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Seasonal Variation in Histologic and Endoscopic Activity of Pediatric Eosinophilic Esophagitis: A Repeated Endoscopy Cohort

Pediyatrik Eozinofilik Özofajitte Histolojik ve Endoskopik Aktivitenin Mevsimsel Değişimi: Tekrarlayan Endoskopi Kohortu

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ABSTRACT

Objective: The pathogenesis of eosinophilic esophagitis (EoE) is not fully understood, food allergens are considered the primary triggers. Nevertheless, the frequent coexistence of EoE with atopic diseases suggests that aeroallergens may also play an important role in disease development and exacerbation. The aim of this study was to assess the relationship between seasonality and disease activity, as determined by esophageal eosinophil counts and endoscopic findings, in children with EoE.

Methods: This retrospective cohort study included pediatric patients diagnosed with EoE who were followed at our center between January 1, 2010, and June 1, 2026. Demographic, clinical, laboratory, endoscopic, and histopathological data were retrospectively collected from the medical records and analyzed. The spring and summer months were defined as the high-pollen season, whereas the autumn and winter months were defined as the low-pollen season.

Results: A total of 526 upper gastrointestinal endoscopic examinations were performed in the 130 patients during the study period. An accompanying allergic disease was present in 55 patients (42.3%), whereas 75 patients (57.7%) had no history of allergic disease. Asthma was the most common allergic comorbidity, affecting 33 patients (25.4%). Compared with the low-pollen season, the high-pollen season was associated with significantly higher median EREFS scores [2 (interquartile range [IQR], 0-4) vs. 1 (IQR, 0-3), $p = 0.012$] and significantly higher median peak histologic eosinophil counts [35 (IQR, 0-71) vs. 25 (IQR, 0-60)] eosinophils per high-power field, $p = 0.013$.

Öz

Amaç: Eozinofilik özofajitin (EoE) patogenezi tam olarak aydınlatılmamış olmakla birlikte, gıda alerjenleri hastalığın başlıca tetikleyicileri olarak kabul edilmektedir. Bununla birlikte, EoE'nin atopik hastalıklarla sıklıkla birlikte görülmesi, aeroalerjenlerin de hastalığın gelişimi ve alevlenmesinde önemli bir rol oynayabileceğini düşündürmektedir. Bu çalışmanın amacı, eozinofilik özofajitli çocuklarda özofagus eozinofil sayıları ve endoskopik bulgular ile belirlenen hastalık aktivitesi ile mevsimsellik arasındaki ilişkiyi değerlendirmektir.

Yöntemler: Bu retrospektif kohort çalışmasına, 1 Ocak 2010 ile 1 Haziran 2026 tarihleri arasında merkezimizde izlenen ve EoE tanısı alan pediatrik hastalar dahil edildi. Demografik, klinik, laboratuvar, endoskopik ve histopatolojik veriler tıbbi kayıtlardan geriye dönük olarak elde edilerek analiz edildi. İlkbahar ve yaz ayları yüksek polen sezonu, sonbahar ve kış ayları ise düşük polen sezonu olarak tanımlandı.

Bulgular: Çalışma dönemi boyunca 130 hastaya toplam 526 üst gastrointestinal sistem endoskopisi uygulandı. Hastaların 55'inde (%42,3) eşlik eden alerjik hastalık bulunurken, 75'inde (%57,7) alerjik hastalık öyküsü yoktu. Astım, 33 hastayı (%25,4) etkileyerek en sık görülen alerjik komorbiditeydi. Düşük polen sezonu ile karşılaştırıldığında, yüksek polen sezonunda medyan EREFS skorları [2 (çeyrekler arası aralık [IQR], 0-4) vs. 1 (IQR, 0-3), $p = 0,012$] ve medyan pik histolojik eozinofil sayıları [35 (IQR, 0-71) vs. 25 (IQR, 0-60)] yüksek büyütme alanındaki eozinofiller, $p = 0,013$ anlamlı olarak daha yüksekti.

Sonuç: Bu bulgular, aeroalerjenlerin EoE aktivitesinin mevsimsel modülasyonunda potansiyel bir rol oynadığını desteklemekte ve EoE'li

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ABSTRACT

Conclusion: These findings support a potential role for aeroallergens in the seasonal modulation of EoE activity and suggest that seasonal aeroallergen exposure should be considered during the clinical follow-up of pediatric patients with EoE.

Keywords: Eosinophilic esophagitis, pediatric, seasonality, aeroallergens, endoscopy

Öz

pediyatrik hastaların klinik izlemi sırasında mevsimsel aeroalerjen maruziyetinin dikkate alınması gerektiğini düşündürmektedir.

Anahtar Sözcükler: Eozinofilik özofajit, pediyatrik, mevsimsellik, aeroalerjenler, endoskopi

INTRODUCTION

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated inflammatory disorder of the esophagus characterized by symptoms of esophageal dysfunction. In children, clinical presentation is age-dependent and may include feeding difficulties, vomiting, abdominal pain, dysphagia, food impaction, poor growth, and failure to thrive. According to the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guideline, the histological diagnosis of EoE is established by the presence of a peak eosinophil count of ≥ 15 eosinophils per high-power field (eos/HPF) in esophageal biopsy specimens in the appropriate clinical setting (1). Over the past two decades, both the incidence and prevalence of EoE have increased markedly, particularly in the pediatric population (2). Although the pathogenesis of EoE is not fully understood, food allergens are considered the primary triggers. Nevertheless, the frequent coexistence of EoE with atopic diseases, particularly allergic rhinitis and asthma, suggests that aeroallergens may also play an important role in disease development and exacerbation (3). Allergic comorbidities, including allergic rhinitis, asthma, and urticaria, are present in approximately 41% of patients with EoE (4). The aim of this study was to assess the relationship between seasonality and disease activity, as determined by esophageal eosinophil counts and endoscopic findings, in children with EoE.

MATERIALS AND METHODS

This retrospective cohort study included pediatric patients diagnosed with EoE who were followed at the Division of Pediatric Gastroenterology, Hepatology and Nutrition, Gazi University, Faculty of Medicine, between January 1, 2010, and June 1, 2026. Demographic characteristics, clinical features, laboratory findings (peripheral blood eosinophil percentages obtained within the one month preceding each endoscopic examination), endoscopic findings, and histopathological results were retrospectively extracted from the medical records and analyzed. Because patients underwent multiple follow-up endoscopic examinations during the study period, all endoscopic assessments were included in the analysis and categorized according to the season in which they were performed, regardless of treatment status. The diagnosis of EoE was made according to the ESPGHAN guideline after excluding secondary causes of esophageal eosinophilia, including gastroesophageal reflux disease, Crohn's disease, vasculitis, infections, and connective tissue disorders, and demonstrating a peak eosinophil count of ≥ 15 eos/HPF in esophageal biopsy specimens obtained during upper gastrointestinal endoscopy (1). Biopsy specimens obtained from the proximal, middle, and distal esophagus were reviewed. The highest

eosinophil count identified in any biopsy specimen was recorded as the peak eosinophil count. Endoscopic findings were assessed using the Eosinophilic Esophagitis Endoscopic Reference Score (EREFS), which evaluates edema, rings, exudates, furrows, and strictures (5). Endoscopic examinations were categorized according to the season in which they were performed: Winter (December-February), spring (March-May), summer (June-August), and autumn (September-November). To evaluate the potential effect of aeroallergen exposure, seasons were dichotomized into a high-pollen season (spring/summer) and a low-pollen season (autumn/winter), reflecting the typical pattern of airborne pollen exposure in Türkiye (6-8). The study protocol was approved by the Ethics Committee of Gazi University (approval number: 1450; date: July 28, 2026).

Statistical Analysis

Data analysis was undertaken using IBM SPSS Statistics for Windows (version 22.0; IBM Corp., Armonk, NY, USA). The normality of continuous variables was evaluated with the Shapiro-Wilk test before statistical testing. Normally distributed data are presented as mean $\pm$ standard deviation, whereas skewed data are summarized as median and interquartile range (IQR). Categorical variables are reported as frequencies with corresponding percentages. Comparisons between the high- and low-pollen seasons were performed using the independent-samples t-test or the Mann-Whitney U test, according to data distribution. Associations involving categorical variables were examined using Pearson's chi-square test or Fisher's exact test when appropriate. Statistical significance was defined as a two-sided p-value below 0.05.

RESULTS

A total of 130 pediatric patients with EoE were included in the study. Of these, 96 (73.8%) were male and 34 (26.2%) were female. A total of 526 upper gastrointestinal endoscopic examinations were performed in the 130 patients during the study period. The mean age at the first endoscopic examination was 7.5 ± 4.4 years. An accompanying allergic disease was present in 55 patients (42.3%), whereas 75 patients (57.7%) had no history of allergic disease. Asthma was the most common allergic comorbidity, affecting 33 patients (25.4%), followed by food allergy in 12 (9.2%), allergic rhinitis in 7 (5.4%), and urticaria in 3 (2.3%). At the time of endoscopy, 50.5% of the patients were asymptomatic. The most common symptoms were food impaction (16.5%), vomiting (11.6%), dysphagia (9.1%), abdominal pain (4.3%), prolonged chewing/selective eating (4.2%), and drinking lots of water with meals (3.3%). The monthly distribution of the mean endoscopic EREFS scores and mean peak histologic eosinophil counts is shown in Figure 1.

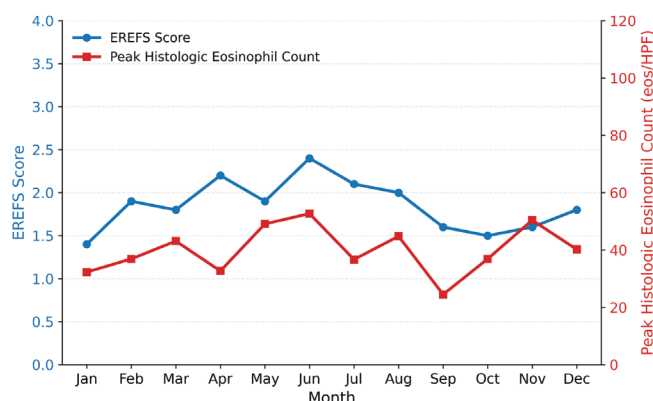


Figure 1. Monthly distribution of the mean endoscopic EREFS scores and mean peak histologic eosinophil counts.

EREFs: Eosinophilic Esophagitis Endoscopic Reference Score.

Both parameters demonstrated a similar temporal pattern, with higher values during the spring and summer months and lower values during autumn. When EREFS scores and peak histologic eosinophil counts were compared across the four seasons, both parameters were higher during spring and summer than during autumn and winter; however, these differences did not reach statistical significance ($p = 0.071$ and $p = 0.086$, respectively). In a prespecified secondary analysis, spring and summer were grouped as the high-pollen season, whereas autumn and winter were grouped as the low-pollen season. Compared with the low-pollen season, the high-pollen season was associated with significantly higher median EREFS scores [2 (IQR, 0-4) vs. 1 (IQR, 0-3), $p = 0.012$] and significantly higher median peak histologic eosinophil counts [35 (IQR, 0-71) vs. 25 (IQR, 0-60) eos/HPF, $p = 0.013$]. When the findings from patients' initial endoscopies were compared between the high- and low-pollen seasons, no significant differences were observed in EREFS scores or peak eosinophil counts ($p = 0.600$ and $p = 0.847$, respectively). However, when follow-up endoscopies were compared after excluding the patients' initial endoscopies, significant differences were observed in both EREFS scores and peak eosinophil counts ($p = 0.005$ and $p = 0.002$, respectively). Similarly, the median serum eosinophil percentage was significantly higher during the high-pollen season than during the low-pollen season [4.6% (IQR, 2.3-6.5) vs. 3.8% (IQR, 2.0-6.3), $p = 0.042$]. The odds of active histologic disease (peak eosinophil count ≥ 15 eos/HPF) were significantly higher during the high-pollen season than during the low-pollen season (odds ratio = 1.66, 95% confidence interval = 1.15-2.38; $p = 0.006$).

DISCUSSION

In the present study, we demonstrated that EoE activity was significantly greater during the high-pollen season (spring and summer) than during the low-pollen season. Patients evaluated during the high-pollen season had higher endoscopic disease severity, higher peak histologic eosinophil counts. Although previous studies have investigated the seasonal variation of EoE, our study differs from the existing literature in several important aspects.

Unlike many earlier reports focusing solely on newly diagnosed patients or on individuals presenting with food impaction, our cohort included both newly diagnosed and follow-up patients, including those receiving treatment whose symptoms had improved (9). In our study, no significant seasonal differences in EREFS scores or peak eosinophil counts were observed at the initial endoscopy, whereas significant differences emerged in follow-up endoscopies. This discrepancy may partly be explained by the variable interval between symptom onset and diagnosis, as patients may undergo their initial endoscopy at different stages of disease activity. In addition, follow-up endoscopies may be more frequently performed in response to treatment assessment, recurrence of symptoms, or other clinical indications, potentially resulting in a greater representation of periods of active disease and thereby contributing to the observed seasonal differences. Furthermore, all data were derived from a single tertiary referral center with standardized endoscopic, histopathological, and clinical evaluation, minimizing concerns regarding heterogeneity that may arise in multicenter or nationwide database studies.

The etiology and pathogenesis of EoE have not yet been fully elucidated. Although EoE is primarily considered a food antigen-driven disease, its frequent coexistence with other atopic conditions raises the possibility that aeroallergens may also contribute to disease activity (10). A distinct seasonal pattern has been demonstrated for asthma exacerbations, with Harju et al. (11) reporting significant seasonal variation in asthma-related hospitalizations. Similarly, seasonal allergic rhinitis is well known to peak between April and June, corresponding to periods of increased airborne pollen exposure (12). In Türkiye, although regional variations exist, airborne pollen concentrations are highest during the spring and summer months (6). Considering these observations, the increased EoE activity observed during the high-pollen season in our study supports the hypothesis that aeroallergen exposure may contribute to the etiopathogenesis and seasonal exacerbation of EoE.

Several studies have previously investigated the seasonal distribution of EoE. In one of the largest published cohorts, Wang et al. (9) evaluated 234 patients with newly diagnosed EoE and found that the number of diagnoses was significantly lower during the winter months than during the other seasons. Similarly, Watanabe et al. (13) reported that EoE diagnoses were more frequent during spring and summer and less common during winter. In a study conducted in the United States including 79 children with EoE, 45% of patients were diagnosed during the spring months (14). In addition, several case reports have described seasonal exacerbations of EoE during the pollen season in patients with concomitant allergic rhinitis or asthma (15,16). Our findings are consistent with these previous observations, demonstrating increased EoE activity during the high-pollen season. From a clinical perspective, these findings suggest that, particularly in patients with concomitant allergic diseases such as asthma or allergic rhinitis, withdrawal or step-down of maintenance therapy may be more appropriately considered after the high-pollen season rather than during periods of peak aeroallergen exposure. However, prospective studies are needed to determine whether such a strategy improves long-term disease control.

Study Limitations

This study has several limitations. First, its retrospective design may have resulted in incomplete clinical documentation and limited the availability of potentially relevant variables, such as detailed environmental exposure data and individual pollen sensitization profiles. Second, although our institution is located in Ankara and most of our patients reside in Ankara, it is a tertiary referral center that receives patients from many regions of Türkiye. Therefore, regional differences in pollen calendars and aeroallergen exposure may have influenced the observed seasonal patterns. Because the analyses were based on the timing of endoscopy rather than patients' geographic residence or region-specific pollen counts, regional variability in aeroallergen exposure could not be accounted for. Third, the severity and activity of concomitant allergic diseases, including asthma and allergic rhinitis, were not systematically documented at the time of endoscopy. Consequently, the temporal relationship between seasonal exacerbations of these allergic diseases and EoE activity could not be directly evaluated. Finally, due to incomplete treatment-related data in the medical records, we were unable to perform a detailed comparison of seasonal disease activity according to specific treatment modalities, such as elimination diets, proton pump inhibitors, or topical corticosteroids.

CONCLUSION

In conclusion, our study demonstrated that EoE activity was significantly higher during the high-pollen season in a cohort including both newly diagnosed and follow-up patients. Increased endoscopic severity, histologic eosinophilic inflammation, peripheral eosinophilia, and a higher prevalence of active histologic disease during spring and summer support a potential role for aeroallergens in the seasonal modulation of EoE activity. These findings suggest that seasonal aeroallergen exposure should be considered during the clinical follow-up of patients with EoE, particularly in those with concomitant atopic diseases such as asthma or allergic rhinitis. Prospective multicenter studies incorporating regional pollen monitoring and allergen sensitization data are warranted to confirm these observations and to determine whether seasonally tailored monitoring and treatment strategies can improve disease outcomes.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Gazi University (approval number: 1450; date: July 28, 2026).

Informed Consent: Informed consent was not required as this was a retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.Ö., Ö.E.G., S.S., B.D., Concept: H.Ö., B.D., Design: H.Ö., S.S., Data Collection or Processing: A.C., F.E.K., Analysis or Interpretation: H.Ö., S.S., Literature Search: H.Ö., Writing: H.Ö., S.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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