

# Eosinophilic esophagitis has association with the childbirth type

## Abstract

The objective of this study was to identify the relationship between the type of childbirth and the prognosis of eosinophilic esophagitis in cow's milk protein allergy. A cross-sectional, quantitative, descriptive and analytical study with 141 children aged 0-5 years, diagnosed with cow's milk protein allergy at a tertiary-level Infant Institutional Hospital. We collected in the Hospital information's about Sociodemographic, anthropometric data, food consumption, specific allergic alterations of eosinophilic esophagitis and type of delivery. The sample consisted of 113 children with a mean age of 12 months, most of them female (59.6%). The type of delivery was associated with eosinophilic esophagitis; about 83.5% of the diagnosed children were born of cesarean delivery. It was verified the presence of vomiting, diarrhea and predominant abdominal pain in males. Weight loss was a prevalent symptom in females. The confidence interval was 95%, which reflected the value of  $p=0.05$ . Individuals born with cesarean delivery can manifest exacerbated immune reactions, unlike those born by normal delivery. We suggest additional studies with nutritional interventions relating nutritional status, breastfeeding, the onset of infant formula and complementary food with eosinophilic esophagitis.

**Keywords:** food allergy, food, food hypersensitivity, cow milk

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## Introduction

Food allergy is a specific immune response caused by a protein component of a given food developed after ingestion, consumption or inhalation.<sup>1</sup> Worldwide, 5% of children under five years of age have some food allergy,<sup>2</sup> affecting 3 to 5% of the population.<sup>3</sup>

In fact, cow's milk protein allergy (APLV) is responsible for 90% of food allergies, manifesting rapidly through immunoglobulin E (IgE), causing skin reactions (urticaria, atopic dermatitis and angioedema), gastrointestinal (vomiting, diarrhea, abdominal pain isolated or involving other systems), respiratory (asthma or rhinitis) and systemic (anaphylaxis, hypotension or shock).<sup>4</sup>

In this context, one of the main symptoms of mixed APLV (with reactions mediated and not mediated by IgE) is eosinophilic esophagitis (EoE), with gastrointestinal symptoms such as nausea, vomiting and abdominal pain.<sup>5</sup> It is important to highlight that the family history of APLV is an indicator for the incidence of EoE.<sup>6</sup>

It should be noted that some factors of early childhood are associated with the development of EoE in the pediatric population, such as: use of antibiotics, cesarean delivery, premature delivery and exclusive feeding with infant or mixed formula (infant formula and breast milk).<sup>7</sup>

In fact, EoE is a chronic inflammatory pathology restricted to the esophageal region due to mixed hypersensitivity, that is, by immunological reactions mediated by IgE and not mediated by IgE. Its main characteristic is the infiltration of eosinophils in the esophageal tube.<sup>8</sup>

In Brazil, the frequency of eosinophilic esophagitis in adults is not known, but in children its prevalence is 5.2%, being 2.5 times higher in males (71.4% in males and 28.6% in female).<sup>9</sup>

The diagnosis of this disease has been increasing in children and adults. The incidence rate is 0.2 per 100,000 children per year in the

United Kingdom, 8.9 per 100,000 children per year in Australia and 43 per 100,000 children per year in the United States of America.<sup>10</sup> Furthermore, EoE affects a large majority of male patients with a history of allergic diseases, such as allergic rhinitis, asthma, food allergy and atopic dermatitis.<sup>9</sup>

Based on what has been exposed, the present study aims to identify the relationship of the type of delivery in the prognosis of eosinophilic esophagitis in allergies to cow's milk protein. We select the theme based on aggressiveness the aggressiveness of the symptoms presented in eosinophilic esophagitis and the concern with the nutritional status of the affected individuals, since the public is predominantly childish and are in the growth phase; therefore, they need an adequate energy supply.

## Methods

This is a quantitative, descriptive and analytical cross-sectional study. The study was carried out in a population of 141 children, for convenience, 0 to 5 years of age, diagnosed with a cow's milk protein allergy, and followed up by the cow's milk protein allergy program, at Hospital Infantil Albert Sabin (HIAS), located in the Vila União neighborhood, in the city of Fortaleza, Brazil, from January to April 2019.

However, the inclusion criteria for the research are patients whose guardians agree to participate in the study by signing the Free and Informed Consent Form; patients diagnosed with allergy to cow's milk protein; patients seen on Wednesday mornings. While the exclusion criteria are: patients diagnosed with allergy to cow's milk protein who hospitalized and patients using immunosuppressive drugs.

We perform data collection using by completing the Food Hypersensitivity Protocol already used by Hospital Infantil Albert Sabin, during consultations with gastro pediatricians, between the months of January and April 2019, every Wednesday by morning.

We collect data on food consumption, as well as the 24-hour food record. Through the service protocol, we record the type of milk consumed and the start of complementary feeding. At the end of the consultation, we assessed the children's nutritional status using anthropometric measures of weight and height, measured by the researchers. We measured the weight with a portable digital scale - Glass Tech Line Model (supports up to 180 kg), We checked with an infantometer (lying child) in patients up to 2 years old and in children over the age, the stadiometer - Capri Sanny Stadiometer model, according to the recommendations of the Ministry of Health.<sup>11</sup>

The Z score according to the classification for children of the World Health Organization<sup>12</sup> established the nutritional diagnosis. With this information, we performed a check to determine whether cow's milk is present in the individuals' diet. In addition, through this same protocol, we analyzed the type of delivery and specific allergic changes of eosinophilic esophagitis, such as abdominal pain, nausea, vomiting, dysphagia, gastroesophageal reflux symptoms, growth deficit and low weight gain.

However, the main variable evaluated was the association of the type of delivery in the prognosis of eosinophilic esophagitis in people allergic to cow's milk protein. After collection, we analyzed the data in the program IBM SPSS 22.0 for Windows. We used the Levene and Shapiro-Wilk tests to verify homogeneity and normality, respectively. We used data with normal distribution by means and standard deviation, while those with distribution, while the others organized in medians and percentiles.

We adopted a 95% confidence interval, which reflected in the value of  $p=0.05$ . To check the association between qualitative variables, we used the Chi-Square Test. The Research Ethics Committee (CEP) of the University of Fortaleza, in accordance with resolution 466/2012 of the National Health Council (CNS) of the Ministry of Health (MS), regarding research involving human beings approved this research.

In addition, those responsible for the participating children signed the Informed Consent Form, prior to participating in the research.

## Results

One hundred thirteen children participated in this study, as they met the inclusion criteria of the research. The average age of the survey participants was 12 months, with 59.6% ( $n=96$ ) being female. Children were diagnosed with eosinophilic esophagitis (EoE) on average 60 days after birth. Table 1 shows the association of EoE with sex, type of breastfeeding and type of delivery.

An association of type of delivery with EoE was verified. The children who were born by cesarean delivery, about 83.5% ( $n=94.35$ ) were diagnosed with the pathology, while those with normal delivery, the percentage value was 50% ( $p=0.03$ ).

When observing breastfeeding, we found that children who received breastfeeding presented lower percentage values than the others, but this value is not statistically significant ( $p>0.05$ ). With regard to sex, about 80% of participants in both groups had EoE, with no statistically significant result ( $p>0.05$ ). Table 2 shows the relationship between the presence of EE with sex, the presence of vomiting, abdominal pain, low weight gain and urticaria.

The relationship between the presence of vomiting and (EoE) was verified. Of the children with this disease, 84.3% had vomiting. In addition, there was a strong relationship between diarrhea and

abdominal pain with the presence of the disease 76% and 84.2% of the individuals had these symptoms, respectively. Low weight gain was also associated with pathology in 84.4% of people. However, urticaria showed no significant relationship with (EoE) (Table 3).

**Table 1** Association of children diagnosed with eosinophilic esophagitis with sex, type of breastfeeding and delivery

	Eosinophilic esophagitis		
	Yes	No	p
<b>Gender</b>			
Masc	79.30%	20.70%	0.759
Fem	81.40%	18.60%	
<b>Breastfeeding</b>			
Yes	78.90%	21.10%	0.465
No	85.20%	14.80%	
<b>Type of childbirth</b>			
Cesariano	83.50%	16.50%	0.03
Normal	50%	50%	

Yes, received exclusive breastfeeding; No, you did not receive exclusive breast feeding,  $p$ =significance test with a 95% confidence interval reflected in the value of  $p<0.05$  for chi-square test

**Table 2** Association between 113 children diagnosed with eosinophilic esophagitis and allergic manifestations

	Eosinophilic esophagitis	
	Presence(n)	Absence (n)
Vomiting	43 (84.3%)	8 (15.7%)
Diarrhea	57 (76%)	10 (24%)
Abdominal Pain	32(84.2%)	6 (15.8%)
Low Weight Gain	27(84.4%)	5 (15.6%)
Dermatitis	50 (79.4%)	13 (20.6%)

$n$ , number of children

**Table 3** Association between the sexes of children diagnosed with eosinophilic esophagitis and allergic manifestations of the disease

	Diagnosed with esophilic esophagitis		
	Male	Female	P
<b>Vomiting</b>			
Yes	29 (44.6%)	14 (29.2%)	0.095
No	36 (55.4%)	34 (70.2%)	
<b>Diarrhea</b>			
Yes	36 (55.4%)	21 (43.8%)	0.221
No	29 (44.6%)	27 (56.2%)	
<b>Abdominal pain</b>			
Yes	21 (65.6%)	11 (43.4%)	0.273
No	44 (34.4%)	37 (56.6%)	
<b>Low Weight Gain</b>			
Yes	14(21.5%)	13 (27.1%)	0.342

Table Continued

	Diagnosed with esophilic esophagitis		
	Male	Female	P
No	51 (79.5%)	55 (63.9%)	
<b>Urticaria</b>			
Yes	28(43.1%)	22 (45.8%)	0.848
No	37 (56.9%)	26 (54.2%)	
<b>Dermatitis</b>			
Yes	19(29.2%)	15 (31.3%)	0.817
No	46 (70.8%)	33 (68.7%)	

p, significance test with a 95% confidence interval reflected in the value of  $p < 0.05$  for testing independent variations

Regarding symptoms, in association with sex, the presence of diarrhea was more common in males with 55.4%, demonstrating a significant relationship with sex ( $p = 0.221$ ). In the same way, in relation to abdominal pain, it was more prevalent in males, with 65.5%, a strong significant relationship with sex is perceived ( $p = 0.273$ ). The vomiting symptom was present in male children (44.6%), but also did not present significant values ( $p > 0.05$ ). In contrast, low weight gain was more common among females (27.1%), with a significant result ( $p = 0.342$ ). When observing dermatitis, we found that female children had higher percentage values (31.3%); however, this value was not statistically significant ( $p > 0.05$ ).

## Discussion

The present study aimed to identify the type of delivery association in the prognosis of eosinophilic esophagitis in allergies to cow's milk protein, noting that the majority of individuals affected with eosinophilic esophagitis (EoE) are children. Linhares<sup>6</sup> states in his study that most of the time, this happens because children are exposed to proteins early on through the infant formula, proteins that are responsible for early stimulating the child's immature immune system.

In this context, it is important to note the association of cesarean delivery with EoE, in the research it was found that most of those diagnosed with the pathology were born from cesarean delivery. Sabra<sup>13</sup> corroborates with the present study by revealing that cesarean delivery delays the descent of breast milk, contributing to early bottle-feeding in infants, and often before breastfeeding.

It is important to point out that the newborn (NB) ingests proteins conveyed in the infant formula through the bottle and this will cause an immune response through the activation of the allergic response of the gastrointestinal lymphoid tissue (GALT). Still according to Sabra,<sup>14</sup> newborns ingest hospital bacteria, with a coliform microbiota, consisting of pathogenic bacteria that cause intestinal dysbiosis, different from the maternal microbiota that is predominantly composed of bifidobacteria and lactobacilli. This causes a delay in the growth of the intestinal microbiota and these factors end up inducing the NB to have exacerbated immune reactions and the appearance of allergies.

Breastfeeding had no statistically significant association. However as previously mentioned, the use of infant formulas instead of breastfeeding triggers several immunological reactions leading to the appearance of several symptoms, such as vomiting, hives, diarrhea, abdominal pain and low weight gain. We found these clinical signs in research.

In agreement with the Santos<sup>15</sup> survey, the children on exclusive breastfeeding have better nutritional status according to the BMI and fewer children with low weight, when compared to breastfeeding using infant formulas.

We emphasize that low weight gain was a relevant factor according to the analysis of the results and must be taken into account since the public is predominantly childlike, a stage of life that requires nutrients for them to grow and develop in an appropriate and healthy way.

Regarding the appearance of these symptoms, the study indicated that male children presented most symptoms; this was explained in the study by Sherrill et al.<sup>16</sup> that there is a polymorphism in the male genes and thus express the stromal thymic lymphopoietin, responsible stimulate Th2 lymphocyte responses.

Although the presence of urticaria was not statistically significant, in the research, female children indicated a higher prevalence of this symptom in relation to males. Sabra<sup>17</sup> confirms this fact, as he mentioned that chronic urticaria is present in female individuals and justifies that cow's milk is the main cause in the first year of life, and states that urticaria is the most common clinical sign in food allergies.

Furthermore, in relation to gastrointestinal symptoms, such as vomiting, diarrhea and abdominal pain, they presented a strong relationship with the disease, according to Rocha Filho et al.<sup>18</sup> these symptoms are the late manifestation of eosinophilic esophagitis.

In this context, it is important to note that EoE is associated with the type of delivery and cow's milk enters as the main trigger of immunological reactions, due to the presence of proteins that generate this hypersensitivity process causing allergy to cow's milk protein and esophagitis eosinophilic would be a consequence of that allergy. In addition, it suggests a study with a larger number of participants in order to verify a significant relationship between EoE and nutritional status as well as breastfeeding.

## Conclusion

Given the above, there was a positive relationship for patients with eosinophilic esophagitis born by normal delivery, unlike cesarean delivery, since individuals who are born by cesarean delivery may have exacerbated immune reactions. We suggest additional studies with a larger number of participants and, if possible, nutritional interventions related to nutritional status, breastfeeding, beginning of infant formula and complementary feeding with eosinophilic esophagitis.

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## Conflicts of interest

The authors declare there are no conflicts of interest.

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## References

1. Lopes JDP, Ramos NCV, Providelo CF, et al. Prevalence of food-related allergic reactions among college students. *Revista Uningá*. 2018; 55(1):195–205.

2. ASBAI and SBAN. Practical guide for diagnosis and treatment of cow's milk protein allergy mediated by immunoglobulin E. *Revista Brasileira de Alergia*. 2018.
3. Oliveira ARV, Pires TO, Nascimento LPC, et al. Food allergy: prevalence through epidemiological studies. *Revista de Ciencia da saúde Nova Esperança*. 2018;16(1): 7–15.
4. Ferreira S, Pinto M, Carvalho P, et al. Allergy to milk proteins with gastrointestinal vaccines. *Revista Nascer e Crescer*. 2014;23(2):72–79.
5. Nunes MPO, Van Tilburg MF, Tramontina FEOP, et al. Detection of serum and salivary IgE and IgG1 immunoglobulins specific for diagnosis of food allergy. *PLoS One*. 2019;14(4):1–13.
6. Nunes MPO, Candido FNM, Vieira NM, et al. Analysis of acceptance of cow milk-free food by allergic children. *Nutrition & Food Science International Journal*. 2020;9:100–105.
7. Chehade M. In time: Eosinophilic esophagitis: when to suspect it and how to diagnose it in children and adolescents. *Rev Paul Pediatr*. 2016; 34(4):395–396.
8. Guaitolini BP, Santos PFAM. Case report: Eosinophilic esophagitis associated with cow's milk protein allergy. *Residência Pediátrica*. 2016; 3(6):149–151.
9. Lucendo AJ, Molina-Infante J, Arias Á, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. *United European Gastroenterol J*. 2017;5(3):335–358.
10. Sousa MJ, Lopes I, Guilherme A, et al. Pediatric age eosinophilic esophagitis. *Revista Nascer e Crescer*. 2017;26(2):114–121.
11. Brazil. Ministry of Health. Department of Health Care. Department of primary care. Anthropometry: how to weigh and measure. 2004.
12. World Health Organization (WHO). WHO child growth standards: methods and development. Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age. 2006.
13. Ferreira CT, Vieira MC, Furuta GT, et al. Eosinophilic esophagitis-Where are we today? *Pediatr (Rio J)*. 2019;95(3):275–281.
14. Sousa F, Costa AC, Barbosa M. Eosinophilic esophagitis and allergy. *Jornal Português de Gastreenterologia*. 2013;20(1):10–15.
15. Santos, AJAO, Bispo AJB, Cruz LD. Breastfeeding pattern and nutritional status of children up to six months of age. *HU Journal*. 2016;42(2):119–124.
16. Sherrill JD, Gao PS, Stucke EM, et al. Variants of thymic stromal lymphopoietin and its receptor associate with eosinophilic esophagitis. *J Allergy Clin Immunol*. 2010;126(1):160–165.
17. Lozinsky AC, Morais MB. Eosinophilic colitis in infants. *J Pediatr (Rio J)*. 2014;90(1):16–21.
18. Rocha Filho WR, Scalco MF, Pinto JA. Allergy to cow's milk protein. *Med Minas Gerais Journal*. 2014;3(24):374–380.