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Clinical Features of Eosinophilic Esophagitis: A Single Center Experience in Ecuador

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Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Purpose: Data on eosinophilic esophagitis (EoE) in South America is scarce. Moreover, no studies are available in Ecuador. We evaluated the clinical, endoscopic, and histological characteristics of Ecuadorian children with EoE.
Methods: Medical records of 2,711 children who underwent upper gastrointestinal endoscopy (UGE) between 2009 and 2020 at Hospital Metropolitano de Quito, Ecuador were reviewed. Esophageal mucosal biopsies were obtained from 72 patients and the features of 35 children with EoE were described. EoE was diagnosed when there were more than 15 eosinophils in the esophagus, per high power field.
Results: EoE was diagnosed in 35 children (9.4±4.5 years) with a male predominance (74%). Abdominal pain (51.4%) and vomiting (31.4%) were dominant symptoms. A history of allergic diseases was noted in 47.1% of the children, which mainly included allergic rhinitis (37.1%) and atopic dermatitis (11.4%). The most common endoscopic findings were furrowing (82.9%) and edema (74.3%). All patients were initially treated with proton-pump inhibitors (PPIs). Those who did not respond to PPIs received steroids (5.7%) and diet therapy (5.7%), and five patients were referred to an allergist. Clinical and histological resolution was observed in 65% of the patients who underwent a second UGE after 6–8 weeks of PPI.
Conclusion: Our study describes the clinical features of pediatric EoE in Ecuador. This is the first retrospective study in Ecuador that describes the clinical, endoscopic, and histological manifestations of EoE in a small pediatric population. Almost half of the children who underwent a biopsy had EoE.

Keywords: Eosinophilic esophagitis; Pediatrics; Proton pump inhibitors

INTRODUCTION

Eosinophilic esophagitis (EoE) is a relatively new condition, and its definition has evolved over time. Currently, it is considered an antigen-immune inflammatory mediated disease, in which eosinophils infiltrate the esophageal mucosa and more than 15 eosinophils can be observed per high power field (HPF), with no other causes of esophageal eosinophilia [1].

The incidence and prevalence of EoE have gradually increased over time. Currently, in the United States of America, the prevalence of EoE is 30–90 cases per 100,000 and the incidence is 1/2,000 [1].

EoE arises from the interaction between genetic and environmental factors [2]. It is pathogenically related to Th2 inflammation, described by a combined immunoglobulin E (IgE) and non-IgE-mediated reaction to environmental and food agents, which is determined by thymic stromal lymphopoietin secreted by esophageal epithelial cells [3].

In the last two decades, EoE has evolved from a relatively rare disease to one of the leading causes of dysphagia and food impaction in adults. In children, vague reflux symptoms have been described as the main clinical manifestations [4]. Other symptoms in children include dysphagia, food impaction, and/or food refusal.

The progressive course of EoE is characterized by repeated mucosal inflammation, damage and remodeling of the esophageal wall, collagen deposition, and lamina propria fibrosis [2]. If EoE is left untreated, it may lead to esophageal strictures. Pharmacological therapy, dietary elimination, and mechanical dilation of the esophagus are some of the available treatment strategies.

Currently, there are no studies that evaluate the characteristics of EoE in Ecuador. Therefore, the aim of this report was to establish clinical, endoscopic, and histological characteristics of EoE in pediatric patients in a single center in Quito, Ecuador.

MATERIALS AND METHODS

Study design

We conducted a retrospective study of patients evaluated from 2009 to 2020 by the Pediatric Gastroenterology Department in Hospital Metropolitano in Quito, Ecuador. Medical records of patients under 18 years of age who underwent an upper gastrointestinal endoscopy (UGE) from January 2009 to May 2020 were reviewed. During this period, 2,711 upper endoscopies were performed (**Fig. 1**).

Subjects

Thirty-five children (male and female) aged 11 months to 18 years with ≥15 eosinophils per HPF in the esophageal mucosa were included. Patients with infectious esophagitis, eosinophilic gastroenteritis, gastroesophageal reflux disease (without eosinophilia), or hypereosinophilic syndrome were excluded. In every patient, personal history of allergy, clinical manifestations, and endoscopic and histological findings were analyzed.

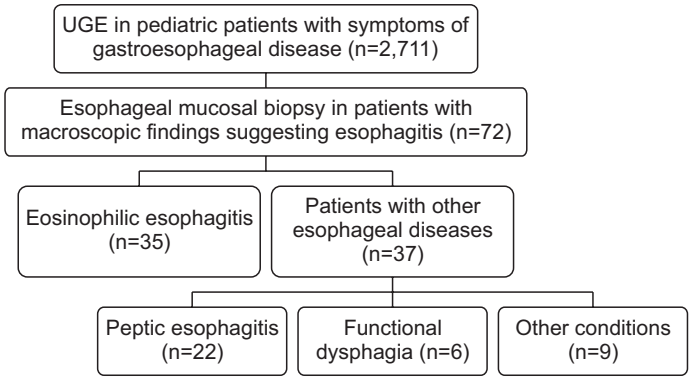

Fig. 1. Study design of eosinophilic esophagitis.
UGE: upper gastrointestinal endoscopy.

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Endoscopy and histopathology

UGE was performed using a GIF-XP 190N (Olympus Corporation, Tokyo, Japan) in 2,711 patients. In 72 children with macroscopic findings suggesting esophagitis (mucosal edema, furrowing, rings, exudates, and strictures), biopsies were obtained from the upper, mid, and lower esophagus (total: 6 biopsies).

Histopathological analysis was performed using hematoxylin-eosin staining. Reported findings included the number of eosinophils per HPF, eosinophil microabscesses, basal-zone hyperplasia, and lamina propria fibrosis.

Statistical analysis

After collecting medical records, the data were analyzed to estimate the number and percentage of EoE. The clinical characteristics, endoscopic findings, and initial treatment protocols were described.

Data were collected in Microsoft Office Excel 2013 (Microsoft, Redmond, WA, USA), and the variables were evaluated using SPSS version 23 (IBM Co., Armonk, NY, USA). Percentages were calculated for qualitative variables, and mean and standard deviation were calculated for quantitative variables.

Ethics

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed in this study. Due to the retrospective nature of the study, ethical approval from the Human Research Ethics Committee was not required. This was a descriptive study, comprised of non-experimental research with secondary data and anonymized patients.

RESULTS

Clinical characteristics

Thirty-five children with EoE were included in the study, and the mean age at diagnosis was 9.4±4.5 years. The sex ratio of males to females was 2.8:1 with 26 boys (74%) and 9 girls (26%).

Sixteen of the 35 patients with EoE had a history of one or more allergic diseases, including allergic rhinitis in 37.1% (n=13), atopic dermatitis in 11.4% (n=4), food allergy in 8.6% (n=3), allergic sinusitis in 5.7% (n=2), and asthma in 5.7% (n=2) (**Table 1**).

Symptoms were experienced 11.7±17.8 months before the initial diagnosis. At diagnosis, abdominal pain was the main symptom observed (n=18, 51.4%), followed by vomiting (n=11, 31.4%) and dysphagia (n=8, 22.9%). Less frequent symptoms included heartburn, foreign body sensation, nausea, and other symptoms, such as rumination; gastrointestinal bleeding; food impaction; chest pain; and food avoidance (**Table 1**).

Endoscopic findings of the esophagus in EoE

The main endoscopic findings were furrowing (n=29, 82.9%), edema (n=26, 74.3%), rings (n=16, 45.7%), and exudates (n=8, 22.9%). Stricture, crepe paper esophagus, and normal mucosa were found in one case each (**Fig. 2**).

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Table 1. Allergic diseases and clinical symptoms in patients with eosinophilic esophagitis

Variable	Value (n=35)
Allergic diseases	
Allergic rhinitis	13 (37.1)
Atopic dermatitis	4 (11.4)
Food allergy	3 (8.6)
Asthma	2 (5.7)
Allergic sinusitis	2 (5.7)
Symptoms	
Abdominal pain	18 (51.4)
Vomiting	11 (31.4)
Dysphagia	8 (22.9)
Heartburn	4 (11.4)
Foreign body sensation	4 (11.4)
Others	11 (31.4)

Values are presented as number (%).

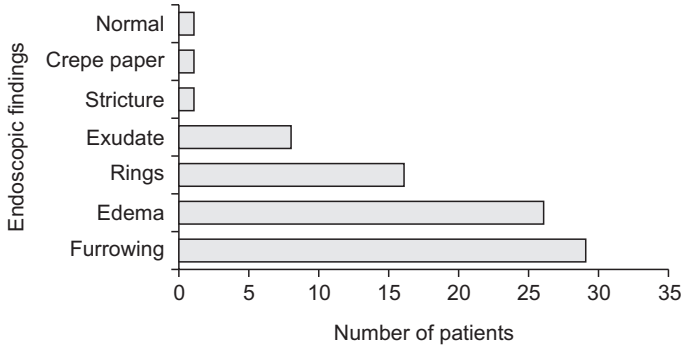

Fig. 2. Endoscopic findings of the esophagus in patients with eosinophilic esophagitis at diagnosis.

Other findings were basal-zone hyperplasia (n=16, 45.7%), lamina propria fibrosis (n=1, 2.9%), and eosinophil microabscesses (n=1, 2.9%).

Initial treatment for EoE

All patients were initially treated with PPIs (n=35, 100%) for 6-8 weeks, and one patient simultaneously underwent an esophageal dilation. Twenty-six children (74.2%) underwent a second UGE; 65% had normal endoscopic findings and in the rest, the number of eosinophils per HPF in the esophageal mucosa was found to be more than 15 despite treatment with PPIs. The group of patients not responding to PPIs required other treatments, such as swallowed steroids with fluticasone (n=2) and targeted elimination diet based on the results of allergen tests (cow's milk and eggs [n=1], empiric diet cow's milk [n=1]), and five patients were referred to an allergist. Additionally, we discovered nine patients with *Helicobacter pylori* infection who received triple therapy (esomeprazole, amoxicillin, and clarithromycin).

DISCUSSION

Over the past 20 years, the global prevalence and incidence of EoE have increased rapidly, which may be explained by improved recognition of EoE and higher use of diagnostic endoscopy for pediatric biopsies [3].

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EoE can occur at any age in children. The mean age at the time of diagnosis ranges from 5.4 to 9.6 years [5]. The presentation age in our study was 9.4±4.5 years (range, 1–18 years), which is similar to that of other studies.

The sex ratio of males to females was 2.8:1 in our cohort. There is a difference in the sex ratio of patients with EoE. Males are known to have a higher prevalence than females among both children and adults. In two different studies, the ratio between men and women ranged from 2.5:1 to 3:1 [3,6], comparable with our ratio.

Clinical presentation depends on the patient's ability to report symptoms associated with esophageal dysfunction, and it can take a long time to reach a diagnosis of EoE [3]. On an average, our study participants experienced symptoms 11.7±17.8 months before diagnosis. This wide variation may be explained by symptoms exhibiting an acute presentation, as in the case of food bolus impaction, and at other times, the presentation might be more insidious.

The variation in presentation may lead to misdiagnosis. For example, children who avoid certain foods can be labeled as picky eaters [7], whereas adolescents may be misdiagnosed as having eating disorders [3,7]. In the pediatric population, the most prevalent symptoms are vomiting, abdominal pain, dysphagia, and food bolus impaction [3]. This study revealed that abdominal pain was the most common symptom, followed by vomiting and dysphagia, while bolus impaction was observed in only one patient.

Children and adults with EoE frequently present with concomitant allergic diseases, such as asthma, allergic rhinitis, food allergies, and atopic dermatitis [6]. The rates of these diseases are approximately three times higher in children with EoE than those in the general population [3]. In this study, almost half of the patients (45.7%) had concomitant allergic diseases. A meta-analysis study reported that EoE patients of all ages have a significantly higher chance of presenting with bronchial asthma, allergic rhinitis, and eczema, as opposed to the control population [8]; which is comparable with our study, where allergic rhinitis and atopic dermatitis were the main concomitant allergic diseases in children with EoE. However, asthma was not as common in this study as it was in others.

Endoscopic findings are not pathognomonic. The pattern of abnormality varies between patients [7], and each sign may occur in isolation or in combination. Typical endoscopic findings in patients with EoE include edema, exudates, furrowing, concentric rings, and strictures [9]. In our study, the most common endoscopic features were furrowing (82.9%), edema (74.3%), rings (47.5%), and exudates (22.9%). Normal endoscopic findings of the esophageal mucosa have been reported in approximately 32% of the children diagnosed with EoE [5]. In contrast, in the present study, visually normal esophageal mucosa was observed in only one patient. Although this was observed in only one case, it demonstrates the importance of regularly performing esophageal biopsies when performing UGE.

EoE is a chronic, progressive disease and therapeutic strategies aim to resolve clinical symptoms and esophageal inflammation to avoid long-term complications related to fibrosis and deterioration of health-related quality of life [5]. Therapeutic options currently available for EoE include elimination diets, PPIs, and steroids. PPIs are the most common first-line therapy used for patients with EoE, and in our study, all patients received PPI as the initial treatment. The efficacy of PPIs in inducing remission appears to be related to the reduction of esophageal damage caused by acid exposure and to the anti-inflammatory effect [2,10]. Some studies have

https://doi.org/10.5223/pghn.2022.25.4.293

reported that PPIs induced histologic remission and clinical improvement in more than half of the patients with symptomatic esophageal eosinophilia [11-13]. Correlated with our study, 65.3% of the patients who underwent a second UGE after 6–8 weeks of PPI treatment achieved histological remission (<15 eosinophils per HPF) and symptom improvement.

Dietary therapy is the only treatment targeting the cause of the disease; three major classes of elimination diets are used: elemental diet, targeted diet by allergy testing, and empiric diet [2]. In this study, two patients were treated with dietary therapy, and the patient who received targeted diet therapy devoid of eggs and cow's milk was found to have normal histological findings and symptomatic relief on a follow-up UGE.

Topical steroids have emerged as first-line induction agents due to their anti-inflammatory mechanisms, and are effective in inducing clinical, endoscopic, and histologic remission [14-16]. Laserna-Mendieta et al. [15] found that topical steroids were the most effective in inducing clinical (decrease ≥50% in the dysphagia symptom score) and histologic remission (count <15 eosinophils per HPF); however, PPIs were the most frequently prescribed . Similar to our study, all patients were initially treated with PPIs, and the two patients who did not respond, received swallowed steroids.

Conclusion

Our study describes the clinical features of pediatric EoE in Ecuador. It is the first retrospective study in Ecuador that describes the clinical, endoscopic, and histological manifestations of EoE in a small pediatric population. Clinical characteristics of symptoms, endoscopic findings, and associated co-morbid allergic diseases, were comparable to those of other studies. Most patients in this study showed good clinical response to PPI treatment. A population-based, multi-center study with long-term follow-up is warranted to estimate the prevalence and incidence of EoE in Ecuadorian children.

Limitations

This study was a retrospective and single-center observational analysis. As this was a single center study, our sample size was small. A population based multi-center study would provide more insights into the epidemiology of this disease in Ecuador.

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