



ORIGINAL ARTICLE

OPEN ACCESS

Characterization of a group of children with eosinophilic esophagitis in Cali, Colombia

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Received 13 July 2022; Accepted 22 November 2022

Available online 1 May 2023

KEYWORDS

Child;
Eosinophilic
Esophagitis;
Gastrointestinal
Disease;
Histologic
Techniques;
Hospitalized;
Immunoglobulin;
Inv Allotype

Abstract

Purpose: Eosinophilic esophagitis (EoE) is an immunologically mediated chronic disease of the gastrointestinal tract. The objective of this study was to clinically and demographically describe a child population with EoE diagnosed in a high-complexity hospital in Cali, Colombia. **Methods:** A retrospective study was carried out. The clinical histories of patients between 0 and 18 years with clinical suspicion and a histological diagnosis of EoE were analyzed. All patients underwent an allergy study, either by measurement of specific immunoglobulin (Ig) E and/or an intraepidermal skin-prick test.

Results: Thirty-five patients were included in the study, of which 21 (60%) women. The median age was 8 years (interquartile range [IQR] 5-12), and the age of onset of symptoms was 5 years (IQR 2-10). Thirty patients (85.7%) reported a history of allergic disease, with rhinitis being the most frequent (n = 25, 71.4%). Only one patient reported with food allergy mediated by IgE. The main symptoms in patients included abdominal pain (17 [48.6%]), refractory gastroesophageal reflux (16 [45.7%]), and choking (9 [25.7%]). Upper gastrointestinal endoscopy was normal in 10 patients (38.5%). The median number of eosinophils in the biopsy was 42 (IQR 31-92). Allergic sensitization was verified in 25 of 35 patients (71.4%). Of these, dust mite allergy was positive in 21 patients (84%), while the most frequent food allergy was toward cow's milk, in five patients (31.3%).

Conclusions: The majority of patients with EoE were females. The most frequent symptom was abdominal pain. Endoscopic abnormalities were also observed frequently, and the prevalence of other allergic diseases (especially rhinitis) and allergic sensitization (especially to mites) was high. © 2023 Codon Publications. Published by Codon Publications.

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<https://doi.org/10.15586/aei.v5i13.729>

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Introduction

Eosinophilic esophagitis (EoE), first described in the 1970s, is an immunologically mediated chronic disease of the gastrointestinal tract.¹ It is characterized clinically by a wide range of symptoms and histopathologically by eosinophilic infiltration of the esophageal epithelium.^{2,3} EoE can generate short- and long-term complications such as stenosis and esophageal motility alterations, which can seriously lower the quality of life and the functionality of patients and their families,⁴ all of which add to the high cost for the health system.⁵

Initially, EoE was considered a rare disease, but in recent years there has been an increase in its frequency, possibly due to diagnostic suspicion. The general incidence is 3.7 per 100,000 inhabitants per year; however, its incidence is higher in adults, where it reaches 7.0 per 100,000 inhabitants per year. The global prevalence is 22.7 per 100,000 inhabitants, varying according to the population studied and its geographical location.⁶ In pediatric population, EoE is found in approximately 1-4 of every 10,000 children, and in the adult population with respect to sex, a male predominance (66%) was found. In Latin America, a prevalence of 3.69 cases per 1000 children has been described, while in Colombia it is 18.2 per 1000.⁷

EoE is characterized by a wide range of symptoms that appear to be related to age.⁸ Thus, in younger children, regurgitation, vomiting, abdominal pain, and refusal of food are more frequent, while in older children, dysphagia, impaction of the bolus, and chest pain are more frequent.⁸ It has been suggested that these differences may represent a progression of the disease.^{4,9}

In the presence of symptoms of esophageal dysfunction, it is necessary to perform upper digestive tract endoscopy. There is no macroscopic finding within the endoscopy that is pathognomonic for EoE, though the presence of esophageal rings or trachealization of the esophagus, stenosis, decrease of the lumen due to edema, longitudinal grooves, mucosal edema, decreased mucosal vascularization, white plaques, or exudates highly suggest the diagnosis.¹⁰ These changes in the mucosa are a result of chronic infiltration of eosinophils, which induces remodeling of the esophagus wall.^{3,11} However, 5-32% of endoscopic samples were normal despite having an eosinophilic infiltrate.^{12,13} The essential histological finding in esophageal biopsies was the presence of at least 15 eosinophils per high-power field, which confirmed EoE diagnosis.^{1,10}

Sensitization to foods or aeroallergens can be studied by skin tests or by measurement of specific IgE. A sensitization of 71-93% to aeroallergens and 50% to foods has been described.¹⁴ Skin tests are more frequently positive for peanuts, eggs, soybeans, cow's milk, and wheat and, to a lesser extent, for legumes, rye, and meat. On the other hand, house dust mites, dog and cat dandruff, and tree pollen have been the most frequently described aeroallergens.^{1,15-17}

The treatment of EoE should be a multidisciplinary effort of the gastroenterologist, the allergist, and the nutritionist. The following goals should be set: control of symptoms, histological remission, management of complications, and prevention of long-term sequelae.^{8,18,19}

Because most of studies on EoE have been conducted in American and European populations, little is known about the characteristics of these patients in Latin America and Colombia. The objective of the present study was to describe the demographic, clinical, and allergological characteristics in a group of pediatric patients with eosinophilic esophagitis in a high-complexity hospital in Cali, Colombia.

Methods

A descriptive, retrospective, cross-sectional study was conducted. The clinical records of patients aged 0-18 years with a diagnosis of EoE who attended pediatric allergology or gastroenterology outpatient clinic of the Fundación Valle de Lili in Cali, Colombia, between January 2013 and December 2019, were reviewed.

The presence of more than 15 eosinophils per high-power field, associated with gastrointestinal symptoms, was used as the diagnostic criterion. Demographic and clinical data, concomitant allergic diseases, and family history of first-degree allergic disease and eosinophilic esophagitis were analyzed. The eosinophil count in peripheral blood was analyzed. Refractory gastroesophageal reflux (RGER) was considered present when the patient remained symptomatic despite management with antireflux measures and first-line treatment with proton pump inhibitors and/or prokinetics. Eating disorder was defined as rejection of solid foods, delayed intake, or predilection for soft and/or liquid foods. The presence of symptoms was analyzed according to the growth and development standards of the patients as follows: preschool children under 5 years of age; school children from 6 to 11 years; and adolescents over 12 years.

An allergological study was performed with intraepidermal tests and/or specific IgE measurement (ImmunoCAP), according to the medical criteria and clinical condition of the patient, to the foods most related to EoE according to the available literature (milk, eggs, and major proteins of fish, nuts, shellfish, legumes), and to the prevalent aeroallergens in the area.

For statistical analysis, data were collected from the patient clinical records and organized in a database. Dichotomous variables are reported as percentages. Continuous variables are presented as medians and interquartile ranges or means and standard deviations, depending on their distribution. The normality of the variables was estimated using Shapiro-Wilk test.

Results

Between January 2013 and December 2019, 35 patients were included. Twenty-one of them were females (60%). The median age of consultation was 8 years (IQR 5-12) and that of presentation of symptoms was 5 years (IQR 2-10). The diagnosis was made on an average of 2 years (IQR 1-3) after the onset of symptoms. In 22 patients (62.9%), there was a family history of allergic disease, and 2 (5.7%) had a first-degree relative diagnosed with eosinophilic esophagitis. Concomitant allergic diseases were present in 30 patients (85.7%). Twenty-five patients (71.4%) had

allergic rhinitis, 11 (31.4%) had asthma, 2 (5.7%) had atopic dermatitis, and 1 (2.9%) reported with IgE-mediated food allergy (Table 1).

The main symptoms presented were abdominal pain in 17 patients (48.6%), RGER in 16 (45.7%), choking in 9 (25.7%), vomiting and nausea in 6 (14.3. %), eating disorders in 5 (14.3%), chest pain in 5 (14.3%), and dysphagia and food bolus impaction in 1 (2.9%) each (Table 1). Figure 1 shows the distribution of symptoms by age group.

As part of the diagnostic approach, the number of eosinophils in peripheral blood was determined, yielding a median of 545 eosinophils (IQR 440-590) (Table 1). All patients underwent upper digestive tract endoscopy, but only 26 of them (74.2%) had a macroscopic report. The rest were conducted in external institutions, and we had no access to the report. However, the eosinophil count was obtained in the esophageal biopsies of all patients, with a median of 42 (IQR 31-92) (Table 2). Intraepidermal skin tests or puncture tests were performed in 32 patients (91.4%). Eleven patients (34.4%) presented sensitization only to aeroallergens, 3 (9.4%) to only food, and 10 (31.2%) to a mixed sensitization. The tests were negative in 8 (25%) patients. In eight cases (22.8%), specific IgE was determined, with four (50%) being positive.

Twenty-one patients (84%) presented sensitization to dust mites, *D. pteronyssinus* being the main allergen (present in all 21 [100%] sensitized patients), followed by *D. farina* in 18 (85.7%) and *B. tropicalis* in 14 (66.7%) patients. The second-most common sensitization was to animal epithelia, in six patients (28.5%), followed by pollen in five (23.8%) and molds in two (9.5%) patients.

Table 3 describes the results of allergologic tests in patients with EoE. Food sensitization was positive in 16 patients (64%). The main sensitizing food was cow's milk, in five patients (31.3%), followed by eggs in four (25%) and soybeans in three (18.5%). Peanuts, white fish, and shrimp

Table 1 Clinical characteristics of pediatric patients diagnosed with EoE.

	n = 35
Sex, n (%)	
Male	14 (40.0)
Female	21 (60.0)
Age [years], median (IQR)	8 (5–12)
Age of onset of symptoms [years], median (IQR)	5 (2–10)
Family history of allergic disease, n (%)	22 (62.9)
Family history of EoE, n (%)	2 (5.7)
Personal history of allergic disease, n (%)	30 (85.7)
Rhinitis	25 (71.4)
Asthma	11 (31.4)
Atopic dermatitis	2 (5.7)
IgE-mediated food allergy	1 (2.9)
Symptoms, n (%)	
Abdominal pain	17 (48.6)
Refractory gastroesophageal reflux	16 (45.7)
Choking	9 (25.7)
Vomiting	5 (14.3)
Chest pain	5 (14.3)
Eating disorder	5 (14.3)
Dysphagia	1 (2.9)
Impaction	1 (2.9)
Blood eosinophil count [n/mL], median (IQR)	545 (440–590)

were each positive in two patients (12.5%), while pork, oats, and chickpea were found to be positive in one patient (6.3%). Of all the above sensitizations, the only food allergy mediated by IgE was found in a patient with cow's milk anaphylaxis.

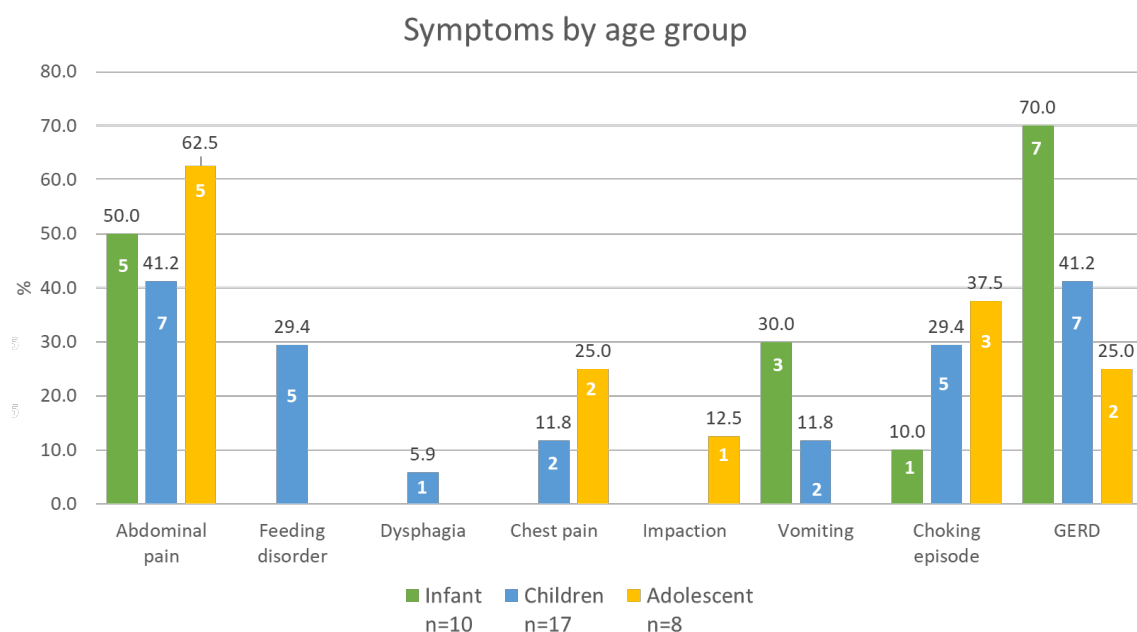


Figure 1 Symptoms by age group. Distribution of symptoms according to the age group of the patients. The numbers above the bars correspond to the percentage (%), and the numbers within the bars are the raw numbers (n).

Table 2 Endoscopic findings and eosinophil count in biopsy.

Endoscopic macroscopic findings, n (%)	n = 26
Normal appearance	10 (38.5)
Exudates	9 (34.6)
Linear grooves	9 (34.6)
Esophageal rings/Trachealization	5 (19.2)
Eosinophil count in biopsy, n (%)	n = 35
≤40	18 (48.7)
41–60	6 (16.2)
61–80	4 (10.8)
81–100	6 (16.2)
>100	3 (8.1)

Discussion

This study describes the demographic and clinical characteristics, allergen sensitization, and endoscopic and histological findings of 35 pediatric patients with EoE. The majority were female, which contrasts with the findings in various international studies^{13,20–22} and studies in Latin America^{7,23,24}, in which the male to female ratio has been as high as 3:1 and even 4:1.^{14,22} The reason for this predominance is unknown, but it is believed that there is a mechanism of inheritance linked to a single-nucleotide polymorphism in the thymic stromal lymphopoietin (TSLP) receptor in the pseudoautosomal regions of chromosomes Xp22.3 and Yp11.3.²⁵ The discrepancy could be explained by our relatively low number of samples.

The median age of consultation was 8 years, compared to the median age of 5 years for the onset of symptoms, which means a delay of 2 years (IQR 1–3) for diagnosis. In a multicenter study, Chehade et al.²⁶ described a delay in diagnosis of 1–2 years after the onset of symptoms, which is similar despite the limited knowledge of the disease in our environment. The majority of patients had eosinophilia in peripheral blood, with a median of 545 eosinophils (IQR 440–590). In other studies, an eosinophilia count of >300–350/mm³ has been described in 40–50% of patients with EoE.¹⁴

A close relationship between EoE and other allergic diseases has been described, with a concomitance of 28–86% in adults and 42–93% in children.¹⁴ In the present study population, this concomitance was found in 30 patients (85.7%), which is in agreement with the literature.^{2,14} Of these patients, 71.4% had allergic rhinitis, which is within the prevalence range reported in other studies (40–75%).¹⁴ Asthma and atopic dermatitis occurred in 31.4% and 5.7% of our patients, respectively, similar to what was previously reported.¹⁴ Only one patient (2.9%) had food allergies mediated by IgE, in contrast to the prevalence of 4.7% reported in patients with EoE.²⁷

The main symptoms were abdominal pain and RGER, in 17 (48.6%) and 16 (45.7%) patients, respectively, followed by choking in 9 (25.7%) patients. Dividing them by age group, preschool patients presented nonspecific symptoms such as abdominal pain, vomiting, and RGER, while elementary school and adolescent patients most often had eating disorders, chest pain, dysphagia, impaction, and choking,

Tables 3 Results of allergological tests in patients with EoE (n = 35).

Allergy tests, n (%)	
Intraepidermal skin tests	27 (77.1)
Specific IgE	3 (8.6)
Intraepidermal + specific IgE	5 (14.3)
Intraepidermal test results, n (%)	
Negative	8 (25.0)
Sensitization to pneumoallergens	11 (34.4)
Food sensitization	3 (9.4)
Mixed sensitization	10 (31.2)
Specific IgE results in blood, n (%)	
Negative	4 (50)
Positive	4 (50)
Sensitized patients	
Patients sensitized to aeroallergens n = 21	
Mites n (%) 21 (100)	
<i>D. Pteronyssinus</i>	21 (100)
<i>D. farinae</i>	18 (86)
<i>Blomia tropicalis</i>	14 (67)
Animal epithelium, n (%)	
Cat	1 (16.7)
Dog	2 (33.3)
Dog and cat	3 (50)
Pollen, n (%)	
Only grasses	2 (40)
Herbs and Grasses 2 (40)	
Herbs, grasses and cypress	1 (20)
Molds, n (%)	
Alternaria and Aspergillus	1 (50)
Aspergillus and Cladosporium	1 (50)
Number of food sensitizations, n (%) n = 16	
1 food	11 (68.8)
2 foods	1 (6.2)
>2 foods	4 (25.0)
Type of food, n (%)	
Cow's milk	5 (31.3)
Egg	4 (25)
Soy	3 (18.5)
White fish	2 (12.5)
Shrimp	2 (12.5)
Peanuts	2 (12.5)
Pig	1 (6.3)
Oats	1 (6.3)
Chickpea	1 (6.3)

symptoms, which have been associated with a longer evolution of the disease. Chronic and diffuse eosinophilic inflammation is believed to progress to fibrotic changes in the esophagus.^{1,8,9} Therefore in younger children, regurgitation, vomiting, abdominal pain, food rejection, and failure to thrive are more prevalent,²⁸ while in older children, dysphagia, impaction of the bolus, and food and chest pain are more frequent.⁸ Even in our small sample, we saw this trend in the progression of symptoms with age. This pattern is not rigid, so, for example, dysphagia has been seen in school children.⁸

The endoscopic appearance of the mucosa was normal in 10 patients (38.5%), similar to that described in other

reports, where this finding has been present in 27-32% of endoscopies performed in the pediatric population.^{13,29} The most frequent abnormal finding was the presence of linear grooves together with exudates, each of which was evident in nine patients (34.6%). In previous studies, grooves have been reported in 37-41% of patients. On the other hand, it is noteworthy that in the present population, five patients (19.2%) presented esophageal rings or trachealization, changes suggesting advanced disease and fibrosis. This finding was higher than those of other studies.^{13,24,29}

In the histological evaluation, the median eosinophil count per high-power field in esophageal biopsies was 42 (range 0-302), a value similar to that reported in a local study, where the median eosinophil count per high-power field was 42.34 (range 10-150),²⁴ and in an international study, where the median was 41 (range 0-288).²⁹

The role of food and environmental allergens in EoE has been the subject of study. When implementing a restrictive diet or a diet with elemental formula, the majority of patients present clinical improvement,¹⁷ which suggests that food can trigger eosinophilic inflammation at the esophageal level. In the present study, the food allergen to which patients were most frequently sensitized was cow's milk, followed by eggs and soy. In other studies, the same foods and wheat have been identified as those that generate greater sensitization in the patients.^{27,30,31} In this series, atopic patch tests were not performed due to the lack of standardization of the method.

Sensitization to aeroallergens was characterized by a clear predominance of positivity to dust mites (84%), followed by animal epithelia and pollens. This high percentage of sensitization to dust mites can be explained by the high prevalence of concomitant allergic respiratory disease, especially rhinitis (71.4%), in the studied population. The clinical relevance of these allergens in EoE is not clear, but due to the high prevalence of EoE during pollen season, there is growing evidence of the importance of aeroallergens in EoE.^{6,27} In this geographical area (the tropics), there is only one season and no pollination season, so it is difficult to conclude an involvement of pollen in this population. However, it is likely that mites have some clinical relevance. These are important because perennial environmental allergens can be related to the lack of response to treatment with corticosteroids in EoE.

Limitations and Strengths

This study has several limitations, and its results should be interpreted within the context of the proposed design. Its retrospective design in which information was taken from medical records implies the loss of some data due to lack of registration. Because the information of the biological samples was taken from the gastroenterologist's reports and not from the tissue directly, it was not possible to classify the patients with the classification proposed by Hirano et al. For this same reason, the correlation between eosinophilic infiltration and macroscopic findings could not be evaluated. The data were obtained in a single center, so they cannot be extrapolated to the entire Colombian population with EoE. Multicenter studies are required to confirm the results.

Conclusions

In this cohort of children with EoE, the majority were females, and the most frequent symptom was abdominal pain. There were frequent endoscopic abnormalities, and other allergic diseases (especially rhinitis) and allergenic sensitization (especially to mites) were common. Multicenter studies are required in Colombia and Latin America to better understand the epidemiological, clinical, and allergological characteristics specific to the region, as well as the response to treatment.

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