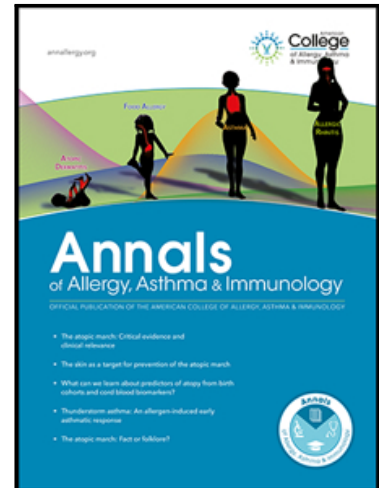


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Association of initial esophageal eosinophil counts with atopic dermatitis in EoE patients.

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Abbreviations/Acronyms.

EoE – eosinophilic esophagitis

AD – atopic dermatitis

GERD – gastroesophageal disease

EoEHSS – Eosinophilic esophagitis histologic scoring system

eos/hpf: eosinophils per high power field

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Table: 1

The estimated prevalence of atopic dermatitis (AD) in esophageal esophagitis (EoE) ranges from 2–19%.¹ We hypothesized that the presence of AD is associated with increased severity of EoE, defined as an increased rate of food impaction, esophageal stricture, or subepithelial fibrosis on biopsy in a cohort of pediatric patients. We further hypothesized that eosinophil counts on endoscopy would be higher in patients with EoE and concomitant AD, than in those without AD.

We performed an IRB-exempt retrospective chart review of patients with a diagnosis of EoE (identified by ICD-10 codes) seen in the Penn State Children's Hospital Allergy, Asthma and Immunology clinic between January 1, 2016 and June 30, 2019, from existing RedCAP databases. Eight patients seen in the Gastroenterology Clinic (but not yet seen in the Allergy Clinic) were also included in the study. 273 charts were reviewed, and 77 charts included with a confirmed diagnosis of EoE, defined as esophageal eosinophilia greater than or equal to 15 eosinophils per high power field on esophageal biopsy with symptoms of esophageal dysfunction. The study excluded 196 patients not seen during the designated time period, and patients who did not have a confirmed (but only suspected) diagnosis of EoE on esophageal biopsy. The prevalence of food impaction, esophageal stricture and subepithelial fibrosis on biopsy was compared

between cases of EoE patients with AD and the control group of EoE patients without AD, using logistic regression. Potential confounders and covariates were tested and adjusted for. A sensitivity analysis was performed. When applicable, data was analyzed with chi-square test, with a p-value less than <0.05 considered significant. For peak eosinophil counts on biopsy, the Wilcoxon Rank Sum test was used.

The age of patients ranged from 3 to 21 years (median of 13 years). Most patients were male (57) with only 20 female patients. Patients were mainly Caucasian (57) with 11 Hispanic, 6 African American and several minority patients.

EoE symptom report is variable. A sensation of choking may not always result in objective episodes of food impaction or be well-differentiated from dysphagia. We defined food impaction as physician-documented episodes of food impaction, noted in 12 (16%) of patients with EoE alone and 1 (6%) of EoE and AD patients. Of 61 patients with EoE alone, 11 (18%) had vomiting, and of 16 patients with EoE and AD, 1 (6%) had vomiting. Many patients have compensatory eating behaviors to minimize symptoms.²

Concomitant GERD was found in 54 (70%) patients by ICD-10 codes. AD was found in 16 (21%) patients, asthma in 39 (51%) patients, allergic rhinitis in 49 (64%) patients and IgE-mediated food allergy in 22 (29%) patients. Subepithelial fibrosis on esophageal biopsy was found in 32 (42%) patients, food impaction in

13 (17%) patients, micro-abscesses in 31 (40%) patients and esophageal strictures in only 1 patient (1.36%). Micro-abscesses were found in 18 (46%) patients with asthma, 24 (49%) patients with allergic rhinitis and 7 (44%) patients with AD. Excluding allergic rhinitis (p-value 0.039), these results were not statistically significant. Of 16 patients with EoE and AD, sub-epithelial fibrosis was found in 4 (25%, p-value 0.119) patients and food impaction in 1 patient (6.25%, p-value 0.288).

We did not find a higher incidence of food impaction, sub-epithelial fibrosis and esophageal stricture in patients with EoE and concomitant AD. Asthma, allergic rhinitis and IgE-mediated food allergy were also not each associated with an increased EoE severity. Of 39 patients with asthma, 13 (33%) had sub-epithelial fibrosis, while 5 (13%) had food impaction. Of 49 patients with allergic rhinitis, 20 (41%) had sub-epithelial fibrosis, while 9 (18%) had food impactions. These results were not statistically significant.

We found a statistically significant and increased median eosinophil count on initial biopsy of the proximal esophagus in patients with concomitant AD (60 vs. 20, p-value 0.011). When assessing median eosinophil count on initial biopsy regardless of location (proximal, mid- or distal esophagus), a statistically significantly increased median eosinophil count was found in patients with concomitant AD (65 vs. 40, p-value 0.005). This finding, in particular, is interesting. Although several studies in the literature note the lack of correlation

of peak eosinophil counts on esophageal biopsy with clinical symptoms or severity of EoE, peak eosinophil count changes are often used as part of histologic remission, together with symptom assessment, to guide EoE management. There is a lack of consensus across the literature on a specific definition of histologic remission.³ This suggests that one may consider a higher threshold of esophageal eosinophil count in EoE patients with AD to be considered in remission. It would also be of value to assess other histologic variables of the EoEHSS (eosinophilic esophagitis histologic scoring system).

Considering limitations of our study, we note that a determination of the absence of a difference in disease severity between EoE with AD vs EoE is difficult to conclude without a longitudinal study over time involving each patient. While a lower incidence of fibro-stenotic complications is expected in children, our small retrospective study is underpowered, with subepithelial fibrosis and food impaction found in only a few patients. Other limitations include the lack of documentation of atopic dermatitis severity. Additionally, peripheral eosinophil counts were not available for all patients and were not assessed. Peripheral eosinophilia has been reported in 50-70% of patients with EoE but as Choudhury reported, peripheral eosinophilia is not a sensitive indicator of active EoE.⁴ We note this is a limitation of the study as peripheral eosinophilia correlates with severity of AD, which would be of interest.⁵ The variation of pathology reports (some performed at other institutions) was a limitation. The use of a standardized

scoring system such as the EoEHSS on pathology reports would confer uniformity in assessment.

Further studies with larger sample sizes may be of value to determine if findings are reproducible across various populations. Our findings certainly may impact therapeutic decision-making and indicate a need for a more targeted approach for patients with EoE and AD. It raises the question of whether improved control of AD would impact EoE remission.

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Table 1: Comparison of findings of our study in patients with EoE and AD, EoE without EoE

Variable	EoE with AD	EoE without AD	All EoE patients	P-value for condition:
Biopsy findings:				
Microabscesses	7 (44%)	24 (39%)	31 (40%)	0.749 **24/49 with allergic rhinitis had microabscesses with p-value of 0.039.
Subepithelial fibrosis	4 (25%)	28 (46%)	32 (42%)	0.119
Esophageal stricture	0	1 (2%)	1 (1.3%)	1.00
Food impaction	1 (6%)	12 (20%)	13 (17%)	0.288
Median eosinophil count in proximal esophagus on endoscopy	60 eos/hpf	20 eos/hpf		0.011
Median eosinophil count in esophagus on endoscopy, regardless of location	65 eos/hpf	40 eos/hpf		0.005
Total Patients	16	61	77	

and all EoE patients.