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Insights into the emerging epidemic of eosinophilic oesophagitis

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A B S T R A C T

Eosinophilic oesophagitis (EOE) is a relatively recently recognised condition characterised by an increase in oesophageal eosinophils. EOE occurs in children and adults with a strong male preponderance. There has been a sharp increase in EOE in North America, Europe and Australia. The reasons for this increase remain unclear but are likely to be influenced by genetic and environmental factors, as well as early-life exposures. Based on recent population-based data, the estimated EOE prevalence in the USA is 56.7 per 100,000 persons. The peak prevalence was observed in patients between 35 and 39 years of age. Prevalence figures in Asia and the Middle East generally appear to be lower than in Western countries, but population-based studies are not available. A causal association between coeliac disease and EOE appears unlikely. Data on the seasonal variation of EOE remain inconclusive. Further population-based studies are needed to define the epidemiology of EOE.

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Eosinophilic oesophagitis (EOE) is a relatively recently recognised clinical entity characterised by an increase in oesophageal mucosal eosinophils, in conjunction with symptoms attributable to upper gastrointestinal tract dysfunction [1]. The initial description of EOE as a cause for dysphagia in adults was made by Atwood et al. in 1993 and Straumann in 1994 [2,3]. Before then, cases reports had often misaligned oesophageal eosinophilia with gastro-oesophageal reflux disease (GORD). Over the past two decades, there has been a rapid increase in reported cases of EOE in most developed countries. The molecular pathways in the biology of EOE have also largely been mapped out [4–7]. However, despite these significant advances the recognition and treatment of EOE remains cumbersome. One of the main reasons for this is the lack of non-invasive diagnostic markers as the diagnostic and monitoring process continues to rely on endoscopic procedures, including collection of multiple oesophageal biopsies [1,8].

EOE occurs in children and adults, males and females, and has been described in patients from a range of ethnic backgrounds. While the underlying pathological mechanisms appear to be shared, there are significant differences in the epidemiology between groups. Phenotypic subtypes of EOE have been recognised, including proton pump-responsive oesophageal eosinophilia (PPI-ROE) [8]. There is familial clustering of EOE which points to genetic susceptibility factors [9]. EOE also strongly aligns with food allergy [10]. In addition, environmental factors and early-life exposures appear to be important risk factors [11,12].

Problems with obtaining reliable, population-based data

Upper gastrointestinal endoscopy and biopsy remain essential elements in the diagnosis of EOE. Current diagnostic criteria require demonstration of 15 eosinophils or more per microscopic high-power field (HPF) on oesophageal histology [1]. As access to gastroscopies is limited in many clinical settings, this may lead to a delayed diagnosis or significant under-recognition of EOE. A recent population-based Canadian study found that the 5-fold increase in the incidence from 2.1 per 100,000 to 11.0 per 100,000 persons was significantly influenced by a higher rate of obtaining oesophageal biopsies [13]. The proportion of patients with dysphagia undergoing gastroscopy has also significantly increased [14]. However, a recent Danish study suggests that the rise in EOE cannot explained by the rising number of endoscopic procedures alone [15]. The recent rise in diagnosed cases of EOE is therefore most likely influenced by a range of factors, including improved clinical awareness, better access to endoscopies and increased rates of biopsy ascertainment [13].

Although there are American and European consensus guidelines for EOE, there are aspects in the diagnostic process that require further standardisation [1,8,16]. Several methods are currently used for the quantification of eosinophils, either by counting the peak number in any HPF or an averaged number derived from several HPFs. Even the size of a single HPF at 400-times magnification is not standardised, and it has been suggested to move to report mucosal eosinophils counts per mm^2 as a more objective diagnostic measure. These inconsistencies are likely to affect the accuracy of the histopathological diagnosis of EOE. In addition, most epidemiological studies so far have not clearly distinguished between EOE and other causes of oesophageal eosinophilia, such as PPI-ROE. This issue may be overcome in the future if the diagnosis of EOE can be made by molecular techniques and gene array profiles in biopsies [6]. This approach would potentially offer a more reproducible process in diagnosing EOE and would make the comparison between international epidemiological data more reliable.

EOE is a global disease

Over the past decade, case series have emerged from both developed and developing regions in the world. Most studies were conducted in North America [17–19], Europe [15,20,21] and Australia [22,23]. Fewer studies are available from Asia [24–27] and the Middle East [28]. The quality of epidemiological data varies considerably, and population-based epidemiological data are often unavailable. Most studies examining the past two decades have demonstrated a significant increase in the prevalence of EOE. The highest prevalence of EOE has been reported from North America and Sweden [20,29]. The Olmstead County study identified 78 paediatric and adult patients with EOE between 1976 and 2005, corresponding with an incidence of 9.45 per 100,000 and prevalence of 55 per 100,000 persons [18].