



Original Article

A study of eosinophil count in oesophageal and gastric mucosal biopsies at a tertiary care centre

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ABSTRACT

Background: Eosinophils are inflammatory cells and can infiltrate several organs playing a major role in causing tissue damage and organ dysfunction. This study was conducted to establish the baseline eosinophil count in normal states and to correlate mucosal eosinophil count with abnormalities of the oesophagus and stomach.

Materials and methods: A retrospective observational study was conducted at the surgical pathology department of a tertiary care hospital in Mumbai. A total of 124 biopsies were studied. Oesophageal and stomach biopsies with some pathology including oesophagitis, gastritis, ulcer, nonspecific inflammation, etc, were considered abnormal.

Results: Out of 124 biopsies, 36 (29.03%) were normal, while 88 (70.97%) were abnormal. Eosinophilic gastrointestinal disease had male predilection. In abnormal oesophageal biopsies, 16 (88.9%) of 18 oesophageal biopsies had an eosinophil count in the 0-5 eos/hpf band, whereas 50 (71.4%) of 70 abnormal stomach biopsies had eosinophils in the 0-5 eos/hpf band. The eosinophil count reported was 24/hpf in eosinophilic oesophagitis.

Conclusions: Almost all normal oesophageal biopsies (90.9%) and stomach biopsies (100%) showed eosinophil count as 0 eos/hpf and <10/hpf respectively. So if one finds eosinophils in a biopsy sample, one needs to look for other specific pathology.

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INTRODUCTION

Eosinophils are inflammatory cells, originating in the bone marrow, playing an important role in defending the host against parasitic pathogens.¹ During inflammatory conditions, eosinophils can infiltrate several organs, e.g. lungs, gastrointestinal tract and skin, playing a major role in causing tissue damage and organ dysfunction. Eosinophil-associated gastrointestinal disorders are being recognized with increasing frequency, and recent epidemiological analysis indicates that there is a bona fide increase in disease prevalence.^{2,3}

The majority of investigations focusing on Eosinophilic gastrointestinal disorders (EGID) have been limited to eosinophilic oesophagitis (EE). Because the oesophagus is normally devoid of eosinophils, the diagnosis and investigation of EE are relatively simple compared with other forms of EGID. Prior studies have indicated that the number of eosinophils, their regional distribution in gastrointestinal biopsy samples, as well as the level of eosinophil degranulation may be critical determinants for defining disease.^{4,5} Clarity concerning the diagnostic criteria, which has to be based on intestinal pathology, is confounded by the lack of a clear description of the normal number and regional distribution of eosinophils in the intestinal tract. The current study was conducted to establish the baseline eosinophil count in normal states and to correlate mucosal eosinophil count with abnormalities of the upper gastrointestinal tract, in particular, the oesophagus and stomach.

MATERIALS AND METHODS

The current study was a retrospective observational study conducted at the surgical pathology department of a tertiary care hospital in Mumbai. Total of 147 oesophageal and stomach biopsies were received during the one-year study period. Only biopsies of oesophageal and gastric origin having had upper digestive tract symptoms such as dysphagia, epigastric pain, vomiting, nausea, association with other conditions such as chronic kidney disease, chronic liver disease, anemia, having nonspecific symptoms such as abdominal pain, bleeding per rectum, etc and having some endoscopic findings were included. Biopsies revealing neoplasia of the oesophagus or stomach were excluded from the study. Considering these inclusion and exclusion criteria, a total of 124 biopsies were studied. Biopsies diagnosed to have 'no significant pathology' showing normal mucosal architecture without any significant inflammation, granuloma, dysplasia, or malignancy, were considered to be normal. Biopsies showing 'some pathology' or other including oesophagitis, gastritis, ulcer, nonspecific inflammation, etc, all were considered to be abnormal. Those biopsies with no pathological lesion found, which included follow-up biopsies from malignant lesions operated previously were taken as normal biopsies. All others, which showed any pathology including mild inflammation, were categorized as abnormal biopsies.

Biopsy specimens were placed in 10% buffered formalin for fixation and were subjected to routine processing. Sections were cut at right angles to the mucosal surface followed by staining using hematoxylin and eosin stains. Special stains

were done wherever indicated. A detailed microscopic examination was carried out on all biopsies. Areas where the surface epithelium was well-oriented were selected for analysis. The number of eosinophils was counted in each biopsy in five different high-power fields (400X) and the average number was noted for both normal and abnormal biopsies. Lwin et al used this method for counting eosinophils in gastric biopsies.⁶ The eosinophil counts were clubbed as 0-5, 6-10, 11-15, and so forth. Features looked for in the biopsies showing an increase in eosinophil count in the surface epithelium were: hyperplastic basal cell layer in the oesophagus, dense aggregates of eosinophils in lamina propria and muscularis mucosa and degranulations of eosinophils, other inflammatory cells such as neutrophils, lymphocytes. Special stains were used to look for intestinal metaplasia, *Helicobacter pylori* bacilli, fungal infection, etc. In all normal and abnormal biopsies, detailed eosinophil counts per high-power field were documented. A detailed pathological examination was carried out to note the type of inflammation, cause of inflammation, etc.

RESULTS

Out of 124 biopsies, 36 (29.03%) were normal while 88 (70.97%) were abnormal. The age of presentation ranged from 2 to 80 and showed that the majority of abnormal biopsies were between 21-60 years of age (fig. 1). Male to Female ratio was 1.77:1 in normal biopsies and 1.38:1 in abnormal biopsies depicting male preponderance. 11 of the 36 normal biopsies were from the oesophagus, while 25 were from the stomach, and 18 of the 88 abnormal biopsies were from the oesophagus, while 70 were from the stomach (Table 1). The average eosinophil count in five high power fields (400x) of each of the normal biopsies was 3. The eosinophil count was clubbed in bands as 0-5 eos/hpf, and 6-10 eos/hpf.

Out of 18 abnormal oesophageal biopsies, 16 (88.9%) had an eosinophil count in the 0-5 eos/hpf band, whereas 50 (71.4%) of 70 abnormal stomach biopsies had eosinophils in the 0-5 eos/hpf band. Eosinophils were found in a wide range of 11-50 eos/hpf in 9 stomach biopsies (12.9 percent) (Table 2).

Table 1: Association of Eosinophil count with the site of biopsy in normal samples

Region/ Eosinophil band	0-5	6-10	Total
Oesophagus	11	0	11
Stomach	24	1	25
Total	35	1	36

Table 2: Association of Eosinophil count with the site of biopsy in abnormal samples

Region / Eosinophil Band	0-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	46-50	Total
Oesophagus	16	0	0	1	1	0	0	0	0	0	18
Stomach	50	11	1	1	2	2	1	0	0	2	70
Total	66	11	1	2	3	2	1	0	0	2	88

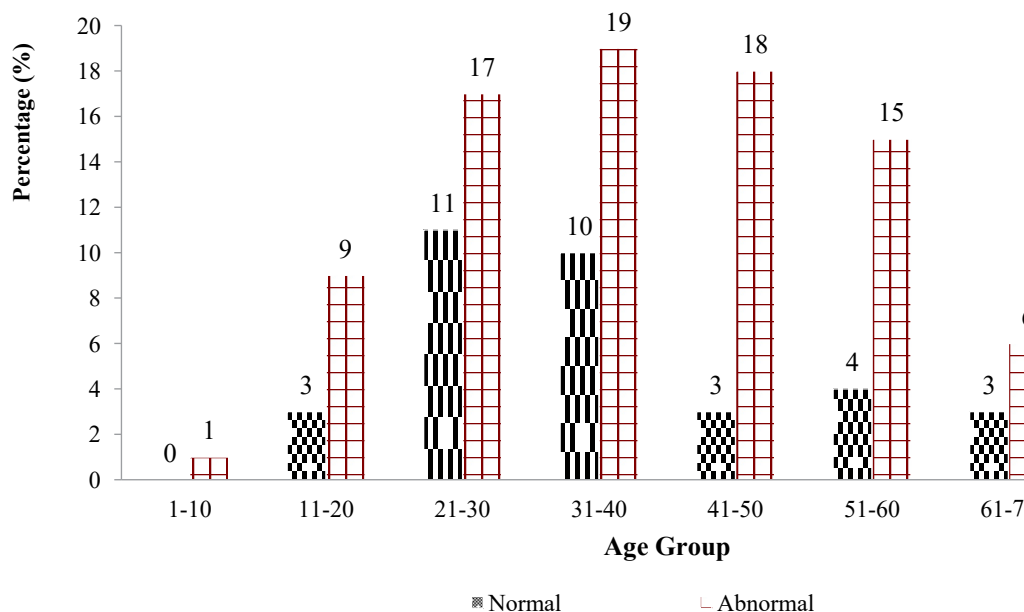


Figure 1: Bar graph showing age-wise distribution of patients.

Barett’s oesophagus was seen on 4/18 (22.2 %) oesophageal biopsies having eosinophil count between 0 to 5 eos/hpf and dysphagia (Table 3). One patient was experiencing epigastric discomfort, while the other had a history of

chronic alcoholism along with regurgitation and heartburn. On endoscopy, three patients had Barett’s oesophagus (one with hiatus hernia) and the fourth had a stricture.

Table 3: Eosinophil count in various diagnoses of abnormal oesophageal biopsies

Region / Eosinophil Band	0-5	6-10	11-15	16-20	21-25	Total
Barett’s oesophagus	4	0	0	0	0	4
Esophagitis	2	0	0	1	1	4
GERD	2	0	1	0	0	3
NSIP&	7	0	0	0	0	7
Total	15	0	1	1	1	18

*NSIP – Nonspecific inflammatory pathology

Histopathological features of oesophagitis were present in 4/18 (22.2%) oesophageal samples. The eosinophil level in two biopsies was in the 0-5 eos/hpf range; these patients exhibited dysphagia, discomfort, regurgitation and heartburn. One patient with eosinophilic oesophagitis presented with epigastric pain, nausea, distention of the abdomen, on and off fever and pyloric obstruction with diffuse thickening of the bowel on endoscopy. One patient with oesophagitis presented with dysphagia, and stricture on endoscopy and band eosinophil count of 20 eos/hpf.

Nonspecific inflammatory pathology (NSIP) showed the highest number of biopsies i.e. 7/18 with eosinophils in the range of 0-5 eos/hpf.

The eosinophil count in various diagnoses of abnormal stomach biopsies showed that the majority (88.5%) of patients with gastritis including one with Helicobacter pylori infection had eosinophil count in the band 0-10 eos/hpf, while 6/52 (11.5%) biopsies had count in the wide band range of 11-50 eos/hpf (Table 4).

Table 4: Eosinophil count in various diagnoses of abnormal stomach biopsies

Region /Eosinophil Band	0-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	46-50	Total
Gastritis	39	7	1	1	2	1	0	0	0	1	52
*PPI	3	0	0	0	0	1	0	0	0	0	4
NSIP	8	3	0	0	0	0	0	0	0	0	11
Peptic ulcer	0	0	0	0	0	0	1	0	0	1	2
Metaplasia	0	1	0	0	0	0	0	0	0	0	1
Total	50	11	1	1	2	2	1	0	0	2	70

*PPI – Proton pump inhibitor induced changes

Symptoms reported in biopsies with eosinophil count in the band 0-10 eos/hpf were epigastric pain (15), regurgitation with heartburn (8), vomiting (7), dysphagia (4) and associated with conditions (11) such as chronic diarrhea, chronic kidney disease, chronic liver disease, ulcerative colitis, follow-up case of carcinoma, etc. They had various endoscopic findings such as erythema (12), nodule (8), ulcer (1), and hiatus hernia (2), while few were normal (9). Symptoms reported in biopsies with eosinophil count in the band 11-50 eos/hpf were epigastric pain and on endoscopy had an ulcer (3), erythema (1), gastritis (1), and other findings such as snake skin appearance, longitudinal furrowing, felinezation/trachealization of oesophagus (fig. 2).

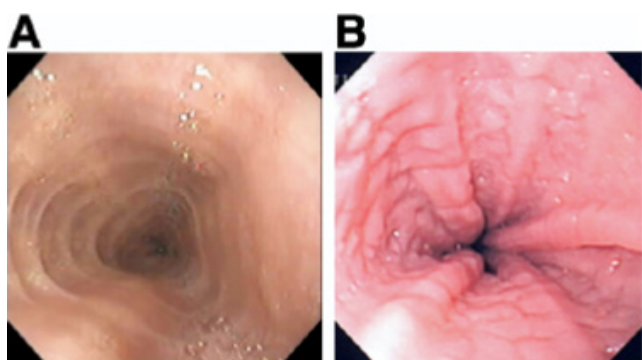


Figure 2: Endoscopic Findings associated with eosinophilic esophagitis (A) Mucosal rings giving appearance of trachealization, also been termed as feline oesophagus. (B) Esophageal furrowing representative of mucosal edema and thickening

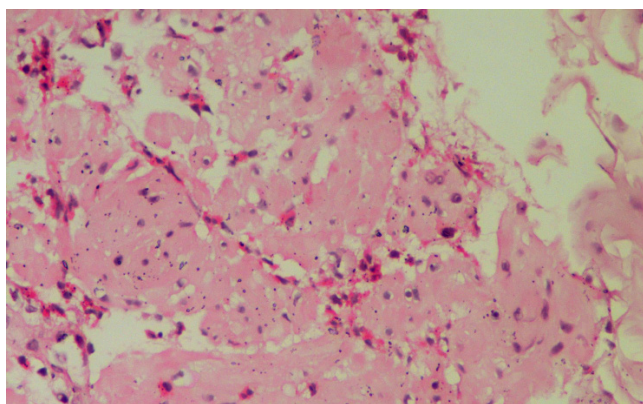


Figure 3: Eosinophilic Oesophagitis showing dense eosinophilic infiltrate in the surface epithelium of oesophagus (H & E, 400X)

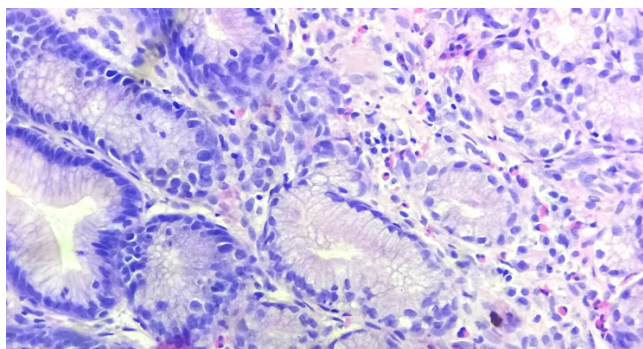


Figure 4: *H. Pylori* induced gastritis showing eosinophilic infiltrate in gastric mucosa (H & E, 400X)

DISCUSSION

There is a lack of Indian studies on the normal range of eosinophils in gastrointestinal tract biopsies. Often Pathologists come across mild to moderate degrees of eosinophilia in gastrointestinal biopsies. There is no established normal range, especially in gastric tissue.

Most of the normal biopsies were in the age bracket 21-40 years while most of the abnormal biopsies were in the age bracket 21-60 years. As per previous studies, eosinophilic oesophagitis was most prevalent in young children and adults, while eosinophilic gastritis more commonly affects children than adults.⁷ In our study there was no difference in the number of eosinophils in oesophagus or stomach between males and females. The eosinophilic gastrointestinal disease has a predilection for males and the findings were in line with other studies.^{5,8,9}

In our studies, the various indications for performing oesophageal biopsies were dysphagia (58.6%), regurgitation with heartburn (34.5%), epigastric pain (27.6%), irrespective of whether the biopsies were normal or abnormal. Studies have described that eosinophilia in the oesophagus is associated with symptoms of dysphagia which may be due to the secretion of compounds that are irritative to oesophageal lining or making the oesophagus stiff and less effective in propelling food downward, thus disrupting the easy passage of food. Yan et al found that dysphagia was the most common symptom in eosinophilic esophagitis.⁸ There was no correlation seen between the eosinophil count and endoscopic appearance in oesophagus and the results were similar to that of Kalach et al.¹⁰

The current study reported that 10 out of 11 histopathologically normal oesophageal biopsies showed an eosinophil count of 0 eos/hpf while only one biopsy showed a single eosinophil per high power field (fig. 3). This was similar to the study done by Rothenberg et al.²

Oesophageal abnormal biopsies of cases of gastroesophageal reflux disease (GERD) in our study had an eosinophil count of 0 eos/hpf. This finding was comparable with the study by Zuo et al where oesophageal eosinophil count in GERD was under 7.¹¹ One biopsy taken from the lower end of oesophagus, diagnosed to have GERD, showed 12 eos/hpf on microscopy. This biopsy presented with regurgitation and heartburn, had a stricture and Barrett's oesophagus on endoscopy. The eosinophil count of this biopsy was contradictory to Zuo et al.¹¹

Rothenberg et al in their endoscopic studies have shown many findings including strictures, mucosal rings, ulcerations, whitish papules, and polyps in eosinophilic oesophagitis, while in eosinophilic gastritis, pyloric obstruction was the most common endoscopic finding.² In the current study, we did not observe any of these findings in the oesophagus; however, pyloric obstruction was observed in the stomach.

Findings in the patient suffering from eosinophilic oesophagitis were comparable with the consensus recommendations of the First International Gastrointestinal Eosinophil Research Symposium about eosinophilic oesophagitis.¹² A study conducted by Dellon et al, also gave similar recommendations for the definition of eosinophilic oesophagitis.¹³ Hurrell et al, in their study, had also recommended degranulated eosinophils as a suggestive histological criterion for diagnosis of eosinophilic oesophagitis.¹⁴ The patient in our study diagnosed to have eosinophilic oesophagitis also showed degranulated eosinophils on microscopy.

The present study reported eosinophil count as 24/hpf in eosinophilic oesophagitis. A comparison of the eosinophil count of the present study with previous studies in eosinophilic oesophagitis was seen as given in [Table 5](#).

Table 5: Comparison of eosinophil count in eosinophilic oesophagitis in various studies

Year	Authors	Eosinophils/ hpf
1985	Lee et al ⁷	10
1993	Attwood et al ¹⁵	20
1999	Walsh et al ¹⁶	31
2002	Fox et al ¹⁷	15-20
2003	Croese et al ¹⁸	30
2004	Potter et al ¹⁹	15
2004	Rothenberg et al ²	7-24
2006	Assa'ad et al ²⁰	24
2013	Dellon et al ¹³	15

It is difficult to distinguish GERD from eosinophilic oesophagitis based on histopathology alone.^{14,15} However, in the present study, eosinophilic oesophagitis had specific findings on microscopy and it was associated with peripheral eosinophilia, which was absent in GERD.

Indications for performing gastric biopsies in our study were epigastric pain (47.4%), vomiting (20%), regurgitation with heartburn (17.9%), etc irrespective of whether the biopsies were normal or abnormal. Rothenberg et al have observed that abdominal pain was the most common symptom in eosinophilic gastroenteritis.² Of all 25 stomach biopsies showing normal findings on histology, 100% showed eosinophil count in the range 0-10 eos/hpf. This was similar to the study conducted by Lwin et al in which the eosinophil count was in the range of 0-8 eos/hpf in normal stomach biopsies.¹

In our study, all the biopsies diagnosed as *Helicobacter pylori* induced gastritis had eosinophil count in the range 0-30 eos/hpf ([fig. 4](#)). Four cases had eosinophil count higher than the range observed by Hurrell et al (0-16 eos/hpf).¹⁴ Some studies conclude that eosinophils and eosinophil released eosinophil cationic protein (ECP) may contribute to inflammatory changes in chronic gastritis, whereas there

is no proof that they play a role in ulcer development.²¹

Chang et al reported the overall range of eosinophils/HPF seen on biopsies from patients diagnosed with EG as 4 to 300, with a median count of 82 eos/hpf. This finding was much greater than the minimum level of 20 eos/hpf commonly used as part of the diagnostic criteria.²²

CONCLUSIONS

In present study, 90.9% of normal oesophageal biopsies showed eosinophil count 0/hpf, while 100% of normal stomach biopsies showed eosinophil count <10/hpf. Presence of eosinophils in a biopsy warrants a search for other specific pathological features.

Conflict of interest: None

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