

Racial Differences in the Clinical Presentation of Pediatric Eosinophilic Esophagitis

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What is already known about this topic? The prevalence of eosinophilic esophagitis (EoE) is increasing. Analysis of current data shows that white males comprise the highest proportion of patients with EoE.

What does this article add to our knowledge? African American patients with EoE comprise a higher proportion of this EoE population than previously reported, present at a younger age than white patients, and have different clinical characteristics than white patients.

How does this study impact current management guidelines? This study raises awareness of the potential diagnosis of EoE in African American children with atopy and esophageal dysfunction. Further research is needed to better understand possible racial differences in pediatric EoE.

BACKGROUND: Analysis of current data suggests that 80% to 90% of children diagnosed with eosinophilic esophagitis are white. Little data exist regarding the presentation of eosinophilic esophagitis and potential clinical differences in minority children.

OBJECTIVE: This study compared the clinical presentation of eosinophilic esophagitis in African American children with white children treated at an urban allergy referral center.

METHODS: At an urban allergy clinic, a 2-year retrospective chart review was performed of 50 consecutive pediatric patients diagnosed with eosinophilic esophagitis. Presenting symptoms, age at diagnosis, coexisting atopic disease, and laboratory parameters were compared between races.

RESULTS: Most of the 50 children identified were boys (74%), as previously described. However, unlike prior literature, most were nonwhite (42% white, 42% African American, 4% Asian, and 12% other). African American children compared with white children had (1) a significantly higher frequency of failure to thrive ($P < .01$) and vomiting ($P < .01$) as presenting symptoms, (2) a higher frequency of comorbid atopic dermatitis ($P < .01$), (3) a younger mean age of symptom presentation and formal diagnosis (3.7 vs 9.1 years; $P < .01$), and (4) a trend toward a longer interval between symptom onset and formal diagnosis. However, after

adjusting for confounding variables of age and insurance type, several of these racial differences were no longer significant.

CONCLUSION: African American children in this series had a larger burden of eosinophilic esophagitis than previously described as well as differences in clinical presentation compared with white patients. Analysis of these findings suggests that providers be aware of this potential diagnosis in young, atopic African American children with symptoms of esophageal dysfunction. © 2014 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2014;2:320-5)

Key words: Eosinophilic esophagitis; Race; African American; Health disparities

Eosinophilic esophagitis (EoE) has been increasing in prevalence,¹⁻⁵ and, likewise, the number of research publications about EoE has doubled between 2007 and 2011.⁶ Yet, despite the rapidly growing body of literature about EoE, few studies to date have examined the demographics and, specifically, the racial distribution of EoE in the pediatric population.⁷⁻⁹ Analysis of current data shows that more than 80% to 90% of children with EoE are white.^{6,10-12} Because of this apparent predominance among white patients, there are fewer data available about the clinical presentation in African American and other minority children. This study serves to characterize the racial distribution of EoE among children at an urban allergy referral center and to examine differences in presentation and phenotype between different racial groups affected by EoE.

METHODS

Study design

A retrospective chart review was performed of all patients younger than 18 years of age who were diagnosed with EoE during a 2-year period (August 2008 to August 2010) at the Children's National Medical Center Allergy Clinic in Washington DC. Patients with EoE were identified from an internally maintained clinical database that captures the diagnosis of every consecutive patient seen in the allergy clinic. A diagnosis

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Abbreviations used

AD- Atopic dermatitis
EoE- Eosinophilic esophagitis
FTT- Failure to thrive
GER- Gastroesophageal reflux
hpf- High-power field

of EoE was based on consensus diagnostic guidelines,^{6,7} which include clinical symptoms of esophageal dysfunction, ≥ 15 eosinophils per high-power field (hpf) on an esophageal biopsy specimen, and a lack of response to high-dose proton pump inhibitor therapy. All subjects underwent endoscopy at the study institution. The subjects had biopsy specimens routinely obtained in the stomach and small intestine, and, if eosinophils were detected in either the stomach or small intestine, thereby suggesting a possible eosinophilic gastrointestinal disorder, then those subjects were excluded. Data were abstracted from charts by a single reviewer (H.S.). Data collected included demographic variables (sex, race, insurance type), clinical variables (presenting symptoms, age at symptom onset, age at diagnosis and comorbid physician-diagnosed atopic disease), and laboratory variables (peak eosinophils/hpf on esophageal biopsy specimen and total serum IgE). Race was self-reported by each patient's parent at the time of the first clinical encounter as "black," "white," "Asian," or "other." Only one race category could be selected per patient. Insurance type was defined as public if the patient was primarily insured by Medicaid and as private for all others. Regarding presenting symptoms, the documented clinical history was used to categorize patients as having one or more of the following symptom types at presentation: failure to thrive (FTT), vomiting and/or gastroesophageal reflux (GER), abdominal pain, and dysphagia and/or food impaction. Therefore, an individual patient could have more than one presenting symptom. The study was approved by the Children's National Medical Center Institutional Review Board.

Statistical analysis

Differences in demographic variables (age at symptom onset and diagnosis) and laboratory values between the racial groups were analyzed by using the Wilcoxon rank sum test because none of these continuous variables were normally distributed. Differences in other demographic variables (sex and insurance type) and clinical presentation (symptom presentation and comorbid atopic disease) between the 2 racial groups were determined by using the χ^2 test or the Fisher exact test for those comparisons that involved small sample sizes. Univariate logistic regression was used to generate odds ratios of each specific symptom presentation that compared African American versus white children. Multivariate logistic regression was then performed to adjust for potential confounding variables, including sex, race, insurance type, and age at diagnosis. Analysis was performed with StataSE 9.0 (StataCorp LP, College Station, Tex).

RESULTS

The study population included 50 children and showed a 3:1 male to female predominance, as has been previously demonstrated.^{1,6,10,13} However, in differing from previous data, a large proportion of minority subjects was observed (with an equal number of African American and white patients). Approximately, one-third of patients had public insurance (Table I). Overall, the

mean age at symptom onset was 3.9 years, which preceded the mean age of diagnosis (5.9 years) by 2 years. Vomiting and/or GER was the most common presenting symptom, almost twice as common as abdominal pain, the second most prevalent (Table I). Consistent with prior literature, comorbid atopic conditions were commonly seen in the study population, with 80% of patients carrying a diagnosis of atopic disease.¹ The most common conditions were asthma and allergic rhinitis, followed closely by IgE-mediated food allergy and atopic dermatitis (AD) (Table I).

Comparison of African American and white children

After reviewing the entire cohort, data between the different racial subgroups were examined. Comparisons were limited to the African American and white groups because the sample size was too small to show significant findings for Asian and other racial groups. There were no significant sex differences noted between the 2 racial groups. However, almost two-thirds of African American patients had public insurance compared with 5% of white patients. Laboratory data also differed by race. Gross pathologic comparison showed that the mean number of peak eosinophils/hpf of an esophageal biopsy specimen was significantly higher in the African American group versus the white group (49 eosinophils/hpf vs 37 eosinophils/hpf, respectively). The location of peak eosinophils (middle esophagus vs distal esophagus) did not significantly differ by race or clinical presentation. Mean total serum IgE levels were higher in the African American group versus the white group, but this difference was not statistically significant (Table II).

When looking at comorbid atopic disease, there was a striking difference in the frequency of AD by race. Fifty-seven percent of the African American subjects had coexisting AD compared with 9% of the white counterparts (Figure 1). No significant differences by race in other atopic conditions were observed.

Clinically, there were significant differences in the type and timing of symptoms between racial groups in the study population. FTT and vomiting and/or GER were found to be significantly more frequent as presenting symptoms in African American compared with white children by 5-fold and 2-fold, respectively (Figure 2). In addition to differences in symptom type, the age of symptom onset was found to differ by race. For all symptom types except FTT, the age of symptom onset was significantly earlier in African Americans (Table III). For white patients, the mean ages of each symptom onset mirror the prior literature, for example, with abdominal pain presenting at a mean age of 8.7 years and dysphagia and/or food impaction at 11 years.¹ However, African American subjects had a significantly different and remarkably younger age of certain symptom presentation, for example, abdominal pain at a mean age of 3 years and dysphagia and/or food impaction at 3.7 years.

Beyond differences in when symptoms first presented, there also were observed differences by race in when the diagnosis of EoE was made. The age of diagnosis of African American patients was significantly younger than of the white group (Table III). However, despite being diagnosed at a younger age, African American patients were noted to have a longer interval between reported symptom onset and formal diagnosis (approaching significance) (Table III).

Given these data that suggest differences in symptoms and comorbidities between African American and white patients, univariate and multivariate analyses were performed to

TABLE I. Study population (n = 50)

Characteristic	
Sex, no. (%)	
Boys	37 (74)
Girls	13 (26)
Race or ethnicity, no. (%)	
White	21 (42)
African American	21 (42)
Asian	2 (4)
Other	6 (12)
Insurance type, no. (%)	
Public	18 (36)
Other	32 (64)
Age at symptom onset, mean (range) (y)	3.9 (0-14)
Age at diagnosis, mean (range) (y)	5.9 (0-17)
Presenting symptoms, no. (%)	
FTT	14 (28)
Vomiting or GER	37 (74)
Abdominal pain	20 (40)
Dysphagia or food impaction	11 (22)
Atopic disease, no. (%)	
Asthma	20 (40)
Allergic rhinitis	22 (44)
AD	15 (30)
IgE-mediated food allergy	18 (36)
Peak no. eosinophils/hpf, mean (range)	42 (20-100)
Total serum IgE, mean, IU/ml (range)	1153 (4-13956)

TABLE II. Racial differences in demographic and laboratory values

Characteristic	White	African American	P value
Boys, no. (%)	17 (81)	15 (71)	.47*
Public insurance, no. (%)	1 (5)	13 (62)	<.001†
Peak no. eosinophils/hpf, mean (range)	37 (20-100)	49 (20-100)	.01‡
Total serum IgE, mean, IU/ml (range)	750 (4-4119)	1614 (10-13,956)	.84‡

*By using the χ^2 test.

†By using the Fisher exact test.

‡By using the Wilcoxon rank sum test.

determine if these findings persisted after controlling for potential confounders. Univariate analysis showed significantly higher odds of having FTT and having vomiting and/or GER as presenting symptoms, and significantly higher odds of AD as a comorbid condition in African American compared with white patients (Table IV). However, in multivariate analysis, only the odds of comorbid AD remained significantly higher in African American patients versus white patients, with an odds ratio of 16.2 (95% CI, 1.2-225.3) (Table IV). However, the confidence interval is substantially widened due to collinearity, which makes the significance of even this finding uncertain. Stepwise regression analysis revealed that public insurance and age of diagnosis were both confounding variables (with the African American population in this cohort having a significantly higher proportion of patients with public insurance [Table II] and a significantly younger mean age at diagnosis [Table III]).

Racial distribution of endoscopy at the study institution

Given the larger than expected proportion of minority subjects in this study population, billing data were examined to determine whether minority subjects more frequently underwent endoscopy at the study institution. According to billing data, a total of 1857 endoscopies were performed at the institution during the study period. The racial distribution of patients undergoing endoscopy was as follows: white, n = 982 (53%); African American, n = 526 (28%); and other, n = 349 (19%).

DISCUSSION

This study found a larger burden of EoE among African American children at an urban allergy referral center than previously described. In addition, significant clinical differences were observed in African American children compared with white children, including differing presenting symptom types, younger age of symptom onset and diagnosis, and higher frequency of comorbid AD. It is unclear whether these differences are attributable to race however because most were no longer evident after adjusting for insurance type and age. Although there are well-established data on how EoE presentation varies in different age groups,^{1,6,14} there exists little information about how these clinical characteristics vary among patients of different races.^{15,16} This may be due to the larger numbers of white patients with EoE available for study and the relatively smaller number of minority patients in previous study populations.

In contrast to previous studies that report more than 80% to 90% of patients with EoE being white,^{6,10,11} our study found an equal proportion of affected African American children (42%) and white children (42%). Although this case series of consecutively diagnosed children with EoE is not intended to define prevalence rates in a broader population, this finding is a striking difference from prior literature. To determine whether this difference was attributable to a higher frequency of endoscopy among African Americans at the study institution, billing data were examined. African American patients actually had a lower endoscopy prevalence than white patients (28% vs 53%) but equal prevalence of EoE, which suggests that EoE may disproportionately affect African Americans. However, because study subjects were identified consecutively in the allergy clinic at the study institution, it is possible that some patients underwent endoscopy at the study institution but received allergy care and EoE diagnosis elsewhere, and this may have occurred more frequently among white patients. Nevertheless, the finding of a large proportion of nonwhites in this EoE study population is an important difference from prior studies.

This difference may be explained by the fact that our institution serves a population in the District of Columbia, which has a higher prevalence of African Americans (50.7%) versus the patient populations in cities with institutions that collect earlier demographic data: Cincinnati (44.8%), Philadelphia (43.4%), Milwaukee (40.0%), and Columbia, Missouri (11.3%).⁹ Indeed, similar to our findings, African Americans comprised a large proportion of patients (40%) in another study conducted in Washington DC, among adult patients with EoE at Walter Reed Army Medical Center.¹⁷ However, compared with Washington DC, the prevalence of African Americans is only slightly lower, for example, in Cincinnati and Philadelphia, where whites comprise the vast majority of reported pediatric EoE cases, which

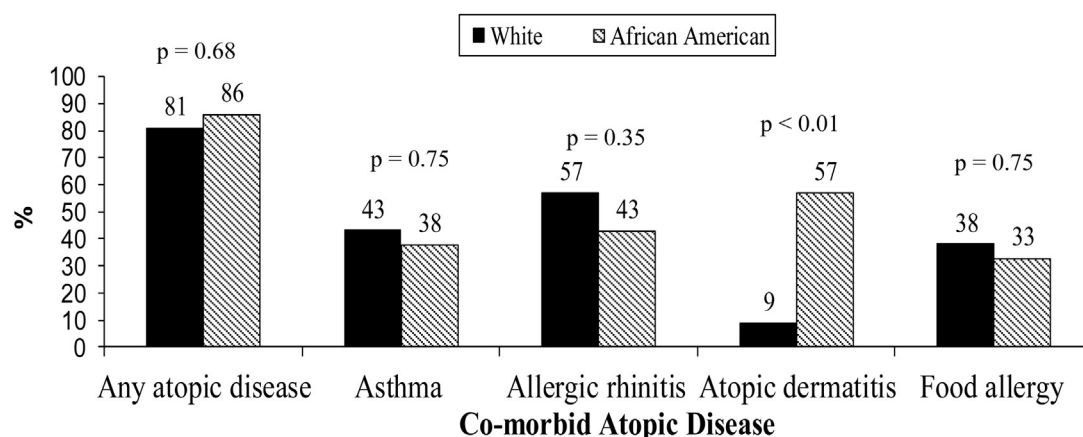


FIGURE 1. Racial differences in comorbid atopic disease.

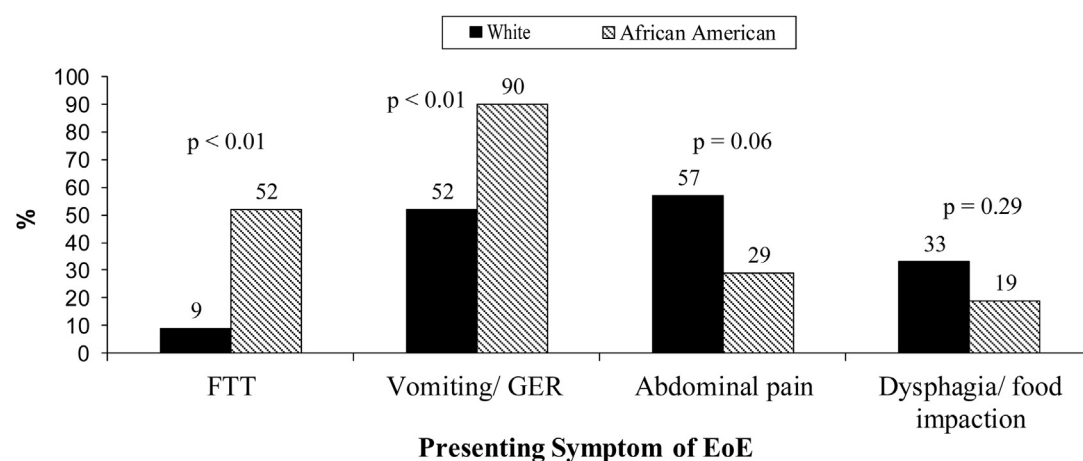


FIGURE 2. Racial differences in symptom presentation.

TABLE III. Racial differences in age of symptom onset and diagnosis

	Mean (range) age, y			P value*
	Study population	White	African American	
Age of symptom presentation				
FTT	0.3 (0-2)	0.5 (0-1)	0.2 (0-2)	.21
Vomiting or GER	2.4 (0-12)	5.9 (0-12)	1.0 (0-7)	<.01
Abdominal pain	6.6 (0-12)	8.7 (3-12)	3.0 (0-8)	.01
Dysphagia or food impaction	7.9 (0-14)	11.2 (8-14)	3.7 (0-8)	.02
Age of diagnosis	5.9 (0-17)	9.1 (1-17)	3.7 (0-13)	<.01
Time between symptom onset and diagnosis	1.5 (0-13)	1.0 (0-6)	2.1 (0-13)	.09

*P values that compare white and African American groups.

suggests that additional factors are responsible for this difference. Perhaps decreased accessibility of health care to African American patients,¹⁸ especially subspecialty pediatric care, may explain the underrepresentation of African American patients in previous cohorts. Other studies have suggested possible barriers to diagnosis of African American children with food allergy. For example, a national study of pediatric food allergy prevalence found higher odds of reported food allergy with African

American versus white children but lower odds of formal diagnosis.¹⁹ Such barriers to the diagnosis of EoE in African American patients may be related to socioeconomic status. Almost two-thirds of African American patients in our series had public insurance compared with 5% in white patients, and perhaps patients with public insurance were more represented in this study population than prior cohorts. Additional larger, population-based studies with inclusion of patients of diverse

TABLE IV. Predictors of clinical presentation

Characteristic	FTT, OR (95% CI)	Vomiting and/or GER, OR (95% CI)	Abdominal pain, OR (95% CI)	Comorbid AD, OR (95% CI)
Univariate analysis				
African American race*	10.4 (1.9-56.6)	8.6 (1.6-46.8)	0.3 (0.1-1.1)	12.9 (2.3-68.9)
Multivariate analyses				
African American race*	2.0 (0.2-17.3)	4.4 (0.5-37.3)	1.3 (0.2-8.1)	16.2 (1.2-225.3)
Public insurance	4.7 (0.8-29.7)	2.8 (0.2-36.1)	0.4 (0.1-2.7)	0.1 (0.004-1.3)
Female sex	1.2 (0.2-7.8)	0.6 (0.1-3.7)	1.4 (0.3-7.6)	0.9 (0.1-6.2)
Age of diagnosis†	0.8 (0.6-1.0)	0.9 (0.8-1.1)	1.2 (1.0-1.5)	0.6 (0.4-0.9)

*Odds of specified clinical presentation for African American vs white children.

†Odds of specified clinical presentation for every 1-y increase in age of diagnosis.

socioeconomic status and adequate access to pediatric subspecialty care are needed to confirm a potential underdiagnosis of EoE among African American children.

The other notable findings of our study relate to differences in the clinical presentation of EoE between African American and white children. As seen in a prior study, African Americans were significantly younger at symptom presentation and diagnosis.⁹ It has been established that younger children are more likely to present with FTT and with vomiting and/or GER.^{6,9,14} Therefore, the younger age of onset for African American children may explain why they also were observed to present more often with FTT and vomiting. Indeed, after adjustment for age in multivariate analyses, these racial differences in symptom presentation were no longer evident. Further studies are needed to explore whether the age of EoE onset is truly younger in African American patients.

In addition to differences in age at initial presentation, the ages at which African American patients in this series experienced certain symptoms types was much younger than with white patients. For whites, the mean ages of each symptom onset in this study mirror the prior literature.¹ However, African American patients had a remarkably younger age of certain symptom presentation, for example, abdominal pain at a mean age of 3 years and dysphagia and/or food impaction at 3.7 years. This raises the question of whether EoE may be a more aggressive disease in African Americans, a possibility that has previously been considered.^{5,9} In addition to progression of symptoms at an earlier age, this study found a higher prevalence of comorbid AD as well as significantly higher peak eosinophils/hpf on esophageal biopsy specimens in African American patients, as has been observed in a prior study.⁹ When taken together, these findings warrant additional study to examine whether a more-severe EoE phenotype may affect African Americans. It is possible that African Americans have different genetic markers that predispose them to a different presentation of EoE. A recent genome-wide association study implicated the 5q22 locus in the pathogenesis of EoE in patients of European ancestry. Thymic stromal lymphopoietin was identified as the most likely candidate gene.²⁰ These findings have not yet been validated in patients with EoE of non-European ancestry. However, genetic markers for EoE may not necessarily differ between African Americans and whites. The racial differences in clinical presentation observed in this series did not persist after adjustment for public insurance. Therefore, socioeconomic status and associated health care access barriers that lead to delays in diagnosis and treatment may contribute more than race to heightened clinical severity in African Americans.

Indeed, this case series observed a trend toward a longer period between symptom onset and diagnosis in African American patients compared with white patients (2.1 vs 1.0 years; $P = .09$). Because previously published data^{6,10,13} reports that EoE predominantly affects whites, this may result in a detection or referral bias, whereby providers are less likely to suspect this disease in African Americans. In addition, because African American children are younger and present with more nonspecific symptoms of FTT and vomiting, their differential diagnosis may be broad, and an etiology of EoE may take longer to identify. However, if white children present later in life with more specific symptoms of dysphagia or food impaction, then this could partially explain their shorter interval between symptom onset and diagnosis. Coupled with a presupposed higher prevalence of EoE in the white population, this may increase the health care provider's suspicion of EoE and the patient's chances of earlier diagnosis.

Strengths of this study include its inclusion of a consecutive sample of children diagnosed with EoE of diverse racial and socioeconomic backgrounds. There are limitations of this study to consider. First, the sample, although diverse, was smaller in size than some prior cohorts and reflective of only one clinical center, thereby limiting generalizability. In addition, there were few Asians and Hispanics in the sample, which restricted analysis to a comparison of African American and whites. To define the true distribution of EoE by race, much larger prevalence studies are needed. National registries of patients with EoE, such as those recently started in Europe and the United States, may facilitate such large studies in the future.^{21,22} Race and socioeconomic data should be entered into the registries to allow better understanding of the distribution of and potential differences in EoE based on those factors. Additional data may have been informative for this study, such as endoscopic characteristics and histologic findings, aside from peak eosinophil counts. A comparison of food and aeroallergen sensitization between African American and white patients may, in addition, have been revealing.

In summary, African American children comprised a larger proportion of patients with EoE in this study than previously reported and had differing clinical presentations compared with whites. The differences observed in symptom presentation may not be primarily related to race but instead to age and socioeconomic status. Additional large studies that are inclusive of nonwhite children are needed to define the true racial distribution of EoE and to explore differences in the disease susceptibility, presentation, and progression by race, social, and environmental factors. Until the true racial distribution of EoE is

better understood, clinicians should be mindful of this potential diagnosis in young African American children with atopy and with symptoms of esophageal dysfunction.

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