based on official residential address at the time of clinical evaluation. Continuous variables are presented as median (IQR) and compared using the Mann–Whitney U test. Categorical variables are presented as n (%) and compared using the Pearson chi-square test. Eosinophilia was defined as a peripheral blood eosinophil count ≥500 cells/μL.

Abbreviations: IgE, Immunoglobulin E; IQR, interquartile range; IU/mL, international units per milliliter; n, number of patients; μL, microliter.

The distribution of clinical phenotypes differed between regions (p = 0.008), whereas the prevalence of eosinophilia was similar (p = 0.781). Although the overall distribution of IgE categories did not differ significantly between regions (p = 0.065), IgE >1000 IU/mL was numerically more frequent in lake-adjacent districts (16.8% vs 8.6%).

Regional Sensitization Patterns

Regional sensitization patterns are shown (Table II). HDM sensitization was more prevalent in lake-adjacent districts than in other Eastern Anatolian provinces (52.1% vs 34.5%; p = 0.006). Conversely, grass and weed pollen sensitization was less frequent in lake-adjacent districts than in other Eastern Anatolian provinces (41.2% vs 52.6%; p = 0.048). Mold and cat dander sensitization did not differ significantly between regions (p = 0.072 and p = 0.434, respectively).

Table II: Distribution of Aeroallergen Sensitization by Province of Residence.

Allergen	Van (n=119)	Other (n=116)	p-value
House dust mite sensitization	62 (52.1)	40 (34.5)	**0.006**
Dermatophagoides pteronyssinus	40 (33.6)	23 (19.8)	**0.017**
Dermatophagoides farinae	36 (30.3)	22 (19.0)	**0.045**
Grass and weed pollen sensitization	49 (41.2)	61 (52.6)	**0.048**
Ambrosia artemisiifolia	14 (11.8)	28 (24.1)	**0.032**
Chenopodiaceae/Amaranthaceae pollen	21 (17.6)	31 (26.7)	0.079
Phleum pratense	32 (26.9)	19 (16.4)	**0.041**
Plantago lanceolata	18 (15.1)	30 (25.9)	0.067
Mold sensitization (Alternaria)	26 (21.8)	15 (12.9)	0.072
Cat dander sensitization	18 (15.1)	22 (19.0)	0.434

Distribution of aeroallergen sensitization stratified by province of residence. Province of residence was categorized a priori as Van (lake-adjacent districts) and other Eastern Anatolian provinces (inland districts), reflecting distinct ecological and climatic settings. Data are presented as n (%), with percentages calculated within each province. Group-level sensitization was defined as a positive reaction to at least one specific allergen within the respective category. Comparisons were performed using the Pearson chi-square test with Yates' continuity correction. All tests were two-sided, and p < 0.05 was considered statistically significant. Abbreviations: n, number of patients; p, probability value.

Airway Outcomes

Among the total cohort, 137 children completed acceptable spirometry (Figure 1). Airway obstruction was identified in 31 children (22.6%).

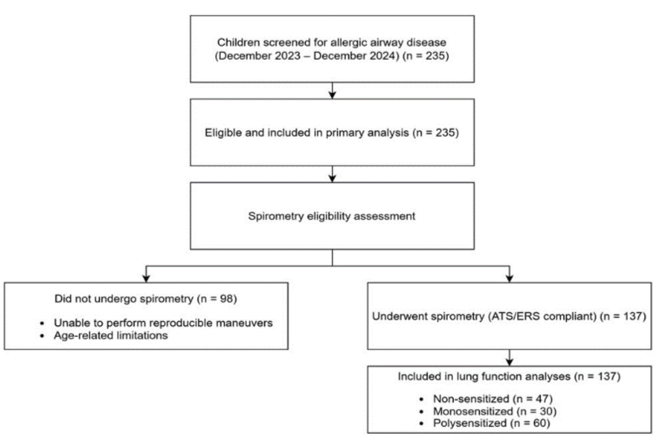

Figure 1. Flowchart of patient recruitment and analytic cohort formation.

Between December 2023 and December 2024, 235 children with physician-diagnosed asthma and/or allergic rhinitis were assessed for eligibility and included in the primary analysis (n=235). Spirometry eligibility was subsequently evaluated; 98 children were excluded due to inability to perform reproducible maneuvers or age-related limitations. A total of 137 participants completed spirometry according to American Thoracic Society/European Respiratory Society (ATS/ERS) standards and were included in lung function analyses.

Among these, 47 participants had no sensitization (0 aeroallergen groups), 30 were monosensitized (1 aeroallergen group), and 60 were polysensitized (≥2 aeroallergen groups).

Abbreviations: ATS/ERS, American Thoracic Society/European Respiratory Society.

Lung function parameters according to sensitization burden are presented (Table III). The prevalence of airway obstruction increased progressively across sensitization categories (8.5%, 20.0%, and 35.0%; p = 0.033). Both FEV_1/FVC and FEF_{25-75} decreased significantly with increasing sensitization burden (p = 0.007 and p = 0.012, respectively) (Figure 2), whereas FEV_1 and FVC did not differ significantly.

Table III: Lung Function Parameters and Clinical Outcomes According to Sensitization Burden

Parameter	0 Groups (n=47)	1 Group (n=30)	≥2 Groups (n=60)	p-value	η²
FEV_1, % predicted	94.8 ± 8.5	91.6 ± 7.6	91.4 ± 7.9	0.071	0.040
FVC, % predicted	97.4 ± 9.8	95.6 ± 8.6	100.0 ± 8.0	0.064	0.042
FEV_1/FVC ratio	0.827 ± 0.022	0.818 ± 0.020	0.807 ± 0.018	**0.007**	0.095
PEF, % predicted	90.4 ± 10.8	91.7 ± 12.6	89.3 ± 12.2	0.681	0.006
$FEF_{25–75}$, % predicted	85.6 ± 6.2	80.4 ± 8.6	74.9 ± 9.0	**0.012**	0.082
Airway obstruction, n (%)	4 (8.5)	6 (20.0)	21 (35.0)	**0.033**	—
BD reversibility, n (%)	10 (21.3)	11 (36.7)	25 (41.7)	**0.048**	—

Lung function parameters and clinical outcomes according to sensitization burden (0, 1, and ≥2 aeroallergen groups). Continuous variables are presented as mean ± standard deviation and were compared using one-way analysis of variance (ANOVA). Categorical variables are presented as n (%) and were compared using the Pearson chi-square test. Effect size is expressed as eta-squared (η²) for continuous variables. Post-hoc pairwise comparisons were not performed due to the exploratory nature of the analysis.

Airway obstruction was defined as FEV_1/FVC < 0.80, as described in the Methods section. Bronchodilator (BD) reversibility was defined as an increase in FEV_1 ≥12% from baseline.

All tests were two-sided, and p < 0.05 was considered statistically significant.

Abbreviations: ANOVA, analysis of variance; BD, bronchodilator; $FEF_{25–75}$, forced expiratory flow between 25% and 75% of forced vital capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; n, number of patients; PEF, peak expiratory flow; p, probability value; η², eta-squared (effect size).

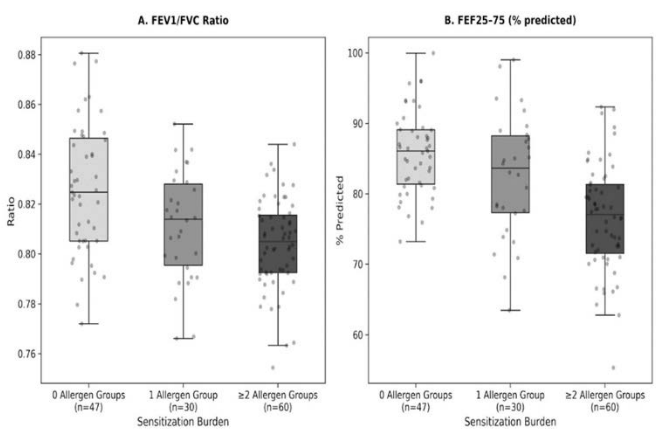

Figure 2. Lung function parameters according to aeroallergen sensitization burden.

Box plots display (A) FEV_1/FVC ratio and (B) $FEF_{25–75}$ (% predicted) across sensitization burden groups: 0 (n=47), 1 (n=30), and ≥2 aeroallergen groups (n=60). The center line indicates the median; boxes represent the interquartile range (IQR); whiskers extend to 1.5 × IQR. Individual data points are shown.

Group comparisons were performed using one-way analysis of variance (ANOVA) or Kruskal–Wallis test, as appropriate.

Abbreviations: ANOVA, analysis of variance; $FEF_{25–75}$, forced expiratory flow between 25% and 75% of forced vital capacity; FEV_1, forced expiratory volume in 1 second; IQR, interquartile range; n, number of patients.

Bronchodilator reversibility was observed in 46 of 137 children (33.6%) and increased across sensitization groups (21.3%, 36.7%, and 41.7%; p = 0.048). Obstruction prevalence stratified by province and sensitization burden is illustrated (Figure 3).

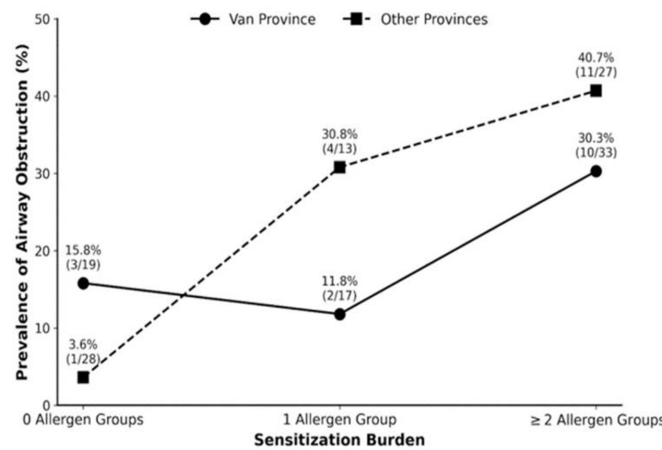

Figure 3. Prevalence of airway obstruction by province of residence and aeroallergen sensitization burden.

Line graph illustrating the prevalence of airway obstruction across sensitization burden groups (0, 1, and ≥2 aeroallergen groups), stratified by province of residence (Van Province vs. other Eastern Anatolian provinces). Airway obstruction was defined as FEV_1/FVC < 0.80. Values represent the percentage of children with airway obstruction within each sensitization group, with corresponding counts (n/N) displayed for each data point. Comparisons were performed using the Pearson chi-square test. Exact p-values are reported in Table III.Abbreviations: n, number of patients.

Multivariable Analysis

Multivariable logistic regression results are presented (Table IV). Sensitization burden was independently associated with airway obstruction (aOR 1.88 per additional aeroallergen group; 95% CI 1.24–2.85; p = 0.003). Age, sex, eosinophilia, and log-transformed IgE were not independently associated with obstruction.

Table IV: Multivariable Logistic Regression Analysis for Independent Predictors of Airway Obstruction.

Predictor Variable	β	Adjusted OR	95% CI (Lower–Upper)	p-value
Age (per 1-SD)	0.134	1.14	0.74–1.77	0.542
Male sex (1 vs 0)	−0.327	0.72	0.30–1.70	0.456
Eosinophilia ≥500 cells/μL	−0.355	0.70	0.26–1.90	0.484
log(Total IgE) (per SD)	0.090	1.09	0.72–1.67	0.675
Sensitization burden	0.630	1.88	1.24–2.85	**0.003**

The multivariable logistic regression model included all listed variables simultaneously (enter method) to evaluate independent predictors of airway obstruction, defined as $FEV_1/FVC < 0.80$, in the spirometry subcohort (n=137).

Adjusted odds ratios (ORs) for continuous variables reflect the risk associated with a 1-standard deviation increase. Sensitization burden reflects the incremental risk per additional positive aeroallergen group. Reference categories for categorical variables are indicated in parentheses. β coefficients represent log odds. All tests were two-sided, and $p < 0.05$ was considered statistically significant. Model calibration was adequate (Hosmer–Lemeshow $\chi^2 = 3.44$, $p = 0.904$), and variance inflation factors for all predictors were <1.05, indicating no significant multicollinearity. Model discrimination was modest (AUC = 0.68). Abbreviations: CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; IgE, immunoglobulin E; OR, odds ratio; SD, standard deviation.

The model demonstrated good calibration (Hosmer–Lemeshow $\chi^2 = 3.44$, $p = 0.904$) and modest discrimination (AUC 0.68, 95% CI 0.59–0.77; $p < 0.001$) (Figure 4).

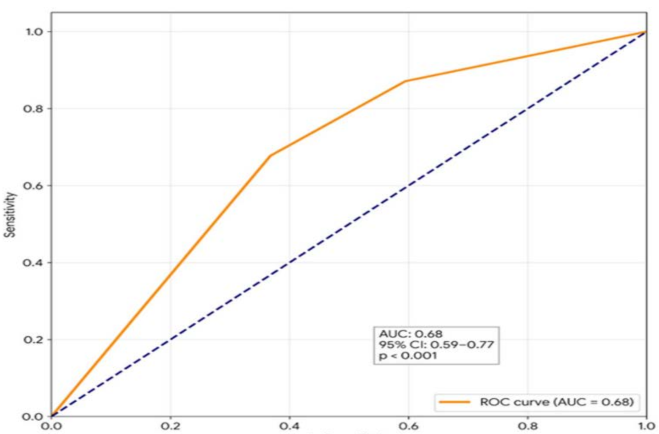

Figure 4. ROC curve for the multivariable logistic regression model predicting airway obstruction.

The ROC curve demonstrates the discriminative performance of the multivariable model for airway obstruction, defined as $FEV_1/FVC < 0.80$. The model included age, sex, eosinophilia, log-transformed total IgE, sensitization burden, and region of residence. The area under the curve (AUC) was 0.68 (95% CI, 0.59–0.77; $p < 0.001$), indicating modest discrimination. The diagonal dashed line represents no discrimination. Abbreviations: AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic.

Sensitivity analyses using the GLI-defined LLN (z-score < −1.64) demonstrated consistent associations between sensitization burden and airway obstruction.

DISCUSSION

This study demonstrates that regional ecological context was associated with distinct aeroallergen sensitization profiles in children with allergic airway disease. In addition, cumulative sensitization burden showed a graded association with spirometrically defined airway obstruction and remained independently associated after adjustment for demographic characteristics and inflammatory biomarkers. These findings indicate that cumulative atopic load is associated with airflow limitation independent of systemic type 2 inflammatory markers within this clinical setting.

Regional differences in sensitization patterns are biologically plausible. Climatic and environmental factors—including humidity, vegetation, altitude, and indoor microenvironmental conditions—are known to influence aeroallergen distribution and exposure intensity[20,21]. Geographic variability in allergen sensitization has been documented across diverse climatic regions[2,22]. Environments characterized by sustained humidity may favor the proliferation of HDM and increased allergen load[23]. The observed predominance of mite sensitization in lake-adjacent districts and higher pollen sensitization in inland provinces is consistent with established ecological patterns of allergen distribution. Similar regional variability has been reported in Turkish pediatric cohorts[24].

The independent association between sensitization burden and airway obstruction underscores the potential contribution of cumulative allergen exposure to persistent airflow limitation. Prior studies evaluating polysensitization and lung function have reported heterogeneous findings, with some demonstrating independent associations and others observing attenuation after biomarker adjustment[7,25]. The present findings support the concept that cumulative sensitization may reflect broader immunologic or structural airway changes not fully captured by systemic inflammatory markers.

In contrast, bronchodilator reversibility increased across sensitization categories in unadjusted analyses but was not independently evaluated in multivariable models. This pattern suggests that dynamic airway responsiveness may not parallel the association observed for fixed airflow obstruction and cumulative sensitization burden. Although eosinophilia and total IgE were not independently associated with fixed obstruction in this cohort, previous literature has demonstrated links between type 2 inflammation and airway variability, and this relationship warrants further investigation[26].

Several limitations merit consideration. The cross-sectional design precludes inference regarding temporality or causality. Spirometry was completed in a subset of participants, introducing the possibility of selection bias. Environmental exposure was inferred from the region of residence rather than directly quantified, which may introduce ecological exposure misclassification. Although sensitivity analyses using LLN criteria yielded consistent results, the primary use of a fixed FEV_1/FVC cutoff (<0.80) may influence classification in borderline cases. The relatively modest model discrimination (AUC 0.68) should also be considered when interpreting predictive performance. Although model complexity was restricted to reduce overfitting, residual confounding from unmeasured environmental, socioeconomic, behavioral, or treatment-related factors remains possible.

Another limitation relates to the scope of the aeroallergen panel. Although commonly relevant aeroallergens in routine clinical practice were included, the panel did not cover certain potentially important sensitizers such as tree pollens, cockroach allergens, and a broader range of molds beyond Alternaria alternata. This limited coverage may have led to an underestimation of the true sensitization burden and may have influenced the observed associations between sensitization patterns and airway outcomes. Future studies incorporating more comprehensive aeroallergen panels are warranted to better characterize the full spectrum of environmental sensitization.

In summary, the ecological context was associated with distinct patterns of aeroallergen sensitization in this pediatric population. Cumulative sensitization burden was independently associated with spirometrically defined airway obstruction, whereas bronchodilator responsiveness appeared less strongly linked to cumulative atopic load. Future longitudinal studies incorporating direct environmental exposure measurements and repeated lung function assessments are needed to clarify temporal relationships and underlying mechanisms.

Ethical Approval: As this study was conducted as a retrospective record review, approval was obtained from a local non-interventional clinical research ethics committee (Decision No: GOKAEK; Reference No: 2025-01-17; Approval Date: 26 January 2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. Patient confidentiality was strictly maintained throughout the study.

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