Diagnostic Delay in Patients with Eosinophilic Gastritis and/or Eosinophilic Duodenitis: A United States Population-Based Study

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BACKGROUND

- Eosinophilic gastritis (EoG) and eosinophilic duodenitis (EoD) are chronic inflammatory diseases characterized by persistent gastrointestinal symptoms and elevated eosinophils in the stomach and small intestine, respectively[1,2]
- There are no standardized diagnostic guidelines, but required steps are esophagogastroduodenoscopy (EGD), collection of biopsies from gastric and duodenal mucosae, and histologic confirmation of tissue eosinophilia
- The nonspecific clinical presentation of patients with EoG and/or EoD (EoG/EoD) combined with limited disease awareness and lack of consensus diagnostic guidelines suggest patients may remain undiagnosed or endure diagnostic delay
- **AIM:** To characterize the path to diagnosis for patients with EoG/EoD in a representative population in the US

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), 12 to 17 y (adolescents), and 0 to 11 y (children), based on age at initial symptom presentation
- Data were analyzed using descriptive statistics; all findings are reported as means with 95% confidence intervals (CIs) unless otherwise noted

Patient selection criteria

- ≥1 claim with ICD-CM diagnostic code for EoG and/or EoD (K52.81)
- ≥1 claim with code for relevant GI symptom, ≥1 claim with code for EGD procedure and ≥1 claim for histopathology procedure prior to EoG/EoD diagnosis
- Evidence of continuous claims coverage for ≥3 years prior to and ≥1 year after first EoG/EoD claim
- A total of 4,108 patients (62% adults, 10% adolescents, 28% children) met all study inclusion criteria; baseline characteristics are presented in Table 1

Table 1. Patient baseline characteristics

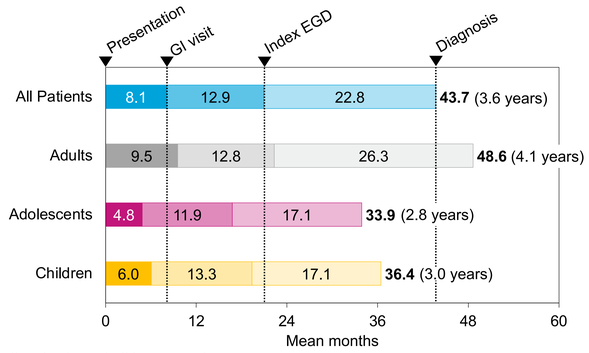
	All Patients	Adults	Adolescents	Children
Demographics				
Number of patients	4,108	2,534	404	1,170
Age, years, mean ±SD	32.9 ±24.1	49.1 ±15.3	14.5 ±1.6	4.0 ±3.7
Female	2,452 (60%)	1,787 (71%)	231 (57%)	434 (37%)
Health insurance provider				
Private/commercial	3,121 (76%)	1,888 (75%)	328 (81%)	905 (77%)
Medicare	309 (8%)	306 (12%)	1 (0%)	2 (0%)
Medicaid	468 (11%)	229 (9%)	52 (13%)	187 (16%)
Self-pay/uninsured	9 (0%)	5 (0%)	1 (0%)	3 (0%)
Other/unknown	201 (5%)	106 (4%)	22 (5%)	73 (6%)
Year of presentation				
2008 to 2011	2,626 (64%)	1646 (65%)	221 (55%)	759 (65%)
2012 to 2015	1,216 (30%)	692 (27%)	158 (39%)	366 (31%)
2016 to 2018	266 (6%)	196 (8%)	25 (6%)	45 (4%)

RESULTS

Patients with EoG/EoD endured an average diagnostic delay of 3.6 years

- Mean time from presentation to diagnosis was 43.7 [95% CI: 42.8, 44.6] months or 3.6 years and was longer in adults (Figure 1)

Figure 1. Mean time between diagnostic steps

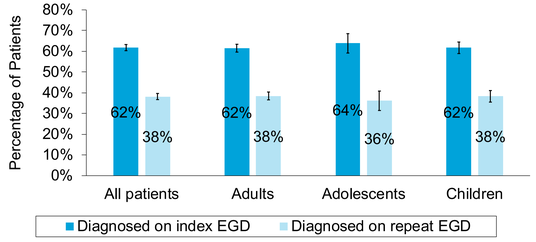


GI, gastroenterologist; EGD, esophagogastroduodenoscopy

- There was an average delay of 8.1 months from presentation to first gastroenterologist (GI) visit, 12.9 months from GI visit to index EGD, and 22.8 months from index EGD to diagnosis of EoG/EoD (Figure 2)
- Patients consulted a mean of 7.2 [95% CI: 7.0, 7.5] clinicians, including 2.2 [95% CI: 2.0, 2.5] gastroenterologists, from presentation to diagnosis
- 44.3% [95% CI: 42.8%, 45.8%] were diagnosed with an alternative, nonspecific gastrointestinal condition, such as irritable bowel syndrome, functional dyspepsia or chronic gastritis, prior to EoG/EoD diagnosis

38% of patients were not diagnosed on index endoscopy

Figure 2. Percentage of patients in whom EoG/EoD diagnosis was established on index vs repeat (i.e., 2 or more) EGD



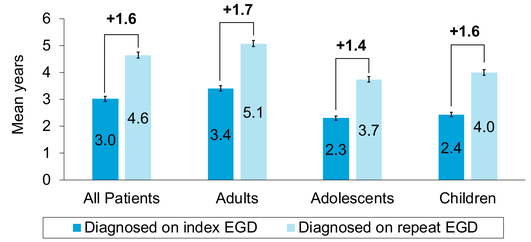
Error bars represent 95% confidence interval (CI)

- 1,569 (38%) patients were not diagnosed on index EGD; this was observed at a similar rate across age groups (Figure 2)
- A mean of 1.74 [95% CI: 1.70, 1.78) EGDs were performed between presentation and EoG/EoD diagnosis across patients

Patients not diagnosed on index endoscopy endured additional diagnostic delay

- In the 1,569 patients not diagnosed on index EGD, mean months between index EGD and repeat EGD was 18.8 [95% CI: 17.9, 19.7]
- Longer delay between index and repeat EGD was observed in adults (22.7 [95% CI: 21.4, 23.9]) vs adolescents (13.3 [95% CI: 10.9, 15.7]) and children (12.2 [95% CI: 10.9, 13.5])

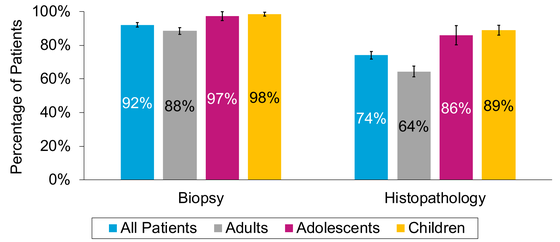
Figure 3. Mean diagnostic delay in patients diagnosed on index vs repeat EGD



- Mean diagnostic delay in patients not diagnosed on initial EGD was 4.6 years, or a mean increase of +1.6 [95% CI: +1.4, +1.8] years compared with patients diagnosed on initial EGD (Figure 3)

Biopsy collection and histopathologic evaluation were not universally performed during index EGD

Figure 4. Rate of biopsy and histopathology procedure in conjunction with index EGD in patients not diagnosed on initial EGD (N=1,569)



- In the subset of patients not diagnosed on index EGD (N=1,569), 7.9% [95% CI: 6.6%, 9.2%] did not have biopsy collection during index EGD
- Of the patients who had biopsy collection, 26.0% [95% CI: 23.8%, 28.3%] did not have documented histopathologic evaluation

Other procedures for differential diagnosis were often used

- Abdominal imaging, colonoscopy, and stool analyses, each of which may help rule out other conditions but are not useful for diagnosing EoG/EoD, were performed in 70.9% [95% CI: 69.5%, 72.3%], 51.9% [95% CI: 50.3%, 53.4%], and 24.0% [95% CI: 22.7%, 25.3%] of patients, respectively

Many EoG/EoD patients have concomitant EoE, allergic disease, and/or peripheral eosinophilia

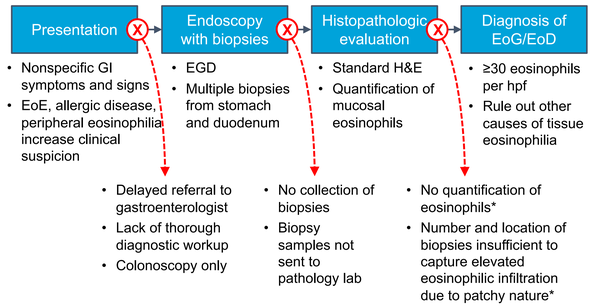
Table 2. Frequency of EoE, allergic conditions and peripheral eosinophilia

	All Patients	Adults	Adolescents	Children
Eosinophilic esophagitis (EoE)	45%	32%	57%	68%
Any allergic disease	77%	71%	82%	88%
Allergic rhinitis	64%	58%	68%	74%
Asthma	43%	35%	52%	59%
Atopic dermatitis	18%	6%	21%	43%
Urticaria	12%	8%	14%	19%
Allergic conjunctivitis	11%	8%	11%	17%
Food allergy	7%	1%	9%	19%
Peripheral eosinophilia	12%	8%	15%	21%

- Comorbid EoE, allergic disease and peripheral eosinophilia were observed in 45%, 77% and 12%, respectively, of patients with EoG/EoD

CONCLUSIONS

Figure 5. Steps required for EoG/EoD diagnosis and points of delay or attrition suggested by this study



GI, gastrointestinal; EGD, esophagogastroduodenoscopy; H&E, hematoxylin and eosin stain; hpf, high-powered field
*speculation not confirmed by present study

- Patients with EoG/EoD endured substantial diagnostic delay; factors identified in this study that contributed to this delay include delayed gastroenterologist visit, delayed EGD, missed diagnosed on first EGD, and lack of routine biopsy and histopathology
- The nonspecific symptoms and signs of EoG/EoD, including abdominal pain, diarrhea and early satiety, contributed to a high rate of misdiagnosis with another gastrointestinal condition; this study identified additional clinical clues to aid in patient identification
- Patients with nonspecific gastrointestinal symptoms with a prior history of dysphagia/EoE, allergic disease and/or peripheral eosinophilia should be referred to a gastroenterologist and evaluated for EoG/EoD
- Current barriers to prompt diagnosis of EoG/EoD and tools to enable a more efficient diagnosis are summarized in Figure 5
- Together with heightened disease awareness and standardized diagnostic guidelines, these findings will help improve the patient's diagnostic journey

References: **1.** Egan and Furuta, Ann Allergy Asthma Immunol 2018;121:162-7; **2.** Fleischer and Atkins, Immunol Allergy Clin North Am 2009;29:53-63, ix.; **3.** Gonsalves, Clin Rev Allergy Immunol 2019;57:272-85; **4.** Ko et al., Am J Gastroenterol 2014;109:1277-85; **5.** Pesek et al. Dig Dis Sci 2019.; **6.** Reed et al. Dig Liver Dis 2015;47:197-201

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