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ORIGINAL ARTICLE

Gastroenterology: Eosinophilic Gastrointestinal Disorders

Impact of gender, race, and age of onset on the phenotype and comorbidities of pediatric eosinophilic esophagitis

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Abstract

Objectives: To investigate differences in symptoms, allergy comorbidities, and eosinophilic inflammation at the time of diagnosis for patients with eosinophilic esophagitis (EoE) based on gender, race, and age of onset.

Methods: A retrospective study was conducted at a multidisciplinary EoE clinic; the correlation between histological findings, previously identified symptoms, associated comorbidities, and demographics including gender, race, as well as age of onset was examined. Chi-squared and Student's *T*-tests were utilized for statistical analysis.

Results: A total of 91 patients were enrolled in this study, with 70% being male and 67% identifying as White. Among the patients, 45% had an early onset of EoE (defined as ≤6 years old). We revealed that White patients and females were significantly more likely to report dysphagia, while non-White patients experienced significantly more vomiting symptoms and had a higher prevalence of asthma as a comorbidity. Early-onset patients exhibited a significantly higher rate of vomiting and had elevated eosinophilic counts compared to patients with EoE onset at a regular age. We also revealed that abdominal pain is associated with a lower average proximal eosinophilic counts.

Conclusions: Our study revealed the significant impact of gender, race, and age of onset on the phenotype and comorbidities of EoE, suggesting these factors should be considered when caring for these patients.

KEYWORDS

comorbidities, eosinophilic, esophagus, inflammation, phenotype

1 | BACKGROUND

Eosinophilic esophagitis (EoE) is recognized as a chronic immunologic disorder of the esophagus resulting in esophageal inflammation due to the accumulation of eosinophils in the epithelium.[1] The improved diagnostic criteria for EoE have led to a natural increase in diagnosis and recognition over the past 20 years.[2,3] Although the precise underlying pathophysiology of EoE is not well understood, various genetic and environmental risk factors are proposed to be associated with the development and phenotypic expression of the disease.[4]

EoE is diagnosed by identification of EoE symptoms, subsequently conducting a biopsy that demonstrates more than 15 eosinophils per high-powered field, and exclusion of any other conditions such as gastroesophageal reflux disease.[5,6] Of note, prolonged untreated inflammation leads to worsening of symptoms as well as increasing fibrosis and scaring, indicating the importance of early

identification and treatment of EoE in preventing symptom progression.[7] Existing literature establishes that EoE manifests differently in adult and pediatric patients.[8,9] There is some overlap in symptoms between adult and pediatric patients, but adolescents and adults tend to present more commonly with dysphagia, solid food impaction, and esophageal fibrosis.[5] In pediatric patients, the most common symptoms can be nonspecific and include vomiting, abdominal pain, failure to thrive, and feeding difficulties.[10,11] The presence of these vague symptoms can make early diagnosis more difficult, emphasizing the need for a better understanding of differences in presentation for specific pediatric populations.[8,9] Within the pediatric age group, there has been limited research to describe ethnic, gender, and concomitant atopic symptoms or diagnoses in patients with EoE. Some preliminary studies have described differences in EoE diagnosis between pediatric African American and Caucasian patients but fail to attribute specific symptoms to a particular race.[11,12]

The objective of this study is to systematically evaluate the impact of demographics and age of onset on the phenotype and comorbidities of pediatric EoE. Our hypothesis posits that variations in gender and race among children may give rise to distinct clinical presentations, and that pediatric patients diagnosed at an early age may experience more severe eosinophilic infiltration within the esophagus.

What is Known

- Adult studies have demonstrated both racial and symptom differences with respect to eosinophilic esophagitis.
- Primary symptom differences in children compared to adults are significant, as are eosinophil count on biopsies at the time of diagnosis.

What is New

- Reported symptoms of dysphagia were more likely in females and White patients, compared to asthma and vomiting in non-White patients.
- Early onset patients have higher levels of eosinophils per high powered field compared to regular onset patients, regardless of race or gender.

2 | METHODS

2.1 | Study design

We conducted a retrospective chart review of pediatric patients seen by a multidisciplinary EoE clinic from January 2020 to December 2022. This research project had received IRB approval. Cases of EoE were defined as per 2018 consensus guidelines.[6] Patients were characterized based on their demographics (Table 1). Pertinent data extracted from the chart review included age, gender, and race as reported in the general demographic page of the medical record. Previous smaller studies have demonstrated significantly higher incidence differences of EoE in the White population,[13] and symptom presentation.[14] Non-White individuals—including Blacks, Hispanics, and others—will be analyzed together and compared with White patients. We defined early onset as ≤6 years old, and regular pediatric onset as >6 years old. Age cutoffs were determined based on previously reported ages of diagnosis commonly seen at >6 years old,[15] as well as very early onset being defined as <1 year old in earlier studies.[16] These patients with known EoE diagnosis were retrospectively assessed for eosinophilic counts on the initial distal and proximal esophageal biopsies as well as previously reported symptoms (e.g., abdominal pain, dysphagia or food impaction, oral aversion or failure to thrive, vomiting) and identified comorbidities (e.g., allergic rhinitis, asthma, eczema, food allergy). The eosinophilic counts were measured in eosinophil count per high-power field (eos/hpf). Histologic findings were extracted from the pathology reports and reviewed again by the same pathologist of our single center.

TABLE 1 Patient descriptive statistics.

	Age category at diagnosis		Total patients
	Early onset (≤6 years old) 41 (45%)	Regular onset (>6 years old) 50 (55%)	91
Gender			
Male	29 (71%)	35 (70%)	64 (70%)
Female	12 (29%)	15 (30%)	27 (30%)
Race			
White	23 (56%)	38 (76%)	61 (67%)
Non-White	18 (44%)	12 (24%)	30 (33%)
Known atopic history	24 (58%)	23 (46%)	47 (52%)
Mean age, years (range)	2.9 (1–6)	11.5 (7–20)	

2.2 | Statistical analysis

Demographic and age of onset information were summarized descriptively. The eosinophilic counts of different gender (Male or Female), race (White or non-White), and age of onset (early onset defined as ≤6 years old, regular pediatric onset defined as >6 years old) were compared

using Student's *T*-test. The percentage of clinical symptoms and associated comorbidities in different gender, race, and age of onset were compared using Chi Square. The correlation of individual symptoms and eosinophilic counts was analyzed using Pearson coefficient. A p value of <0.05 was considered as significant.

3 | RESULTS

Ninety- one patients with a confirmed diagnosis of EoE were included in this study, of whom 70% were male and 30% were female. Among the participants, 67% were White and 33% were non-White. The age of onset ranged from 1 to 17 years, with 45% classified as early onset and 55% as regular onset (Table 1).

3.1 | Histologic findings

Our findings indicated that there was no significant difference of eosinophilic count on both proximal and distal esophageal biopsies between different gender or race. However, early onset (EO) patients had significantly higher average eosinophil counts (distal: 56, proximal: 50) as compared to regular onset (RO) (distal: 39, proximal: 39), ($p < 0.05$.) (Figure 1A,B).

3.2 | Clinical findings

On evaluation of four different types of clinical manifestations (Figure 1C), female patients and White individuals were significantly more likely to present with dysphagia, 56% (vs. 29%) and 43% (vs. 21%), respectively ($p < 0.05$). Non-White patients and patients with early-onset EoE were found to have a significantly higher incidence of vomiting 61% versus 13% and 36% versus 10%, respectively ($p < 0.05$). There was not a statistically significant difference between the number of non-White patients in the early onset group versus the late onset group to suggest a level of confounding for the differences in symptoms. Regarding the association of atopic comorbidities (Figure 1D), non-White patients were found to have a higher incidence of asthma than White patients (39% vs. 11%) ($p < 0.05$), but no difference was found between different gender and race.

3.3 | Symptom–histology correlation

Considering that the correlation between the patient-reported symptoms and histological findings could potentially have a significant clinical impact for possibly reducing the frequency of endoscopies, we also performed this statistical analysis on all enrolled patients together, regardless of gender, race, or age of onset. Among these four different symptoms, our findings suggested that abdominal pain is associated with a lower average proximal eosinophilic count (35 compared to 48 in patients without abdominal pain) ($p < 0.05$). There is no significant correlation for abdominal pain and distal eosinophilic count, as well as other individual symptoms and eosinophilic counts.

4 | DISCUSSION

EoE, a condition with a rising prevalence in both adults and children, has been shown to have a higher incidence in male and Caucasian individuals.[3,17] Despite this, there has been a paucity of research investigating the impact of demographics and age of onset on EoE symptoms and histology.[12,13] Our study adds to the literature on how gender, race, and age of onset are associated with histological features, clinical symptomatology, and comorbidities in children affected by EoE.

Our study shows that histology may differ within pediatric patients based on age of onset. Pediatric patients diagnosed at earlier ages in our cohort had higher esophageal eosinophil counts, which was not seen when examining gender or race at the time of diagnosis. Our study showed differing symptom patterns in patients with EoE associated with different demographic variables. Female patients and White patients were notably more likely to present with dysphagia. Additionally, non-White patients exhibit a higher incidence of asthma and vomiting compared to White patients, which is consistent with previous literatures.[18,19] The underlying mechanisms of action for these differences in symptoms despite similar eosinophil counts are unknown, and more research for identifying the relationship between these unique disease presentations is necessary. However, knowing different presentation patterns among varying demographics may aid in more expedited diagnosis.

This study possesses several noteworthy strengths as well as limitations that warrant consideration. We were able to access a relatively large and diverse cohort of patients diagnosed with EoE, residing within a specific geographic region of the United States, with a notable representation of Black and Hispanic individuals.[17] This enabled us to conduct in-depth stratification of the population based on race and gender, facilitating a comprehensive characterization of the patients concerning both clinical symptoms and histological features. However, it is essential to acknowledge the limitations of this research. The study design was retrospective and limited to a single-center setting, potentially introducing biases and confounding factors that may influence the results. Because of the single center and retrospective design, we had small sample sizes and attempted to overcome this by our ethnicity

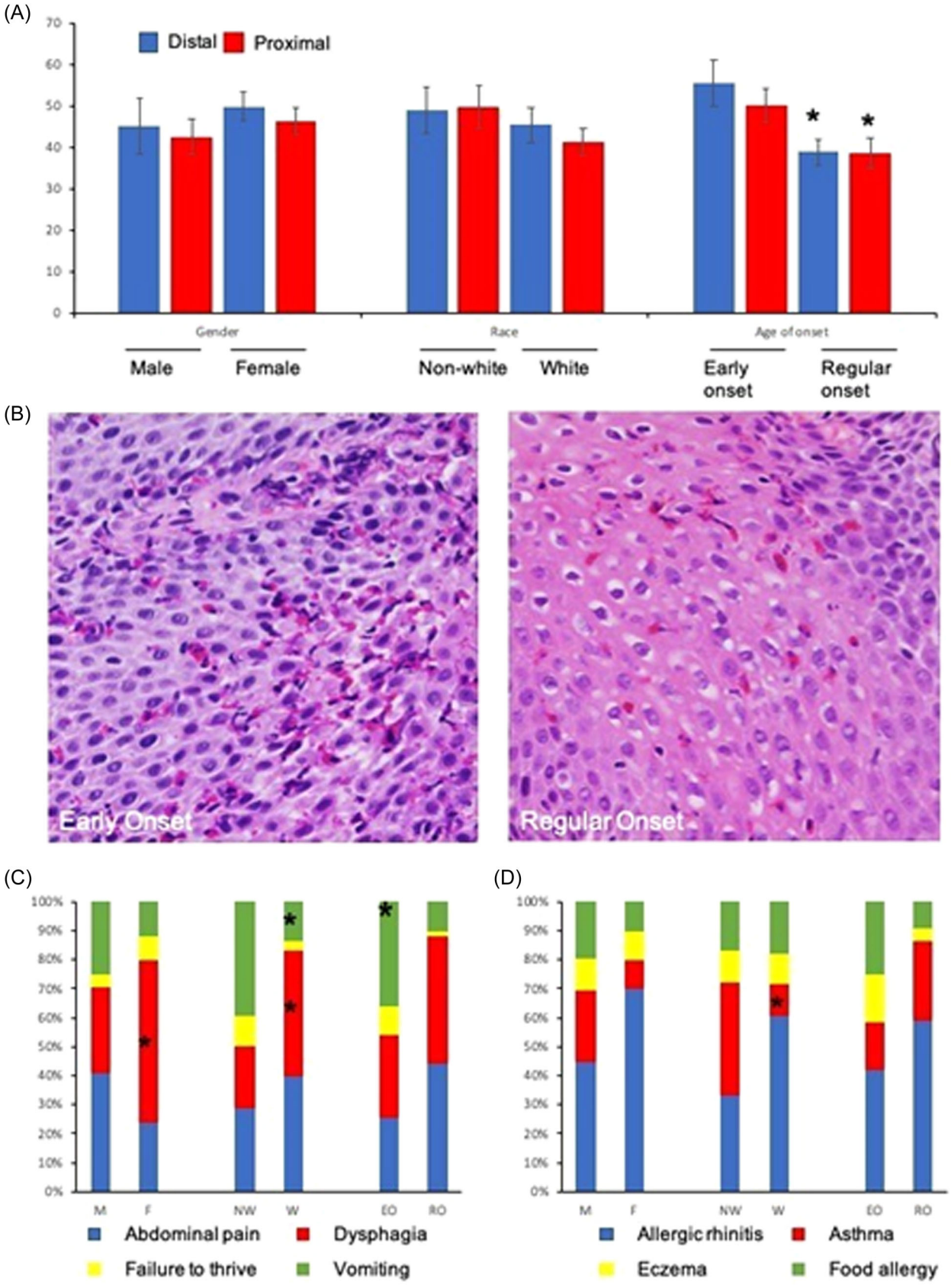

FIGURE 1 Esophageal eosinophilic counts (A), Representative images of eosinophilic inflammation (B), gastrointestinal symptoms (C), and associated comorbidities (D) between different gender (Male [M] vs. Female [F]), race (non-White [NW] vs. White [W]), and age of onset (EO vs. RO). * Indicates statistically significant ($p < 0.05$) findings. EO, early onset; RO, regular onset.

groupings. Based on the current sample size, statistical significance has been successfully found. Including more patients by extending the retrospective time frame may alleviate small sample size issues for future research. We also could not retrospectively utilize symptom scoring tools, however had to use self-reported and documented symptoms instead. Consequently, the findings might not be readily generalizable to other populations or healthcare settings.

Overall, this study reaffirms that pediatric patients present differently from adults, and highlights that there is elevated eosinophil counts in patients with early-onset disease, as well as significant presentation differences between different gender and race. Follow-up review of subsequent endoscopies in these patients to assess response to specific therapies could further highlight differences in response based on age of onset, gender, and ethnicity. In patients with various demographics, this research will help make an earlier diagnosis and ultimately achieve equitable and better patient outcomes.

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CONFLICTS OF INTEREST STATEMENT

The authors declare no conflict of interest.

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REFERENCES

1. Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology*. 2007;133(4):1342-1363.
2. Thomsen SF. Epidemiology and natural history of atopic diseases. *Eur Clin Respir J*. 2015;2. doi:10.3402/ecrj.v2.24642
3. Dellon ES. Epidemiology of eosinophilic esophagitis. *Gastroenterol Clin North Am*. 2014;43(2):201-218.
4. Alexander ES, Martin LJ, Collins MH, et al. Twin and family studies reveal strong environmental and weaker genetic cues explaining heritability of eosinophilic esophagitis. *J Allergy Clin Immunol*. 2014;134(5):1084-1092.e1.
5. Dellon ES, Gibbs WB, Fritchie KJ, et al. Clinical, endoscopic, and histologic findings distinguish eosinophilic esophagitis from gastroesophageal reflux disease. *Clin Gastroenterol Hepatol*. 2009;7(12):1305-1313; quiz 1261.
6. Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018;155(4):1022-1033.e10.
7. Schoepfer AM, Safroneeva E, Bussmann C, et al. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation in a time-dependent manner. *Gastroenterology*. 2013;145(6):1230-6.e1-2.
8. Straumann A, Aceves SS, Blanchard C, et al. Pediatric and adult eosinophilic esophagitis: similarities and differences. *Allergy*. 2012;67(4):477-490.
9. Lucendo AJ, Sánchez-Cazalilla M. Adult versus pediatric eosinophilic esophagitis: important differences and similarities for the clinician to understand. *Expert Rev Clin Immunol*. 2012;8(8):733-745.
10. Muir A, Falk GW. Eosinophilic esophagitis: a review. *JAMA*. 2021;326(13):1310-1318.
11. Weiler T, Mikhail I, Singal A, Sharma H. Racial differences in the clinical presentation of pediatric eosinophilic esophagitis. *J Allergy Clin Immunol Pract*. 2014;2(3):320-325.
12. Chatham D, Cavender CP, Lieberman JA. Racial disparity in eosinophilic esophagitis from a single, defined population. *Ann Allergy Asthma Immunol*. 2014;113(4):489-491.
13. Sperry SL, Woosley JT, Shaheen NJ, Dellon ES. Influence of race and gender on the presentation of eosinophilic esophagitis. *Am J Gastroenterol*. 2012;107(2):215-221.
14. Ito J, Fujiwara T, Kojima R, Nomura I. Racial differences in eosinophilic gastrointestinal disorders among Caucasian and Asian. *Allergol Int*. 2015;64(3):253-259.
15. Shaheen NJ, Mukkada V, Eichinger CS, Schofield H, Todorova L, Falk GW. Natural history of eosinophilic esophagitis: a systematic review of epidemiology and disease course. *Dis Esophagus*. 2018;31(8):doy015. doi:10.1093/dote/doy015
16. Lyles JL, Martin LJ, Shoda T, et al. Very early onset eosinophilic esophagitis is common, responds to standard therapy, and demonstrates enrichment for CAPN14 genetic variants. *J Allergy Clin Immunol*. 2021;147:244-254.e6.
17. Moawad FJ, Dellon ES, Achem SR, et al. Effects of race and sex on features of eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2016;14(1):23-30.
18. Malleske DT, Bryant-Stephens TC, Montoya-Williams D. Childhood asthma disparities-race, place, or not keeping pace? *JAMA Pediatr*. 2022;176:739-740.
19. Zanobetti A, Ryan PH, Coull B, et al. Childhood asthma incidence, early and persistent wheeze, and neighborhood socioeconomic factors in the ECHO/CREW Consortium. *JAMA Pediatr*. 2022;176(8):759-767.

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