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The Effects of Patient Demographics on Outpatient Endoscopy Utilization in Children with Eosinophilic Esophagitis

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Abstract

Objectives: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus that requires esophagogastroduodenoscopy (EGD) for diagnosis and treatment monitoring. We aimed to identify frequency of endoscopic monitoring in children with EoE and observe the effect of age, race, socioeconomic factors, and atopy on the rate of endoscopy.

Methods: We queried the Pediatric Health Information System over a 15-year period for ambulatory EGDs in children with EoE. Subjects with at least 1 year of data were included. Age, gender, ethnicity, race, insurance type, median household income, and atopy were collected for each subject.

Results: 16,517 subjects were included (mean age 8.5y). 3,211 (19%) of subjects had ≥1 EGD per subject year (EGD/SY). Subjects >13 years old were more likely to have ≥1 EGD/SY compared to children 6-12 years (OR 2.29, p<0.001, 95%CI = 2.06-2.54). Males were more likely to have ≥1 EGD/SY compared to females (OR 1.18, p<0.001, 95%CI = 1.08-1.31). African-American subjects were 16% less likely than Caucasian subjects to have ≥1 EGD/SY (OR 0.84, p=0.05, 95%CI = 0.71-1.00). Subjects with allergic rhinitis or

anaphylaxis, food allergy, and/or oral allergy syndrome were more likely to have ≥1 EGD/SY (OR 1.67, p<0.001, 95%CI = 1.47-1.90 and OR 3.65, p<0.001, 95%CI = 3.25-4.11 respectively).

Conclusions: 19% of subjects had ≥1 EGD/SY. Older age, male gender, allergic rhinitis, and food allergies were associated with more frequent endoscopic monitoring in children with EoE. Caucasian subjects had more frequent endoscopy than African-American subjects. This study raises awareness about underrecognized variation in the care of children with EoE.

Keywords = pediatric eosinophilic esophagitis, endoscopy, implicit bias

What is Known?

- Eosinophilic esophagitis (EoE) is most common in males and Caucasians.
- There are variations in the presentation of EoE and disease severity based on age and race.
- Young children present with vomiting, feeding aversion, or growth failure, compared to adolescents and adults who present with dysphagia and food impactions.

What is New?

- Adolescents and children younger than 5 years of age with EoE undergo more frequent endoscopy compared to children 6-12 years of age.
- African-American children with EoE undergo less frequent endoscopy compared to Caucasian children, which may be due to implicit bias in healthcare.
- There is underrecognized variation in endoscopic monitoring in the management of EoE in children.

Introduction

Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease involving eosinophilic-predominant esophageal inflammation (1). A diagnosis of EoE requires symptoms of esophageal dysfunction plus at least 15 eosinophils/high powered field on a mucosal biopsy from the esophagus (1). Chronic inflammation in EoE can lead to esophageal fibrosis and strictures. Treatment of the inflammation, with proton pump inhibitors, topical swallowed steroids, and dietary elimination of common food allergens, reduces these fibrostenotic changes (1-4). Treatment monitoring remains a challenge in EoE, because symptoms often do not correlate with degree of esophageal eosinophilia (5, 6). Although other modalities are being explored (3), esophagogastroduodenoscopy (EGD) is currently the standard tool to assess for mucosal disease, but usually requires sedation or anesthesia in pediatric patients (7). There is considerable variation in practice in disease monitoring (8), and the frequency of EGD is left to the provider's discretion (1, 6).

The presentation of EoE and disease severity differ based on age and race. Adults and adolescents often present with dysphagia or food impactions, whereas young children and infants present with vomiting, feeding dysfunction, growth failure, and abdominal pain (9-11). It has been well described that EoE has a higher prevalence in Caucasians (10-12), although some recent pediatric studies have demonstrated that African-Americans may be equally affected but underdiagnosed (13, 14). Additionally, African-American patients present at a younger age (13, 15). Although these epidemiologic differences have been identified, differences in treatment management based on age, race, or socioeconomic status remain unknown. One study of 508 children found that median household income (MHI) was higher in patients with EoE compared to control subjects in their gastroenterology (GI) and allergy clinics, and Caucasian race was a confounding variable that accounted for this difference (16). Another retrospective study observed that 89 pediatric patients with EoE underwent 471 esophagogastroduodenoscopies (EGDs), with a mean of 2.8 EGDs in children with resolved EoE to 6.6 EGDs in children with relapsed EoE (9). Racial disparity between patients undergoing EGDs for EoE was identified in a single center study, where of 1,857 EGDs performed in patients with EoE at their institution, 53% were in Caucasian children versus 28% in African-American children (14).

We performed a retrospective cohort study using the Pediatric Health Information System to identify EGDs performed in ambulatory surgery centers on children with EoE. We sought to identify the frequency of endoscopic monitoring in pediatric patients with EoE with a national sample. Our secondary aim was to identify the variation in frequency of EGD utilization based on age, gender, ethnicity, race, median household income, insurance type, and concurrent atopic diagnoses. We hypothesized that there were one or more patient-level factors that influenced the rate of endoscopy utilization in children, most likely race.

Methods

This study was approved by the Indiana University Institutional Review Board under exempt status prior to acquiring or analyzing data.

Data Source

The data for this study were obtained from the Pediatric Health Information System (PHIS), an administrative database that contains inpatient, emergency department, ambulatory surgery and observation encounter-level data from over 52 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children's Hospital Association (Lenexa, KS). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the PHIS are managed by IBM Watson Health (Ann Arbor, MI). For the purposes of external benchmarking, participating hospitals provide discharge/encounter data including demographics, diagnoses, and procedures. Nearly all of these hospitals also submit resource utilization data (e.g. pharmaceuticals, imaging, and laboratory) into the PHIS. The data are de-identified at the time of data submission, and the data are subjected to a number of reliability and validity checks before being included in the database. For this study, data from 44 hospitals were included, since not all hospitals contribute ambulatory surgery data.

Specific Data Elements Obtained

We queried the PHIS from 01/01/2004 to 12/31/2019 and obtained all ambulatory surgery encounters associated with a diagnosis of EoE where an EGD was performed (see Supplemental Digital Content for ICD-9 and -10 codes, http://links.lww.com/MPG/C354).

To improve the odds that all subjects analyzed were followed by the institution over time, we limited our analysis to subjects with at least 1 year of data in the PHIS, as defined by at least two encounters of any type separated by 12 months or more. This provided the structure to observe frequency of endoscopy over a minimum of 1 year per subject (EGD per subject year or EGD/SY) and reduced the risk of overestimating endoscopic monitoring. We obtained the following data elements for each subject: age at their first encounter, gender, ethnicity, race, insurance type, and median household income (MHI). Atopic disorders associated with medical record numbers in our dataset were obtained by querying the PHIS for the ICD-9 and -10 codes related to status asthmaticus, unspecified asthma, eczema, atopic dermatitis, allergy rhinitis, allergy unspecified, anaphylaxis, food allergy, allergy to other food, and oral allergy syndrome during any encounter (see Supplemental Digital Content, http://links.lww.com/MPG/C354).

Statistical Analysis

We performed univariate statistics (ANOVA and chi-squared) for age, gender, ethnicity, race, insurance type, and median household income to assess how these varied with EGD/SY. We then built a multivariable regression model using mixed effects logistic and linear regression. Hospital was modeled as a random effect, and age, gender, ethnicity, race, insurance type, and median household income as fixed effects. The number of EGDs performed (linear model) and whether 1 or more EGDs were performed (logistic model) were used as dependent/outcome variables. All statistics were performed using R (https://www.r-project.org/) and the lme4 package for mixed effects regression. Statistical significance was determined to be a $p < 0.05$ for all comparisons.

Results

16,517 subjects were included in our study. The mean age of our cohort at their first encounter was 8.5 years, and the median age was 9 years. Thirty percent of subjects were female, 23% were non-Caucasian, and 38% of subjects had Medicaid or other non-commercial health insurance. Number of years of entry in the PHIS per subject ranged from 1-10.25 years. Complete subject characteristics are displayed in Table 1.

3,211 (19%) of subjects had at least 1 EGD/SY. On univariate analysis, subjects with ≥1 EGD/SY were significantly older than those with <1 EGD/SY. The mean age of subjects with 4+ EGD/SY was 13.6 years compared to 8.4 years in subjects with <1 EGD/SY ($p < 0.001$). The distribution among all EGD/SY frequencies showed male and Caucasian predominance, as well as a predominance of subjects with commercial insurance ($p < 0.001$) (Table 2).

On multivariate analysis, subjects < 2 years of age were more likely to have ≥1 EGD/SY compared those 6-12 years of age (OR 1.35, $p < 0.001$, 95%CI = 1.13-1.62). Subjects 2-5 years of age were also more likely to have ≥1 EGD/SY compared those 6-12 years of age (OR 1.33, $p < 0.001$, 95%CI = 1.19-1.48), as were subjects > 13 years old compared to those 6-12 years of age (OR 2.29, $p < 0.001$, 95%CI = 2.06-2.54). Male subjects were more likely to have ≥1 EGD/SY (OR 1.18, $p < 0.001$, 95%CI = 1.08-1.31) compared to female subjects. African-American subjects were 16% less likely than Caucasian subjects to have ≥1 EGD/SY (OR 0.84, $p = 0.05$, 95% CI = 0.71-1.00). Ethnicity (OR 0.88, $p = 0.19$, 95%CI = 0.73-1.07), MHI (OR 1.08, $p = 0.54$, 95%CI = 0.84-1.39) and Medicaid insurance type (OR 0.92, $p=0.12$, 95%CI = 0.83-1.02) did not affect frequency of endoscopy (Table 3).

Subjects with allergic rhinitis were more likely to have ≥1 EGD/SY (OR 1.67, $p < 0.001$, 95%CI = 1.47-1.90). Subjects with other allergy (anaphylaxis, food allergy, oral allergy syndrome, and allergy not specified) were considerably more likely to have ≥ 1 EGD/SY (OR 3.65, $p < 0.001$, 95%CI = 3.25-4.11). Asthma (OR 0.90, $p = 0.35$, 95%CI = 0.73-1.12) and eczema (OR 0.94, $p =0.37$, 95%CI = 0.81-1.08) did not affect frequency of endoscopy (Table 3).

Discussion

We present a large retrospective cohort study of children with EoE undergoing EGD in ambulatory surgery centers to identify rates of outpatient endoscopy utilization in this population as well as demographic and socioeconomic factors that affect this rate. Of 16,517 subjects, 3,211 (19%) of subjects had ≥1 EGD/SY.

Age

Adolescents > 13 years were more likely to have ≥1 EGD/SY compared to school-aged children 6-12 years of age. Younger age groups of < 2 years and 2-5 years of age were more likely to have ≥1 EGD/SY compared to school-aged children as well. There are likely physician and subject factors that contribute to these findings. Gastroenterologists may be more willing to perform endoscopy on older subjects since they have less anesthesia risk compared to young children (7). Older subjects and adolescents are also more likely to have poor medication adherence with frequent flare of symptoms (17), or perhaps have more disease burden due to long-standing inflammation. On the other hand, young children are more often treated with diet elimination, for which repeat endoscopy is recommended to assess treatment response and upon food reintroduction (4). This is likely the reason we see an increase in endoscopy frequency in the younger age groups.

Gender

Males were 18% more likely to have ≥1 EGD/SY, which may represent increased disease burden in males or be a function of a male-predominant disease (10, 12, 18). Additionally, males are more likely to report dysphagia and food impactions, which prompts EGDs, compared to females who report abdominal pain and nausea (15).

Race

African-American children were 16% less likely to have ≥1 EGD/SY compared to Caucasian children. Our findings are consistent with a 2014 retrospective study that examined billing data and found that 53% of endoscopies done in children with EoE were performed in Caucasian children versus 28% in African-American children (14). Symptom variation between races, which has been seen in adults (19), may play a role in endoscopic monitoring, since Caucasian children often report dysphagia compared to African-American children who exhibit more failure to thrive (15). There may be unidentified variation in treatment strategies based on race which affects endoscopy frequency as well.

A more alarming consideration for less frequent endoscopic monitoring in African-American children with EoE is implicit bias. Multiple studies have shown that healthcare professionals exhibit the same degree of implicit racial bias compared to community members (20, 21). As a result of implicit and historical explicit biases, African-American individuals are more concerned about privacy and harmful experimentation in hospitals compared to Caucasians

(22), which can result in decreased or delayed healthcare utilization. For example, the prevalence of food allergies is higher in African-American children compared to Caucasian children (23, 24). Despite this higher prevalence, minority children with food allergies have shorter follow-up duration with a specialist but higher rates of food-induced anaphylaxis (24). African-American children with EoE have more severe inflammation at diagnostic endoscopy compared to Caucasian children, which raises suspicion for delays in care based on race in EoE (13). Implicit bias and its downstream effects may be underrecognized but important reasons for less frequent endoscopic monitoring in these children.

Insurance and Median Household Income

Insurance type has been posited as a barrier to timely EoE diagnosis, especially among African-Americans (14). However, in our study we found that MHI, as well as insurance type, did not affect rate of endoscopy utilization in children with EoE.

Other Atopic Diseases

A history of allergic rhinitis and food allergies significantly increased the likelihood of having ≥1 EGD/SY. These findings support the idea that environmental or food allergens trigger disease. A recent retrospective study found that 1-2% of children and adults with existing diagnosis of EoE had seasonal exacerbation of symptoms in the summer and fall months (28). Of those subjects with seasonal exacerbations, 85% had a comorbid atopic condition, most commonly allergic rhinitis (85%) and food allergy (61%) (28). Subjects with these comorbid atopic conditions may also have more severe EoE which leads to more frequent endoscopic monitoring.

Limitations

This study had several limitations related to our dataset. First, we used an administrative dataset where subjects were identified retrospectively. We did not have information on why patients had repeat EGDs or granular clinical information that may differ from one patient to the next, such as treatment modality, biopsy results, or response to treatment. Our dataset did not include inpatient encounters, and therefore endoscopy performed in inpatient hospital units were not captured. Our study would have been strengthened by identifying the relationship between EoE treatment type and frequency of endoscopy. Second, we used ICD-9 and -10 codes to determine diagnoses, which carries a risk of miscoding or misrepresenting the true indication of a procedure. Our data do not account for a subject's initial diagnostic EGD for which the diagnosis codes of EoE may not be associated. We may have a dataset enriched for follow up EGDs, and a cohort enriched for subjects that had more frequent endoscopic monitoring. Lastly, the PHIS includes information from tertiary care centers for pediatrics, which does not include community-based centers. Only one pediatric hospital is allowed in the PHIS per metropolitan area, and so cities with multiple tertiary care centers are also underrepresented.

Conclusions

Treatment of EoE prevents the development of fibrostenotic changes and esophageal strictures (2). Endoscopic monitoring in EoE is helpful in tracking treatment response, but the frequency of endoscopy is variable. We found that 19% of pediatric patients with EoE undergo at least 1 EGD per year. Adolescent and toddler age groups, male gender, Caucasian race, allergic rhinitis, and food allergies increase the likelihood of having ≥1 EGD/SY. Identifying demographic and socioeconomic factors that affect endoscopy utilization in children with EoE is valuable, and this study raises awareness about underrecognized variation in care. We hope for continued research of the management of children with EoE, and future work in this area should focus on investigation of frequency of EGDs in relation to age, race, and treatment modality.

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Table 1. Subject demographics and EGD/SY

	N=16,517
Mean age in years (SD) **Median age in years** (SD)	8.5 (4.7) 9
Gender – n (%) • Male • Female	 11,583 (70) 4,934 (30)
Ethnicity – n (%) • Not Hispanic/Latino • Hispanic/Latino	 13,805 (84) 1,315 (8)
Race – n (%) • Caucasian • African-American • Other	 12,752 (77) 1,431 (9) 2,334 (14)
Insurance Type – n (%) • Commercial • Medicaid • Other	 10,215 (62) 4,922 (30) 1,380 (8)
Mean household income (SD) **Median household income**	$50,167 ($22,030) $49,955
EGD/SY - Number of subjects (%) <1 1 2 3 4+	 13306 (81) 2481 (15) 546 (3) 114 (<1) 70 (<1)

Table 2. Number of EGD/SY in relation to subject demographics (univariate analysis)

Number of EGDs/Subject Year	**< 1**	**1+**	**2+**	**3+**	**4+**	**p-value**
N	13306	2481	546	114	70	
Mean Age (years)	8.4	8.8	9.6	11.3	13.6	<0.001
Median Age (years)	9	9	11	14	16	
Gender – n (%)						<0.001
Males	9219 (69)	1823 (73)	402 (74)	84 (74)	55 (79)	
Females	4087 (31)	658 (27)	144 (26)	30 (26)	15 (21)	
Ethnicity – n (%)						<0.001
Hispanic/Latino	1090 (8)	187 (8)	32 (6)	4 (4)	2 (3)	
Not Hispanic	11018 (83)	2141 (86)	481 (88)	106 (93)	59 (84)	
Race – n (%)						0.006
Caucasian	10204 (77)	1948 (79)	441 (81)	98 (86)	61 (87)	
African-American	1189 (9)	205 (8)	30 (5)	4 (4)	3 (4)	
Insurance Type – n (%)						<0.001
Commercial	8043 (60)	1637 (66)	387 (71)	93 (82)	55 (79)	
Medicaid	4028 (30)	731 (29)	133 (24)	19 (17)	11 (16)	
Mean MHI ($)	51,822	52,466	53,281	56,894	55,740	0.01
Median MHI ($)	48,223	48,651	49,664	57,770	52,621	

Table 3. Demographic and socioeconomic factors in relation to ≥1 EGD/SY (multivariable analysis)

	OR (Odds Ratio)	95% CI	p-value
Age			
6-12 years	-	-	-
< 2 years	1.35	1.13-1.62	0.001
2-5 years	1.33	1.19-1.48	<0.001
>/= 13 years	2.29	2.06-2.54	<0.001
Gender			
Female	-	-	-
Male	1.19	1.08-1.31	<0.001
Ethnicity			
Not Hispanic or Latino	-	-	-
Hispanic or Latino	0.88	0.73-1.07	0.19
Race			
Caucasian	-	-	-
African-American	0.84	0.71-1.00	0.05
Asian	0.84	0.59-1.18	0.30
Insurance Type			
Commercial	-	-	-
Medicaid	0.92	0.83-1.02	0.12
Household Income	1.08	0.84-1.34	0.54
<$25,000	0.85	0.64-1.33	0.27
$50,000-75,000	0.96	0.87-1.07	0.45
$75,000-100,000	0.93	0.79-1.09	0.37
>$100,000	0.89	0.67-1.18	0.42
Atopy			
Asthma	0.90	0.73-1.12	0.35
Eczema	0.94	0.81-1.08	0.37
Allergic Rhinitis	1.67	1.47-1.90	<0.001
Anaphylaxis, Food Allergy, Oral Allergy Syndrome, Allergy Unspecified	3.65	3.25-4.11	<0.001