Original Article

Frequency of Eosinophilic Esophagitis in patients undergoing upper GI Endoscopy
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ABSTRACT

Objective: To determine the frequency of Eosinophilic Esophagitis (EoE) in patients undergoing upper GI endoscopy.

Methodology: Patients undergoing upper GI endoscopy for any indication were subjected to additional esophageal biopsies for determination of eosinophilic esophagitis. The additional biopsy protocol was two each from proximal esophagus, distal esophagus, stomach & duodenum. Presence of >15 eosinophils in one high power field was criteria for diagnosis of EoE.

Results: Ninety four patients were included according to sample size estimations. Eosinophilic esophagitis was found in 7 (7.4%) of patients undergoing upper GI endoscopies.

Conclusion: Eosinophilic esophagitis should be considered as active diagnosis in presence of suggestive symptoms.

KEY WORDS: Eosinophilic Esophagitis, Allergic Esophagitis, Dysphagia, Eosinophilic Gastroenteritis.

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INTRODUCTION

Eosinophilic Esophagitis (EoE) is a relatively new entity in gastroenterology. Although eosinophilic gastroenteritis (EG) has been first reported in 1937 by Kaijser R and then subsequently in 1961 by Ureles AL but first detail report of EoE was given in 1978 by Landres RT.¹ ² EoE can present with variety of different symptoms including dysphagia, reflux, nausea, vomiting, chest pain and food impactions.³ It has now become an important diagnosis to be considered in patients with dysphagia.³ ⁶ Frequently patients also have other concomitant disorders like asthma, atopic dermatitis or allergies.⁷ ⁸ It mimics gastro esophageal reflux disease (GERD) and could also cause esophageal strictures.⁹ ¹² Among the various etiologies suggested, food allergy and a unique T helper type 2 cytokine profile has been well documented.¹³ ¹⁴ EoE appears to be an antigen-driven hypersensitivity reaction characterized by a mixed IgE-dependent/delayed-type reaction.¹⁴ The diagnosis of EoE should be considered in patients with history of food impaction; persistent dysphagia and in patients having a history of atopy; or GERD refractory to medical therapy. According to the First International Gastrointestinal Eosinophilic Research Symposium
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(FIGERS) an eosinophil count of >15/HPF, along with normal gastric and duodenal biopsies, can substantiate the diagnosis of EoE. Uniformity in endoscopic reporting for esophagitis was established in Los Angeles Classification of Esophagitis which is given as under:

**Grade A:** One (or more) mucosal break no longer than 5 mm, that does not extend between the tops of two mucosal folds.

**Grade B:** One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds.

**Grade C:** One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involves less than 75% of the circumference.

**Grade D:** One (or more) mucosal break which involves at least 75% of the oesophageal circumference.

In our clinical practice we see lot of patients with complaints similar to the one with EoE but there is no published report of these cases from our country. There is lack of awareness of this disorder not only in general practitioners but also in physicians. The current study was designed to see the frequency of EoE in patients undergoing upper GI endoscopy. This will not only provide the data regarding magnitude of the problem but will also document the baseline data of EoE for further studies and also help to generate general awareness about this potentially treatable disorder.

**METHODOLOGY**

All patients of both genders with age 18-90 years undergoing upper GI endoscopy for any reason in our unit were included after taking informed consent. Patients previously diagnosed as EoE, EG, GI malignancies, Crohn’s disease and pregnant women, coagulopathy or thrombocytopenia and varices were excluded. Demographic data was collected. Blood for CBC & PT/INR was withdrawn. Endoscopies were done by single consultant gastroenterologist or by post-graduate trainee in the presence of same consultant. LA classification was used to define grading of erosive esophagitis.

Any further intervention (additional biopsies, polypectomy, dilatation, etc.) done on discretion of endoscopist was recorded. Additional biopsies for study were done as per study protocol which included two each from proximal esophagus (>10 cm form lower esophageal sphincter, (LES)), distal esophagus (<5 cm from LES), stomach & duodenum. All biopsies were taken using standard biopsy forceps and kept in 10% fomaline solution and was submitted for histopathology same day. A single histopathologist who was single blinded evaluated and reported the biopsy specimens. Presence of eosinophilia in stomach or duodenal biopsy categorized the patient as EG & these were excluded. Diagnostic criteria for EoE was presence of >15 eosinophil in one high power field of microscope on histopathology.

Sample size of the study was calculated from recently reported prevalence of EoE of 6.5% in patients undergoing endoscopy. Using confidence level (1-ß) of 95%, and absolute precision (d) of 0.05, the sample size was calculated as 94 patients. PASW Statistics version 18.0 was used for analysis. Means of continuous variables like age, hemoglobin, platelet count and INR were calculated. Frequencies of endoscopic and histopathological findings were reported.

**RESULTS**

Ninety four consecutive patients undergoing upper GI endoscopies in our unit satisfying the inclusion/exclusion criteria were selected. These included 53 (56.4%) males and 41 (43.6%) females. The mean age of males was 38.4 ±5.4 years while that of females was 34.1 ±6.0 years. Mean hemoglobin was 10.3 ± 4.1 gm/dl, platelets were 190 ± 50 x 10^9 /mm3 and INR was 1.12 ± 0.92. Biopsies of 7 (7.4%) patients were consistent with the diagnosis of EoE and 1 (1.1%) of EG, 2 (2.1%) of Barrett’s esophagus & 11 (11.7%) with non-specific esophagitis.

The clinical characteristics of seven patients which were confirmed as EoE are detailed as under.

Male:Female Ratio was 5:2 with mean age of males 39.1 ±3.3 years and that of females was 33.9 ±4.1 years. All seven patients had some degree of dysphagia and two male patients also had complaints of food sticking in esophagus for which they had to take water to help glide it down. All female and one male patients were known patients of asthma and were taking medications for the same. On endoscopy all seven patients had transverse ridges in esophagus called ‘feline esophagus’, one male patients also had small rounded white spots in esophagus which were reported as micro-absceses.

**DISCUSSION**

EoE is a relatively new and uncommon diagnosis in our area and this is perhaps the first report of this disorder from Pakistan. It is a clinicopathological disease characterized by a wide variety of GERD-like symptoms, dysphagia and vomiting that occur in conjunction with dense esophageal eosinophilia.
Esophageal eosinophilia is a common finding associated with GERD, eosinophilic esophagitis, IBD, hyper-eosinophilic syndrome and celiac disease. No pathognomonic findings in the patient's history, or laboratory, endoscopic, or histological results define eosinophilic esophagitis.

We found its frequency at 7.4% in patients undergoing upper GI endoscopies and this figure could be different if patients are investigated with EoE as active consideration in differential diagnosis. It is often an overlooked diagnosis in patients presenting with dysphagia. Males are more frequently affected as compared to females and this was also the case in our study, a systemic review has reported that about 76% of sufferers are from male gender.

Majority of studies have demonstrated allergic etiologies as evident from the fact that most of these patients were also having some other allergic disorder like asthma, atopic dermatitis, allergic rhinitis and the presence of allergic antigen sensitization based on skin prick testing or measurement of plasma antigen-specific IgE. Food allergy is categorized as IgE mediated, non-IgE-mediated or combination of both types. Exposure of a genetically predisposed individual to an appropriate food results in the generation of allergen-specific IgE resulting in allergic sensitization. Re-exposure of the individual to this food results in binding of allergen-specific IgE molecules, release of histamine, and the generation of newly formed mediators, some of which are chemotactic for eosinophils. A role for eotaxin-3 (CC126) in the pathogenesis of EoE has been well documented. Quantitative microarray analyses have shown increased expression of interleukin-15 (IL-15) messenger RNA in the esophagus of patients with EoE. IL-15 mediates in the pathogenesis of EoE. IL-15 activates CD4(+) T cells to produce cytokines that act on eosinophils.

Not only that caliber of esophagus is small in patients with EoE as demonstrated in radiological studies but esophageal distensibility has been shown to be reduced in these patients. The features of fibrosis in EoE include uniformity and hyalinization, whereas the fibrosis in GERD is predominantly associated with lymphoid tissue.

**CONCLUSION**

EoE is an allergic disorder of esophagus and should be actively sought in patients as this is a potentially treatable disease.
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Authors Contribution:
Study was conceived by BFZ, designed and planned by SS & BFZ, data collection was done by SS, ARM, RQ & BFZ. Manuscript was written by SS & RQ, while SA did final editing and gave approval of manuscript for publication.