

**ORIGINAL ARTICLE:**

**TITLE:THE HISTOMORPHOLOGICAL STUDY OF EOSINOPHILIC GASTROENTERITIS AND IT'S FOLLOW-UP**

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**ABSTRACT:**

**BACKGROUND:** Eosinophilic gastrointestinal disorders (EGID) are the group of chronic, inflammatory conditions of the gastrointestinal tract. Little is known about the histomorphology as well as outcome of these after follow-up. The aims of the study are to study the histomorphological pattern of EGIDs and also to determine the changes post follow-up for a period of 24 months.

**METHODS AND REESULTS:** A total of 65 cases reported as Eosinophilic gastroenteritis for a period of two year has been considered and followed-up for a period of next 24 months. Most of them were colonic biopsies (n=30) followed by gastric biopsies (n=14), small bowel biopsies (n=9), esophageal biopsies (n=5) and then duodenal biopsies (n=7). On follow-up, 7 patients (11%) developed Crohn's disease, 10 of them (15%) developed Ulcerative colitis, 4 (6%) developed microscopic colitis, 10 (15%) developed persistent eosinophilia, 27(42%) were asymptomatic and 7 (11%) of them lost for follow-up.

**CONCLUSION:** The identification and histopathological reporting of eosinophilic gastroenteritis is important and follow-up of these patients is also crucial since there are high chances of development of Inflammatory Bowel Disease (IBD) in them.

**INTRODUCTION:** Eosinophilic gastrointestinal disorders (EGID) are a group of disorders which are characterized by pathologic eosinophilic infiltration of the esophagus, stomach, small intestine, or colon leading to organ dysfunction and clinical symptoms.<sup>(1)</sup> Collins defined EGIDs as diseases that characteristically display increased numbers of eosinophils, in normal and abnormal locations, in one or more gastrointestinal (GI) segments<sup>(2)</sup>. Eosinophils normally reside in the GI tract<sup>(3)</sup>, so mere presence of eosinophils (Eo) does not postulate a diagnosis of EGID.

Eosinophilic esophagitis is characterized by eosinophilic infiltration of  $\geq 15$  Eo/high power field (HPF) with secondary fibrosis<sup>(4)</sup>. No such criteria exist for eosinophilic colitis. According to few studies eosinophilic gastroenteritis is defined as an Eo density of  $\geq 30$  Eo/HPF<sup>(5,6)</sup>. However, the most accepted definition of Eosinophilic gastroenteritis in the rest of the gastrointestinal tract, is an Eo count that exceeds 20 Eo/HPF<sup>(7-9)</sup>.

### **AIMS AND OBJECTIVES:**

- 1) To study the histomorphological spectrum of eosinophilic gastrointestinal disorders.
- 2) To examine the different changes seen in the eosinophilic gastrointestinal disorders after follow-up.

### **MATERIALS AND METHODS:**

A prospective study was carried out in the Department of Pathology for a period of two years from June 2016 to June 2018 and followed up for a period of two years till June 2020. The endoscopic biopsies performed in the Department of Gastroenterology were submitted to the Department of Pathology for histopathological examination.

### **INCLUSION CRITERIA:**

- 1) Patients with age  $>18$  years.
- 2) The presence of gastrointestinal symptoms.
- 3) The presence of eosinophils in gastrointestinal biopsies (defined as  $>15$  Eo/HPF for esophageal involvement and  $>20$  Eo/HPF for the rest of the gastrointestinal tract)

### **EXCLUSION CRITERIA:**

- 1) Patients with age  $<18$  years of age.
- 2) Previous diagnosis of inflammatory bowel disease (IBD) and/or celiac disease
- 3) Drug-induced pathologies
- 4) History of connective tissue disorders and/or vasculitis
- 5) Previous radiotherapy to the abdomen
- 6) Primary hypereosinophilic syndrome and
- 7) Myeloproliferative neoplasms.

## BIOPSY AND HISTOPATHOLOGICAL ANALYSIS:

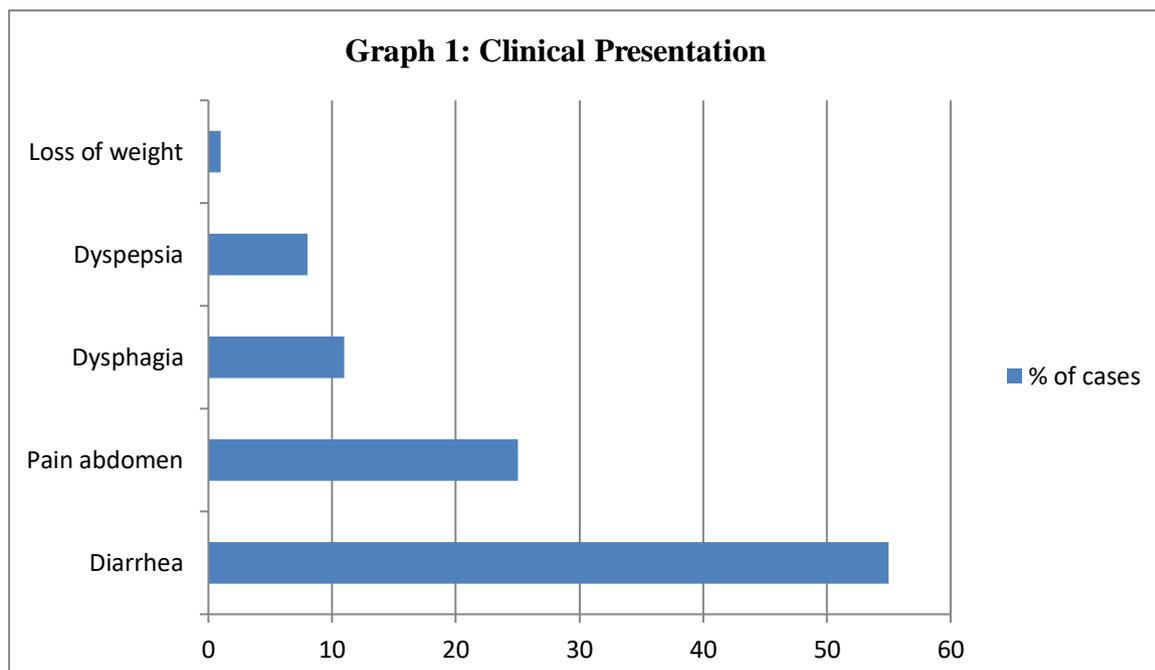
The biopsy specimen was sent in 10% formalin and the biopsies underwent routine fixation and processing procedures. Later the paraffin blocks were prepared and the slides were made. Sections were stained with routine Hematoxylin and Eosin stain (H and E) and mounted with coverslips using Distyrene Plasticizer Xylene (DPX) as mountant. Additional sections were stained with Giemsa to observe H. Pylori and Periodic Acid Schiff (PAS) stain were performed wherever necessary. The histopathological reporting and analysis has been done by two pathologists independently.

Gastrointestinal biopsies from both normal and abnormal appearing mucosae have been taken endoscopically because even normal areas can harbour diagnostic microscopic appearance<sup>(10)</sup>. The following diagnostic criteria have been followed in the histopathological diagnosis of eosinophilic gastroenteritis in different anatomic locations. Normal eosinophil count varies depending on the anatomic site of biopsies of the GIT. In the esophagus, eosinophilic count of  $\geq 15$  Eo/hpf along with the gastrointestinal symptoms is considered as the diagnostic criteria for eosinophilic esophagitis<sup>(11)</sup>. In asymptomatic individuals, less than 10 Eo/hpf in gastric and duodenal biopsies have been considered normal. Eosinophil counts higher than 30 Eo/hpf in the stomach, 50 Eo/hpf in the duodenum and 30 Eo/hpf in the large intestine in an affected segment have been suggested when eosinophilic gastroenteritis is suspected<sup>(12)</sup>.

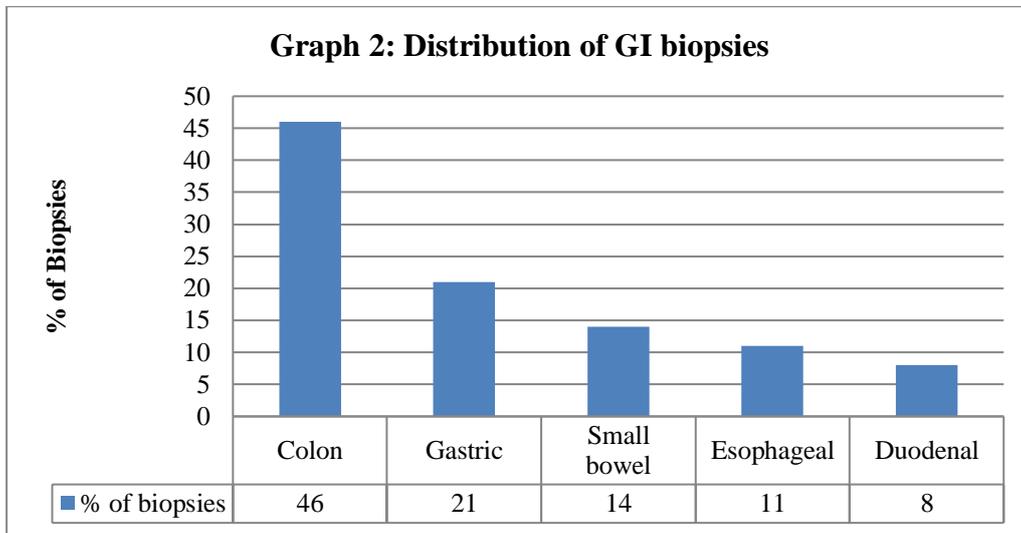
The patients were followed up for a period of 24 months and the clinical information and the information regarding repeat biopsy have been retrieved.

## RESULTS:

A total of 65 cases reported as eosinophilic gastrointestinal disorders have been studied. Most of the patients were males (n=42, 65%) with the remaining females (n=23, 35%) with a male to female ratio of 1.8:1. Most of the patients presented with diarrhoea (n=36, 55%) followed by pain abdomen (n=16, 25%), dysphagia (n=7, 11%), dyspepsia (n=5, 8%) and loss of weight (n=1, 1%) [Graph 1]



The present study included most of the colonic biopsies (n=30) followed by gastric biopsies (n=14), small bowel biopsies (n=9), esophageal biopsies (n=5) and then duodenal biopsies (n=7) [Graph 2].



The eosinophil count in the lining epithelium or in the lamina propria has been counted and the average of 10 high power fields has been determined. The criteria mentioned above have been applied in the diagnosis of spectrum of eosinophilic gastroenteritis. The distribution of various sites of eosinophilic infiltration has been shown in table 1.

**Table 1: Site of eosinophilic infiltration**

Site	Number of patients	% of patients
Esophagus	7	11
Stomach	14	21
Duodenum	5	8
Small intestine	9	14
Colon	30	46

The histomorphological picture of GI biopsies is as under-

In case of esophageal biopsy, presence of >15Eo/hpf, sheets of eosinophils, gland abscesses present in the muscularis and submucosa.

In case of Eosinophilic gastroenteritis or enteritis, >30Eo/hpf in stomach and >50Eo/hpf in duodenum with sheets of eosinophils, present in surface epithelium and gland epithelium; gland abscesses, present in muscularis and submucosa; absence of neutrophils.

In case of eosinophilic colitis, >30Eo/hpf with sheets of eosinophils, present in surface epithelium and crypt epithelium; crypt abscesses, present in muscularis and submucosa; absence of neutrophils.

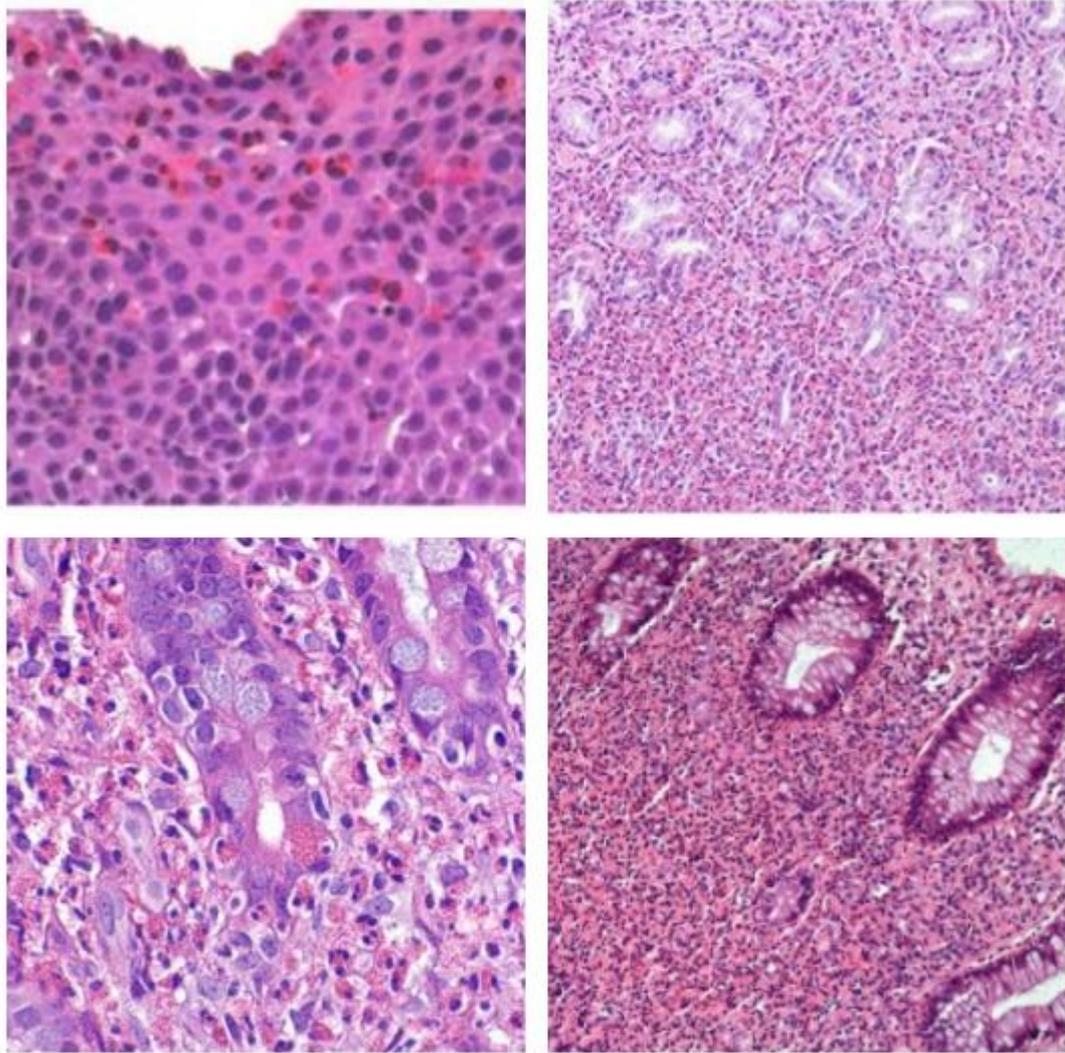


Figure 1: Photomicrograph showing – a) Eosinophilic esophagitis b) Eosinophilic gastritis c) Eosinophilic duodenitis d) Eosinophilic colitis

After histopathological reporting of the eosinophilic gastroenteritis using the above criteria, the patient follow-up has been done for a period of 24 months and these findings has been retrieved. The gastrointestinal symptoms of the patients with eosinophilic esophagitis have been relieved within a period of 3 months and repeat endoscopy was not performed. Twenty patients with colonic eosinophilia became asymptomatic during the follow-up period and repeat endoscopy was not performed. Seven patients were lost for follow-up.

More than one-fourth of the patients diagnosed with eosinophilic gastroenteritis developed inflammatory bowel disease (IBD). Seven patients developed Crohn's disease on repeat gastrointestinal biopsy, ten of them diagnosed with Ulcerative colitis, four with microscopic colitis and other eight had persistent eosinophilia with persistent symptoms.

Table 2: Characteristic features of patients during follow-up period

Type of lesion	Number of patients	% of patients
Crohn's disease	7	11
Ulcerative colitis	10	15
Microscopic colitis	4	6

Persistent eosinophilia	10	15
Asymptomatic	27	42
Lost for follow-up	7	11

## DISCUSSION:

In healthy people, eosinophils reside in the lamina propria of the stomach and intestine. On stimulation these eosinophils can release certain cytokines which can attract more inflammatory cells, such as neutrophils to the intestinal lining. Eosinophils can also act as antigen presenting cells which help in T-cell proliferation and activation. This mechanism occurs in patients with eosinophilic gastroenteritis, IBD and atopic asthma. Eosinophils can be proinflammatory and their numbers in the lining epithelium are greatly increased in active disease<sup>(13)</sup>.

Eosinophils also play a role in tissue repair. According to studies done by Lampinen et al., the eosinophil count was higher in the inactive phase than in the active phase of Crohn's disease and ulcerative colitis<sup>(14, 15)</sup>.

Few studies have documented the development of inflammatory bowel disease in the follow-up period of cases diagnosed with eosinophilic gastroenteritis<sup>(13, 16, 17)</sup>. This finding is in close correlation with the data obtained from our study. Eosinophilic gastroenteritis and IBD share the common clinical manifestations as well as pathogenesis, hence its supporting the fact that 32% of patients with eosinophilic gastroenteritis developed IBD in our study. Hence it's recommended for close follow-up of patients with eosinophilic gastroenteritis. In a study by Bischoff et al, it's shown that eosinophils number and activation will be increased in eosinophilic gastroenteritis whereas in case of IBD, eosinophilic activation will be increased but not the number<sup>(18)</sup>.

## CONCLUSION:

Our study demonstrates the histomorphology of eosinophilic gastroenteritis which is limited in the literature. The various histopathological changes seen in the gastrointestinal biopsies in various anatomic locations have been explained. The study also highlights the development of IBD in case of eosinophilic gastroenteritis and the importance of follow-up in these cases.

## REFERENCES:

- 1) Spergel JM, Book WM, Mays E, Song L, Shah SS, Talley NJ, Bonis PA (2011) Variation in prevalence, diagnostic criteria, and initial management options for eosinophilic gastrointestinal diseases in the United States. *J Pediatr Gastroenterol Nutr* 52:300–306
- 2) Collins MH (2009) Histopathology associated with eosinophilic gastrointestinal diseases. *Immunol Allergy Clin N Am* 29(1):109–117. <https://doi.org/10.1016/j.iac.2008.10.005>
- 3) Jung Y, Rothenberg ME (2014) Roles and regulation of gastrointestinal eosinophils in immunity and disease. *J Immunol* 193(3):999–1005. <https://doi.org/10.4049/jimmunol.1400413>
- 4) Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol* 2011;128:3-20.
- 5) Lwin T, Melton SD, Genta RM. Eosinophilic gastritis: histopathological characterization and quantification of the normal gastric eosinophil content. *Mod Pathol* 2011;24:556-563.

- 6) Wong GW, Lim KH, Wan WK, Low SC, Kong SC. Eosinophilic gastroenteritis: Clinical profiles and treatment outcomes, a retrospective study of 18 adult patients in a Singapore tertiary hospital. *Med J Malaysia* 2015;**70**:232-237.
- 7) Uppal V, Kreiger P, Kutsch E. Eosinophilic gastroenteritis: a comprehensive review. *Clin Rev Allergy Immunol* 2016;**50**:175-188.
- 8) Chen MJ, Chu CH, Lin SC, Shih SC, Wang TE. Eosinophilic gastroenteritis: clinical experience with 15 patients. *World J Gastroenterol* 2003;**9**:2813-2816.
- 9) Gaertner WB, Macdonald JE, Kwaan MR, et al. Eosinophilic colitis: university of Minnesota experience and literature review. *Gastroenterol Res Pract* 2011;**2011**:857508.
- 10) Lee M, Hodges WG, Huggins TL, Lee EL. Eosinophilic gastroenteritis. Southern medical journal. 1996 Feb 1;**89**(2):189-94.
- 11) Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N, Spechler SJ, Attwood SE, Straumann A, Aceves SS, Alexander JA. Updated international consensus diagnostic criteria for eosinophilic esophagitis: proceedings of the AGREE conference. *Gastroenterology*. 2018 Oct 1;**155**(4):1022-33.
- 12) Grandinetti T, Biedermann L, Bussmann C, Straumann A, Hruz P. Eosinophilic gastroenteritis: clinical manifestation, natural course, and evaluation of treatment with corticosteroids and vedolizumab. *Digestive diseases and sciences*. 2019 Aug;**64**(8):2231-41.
- 13) Zammit SC, Cachia M, Sapiano K, Gauci J, Montefort S, Ellul P. Eosinophilic gastrointestinal disorder: is it what it seems to be?. *Annals of gastroenterology*. 2018 Jul;**31**(4):475.
- 14) Lampinen M, Rönblom A, Amin K, et al. Eosinophil granulocytes are activated during the remission phase of ulcerative colitis. *Gut* 2005;**54**:1714-1720.
- 15) Lampinen M, Backman M, Winqvist O, et al. Different regulation of eosinophil activity in Crohn's disease compared with ulcerative colitis. *J Leukoc Biol* 2008;**84**:1392-1399.
- 16) Uzunismail H, Hatemi I, Doğusoy G, Akin O. Dense eosinophilic infiltration of the mucosa preceding ulcerative colitis and mimicking eosinophilic colitis: report of two cases. *Turk J Gastroenterol* 2006;**17**:53-57.
- 17) Mutalib M, Blackstock S, Evans V et al. Eosinophilic gastrointestinal disease and inflammatory bowel disease in children: is it a disease continuum? *Eur J Gastroenterol Hepatol* 2015;**27**:20-23.
- 18) Bischoff SC, Mayer J, Nguyen QT, Stolte M, Manns MP. Immunohistological assessment of intestinal eosinophil activation in patients with eosinophilic gastroenteritis and inflammatory bowel disease. *Am J Gastroenterol* 1999;**94**:3521-3529.