











Eosinophilic oesophagitis (EoE): Risk factors, relationship with disorders of gut-brain interactions (DGBI), and mortality

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Introduction

The role of eosinophils in unexplained gastrointestinal diseases is an area of increasing interest (1). However, there remains a lack of quality data available to determine the relationship between eosinophilic esophagitis (EoE) and DGBIs (e.g., functional dyspepsia (FD), associated duodenal with Several other gastrointestinal eosinophilia)(2). diseases are also characterised by an increased eosinophils, number tissue including gastroesophageal reflux, inflammatory bowel disease, diverticular disease and rumination syndrome (3, 4). Risk factors for EoE still remain to be clearly defined in large population-based studies.

Aim

The aim of this study was to determine the relationship between EoE and DGBIs as well as other potential risk factors for EoE, and mortality in EoE.

Methods

General practice electronic medical records were sourced from the United Kingdom (UK) via The Health Improvement Network which collates and cleans records from across the UK. EoE was identified through Read codes. DGBIs were similarly identified via Read codes and the first date of first record of each was noted.

Results

A total of 1.274 million unique patients were available for analysis. There were 389 EoE cases (0.03%) from the cohort, with age at first diagnoses being mean 21 years (SD=18), and 74% female.

Table 1. Univariate risk factor assessment comparing EoE patients with population.

Factor	Number of Cases	Odds Ratio, 95% CI
Male	287 (73.78%)	3.69, 2.94-4.63
Irritable Bowel Syndrome (IBS)	21 (5.40%)	0.36, 0.23-0.56
Functional Dyspepsia (FD)	64 (16.45%)	0.74, 0.57-0.97
Crohn's Disease	4 (1.03%)	3.85, 1.44-10.31
H. pylori infection	11 (2.83%)	3.35, 1.84-6.10
Gastroenteritis	52 (13.37%)	2.07, 1.55-2.77
Gluten Sensitivity	1 (0.26%)	10.59, 1.48-75.59
Allergy	93 (23.91%)	2.99, 2.37-3.78
Asthma	103 (26.48%)	2.97, 2.37-3.72
Rhinitis	89 (22.88%)	2.46, 1.94-3.12
Eczema	122 (31.36%)	1.92, 1.55-2.37
Gastroesophageal reflux	101 (25.96%)	3.05, 2.43-3.83
Antibiotics	371 (95.37%)	2.79, 1.74-4.48
Proton Pump Inhibitors (PPIs)	361 (92.80%)	11.78, 8.02-17.31
Appendectomy	11 (2.83%)	2.70, 1.49-4.93
Any Surgery	19 (4.88%)	1.95, 1.23-3.10

Table 2. Multivariate risk factor assessment (Model 1) comparing EoE patients with population.

Factor	Number of Cases	Odds Ratio, 95% CI
Male	287 (73.78%)	4.10, 3.27-5.15
Irritable Bowel Syndrome (IBS)	21 (5.40%)	0.19, 0.12-0.30
Functional Dyspepsia (FD)	64 (16.45%)	0.22, 0.17-0.30
H. pylori infection	11 (2.83%)	2.48, 1.35-2.07
Gluten Sensitivity	1 (0.26%)	9.10, 1.25-66.46
Allergy	93 (23.91%)	1.74, 1.36-2.21
Asthma	103 (26.48%)	1.72, 1.36-2.17
Proton Pump Inhibitors (PPIs)	361 (92.80%)	13.29, 10.27-17.20
Gastroesophageal reflux	101 (25.96%)	1.63, 1.28-2.07

For Model 1 (Table 2), we calculated a Receiver Operator Curve (ROC)/Area Under the Curve (AUC) which was 0.86 (95% CI: 0.84-0.88).

A second logistic regression model (Model 2) assessed IBS and FD (adjusting for sex, age at first contact, anxiety, and depression). The result identified that both IBS and FD remained statistically significant and less likely to be associated with EoE (IBS OR: 0.35, 95%CI: 0.22-0.54; FD OR: 0.74, 95%CI: 0.56-0.97). The calculated ROC/AUC: 0.79 (95% CI: 0.77-0.81).

The final logistic regression analysis (Model 3) assessed mortality (adjusting for sex/ age at first contact): mortality (OR: 0.15, 95%CI: 0.03-0.59) was less likely in EoE. The ROC/AUC 0.78 (95% CI: 0.76-0.81).

Conclusions

Individuals with EoE were less likely to have DGBIs (IBS and FD), whereas, they were more likely to have other gastrointestinal diseases (e.g. gluten sensitivity, gastroesophageal reflux, *H. pylori* infection). In addition, they were more likely to have had allergies and asthma and much more likely to have used PPIs before diagnosis of EoE. Mortality for EoE was not increased.

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References

- 1. Hirano I, et al. Ascending to new heights for novel therapeutics for eosinophilic esophagitis. *Gastroenterology* 2023;Sep 8:S0016-5085(23)04979-X.
- 2. Talley NJ, Peterson KA, Genta RM, et al. High discovery rate of duodenal and gastric eosinophilia in patients with unexplained moderate-severe abdominal symptoms: A prospective US multisite study. *Gastroenterology* 2023;164(4):680-683 e2
- 3. Cameron R, Walker MM, Jones M, Eslick GD, Keely S, Pockney P, Cosentino CC, Talley NJ. Increased mucosal eosinophils in colonic diverticulosis and diverticular disease. J Gastroenterol Hepatol 2023;38(8):1355-1364.
- 4.. Zand Irani M, Eslick GD, Brown G, Talley NJ. Letter: eosinophilic duodenitis and increased intraepithelial lymphocytes in rumination syndrome more evidence. *Aliment Pharmacol Ther* 2023;57(11):1353-1354.

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