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Original article

Racial differences in eosinophilic gastrointestinal disorders among Caucasian and Asian

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Abbreviations:

CI, Confidence interval; EGE, Eosinophilic gastroenteritis; EGID, Eosinophilic gastrointestinal disorders; EoE, Eosinophilic esophagitis; GI, Gastrointestinal; HPF, High-power field; IL, Interleukin; Th2, T-helper cell type2

ABSTRACT

Background: Although there is an increasing number of eosinophilic gastrointestinal disorders (EGID) cases including eosinophilic esophagitis (EoE) and eosinophilic gastroenteritis (EGE), being reported globally, no systematic reviews have been conducted to elucidate the racial differences in these disorders. We aimed to show the racial differences, especially among Caucasians and Asians, in the risk of EoE and EGE.

Methods: We conducted a systematic review using PubMed in September 2012. All case reports and case series on EGID that involved human subjects and described race or ethnicity, as well as pathological findings, were included. For the comparison of reported cases between Caucasians and Asians, a chi-squared test was used.

Results: Among the 687 studies found in PubMed, 121 studies fulfilled the eligibility criteria. In total, 2621 patients were reviewed. Among Caucasian EGID patients, 94% had EoE; while among Asian EGID patients, 72% had EGE ($p < 0.001$). Among EoE, Asians were significantly less likely to have dysphagia and heartburn, but more likely to have vomit and abdominal pain, compared to Caucasians ($p < 0.001$). Further, among EGE, Asians were significantly more likely to have eosinophil-infiltrated colon than Caucasians (OR: 3.22, 95% confidence interval [CI]: 1.60–7.04), but were less likely to have eosinophil-infiltrated stomach (OR: 0.29, 95% CI: 0.17–0.49).

Conclusions: We found that EoE occurs more frequently in Caucasian EGID patients than Asian EGID patients, while the reverse is true for EGE. Also, racial disparities in symptoms and eosinophil-infiltrated tissues were observed. Our findings suggest further genetic and environmental studies to elucidate the etiology of EGID.

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Introduction

Eosinophilic gastrointestinal disorders (EGID) are chronic inflammatory disorders characterized by primary eosinophilic infiltration of the gastrointestinal (GI) tract without any known causes of eosinophilia such as parasitic infections, drug reactions, and malignancy.¹ EGID include eosinophilic esophagitis (EoE) and eosinophilic gastroenteritis (EGE); EoE involves only the esophagus, while EGE involves any part of the GI tract.^{1–3} These disorders have been gaining attention in recent years as several

studies reported a rapid rise in their prevalence; in particularly EoE, which saw a 35-fold rise in Philadelphia, USA, and an 18-fold rise in Australia, over the past ten years.^{4,5} However, the exact etiology of EGID has yet to be elucidated, although the role of food-derived antigen or inflammatory mediators such as IL-5, IL-13, thymic stromal lymphopoietin and eotaxin-3 have been described.^{6–9}

Globally, there seems to be a disparity in the incidence rate of the type of EGID being reported; EoE cases have been reported more frequently in Western countries,^{10–18} while EGE were more likely in Asian countries.^{19–64} Although racial and ethnic disparities in the severity and prevalence of immune and allergic disorders such as asthma and atopic dermatitis have been demonstrated before,^{65,66} no such association has not been evaluated for EGID. To that end, we conducted a systematic review on EGID, focusing on Caucasian and Asian populations.

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Methods

Literature reviews

All research articles involving human EoE or EGE cases, which described race or ethnicity, and pathological findings, were included for the study. Articles that were not published in English, had no abstract, or in the form of a review were excluded. A literature search was conducted on PubMed on 22nd September, 2012. The following search strings were used: “eosinophilic esophagitis” [All Fields], “allergic esophagitis” [All Fields], “eosinophilic esophagitis” [All Fields], “eosinophilic gastroenteritis” [All Fields], “allergic gastroenteritis” [All Fields]; together with the following search conditions: English [lang], NOT Review [ptyp], AND has abstract [text]. Initial eligibility screening based on title and abstract was performed independently in a standardized manner by two reviewers (Jun Ito and Takeo Fujiwara). Subsequently, a full-text screening was conducted for further assessment. Discrepancies between reviewers were resolved by consensus. Despite ethnicity not being clearly described in the literature, study subjects from South Korea, China, Taiwan, and Japan were regarded as Asian based on the ethnically homogenous nature of the countries.⁶⁷ If an identical set of subjects were used in multiple articles, the literature which had more detailed information or larger sample size was selected.

Analyses

Through full-text screening of eligible articles, we extracted and compiled patients' characteristics and clinical information. For single case reports or case series, information of each patient was recorded. If a study showed only aggregated sample characteristics and clinical information, aggregated data were used. Finally, we calculated total number of subjects and divided them by race, diagnosis, age and diagnostic criteria.

To stratify subjects by age, samples 18 years old or older were categorized as adults, while those less than 18 years old were categorized as children.⁶⁸ Samples from four studies which showed only aggregated sample data conducted in children's hospitals were assigned for the children category; two studies had mean age 6.4 and 11.4 years old, respectively,^{69,70} and the other two involved samples of 18 and 21 years old, respectively.^{71,72} One study which also showed only aggregated sample data with a 15-year-old patient among 42 EGE patients was assigned for the adult category, as the mean age of the samples was 48.2 years old, with the oldest patient being 72 years old.^{43,68}

The difference in diagnostic criteria for EGID was considered as it may affect the number of reported cases. At present, a peak count of ≥ 15 eosinophils per high-power field (eos/HPF) is the minimum required threshold for the diagnosis of EoE,⁷³ with some studies using >20 or >24 eos/HPF.^{4,8,74} In this review, EoE samples were divided into three groups based on either peak or mean number of eosinophils: ≥ 15 eos/HPF, >20 eos/HPF, and others or unknown. For EGE, no standards for diagnosis exist; however, the majority of studies on EGE follow a Talley criteria⁷⁵ which requires the presence of gastrointestinal symptoms and eosinophil infiltration of one or more areas of the gastrointestinal tract (with no evidence of parasitic or extraintestinal disease). In view of this, we divided EGE samples into two groups; one which met Talley's criteria, and the other one which neither meet the criteria nor mention the diagnostic criteria used.

A chi-squared test was used to compare the reported cases of EoE or EGE between Caucasians and Asians. Further, a logistic regression was conducted to calculate odds ratios (OR) of Asians who had GI symptoms (dysphagia, heartburn, vomit, abdominal

pain and diarrhea), relative to Caucasians, among cases of EoE, EGE, and overall patients. The ORs of Asians who had eosinophilic infiltration for each GI tract (esophagus, stomach, small intestine and colon), relative to EGE Caucasians, were also calculated. All analyses were performed using the STATA SE statistical package, version 12 (Stata Corp., College Station, TX, USA).

Results

Our search identified 687 studies, of which 499 were deemed relevant on the basis of their titles and abstracts. Of these, 378 studies were subsequently excluded: 319 studies were without information on race or ethnicity; 46 studies had samples that were possibly duplicated; six studies had no pathological findings; six studies comprised of subjects whose diagnosis were not of EGID; and one study was a review article. Finally 121 studies were included for further analysis (Fig 1). The number of publications which included Caucasian patients and Asian patients was 59 and 70, respectively. In total, 2621 cases were obtained from these studies (Table 1). The cases included patients ranging from infant to elderly, with men more dominant for both EoE and EGE than women. Across all races, more than half of the EoE patients were diagnosed by the diagnostic criteria of >15 eos/HPF. For EGE, most Asian patients were diagnosed by Talley's criteria, while the same did not apply to Caucasians and other races. Among Caucasians, 94% of EGID patients had EoE, while among the Asian patients, 72% had EGE ($p < 0.001$).

There were significant differences in the number of reported cases of EoE and EGE between Caucasian and Asian samples (Table 2). Caucasian is dominant among EoE, while Asian is dominant among EGE for both in total and adult (both $p < 0.001$). For children, the percentage of Caucasian among EoE (97%) is higher than among EGE (68%) ($p < 0.001$).

Table 3 shows the odds ratios of Asians relative to Caucasians in having GI symptoms among EoE, EGE and EGID (i.e., considering total EoE and EGE cases). For esophagus related symptoms in EoE cases, Asians were 0.27 and 0.32 times less likely to have dysphagia and heartburn, respectively, than Caucasians (95% confidence interval [CI], 0.16–0.47; and 0.15–0.62, respectively). On the other hand, for stomach and lower GI tract related symptoms in EoE

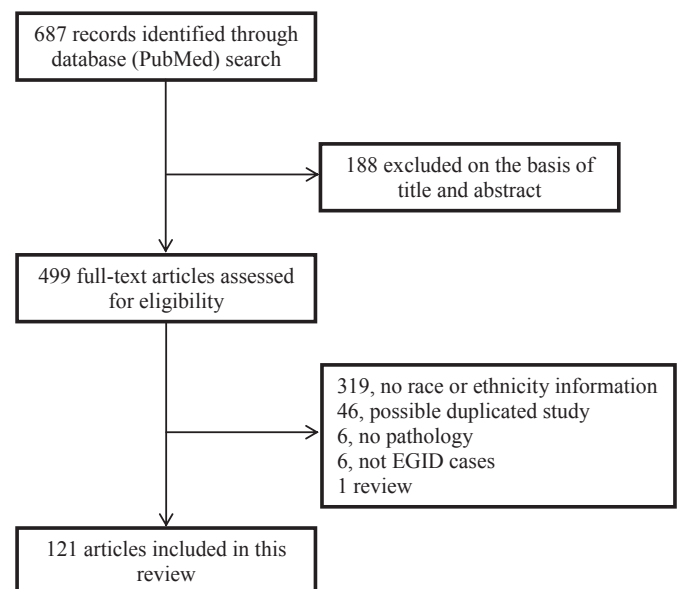


Fig. 1. Flow diagram of literature search.

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