# Eosinophilic Gastritis and Eosinophilic Enteritis Patients Endure a Lengthy Path to Diagnosis and Experience Persistent Symptoms After Diagnosis

Mirna Chehade[1], Lauren T. Gehman[2], Amol P. Kamboj[2], Henrik S. Rasmussen[2]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, United States; [2]Allakos, Inc., Redwood City, CA, United States

## BACKGROUND

- Eosinophilic esophagitis (EoE), eosinophilic gastritis (EG), and eosinophilic enteritis (EEn) are chronic inflammatory diseases characterized by persistent gastrointestinal (GI) symptoms and elevated eosinophils in the esophagus, stomach, and small intestine, respectively[1,2]
- Patients with EG and/or EEn (EG/EEn) often have comorbid allergic conditions such as asthma, rhinitis and atopic dermatitis[1–3]
- Approximately 40% of EG/EEn patients also have esophageal eosinophilia[2]
- There are no FDA-approved treatments for EG/EEn; current disease management often includes diet modification or restriction, and/or topical or systemic corticosteroids[1–3]
- **AIM:** To characterize the real-world experience of patients after EG/EEn diagnosis, including utilization of pharmacologic treatments

## METHODS

### Data source and study design

- Retrospective observational study of Symphony Health's PatientSource® proprietary, longitudinal medical and pharmacy claims database (2008-18)
- Age groups defined as ≥18 years (y) of age (adults), 11 to 17 y (adolescents), and 0 to 10 y (children), based on age at initial symptom presentation
- Statistical significance tested using Wilcoxon Rank Sum test (continuous variables) or Pearson's chi-squared test (categorical variables)

### Patient selection criteria

- ≥1 claim with ICD-CM diagnostic code for EG and/or EEn (K52.81)
- ≥1 claim with code for relevant GI symptom, ≥1 claim with code for endoscopy procedure and ≥1 claim for histopathology procedure prior to EG/EEn diagnosis date
- Evidence of continuous claims coverage for ≥3 years prior to and ≥1 year after 1st EG/EEn claim
- A total of 4,097 patients (62% adults, 11% adolescents, 27% children) met all study inclusion criteria; baseline characteristics are presented in Table 1

**Table 1. Patient baseline characteristics**

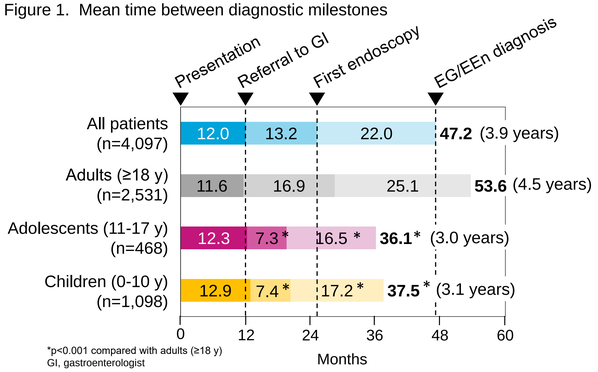
| | All Patients | Adults (≥18 y) | Adolescents (11-17 y) | Children (0-10 y) |
|---|---|---|---|---|
| **Demographics** | | | | |
| Number of patients | 4,097 | 2,531 | 468 | 1,098 |
| Age, years, mean ± SD | 33 ± 24 | 49 ± 15 | 14 ± 3 | 3.6 ± 3.4 |
| Female, n (%) | 2,445 (60%) | 1,785 (71%) | 257 (55%) | 403 (37%) |
| **Insurance coverage, n (%)** | | | | |
| Private/commercial | 3,117 (76%) | 1,886 (75%) | 376 (80%) | 855 (78%) |
| Medicare | 309 (8%) | 306 (12%) | 1 (0%) | 2 (0%) |
| Medicaid | 465 (11%) | 229 (9%) | 65 (15%) | 171 (16%) |
| Self-pay/uninsured | 9 (0%) | 5 (0%) | 1 (0%) | 3 (0%) |
| Other/unknown | 197 (5%) | 105 (4%) | 25 (5%) | 67 (6%) |
| **Year of presentation, n (%)** | | | | |
| 2008 to 2011 | 2,621 (64%) | 1,646 (65%) | 254 (54%) | 721 (66%) |
| 2012 to 2015 | 1,210 (30%) | 690 (27%) | 187 (40%) | 333 (30%) |
| 2016 to 2018 | 266 (6%) | 195 (8%) | 27 (6%) | 44 (4%) |
| **Claims activity** | | | | |
| Years active in data set, mean ±SD | 9.1 ±1.6 | 9.4 ±1.2 | 9.4 ±2.8 | 8.2 ±2.1 |

## RESULTS

### Patients endured a lengthy path to EG/EEn diagnosis

- Median (IQR) time from presentation to diagnosis was 40.4 (17.6–67.1) months, and was significantly longer for adults (47.7, 23.3–73.5) vs adolescents (31.2, 11.4–51.5) and children (32.3, 12.2–55.4)

Figure 1. Mean time between diagnostic milestones

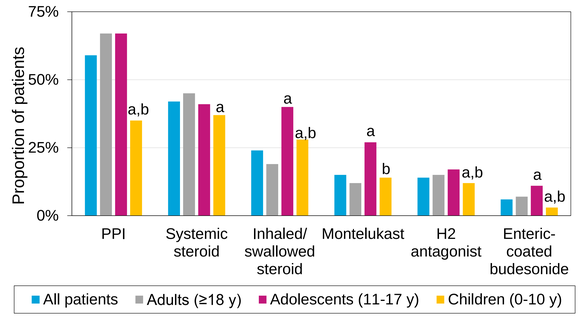



*p<0.001 compared with adults (≥18 y)
GI, gastroenterologist

- Factors contributing to diagnostic delay across age groups include:
  - Delayed gastroenterologist referral and delayed endoscopy (Figure 1)
  - Failure to diagnose on first endoscopy: 46% of patients
  - Failure to biopsy: 7% of first endoscopies did not include biopsies; adults were less likely than adolescents and children to have biopsies taken (11% vs 3% and 2% of first endoscopies did not include biopsy, *P*<0.01)

### Most patients received pharmacologic treatment after EG/EEn diagnosis

Figure 2. Frequency of drug treatments used in ≥5% of patients

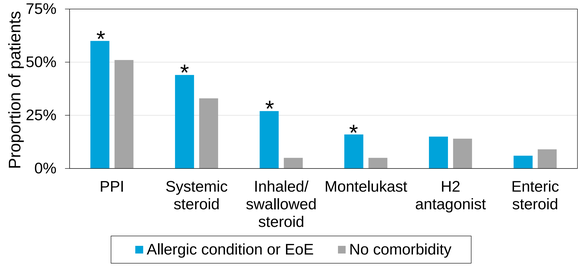



a, *P*<0.001 compared with adults; b, *P*<0.001 compared with adolescents; PPI, proton pump inhibitor

- In the 12 months following EG/EEn diagnosis, 76% of patients received pharmacologic therapy, which was more frequent in adults and adolescents vs children (83% and 89% vs 55%, *P*<0.001)

### Many patients were prescribed pharmacologic treatments even in the absence of comorbid allergic diseases or EoE

Figure 3. Frequency of treatments in patients with and without comorbidities




*P<0.001; PPI, proton pump inhibitor

- Allergic comorbidities (asthma, rhinitis, conjunctivitis, atopic dermatitis, urticaria, food allergy) were common, affecting 77% of patients
- Comorbid EoE was present in 45% of patients
- Proton pump inhibitors (PPIs), steroids (both systemic and inhaled/swallowed), and montelukast were more frequent in patients with a comorbid allergic condition and/or EoE (*P*<0.001), but still prescribed to many patients without these comorbidities
- Other drug treatments indicated for allergic conditions, including cromolyn and antibodies targeting IgE or IL-5, were prescribed in <5% of patients

### Patients experienced persistent symptoms following EG/EEn diagnosis

Table 2. Frequency of documented GI symptoms in 12 months after EG/EEn diagnosis

| | All Patients | Adults (≥18 y) | Adolescents (11-17 y) | Children (0-10 y) |
|---|---|---|---|---|
| **Patients with GI symptom(s) documented by a healthcare provider, n (%)** | **2,453** (60%) | **1,435** (57%) | **315** (67%)[a] | **703** (64%)[a] |
| **Mean (±SEM) unique documented occurrences of GI symptom(s) per year** | **3.4** (±0.1) | **3.6** (±0.2) | **3.5** (±0.1) | **3.2** (±0.1) |

GI symptoms included abdominal pain, vomiting, diarrhea, nausea, failure to thrive, GI bleeding and gas/bloating; symptoms documented by a healthcare provider; claims >10 days apart counted as unique occurrences; a, *P*<0.001 compared with adults

- After EG/EEn diagnosis, a majority of patients experienced persistent GI symptoms, warranting documentation by a healthcare provider, at a mean (±SEM) frequency of 3.4 (±0.1) unique occurrences annually (Table 2)
- The most frequently documented symptoms were abdominal pain (77%), vomiting (38%) and diarrhea (34%)
- In the 1-year period after diagnosis, 21% of patients visited the emergency department (ED) for GI symptoms; ED visits were more likely in children and adolescents vs adults (27% and 25% vs 18%, *P*<0.001 for both)

### EG/EEn patients received substantial volumes of systemic steroids

Table 3. Systemic steroids dispensed to patients with and without GI symptoms in the 12 months following EG/EEn diagnosis

| | All patients (N=4,097) | Patients with persistent GI symptoms (N=2,453) | Patients without GI symptoms (N=1,644) | *P*-value |
|---|---|---|---|---|
| **Patients dispensed systemic steroids, n (%)** | **1,738** (42%) | **1,145** (47%) | **593** (36%) | *P*<0.001 |
| **Median (IQR) annual volume (grams)** | **2.8** (0.2–10.3) | **3.1** (0.2–12.7) | **2.0** (0.1–10.0) | *P*<0.001 |
| **Median (IQR) average daily volume (mg/day)** | **7.8** (0.4–28.3) | **8.6** (0.6–34.7) | **5.6** (0.3–27.4) | *P*<0.001 |

Systemic steroids included oral and i.v. prednisone, prednisolone, dexamethasone and hydrocortisone
Volumes reported in prednisone-equivalent grams or milligrams for annual and average daily volume, respectively

- Patients with GI symptoms persisting after EG/EEn diagnosis were significantly more likely to receive systemic steroids and at higher volumes than patients without persistent symptoms (Table 3); this trend was consistent across age groups:
  - Adults: 13.7 vs 9.6 mg/day, *P*<0.01
  - Adolescents: 11.0 vs 7.3 mg/day, *P*=0.21
  - Children: 5.9 vs 3.9 mg/day, *P*<0.01
- The most common healthcare provider group prescribing systemic steroids was primary care providers (35%), followed by gastroenterology (11%); allergists were responsible for 3% of all systemic steroid prescriptions

## CONCLUSIONS

- Patients with EG/EEn endured a substantial delay across multiple steps in the diagnostic process, highlighting the need for heightened disease awareness and standardized diagnostic criteria
- Most EG/EEn patients received pharmacologic treatment following diagnosis; while these treatments were not necessarily prescribed for EG/EEn, their use may be driven by anecdotal evidence from published case reports[1,2] and the lack of FDA-approved treatment options
- The use of pharmacologic treatments even in patients without allergic comorbidities suggests that many of these treatments were prescribed in an attempt to manage EG/EEn symptoms
- Following diagnosis, most patients with EG/EEn remained symptomatic and visited healthcare providers for their GI symptoms an average of 3.4 times per year, underscoring the need for improved approaches to disease management
- Patients with GI symptoms persisting after EG/EEn diagnosis were more likely to receive systemic steroids, and at higher volumes, than patients without persistent symptoms, suggesting that healthcare providers often resort to systemic steroids to manage EG/EEn symptoms
- Frequent systemic steroid exposure in patients with EG/EEn despite the well-established risks emphasizes the unmet need for targeted therapies that are efficacious and safe for long-term use

**References: 1.** Egan and Furuta, Ann Allergy Asthma Immunol. 2018 Aug;121(2):162-167; **2.** Gonsalves, Clin Rev Allergy Immunol. 2019 Oct;57(2):272-285; **3.** Pesek et al., Am J Gastroenterol. 2019 Jun;114(6):984-994.

Presented at ACG Congress October 2019, San Antonio, Texas