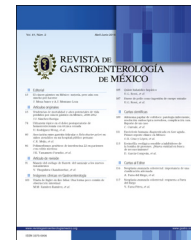




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ORIGINAL ARTICLE

Prevalence of eosinophilic esophagitis: A multicenter study on a pediatric population evaluated at thirty-six Latin American gastroenterology centers[☆]



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KEYWORDS

Esophagitis;
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Abstract

Introduction and objective: Eosinophilic esophagitis is a chronic, immune-mediated disease described in case series and publications worldwide. Over the past twenty years, the authors of different studies have attempted to evaluate its incidence and prevalence. The objective of the present study was to estimate the prevalence of eosinophilic esophagitis in a group of children seen at 36 pediatric gastroenterology centers in ten Latin American countries.

Materials and methods: A multicenter, observational, and cross-sectional study was conducted that estimated the period prevalence of eosinophilic esophagitis in children seen at outpatient consultation and that underwent diagnostic upper gastrointestinal endoscopy for any indication at 36 centers in 10 Latin American countries, within a 3-month time frame.

Results: Between April and June 2016, 108 cases of eosinophilic esophagitis were evaluated. Likewise, an average of 29,253 outpatient consultations and 4,152 diagnostic upper gastrointestinal endoscopies were carried out at the 36 participating centers. The period prevalence of eosinophilic esophagitis in the population studied ($n = 29,253$) was 3.69 cases $\times$ 1,000 (95% CI: 3.04 to 4.44), and among the children that underwent routine upper gastrointestinal endoscopy ($n = 4,152$), it was 26 $\times$ 1,000 (95% CI: 22.6 to 29.4).

Conclusions: The general period prevalence of eosinophilic esophagitis in a group of children evaluated at 36 Latin American pediatric gastroenterology centers was 3.69 $\times$ 1,000, and in the children that underwent endoscopy, it was 26 $\times$ 1,000. There was important prevalence variability between the participating countries and centers. The present analysis is the first study conducted on the prevalence of pediatric eosinophilic esophagitis in Latin America.

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PALABRAS CLAVE

Esofagitis;
 Eosinofílica;
 Niños;
 Prevalencia;
 Latinoamérica

Prevalencia de esofagitis eosinofílica: estudio multicéntrico en población pediátrica evaluada en 36 centros de gastroenterología de América Latina

Resumen

Introducción y objetivo: La esofagitis eosinofílica es una enfermedad crónica, mediada inmunológicamente, descrita en series y publicaciones alrededor del mundo. En los últimos 20 años diversos estudios han intentado evaluar la incidencia y prevalencia de la enfermedad. El objetivo del presente trabajo es estimar la prevalencia de esofagitis eosinofílica en un grupo de niños atendidos en 36 centros de gastroenterología pediátrica de 10 países latinoamericanos.

Materiales y métodos: A través de un protocolo multicéntrico, observacional y transversal se estimó la prevalencia de período de esofagitis eosinofílica entre los niños atendidos en consulta externa y sometidos a endoscopia superior diagnóstica por cualquier motivo en 36 centros de 10 países latinoamericanos durante un período de 3 meses.

Resultados: Entre abril y junio de 2016 108 casos de esofagitis eosinofílica fueron evaluados. Asimismo, un promedio de 29,253 consultas ambulatorias y 4,152 endoscopias superiores de carácter diagnóstico fueron realizadas en los 36 centros participantes. La tasa de prevalencia de esofagitis eosinofílica en la población estudiada ($n=29,253$) fue de $3,69 \text{ casos} \times 1,000$ (IC 95%: 3.04 a 4.44) y entre los niños sometidos a endoscopia superior de rutina ($n=4,152$) fue de $26 \times 1,000$ (IC 95%: 22.6 a 29.4).

Conclusión: La tasa general de prevalencia de período de esofagitis eosinofílica en un grupo de niños evaluados en 36 centros latinoamericanos de gastroenterología pediátrica resultó de $3,69 \times 1,000$, y entre aquellos sometidos a endoscopia fue de $26 \times 1,000$. La prevalencia mostró una importante variabilidad entre los países y centros participantes. Este es el primer estudio de prevalencia de esofagitis eosinofílica pediátrica en Latinoamérica.

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Introduction and aims

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated pathology that is predominantly inflammatory during childhood and progresses to fibrosis in adulthood. It is characterized by signs and symptoms of esophageal dysfunction related to eosinophilic inflammation limited to the esophagus, with infiltration of 15 or more eosinophils per high power field.^{1,2} The majority of population studies conducted in the United States estimate a disease prevalence in the general population between 40 and 90 cases/100,000 inhabitants, and there has been a rapid increase in the number of cases described in recent years.^{3,4} Other epidemiologic studies have demonstrated the following prevalence rates: Australia (89/100,000), Switzerland (43/100,000), Spain (45/100,000), and Canada (34/100,000).^{5,6} A systematic review was conducted by Soon et al., from the University of Calgary, that included at least 25 clinical studies. The results showed incidence between 0.7 and 10/100,000 and a general prevalence rate between 0.2 and 43/100,000, as well as a marked rising trend in recent years.⁷⁻⁹

Even though the prevalence of eosinophilic esophagitis is well known in Latin America and there have been numerous articles, systematic reviews, and epidemiologic studies on the theme, its prevalence in the pediatric population in the region has not yet been studied. In 2014, as an initiative of the Latin American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (LASPGHAN), a Working Group was organized to study eosinophilic esophagitis in children. The results of the different epidemiologic studies carried out to date have shown that the epidemiologic characteristics, clinical behavior, and endoscopic findings in Latin America are similar to those described in the literature.¹⁰⁻¹⁶

The aim of the present study was to calculate the rate of prevalence of eosinophilic esophagitis in a group of children seen at pediatric gastroenterology centers over a 3-month period in 10 Latin American countries.

Materials and methods

An observational, cross-sectional, multicenter study on prevalence was conducted that included an open-question

survey as a data collection instrument, directed at all pediatric gastroenterology and endoscopy centers in Latin America. All the pediatric cases of eosinophilic esophagitis evaluated during the time frame of April to June 2016 were included in the study, incorporating both new cases diagnosed during the study period and already known cases. The definition of EoE cases encompassed all patients under 18 years of age with symptoms of esophageal dysfunction and confirmed endoscopic diagnosis with positive biopsies from the middle and distal thirds of the esophagus that had at least 15 eosinophils per high power field, in the absence of gastritis, enteropathy, or eosinophilic colitis, with secondary causes of eosinophilic esophagitis ruled out. The study population was made up of all the patients evaluated at outpatient consultation that underwent upper gastrointestinal endoscopy for any indication during the time frame specified. The relation between the cases of EoE and the total number of patients that had outpatient consultation and that underwent upper gastrointestinal endoscopy allowed us to calculate the period prevalence rates in the study population and their respective confidence intervals.

The rates were calculated in relation to 1,000 persons/year from the multicenter observations. Confidence intervals were estimated with a 95% probability, using the exact Mid-P method. The Epi Info version 7.2.2.6 package was employed for making the calculations.

The present study was approved by the Research and Ethics Committee of the LASPGHAN and carried out in accordance with the principles of the Declaration of Helsinki.

Results

Thirty-six pediatric gastroenterology and endoscopy centers from 10 Latin American countries participated in the study: Argentina (8), Brazil (1), Colombia (3), Chile (2), Ecuador (1), El Salvador (2), Peru (3), Mexico (7), Uruguay (1), and Venezuela (8). Eighty-three percent (30/36) of the centers were tertiary care and referral hospitals, 36% (13/36) were private hospitals, and 53% (19/36) were located in metropolitan urban zones or State capitals. The centers with the highest number of cases registered were in Brazil, Colombia, Argentina, and Venezuela. During the 3-month study period, 24/36 (66.6%) of the participating centers

reported no cases of EoE. All the participating centers provided their average figures of patients seen at outpatient consultation and the endoscopies performed monthly. An average of 300 to 500 monthly outpatient consultations were reported in 55.5% (20/36) of the centers. An average of 29,253 outpatient consultations and 4,152 diagnostic upper gastrointestinal endoscopies were carried out at the participating centers during the 3-month study period and all patient symptoms and clinical diagnoses were also included.

In that context, 108 cases of eosinophilic esophagitis were evaluated during the same time frame. A total of 71.2% of the patients were males (77/108). With respect to age groups, 2.3% of the cases were breastfeeding infants, 15.7% were pre-schoolers, 45% were school-age children (7 to 10 years), and 37% were adolescents. Symptomatology varied according to age group. Feeding refusal was the most frequent symptom in breastfeeding infants, whereas dysphagia, vomiting, heartburn, and gastroesophageal reflux symptoms were more frequent in pre-schoolers, school-age children, and adolescents. Food impaction was the reason for evaluation in 19% of the patients.

The general prevalence rate of EoE in the children seen at outpatient consultation in the participating centers that reported cases was $3.69 \times 1,000$ (95% CI: 3.04 to 4.44), with a range of 0.2 to $25.4 \times 1,000$ (Table 1). The centers with higher prevalence were located in Brazil ($25.4 \times 1,000$) and Colombia ($18.2 \times 1,000$), the centers with intermediate prevalence were in Chile ($3.1 \times 1,000$), Venezuela ($2.8 \times 1,000$), and Argentina ($2.7 \times 1,000$), and the centers with lower prevalence were in Uruguay ($1.4 \times 1,000$), El Salvador ($0.4 \times 1,000$), and Mexico ($0.2 \times 1,000$). The centers located in Peru and Ecuador reported no cases of EoE during the study period (Table 2).

The general prevalence rate of EoE in children that underwent upper gastrointestinal endoscopy for any indication was $26 \times 1,000$ (95% CI: 22.6-29.4), with a range of 2.6 to $82.3 \times 1,000$. The highest prevalence rates were in

the centers located in Brazil ($82.3 \times 1,000$), Colombia ($57.7 \times 1,000$), Argentina ($32.3 \times 1,000$), and Venezuela ($21.4 \times 1,000$). Only the centers in Brazil, Colombia, and Argentina had a prevalence higher than the general rate of $26 \times 1,000$ (fig. 1).

Discussion and conclusions

Eosinophilic esophagitis (EoE) has become an epidemiologic and editorial phenomenon since the first cases were described in the 1970s.^{17,18} The clinical studies and articles on the subject have multiplied in the medical literature, surpassing 200 scientific publications per year within the last 5 years.¹⁸

In Latin America, since the creation of the Working Group of the LASPGHAN, great efforts have been made to improve our knowledge of the disease, with at least 2 publications by our group that attempt to evaluate the problem from the Latin American perspective. Those articles include a systematic review with evidence-based recommendations on the diagnosis and treatment of eosinophilic esophagitis in children¹⁹ and a multicenter epidemiologic study on the demographic and epidemiologic characteristics of a group of patients with EoE.²⁰ Nevertheless, prevalence figures of the disease are still unknown in Latin America.

Our results show a general prevalence rate in a group of 29,253 children evaluated at a total of 36 pediatric gastroenterology centers, within the time frame of April to June 2016, of $3.69 \times 1,000$ (range: 0.2- $25.4 \times 1,000$). The prevalence of the disease was not regular and varied significantly between the different countries and centers. We identified different areas of prevalence according to the number of cases reported by the centers: low prevalence (Central America and Mexico; the Andes Region: Peru, Ecuador, and Bolivia), intermediate prevalence (the Northern Caribbean: Venezuela; the Southern Cone: Argentina and

Table 1 Prevalence of eosinophilic esophagitis and confidence interval in children that had routine outpatient evaluation for any reason in one of 36 pediatric gastroenterology centers in Latin America (April-June 2016).

Patients/Outpatient consultation	Cases of EoE	Rate x 1,000	95% CI
29,253	108	3.69	3.04-4.44

Table 2 Prevalence of eosinophilic esophagitis by country and number of participating centers in patients that had outpatient consultation evaluation for any reason within the time frame of April-June 2016.

	Number of participating centers	Outpatient evaluations	Cases of EoE	Rate x 1000
Ecuador	1	1,080	0	0
Peru	3	2,910	0	0
Mexico	7	4,500	1	0.2
El Salvador	2	2,430	1	0.4
Uruguay	1	1,350	2	1.4
Argentina	8	6,900	19	2.7
Venezuela	8	5,640	16	2.8
Chile	2	1,590	5	3.1
Colombia	3	1,203	22	18.2
Brazil	1	1,650	42	25.4

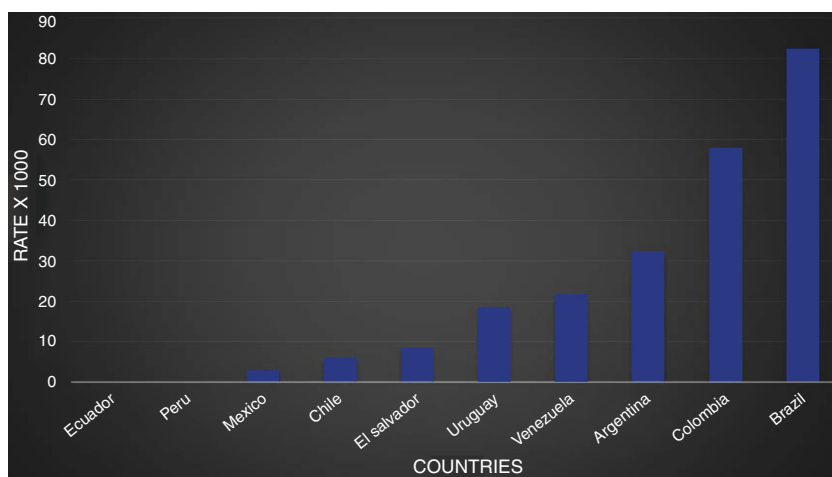


Figure 1 Prevalence of eosinophilic esophagitis by countries in patients that underwent upper gastrointestinal endoscopy for any reason at Latin American centers that reported cases in the April-June 2016 trimester.

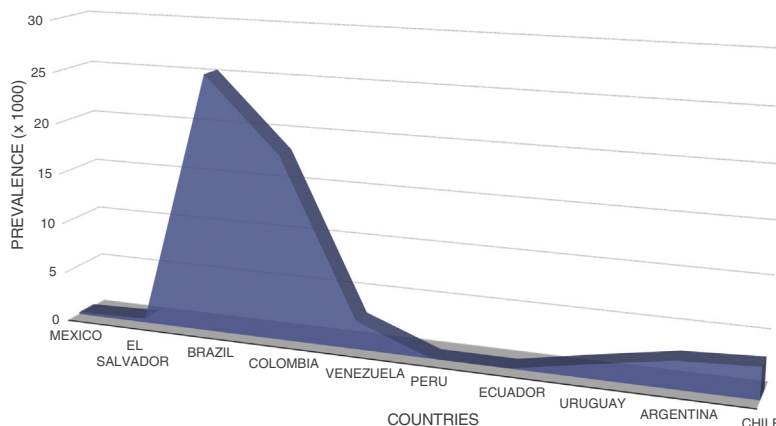


Figure 2 Prevalence of eosinophilic esophagitis by country in patients evaluated at outpatient consultation at Latin American centers that reported cases in the April-June 2016 trimester.

Chile); and higher prevalence (Brazil and Colombia). From a geographic perspective, those results allowed a bimodal curve to be drawn from North to South, with centers reporting low prevalence levels and a straightening of the curve in Central America, Mexico, and the Andes Region, and centers with higher prevalence rates in the North and South of the continent (fig. 2). Brazil merits special consideration, given that with only one center participating in the study, it reported the highest number of cases and the highest prevalence rate. In effect, at least 3 centers in that country are presently dedicated to the study of EoE in children. Perhaps Brazil's geographic density could explain the elevated number of cases and higher prevalence rate of the disease, but Mexico is an intensely populated country with a high participation of centers, and it registered very low prevalence rates.

The estimated prevalence in the group of 4,152 patients that underwent endoscopy was at least 6-times higher: $26 \times 1,000$ (range: $2.6-82.3 \times 1,000$). Our results concur with those described in other case series, in which prevalence is higher in patients that underwent endoscopy, compared

with the general population, and even higher in patients evaluated through endoscopy performed for dysphagia.^{21,22} Two aspects should be considered in relation to those results and the great variability in the prevalence rates found:

1. The influence of the environment and certain sociodemographic factors on the clinical expression of the disease.^{23,24} Latin America is a very heterogeneous continent, characterized by great ethnic diversity and variability with respect to the countries' levels of socioeconomic development. All the aspects related to the immune response pattern necessary for developing EoE, such as exposure to enteropathogens, antibiotic administration within the first year of life, duration of maternal breastfeeding, nutritional status of the population, characteristics of the gut microbiota, prevalence of infectious and immunoallergic diseases, etc., differ throughout the continent and can be influential in the variable prevalence reported by the different centers. Traditionally, in countries with a high prevalence of eosinophilic esophagitis, the disease has more frequently been described in urban populations

with a higher socioeconomic level, which can also be found in Latin American countries and certain sectors of their populations, albeit with lower general prevalence rates.

2. Eosinophilic esophagitis is a condition that requires an endoscopic procedure with biopsies for its evaluation and diagnosis. There has not been a uniform development of pediatric endoscopy as a subspecialty throughout the continent, and so it is logical to assume that the higher prevalence figures in the countries with greater development of the subspecialty can be explained by the fact that there is more probability of the disease being diagnosed. A published study conducted by our group on the situation of pediatric endoscopy in Latin America has shown the existence of at least 256 pediatric endoscopy centers and 39 pediatric endoscopy training centers in 13 Latin American countries, with 70% of them concentrated in 3 countries: Brazil, Argentina; and Venezuela. Likewise, we identified countries with high, medium, and low availability of diagnostic and therapeutic pediatric endoscopy. That reality can influence study results, given that there is very little possibility of evaluating the prevalence of eosinophilic esophagitis in countries with low availability of pediatric endoscopy services.²⁵

In conclusion, the general period prevalence rate of eosinophilic esophagitis in a cohort of Latin American pediatric patients was 3.69 x 1,000 and was at least 6-times higher (26 x 1,000) in the children that underwent upper gastrointestinal endoscopy for any reason or medical indication. Important differences were found between the different countries and centers that participated in the study, most likely due to sociodemographic factors influencing the clinical expression of the disease and to the unequal development of pediatric endoscopy in the different countries. Larger population studies are needed to calculate the incidence and prevalence of eosinophilic esophagitis in both the general population and the pediatric population in Latin America.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Financial disclosure

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Conflict of interest

The authors declare that there is no conflict of interest.

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