

Prevalence of Eosinophilic Esophagitis in Patients with Gastroesophageal Reflux Symptoms: A Cross-Sectional Study

NOOR UL AMIN¹, AZHAR SAEED², SYED MIR USMAN SHAH³, SAADIA ZAINAB⁴, MOEENUL HUQ⁵, MUHAMMAD SHUAIB⁶

¹District Specialist Gastroenterology, DHQ Teaching Hospital, Timargara

²Associate Professor Medicine, Multan Medical and Dental College, Multan

³Assistant Professor Medicine, Postgraduate Medical Institute, Quetta

⁴Assistant Professor Physiology, Isra University Islamabad Campus Al-Nafees Medical College and Hospital Islamabad

⁵Assistant Professor Gastroenterology, DHQ Teaching Hospital / Gomal Medical College Deralsmail Khan

⁶Associate Professor Department of Medicine, Mohiuddin Teaching Hospital, MirpurAJK

Corresponding author: Syed Mir Usman Shah, Email: mirusman573@hotmail.com, Cell: +92 321 8002738

ABSTRACT

Objective: Prevalence of eosinophilic esophagitis in patients with gastroesophageal reflux symptoms.

Study Design: A Cross-sectional Study

Place and Duration: The study was conducted at Gastroenterology department of DHQ Teaching Hospital, Timargara for six months from August 2021 to January 2022.

Methods: There were 300 patients of both genders presented in this study. Individuals who agreed to participate, their personal information such as age, gender, height and weight was recorded with their informed permission. Included patients were had gastroesophageal reflux symptoms. Esophageal biopsies of all the patients were underwent esophagogastroduodenoscopy (EGD). Prevalence of eosinophilic esophagitis was recorded among all cases. SPSS 23.0 was used to analyze all data.

Results: The mean age of the patients was 41.9±8.21 years and had mean BMI 25.7±6.31 kg/m². Majority of the patients were males 190 (63.3%) and 110 (36.7%) were females. We found that frequency of eosinophilic esophagitis among all cases were 27 (9%). Among 27 cases of EoE, males were higher in number 19 (70.4%) than females 8 (29.6%). Among these cases, heartburn was the most common symptom found in 10 (37.03%) cases, followed by dysphagia in 6 (22.2%), epigastric pain in 5 (18.5%). Lower esophagus found in 12 (44.4%) cases and mid in 15 (55.6%) cases. Mean eosinophils was 24.4±7.29 per HPF. As per histological findings, eosinophilic microabscess was found in 20 (70.1%) cases.

Conclusion: Patients with refractory GERD are at risk of developing eosinophilic esophagitis, which can be life-threatening. Dysphagia, heartburn, and food impaction are all possible symptoms. The EoE screening of elderly patients with prolonged GERD, atopy, and non-response to stomach acid inhibitors must be evaluated.

Keywords: Refractory GERD, Eosinophilic Esophagitis, Dysphagia, Heartburn

INTRODUCTION

One of the most common causes of EoE is an allergic/immune response. This condition is characterised by esophageal mucosal eosinophilic infiltration (15/high-power field, HPF). If you suffer from EoE, you may have symptoms such as food impaction, chest pain and dysphagia. Currently, it affects 5-10 persons out of every 100,000, with a prevalence of 0.5-1 instances per 1,000 people [1,2]. White exudates or plaques, as well as friability, are all endoscopic findings in EoE. Serious illness is indicated by narrowing of the lumen and strictures [2].

EoE was first characterised in children, and only lately has it been seen in adults. An increasing number of people have been diagnosed with EoE throughout the years, which may be attributable to genetic and environmental changes or a greater focus on finding the condition. Patients with dysphagia and food impaction had higher rates of EoE than the general population, which may be as low as 12% or as high as 48% [3-5]. EoE may be linked to gastroesophageal reflux disease (GERD) in as many as 30% of patients [6]. Both EoE and GERD have been identified as distinct disease entities despite their clinical similarities. Patients with GERD have eosinophilic infiltration in the esophageal mucosa, and EoE has been identified as a secondary aetiology of GERD. EoE patients benefit from topical steroids, but those with GERD benefit from gastric acid inhibitors [3].

An endoscopic reference score (EREFS) is commonly used to define the five major features of EoE (edoema, rings, exudates, furrows and strictures) [7]. In addition, 10 to 25 percent of individuals with EoE may have a normal endoscopic esophageal look [8]. When there are less than 15 eosinophils per high-power field, a histological diagnosis is confirmed (HPF). Current guidelines propose that at least six biopsies should be taken from two separate locations, often from the distal and proximal oesophagus [9]. With five or more biopsies, the diagnostic sensitivity nearly reached 100% [4]. The "3D" idea of diet, medication, and dilation [4] is used in treatment. For the first therapy of EoE, current United European Gastroenterology recommendations propose STCs, high-dose PPI, or an elimination

diet [10]. According to the Montreal Classification, gastroesophageal reflux disease (GERD) is a disorder that develops when stomach contents flow backward into the oesophagus and cause symptoms such as heartburn and regurgitation. Erosive reflux disease (ERD) and non-erosive reflux disease (NERD) are both forms of GERD. [11,12]

In order to determine the prevalence of EoE in GERD patients who were not responding to treatment, a retrospective study was conducted.

MATERIAL AND METHODS

This study was conducted at Gastroenterology department of DHQ Teaching Hospital, Timargara for six months from August 2021 to January 2022 and comprised 300 patients of GERD. Individuals who agreed to participate had their personal information such as age, gender, and height and weight recorded with their informed permission. Patients who had neoplasia, peptic ulcers, had surgery on their gastrointestinal (GI) tract, had inflammatory bowel disease (IBD), Behcet's disease, fungal esophagitis, eosinophilic gastroenteritis, or did not have records of their eosinophil level were not included in the study.

Patients were aged between 22-70 years. All patients were thoroughly screened, including a thorough history-taking, physical examination, laboratory tests, including a complete blood count (CBC), differential leukocyte count, serum creatinine, liver biochemical tests, abdominal ultrasound, upper GI endoscopy (esophagitis endoscopic reference score was used to minimise observer variability), biopsy (6 esophageal and 4 antral biopsies), and histopathological examination by staining the biopsies with hematoxylin and eosin (H&E). The pathologist tallied the eosinophils using a high-powered microscope. EoE can be diagnosed by the presence of more than 15 eosinophils/HPF, while EE with fewer than 15 eosinophils/HPF is low-grade. Prevalence of eosinophilic esophagitis was recorded among all cases. SPSS 23.0 was used to analyze all data.

RESULTS

The mean age of the patients was 41.9±8.21 years and had mean BMI 25.7±6.31 kg/m². Majority of the patients were males 190 (63.3%) and 110 (36.7%) were females.(table 1)

Table-1: Included patients with baseline details

Variables	Frequency	Percentage
Mean age (years)	41.9±8.21	
Mean BMI (kg/m ²)	25.7±6.31	
Gender		
Male	190	63.3
Female	110	36.7

Among 300 patents, we found that frequency of eosinophilic esophagitis were 27 (9%).(fig 1)

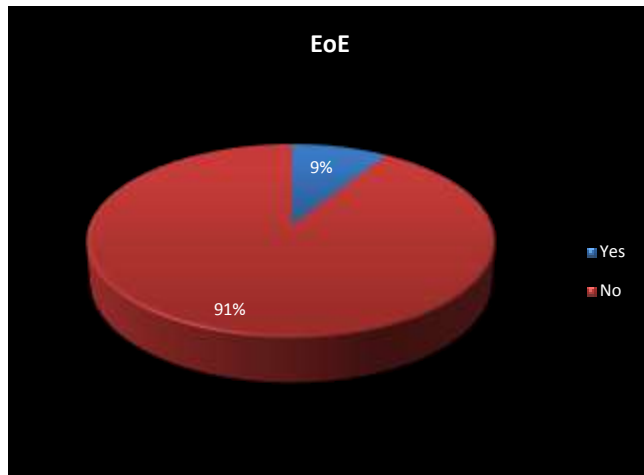


Figure-1: Frequency of eosinophilic esophagitis among GERD cases

Among 27 cases of EoE, males were higher in number 19 (70.4%) than females 8 (29.6%).(fig 2)

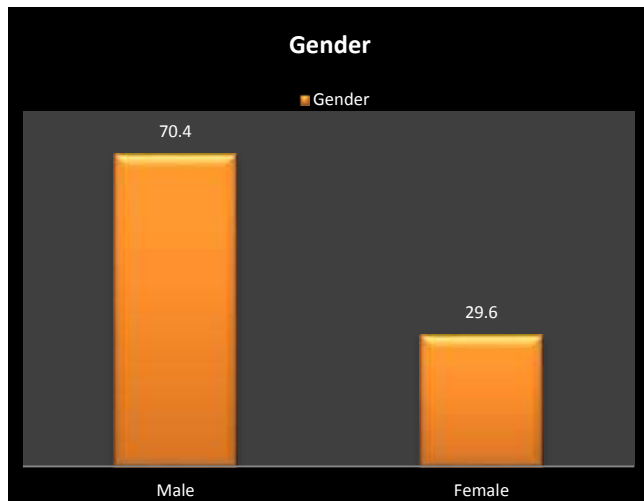


Figure-2: Gender distribution among EoE cases

Among these cases, heartburn was the most common symptom found in 10 (37.03%) cases, followed by dysphagia in 6 (22.2%), epigastric pain in 5 (18.5%). Frequency of smokers was 9 (33.3%). Asthma was found in 5 (18.5%) cases, allergic rhinitis in 4 (14.8%) and food allergy in 2 (7.4%) cases. Lower esophagus found in 12 (44.4%) cases and mid in 15 (55.6%) cases. Mean eosinophils was 24.4±7.29 per HPF.(table 2)

Table-2: Symptomatic profile among EoE cases

Variables	Frequency	Percentage
Symptoms		
heartburn	10	37.03
dysphagia	6	22.2
epigastric pain	5	18.5
dyspepsia	3	11.1
Unknown	3	11.1
Smokers		
Yes	9	33.3
No	18	66.7
Allergy Profile		
asthma	5	18.5
allergic rhinitis	4	14.8
food allergy	2	7.4
Site of EoE		
lower esophagus	12	44.4
mid esophagus	15	55.6
Mean eosinophils per HPF	24.4±7.29	

As per histological findings, eosinophilic microabscess was found in 20 (70.1%) cases, Superficial layering of eosinophils in 4 (14.8%) cases, Basal zone hyperplasia in 22 (81.5%), Rete peg elongation 21 (77.5%), Dilated intercellular spaces in 18 (66.7%) and Epithelial desquamation in 21 (77.5%) cases. (table 3)

Table-3: Histological findings of EoE cases

Variables	Frequency	Percentage
eosinophilic microabscess	20	70.1
superficial layering of eosinophils	4	14.8
basal zone hyperplasia	22	81.5
rete peg elongation	21	77.5
dilated intercellular spaces	18	66.7
epithelial desquamation	21 (77.5%)	77.5

DISCUSSION

With a rising number of cases in the last decade, esophageal inflammation (EoE) is becoming more common. [13] Many studies have been done on EoE's symptoms and prevalence in Western nations. This illness has not yet been thoroughly studied in Asian nations since it is considered unusual. A tertiary care center's endoscopic database was analysed in this study to examine EoE's diagnostic trends and clinical features. As far as we know, Pakistan issued its first EoE report in 2011. [14] In a recent research, 7.4 percent of individuals who had upper gastrointestinal endoscopy for any reason were found to have EoE. Patients were younger and more male-dominated. All patients had 'feline oesophagus' on endoscopy with micro-abscesses visible in some, with a history of atopy, complaints of dysphagia and food impaction. [15]

Comparable to the above mentioned results of previous studies, our studies presented the same results that prevalence of EoE among GERD patients was 9%. Only a few studies have looked at the possibility of GERD and EoE coexisting. The prevalence of EE in patients with gastroesophageal reflux disease (GERD) has been varied. In a Mexican investigation, endoscopy revealed EoE in 4% of refractory GERD patients. Their findings showed that individuals with EoE were substantially younger, had higher dysphagia and atopy as well as poor esophageal peristalsis; they were also more likely to have an esophageal ring or esophageal stricture than patients without EoE. Age 45 years, dysphagia, and atopy were all found to be independent risk factors for EoE [16]. According to an Iranian research, 8.8% of patients with refractory GERD had EoE. Endoscopic examination revealed erosive esophagitis, rings, and white plaques in all patients [17]. 6 percent of GERD patients and 9.7 percent of GERD patients who were resistant to PPIs were found to have EoE in a research done in Japan. Heartburn and trouble swallowing were prominent adverse effects. There was a solitary patient in their investigation who demonstrated typical endoscopic results (longitudinal furrows), and the endoscopy was normal in the five others. They discovered no significant differences in the characteristics of patients with EoE and those without [18].

Among these cases of EoE, heartburn was the most common symptom found in 10 (37.03%) cases, followed by dysphagia in 6 (22.2%), epigastric pain in 5 (18.5%). Frequency of smokers was 9 (33.3%). Asthma was found in 5 (18.5%) cases, allergic rhinitis in 4 (14.8%) and food allergy in 2 (7.4%) cases. Lower esophagus found in 12 (44.4%) cases and mid in 15 (55.6%) cases. Mean eosinophils was 24.4 ± 7.29 per HPF.[19] TEOE's cause is unknown. The high prevalence of food allergies in these individuals has led to a putative relationship between an immune response and numerous ingested allergens.

As per histological findings, eosinophilic microabscess was found in 20 (70.1%) cases, Superficial layering of eosinophils in 4 (14.8%) cases, Basal zone hyperplasia in 22 (81.5%), Rete peg elongation 21 (77.5%), Dilated intercellular spaces in 18 (66.7%) and Epithelial desquamation in 21 (77.5%) cases.[20] Because of the damage and inflammation caused by the chronic acid exposure in GERD, a small increase in eosinophilia might occur. The coexistence of EoE and GERD owing to chance alone is conceivable because GERD is so prevalent in the general population. EoE may be the outcome of long-term GERD in individuals who have chronic acid exposure, as shown by pH measurements in such patients. However, EoE can also cause gastroesophageal reflux disease (GERD). These findings support the concept that eosinophil-induced mucosal breakdown and smooth muscle reorganisation lead to disease progression. GERD symptoms are brought on by the remodelling effect, which relaxes the lower esophageal sphincter and reduces acid evacuation. Patients with reflux symptoms and those who fail to react to gastric acid inhibitors should consider EoE as a possible diagnosis. Globally, the prevalence of EoE varies, although individuals with refractory GERD are at particular risk. Obtaining an EGD and a biopsy quickly is essential for an accurate diagnosis and proper treatment. Corticosteroids for the skin work effectively in EoE cases. [21]

CONCLUSION

Patients with refractory GERD are at risk of developing eosinophilic esophagitis, which can be life-threatening. Dysphagia, heartburn, and food impaction are all possible symptoms. The EoE screening of elderly patients with prolonged GERD, atopy, and non-response to stomach acid inhibitors must be evaluated.

REFERENCES

- Dellon ES, Hirano I: Epidemiology and natural history of eosinophilic esophagitis. *Gastroenterology*. 2018, 154:319-332
- Shi YN, Sun SJ, Xiong LS, Cao QH, Cui Y, Chen MH: Prevalence, clinical manifestations and endoscopic features of eosinophilic esophagitis: a pathological review in China. *J Dig Dis*. 2012, 13:304-309.
- García-Compeán D, González JA, García CA, et al.: Prevalence of eosinophilic esophagitis in patients with refractory gastroesophageal reflux disease symptoms: a prospective study. *Dig Liver Dis*. 2011, 43:204-208.
- Mackenzie SH, Go M, Chadwick B, et al.: Eosinophilic esophagitis in patients presenting with dysphagia--a prospective analysis. *Aliment Pharmacol Ther*. 2008, 28:1140-1146.
- Kerlin P, Jones D, Remedios M, Campbell C: Prevalence of eosinophilic esophagitis in adults with food bolus obstruction of the esophagus. *J Clin Gastroenterol*. 2007, 41:356-361.
- Remedios M, Campbell C, Jones DM, Kerlin P: Eosinophilic esophagitis in adults: clinical, endoscopic, histologic findings, and response to treatment with fluticasone propionate. *Gastrointest Endosc*. 2006, 63:3-12.
- Lucendo AJ, Arias Á (2017) The role of endoscopy in eosinophilic esophagitis: from diagnosis to therapy. *11(12):1135-1149*
- Gomez-Aldana A et al (2019) Eosinophilic esophagitis: current concepts in diagnosis and treatment. *World J Gastroenterol* 25(32):4598-4613.
- Gomez Torrijos E, Gonzalez-Mendiola R, Alvarado M, Avila R, Prieto-Garcia A, Valbuena T, Borja J, Infante S, Lopez MP, Marchan E, Prieto P, Moro M, Rosado A, Saiz V, Somoza ML, Uriel O, Vazquez A, Mur P, Poza-Guedes P, Bartra J (2018) Eosinophilic esophagitis: review and update. *Front Med* 5:247.
- Miehke S et al (2020) Orodispersible budesonide tablets for the treatment of eosinophilic esophagitis: a review of the latest evidence. *Ther Adv Gastroenterol* 13:1756284820927282
- Wong S, Ruszkiewicz A, Holloway RH, Nguyen NQ (2018) Gastroesophageal reflux disease and eosinophilic esophagitis: what is the relationship? *World J Gastrointest Pathophysiol* 9(3):63-72
- Kellerman R, Kintanar T (2017) Gastroesophageal reflux disease. *Prim Care* 44(4):561-573
- Chang F, Anderson S. Clinical and pathological features of eosinophilic esophagitis: a review. *Pathology* 2008;40:3-8
- Saeed S, Zuberi BF, Afsar S, Qadeer R, Memon AR: Frequency of Eosinophilic Esophagitis in patients undergoing upper GI Endoscopy. *Pak J Med Sci*. 2011, 27:545-548.
- Anis K, Chandnani A, Ahmed M, et al. (July 27, 2019) Retrospective Analysis of Eosinophilic Esophagitis in Patients with Refractory Gastroesophageal Reflux Disease. *Cureus* 11(7): e5252.
- García-Compeán D, González JA, García CA, et al.: Prevalence of eosinophilic esophagitis in patients with refractory gastroesophageal reflux disease symptoms: a prospective study. *Dig Liver Dis*. 2011, 43:204-208
- Foroutan M, Norouzi A, Molaei M, et al.: Eosinophilic esophagitis in patients with refractory gastroesophageal reflux disease. *Dig Dis Sci*. 2010, 55:28-31
- Okimoto K, Arai M, Ishigami H, et al.: A prospective study of eosinophilic esophagitis and the expression of tight junction proteins in patients with gastroesophageal reflux disease symptoms. *Gut Liver*. 2018, 12:30-37
- Mackenzie SH, Go M, Chadwick B, et al. Eosinophilic esophagitis in patients presenting with dysphagia--a prospective analysis. *Aliment Pharmacol Ther* 2008;28:1140-1146.
- Molina-Infante J, Bredenoord AJ, Cheng E, et al. Proton pump inhibitor-responsive oesophageal eosinophilia: an entity challenging current diagnostic criteria for eosinophilic esophagitis. *Gut* 2016;65:524-531.
- GaHeeKim, KeeWook Jung, Hwoon-Yong Jung, Kee Don Choi, JungBok Lee, Young Soo Park, So-Woon Kim, JeongHoon Lee, Do Hoon Kim, Ji Yong Ahn, Ho June Song, Gin Hyug Lee, and Jin-Ho Kim. Diagnostic Trends and Clinical Characteristics of Eosinophilic Esophagitis: A Korean, Single-center Database Study. *April 1, 2018*