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Cross-Sectional Comparative Study of Frequency of Eosinophilic Esophagitis in Patients with Upper Gastrointestinal Tract Symptoms

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ABSTRACT

Background: *Eosinophilic esophagitis (EoE) is an increasingly recognized chronic immune-mediated inflammatory condition of the esophagus, now considered the second most common cause of chronic esophagitis after gastroesophageal reflux disease (GERD). This cross-sectional pilot study aimed to determine the frequency of EoE among patients presenting with upper gastrointestinal (GIT) symptoms.*

Methods: *this cross-sectional study included 100 adult patients (50 males and 50 females), aged 18 years and above, all participants were subjected to detailed medical history and underwent upper GI endoscopy for upper GIT symptoms. Exclusion criteria encompassed patients using medications that could induce esophagitis, those with collagen vascular diseases, scleroderma, or achalasia. During endoscopy, six biopsy samples were collected from the proximal, mid, and distal esophagus, even if the mucosa appeared normal, along with additional biopsies from the stomach and duodenum to rule out other conditions. Histopathological examination confirmed EoE based on the presence of ≥15 eosinophils per high-power field (HPF). this study was conducted at 6 October University Hospital and Cairo University Hospital.*

Results: *Among the 100 patients evaluated, 5% were diagnosed with EoE based on histopathological findings. Subjects having EoE were significantly older than who weren't (P value <0.001). The prevalence was higher in males (8%) compared to females (2%) (P value 0.362) and more common in smokers (P value 0.156). Heartburn was the most commonly reported symptom, affecting 96% of patients (P value <0.001), followed by dysphagia 50% (P value 0.056) and vomiting 45% (P value 0.655). Food impaction occurred in 25% of cases (P value NA), with all instances associated with EoE. Endoscopic findings indicative of EoE, such as esophageal erosions, rings and linear furrows, were observed in 49%, 8% and 7% of cases, respectively (P value 0.025, 0.003 and 0.002). Notably, no statistically significant association was found between EoE and allergic rhinitis (24%), bronchial asthma (23%), or food allergy (14%), with p-values of 0.830, 0.605, and 0.587, respectively.*

Conclusion*: These findings suggest that EoE may be underdiagnosed among Egyptian patients with upper GIT symptoms, particularly given the potential overlap with GERD and other conditions. Increased awareness and systematic screening could improve diagnostic rates and inform tailored therapeutic strategies. Further large-scale multicenter studies are needed to validate these results and explore the epidemiological and clinical characteristics of EoE in diverse populations.*

Keywords: EoE, Upper GIT Symptoms, Endoscopy, Biopsy.

INTRODUCTION

Eosinophilic esophagitis (EoE) is an increasingly recognized, chronic and antigen/immune-driven inflammatory disease of the esophagus [1].

EoE has now evolved to the second most common cause of chronic esophagitis after gastroesophageal reflux disease, and now represents the most frequent cause of dysphagia in young male patients. It is also recognized as the most common manifestation of all eosinophilic gastrointestinal disorders [1].

EoE is predominantly found in Westernized countries and geographical areas with a higher socioeconomic development and may affect individuals of every race, gender and age [2].

Several epidemiological studies have reported an increasing incidence and prevalence of EoE, however it is still unclear whether this rise is a real phenomenon or caused by increased awareness, i.e. diagnostic bias [2-5].

The prevalence of EoE in Egypt is still largely undetermined due to lack of wide scale studies addressing this disease.

Most studies on EoE have been performed in the western world and certain populations, such as African [2,3,4,6].

Cases from Middle Eastern Region and female gender, may be underdiagnosed because of their presentation with atypical symptoms[1,5,6].

Sampling Method:

Consecutive non-random sample

Sample Size:

Sample size was calculated according to the results of the study of Hunter and collaborators (2014) which showed a prevalence of 3% among Egyptian adult patients presenting with upper gastrointestinal symptoms [5]

- **Estimated total population:** 10000
- **Accuracy:** 0.05
- **95% confidence interval:** 1.96
- **Provisional sample size:** 45 (approximated to 50).
- **Final sample size:** 100 (50 Males and 50 Females).
- Sample size was calculated using EPIDAT software version 4.1.

Ethical Considerations:

This study ethically approved by the Institutional Review Board (IRB) of the Faculty of Medicine, October 6 University, and Cairo University Hospital. Written informed consent obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Study Methods:

A detailed history of upper GIT symptoms obtained from all cases with special emphasis on dysphagia.

A special questionnaire used for all cases addressing all symptoms related to the presenting complaint with special emphasis on dysphagia for which certain form used (The Dysphagia Symptom Questionnaire, version 4.0) [119].

Upper GI endoscopy done for all cases and in cases of grossly identified esophageal lesions suggesting eosinophilic esophagitis the endoscopic classification and grading that used is that proposed and validated by the international expert group [120].

GERD cases classified according to Los Angeles scoring system [121].

Any other endoscopic findings have been reported.

Six biopsies obtained from the proximal, mid and distal esophagus even if appears normal and two additional biopsies obtained from the stomach and duodenum.

All specimens examined histopathologically, and eosinophilic esophagitis diagnosed according to the specified criteria established for diagnosing eosinophilic esophagitis [122].

Regarding the biopsy procedure, six biopsy samples obtained from the mid and distal esophagus, considering the patchy nature of EoE, in addition biopsies obtained from the stomach to rule out eosinophilic gastroenteritis in patients with compatible symptoms and/or endoscopic abnormalities [123].

The presence of eosinophilia is the key factor for a diagnosis of primary EoE, and therefore it is essential to rule out secondary causes of esophageal eosinophilia. EoE can be associated with other inflammatory intestinal diseases, including inflammatory bowel disease, celiac disease, GERD, and extraesophageal eosinophilic gastrointestinal disorders [124].

Aim of the Work

This study aims at determining the frequency of EoE in group of patients, of both genders, presenting with upper GIT symptoms.

Patients and Methods

Type of Study:

Cross-sectional comparative study

Study Setting:

The cases recruited from the Endoscopy Unit in October 6 University and El-Ebrashy Endoscopy Unit in Internal Medicine Department in Cairo University Hospital.

Study Population:

The study was conducted on subjects presenting with upper GIT symptoms for upper GI endoscopy. Our study included equal samples of both genders; 50% Males and 50% Females.

Inclusion Criteria:

Patients above 18 presenting for upper endoscopy because of upper GIT symptoms

Exclusion Criteria:

1. Patients taking drugs that can cause esophagitis (NSAIDS- antibiotics especially tetracycline-iron supplements-biphosphonates- calcium channel blockers-theophyline- any type of inhalers
2. Patients with Collagen vascular disease.
3. Patients with Scleroderma.
4. Patients with achalasia

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Ethical Considerations:

This study ethically approved by the Institutional Review Board (IRB) of the Faculty of Medicine, October 6 University, and Kasr Al-Aini University Hospital. Written informed consent obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

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Statistical Analysis

The collected data introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 23 for windows. Qualitative data was defined as numbers and percentages. Chi-Square test and Fisher's exact test have been used for comparison between categorical variables as appropriate. Quantitative data tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables described as means and standard deviation (SD), and independent sample t-test/Mann-Whitney

test will be used for comparison between groups. P value ≤0.05 was considered to be statistically significant.

Statistical methods:

Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) vs. 27. Numerical data were summarized using means and standard deviations or medians and/or ranges, as appropriate. Categorical data were summarized as numbers and percentages. Estimates of the frequency were done using the numbers and percentages. Numerical data were explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test. Chi square or Fisher's tests were used to compare between the independent groups with respect to categorical data, as appropriate. Comparisons between two groups for normally distributed numeric variables were done using the Student's t-test.

To measure the independent effect of different factors on presence of eosinophilic esophagitis, factors which had significance level less than 0.10 were selected to enter into stepwise logistic regression analysis**.** Logistic regression was done to give adjusted odds ratio and magnitude of the effect of different risk factors in relation to eosinophilic esophagitis. Odds Ratio (OR) and 95% Confidence Interval (95% CI) were done also (95% CI that doesn't contain 1.0 is considered significant). All tests were two tailed & Probability (p-value) ≤ 0.05 is considered significant.

RESULTS

The current study involved 100 cases recruited from the Endoscopy Unit in October 6 University and El-Ebrashy Endoscopy Unit in Internal Medicine Department in Cairo University Hospital. Average age of the patients was 41 years, ranging from (18-60) years. Male to female ratio was 1:1. Greater than half of cases were nonsmokers (59%). The majority of cases have symptoms for more than six months (67%) (Table 1).

Table (1): Demographic characteristics of study participants

	n=100 (%)
Age (Mean ±SD)	41 ±12
Sex	
Female	50 (50)
Male	50 (50)
Smoking	
Yes	41 (41)
No	59 (59)
Duration of symptoms	
< 6 months	33 (33)
≥ 6 months	67 (67)

SD: Standard deviation

Table (2) shows that, the majority of patients have heart burn (96%). Half of patients suffer from dysphagia (50%). Near half of patients suffer from vomiting (45%). Only one quarter of patients complain of food impaction (25%) (figure 2).

Table (2): Patients symptoms

	n=100 (%)
Heartburn	
Yes	96 (96)
No	4 (4)
Dysphagia	
Yes	50 (50)
No	50 (50)
Vomiting	

Yes	45 (45)
No	55 (55)
Food impaction	
Yes	25 (25)
No	75 (75)

Table (3) shows that, near quarter of patients suffer from allergic rhinitis & bronchial asthma (24%& 23%) respectively. Only (14%) of patients suffer from food allergy.

Table (3): Associated illness

	n=100 (%)
Allergic rhinitis	
Yes	24 (24)
No	76 (76)
Bronchial asthma	
Yes	23 (23)
No	77 (77)
Food allergy	
Yes	14 (14)
No	86 (86)

Table (4) representing endoscopic finding of the patients. Near half of patients have erosions (49%). Rings and linear furrows present in (8%&7%) respectively.

Table (4): Endoscopic finding

	n=100 (%)
Erosions	
Yes	49 (49)
No	51 (51)
Rings	
Yes	8 (8)
No	92 (92)
Linear furrows	
Yes	7 (7)
No	93 (93)

Table (5) shows that, 5% of cases have eosinophilic esophagitis.

Table (5): Histologic finding

	n=100 (%)
Eosinophilic esophagitis	
Yes	5 (5)
No	95 (95)
	Median (range)
Stomach	3 (0-25)
Duodenum	10 (2-25)
Lower esophagus	5 (0-27)
Middle esophagus	0 (0-22)

Upper esophagus	0 (0-19)

Table (6) shows that patients having eosinophilic esophagitis were significantly older than patients not complaining from eosinophilic esophagitis (p value <0.001). Meanwhile, there, there was statistically significant difference in prevalence of eosinophilic esophagitis in relation to gender and smoking status (p value 0.362&0.156 respectively).

Table (6): Demographic characteristics of patients with and without eosinophilic esophagitis

	Eosinophilic esophagitis		**P value**
	Yes	**No**	
	n=5 (%)*	**n=95 (%)***	
Age (Mean ± SD)	57 ±5	40 ±12	<0.001
Gender			
Male	4 (8)	46 (92)	0.362
Female	1 (2)	49 (98)	
Smoking			
Yes	4 (9.8)	37 (90.2)	0.156
No	1 (1.7)	58 (98.3)	
Duration of symptoms			
< 6 months	0 (0)	33 (100)	0.168
> 6 months	5 (7.5)	62 (92.5)	

*Percentages were calculated within rows, P value <0.05 is considered significant

Table (7) shows that, the only symptom associated with eosinophilic esophagitis is heartburn, 20% of patients complaining of heartburn has eosinophilic esophagitis.

Table (7): Symptoms of patients with and without eosinophilic esophagitis

	Eosinophilic esophagitis		**P value**
	Yes	**No**	
	n= 5 (%)*	**n=95 (%)***	
Dysphagia			
Yes	5 (10)	45 (90)	0.056
No	0 (0)	50 (100)	
Food impaction			
Yes	5 (5.2)	91 (94.8)	NA
No	0 (0)	4 (100)	
Vomiting			
Yes	3 (6.7)	42 (93.3)	0.655
No	2 (3.6)	53 (96.4)	
Heartburn			
Yes	5 (20)	20 (80)	<0.001
No	0 (0)	75 (100)	

*Percentages were calculated within rows, P value <0.05 is considered significant, NA: Not applicable

As shown in table (8), there is no statistically significant difference in presence of eosinophilic esophagitis in relation to (allergic rhinitis, food allergy and bronchial asthma).

Table (8): Associated illness in relation to eosinophilic esophagitis:

	Eosinophilic esophagitis		P value
	Yes	No	
	n=5 (%)*	n=95 (%)	
Allergic rhinitis			
Yes	1 (4.2)	23 (95.8)	0.830
No	4 (5.3)	72 (94.7)	
Food allergy			
Yes	0 (0)	14 (100)	0.605
No	5 (5.8)	81 (94.2)	
Bronchial asthma			
Yes	0 (0)	23 (100)	0.587
No	5 (6.5)	72 (93.5)	

Percentages were calculated within rows, P value <0.05 is considered significant

Table (9) shows that, presence of erosion, rings and linear furrows are significantly associated with eosinophilic esophagitis (P value 0.025, 0.003&0.002 respectively).

Table (9): Relation of endoscopic finding to eosinophilic esophagitis

	Eosinophilic esophagitis		P value
	Yes	No	
	n=5 (%)*	n=95 (%)	
Erosions			
Yes	5 (10.2)	44 (89.8)	0.025
No	0 (0)	51 (100)	
Rings			
Yes	3 (37.5)	5 (62.5)	0.003
No	2 (2.2)	90 (97.8)	
Linear furrows			
Yes	3 (42.9)	4 (57.1)	0.002
No	2 (2.2)	91 (97.8)	

Percentages were calculated within rows, P value <0.05 is considered significant

Multivariate analysis

To measure the independent effect of all factors that affect the presence of eosinophilic esophagitis, factors which had significant level less than 0.100 were selected to enter into stepwise logistic regression.

Table (10): Shows the variables which were significant in the stepwise logistic regression

Variables	B	SE	OR	95.0% CI for OR	P value
Rings	2.5	1.2	12.6	1.2-126.9	0.032
Linear furrows	2.8	1.2	16.4	1.6-167.8	0.018

B: regression coefficient, SE: standard error, OR; odds ratio, CI: confidence interval, p value <0.05 is considered significant

The regression coefficient shows the effect of each variable after controlling the effect of other variables in the model. The model shows that the most important factors that predict the presence of eosinophilic esophagitis are the presence of rings and linear furrows. Patients have rings by endoscopy are 12.6 times

more likely to have eosinophilic esophagitis and patients have linear furrows are 16.4 times more likely to have eosinophilic esophagitis.

DISCUSSION

Demographic Characteristics

Our study, which involved 100 participants, had an average age of 41 years, with a male-to-female ratio of 1:1. Greater than half of the participants were non-smokers (59%), and most reported symptoms persisting for more than six months (67%). These demographic details are consistent with a previous study indicating that EoE often presents in middle-aged adults and is more prevalent in males [125].

The high proportion of chronic symptomatology (>6 months) aligns with the chronic nature of EoE, as highlighted by a previous study, which noted that delayed diagnosis increases the risk of complications such as strictures [126].

Symptoms and Their Association with EoE

Our study show that Heartburn was the most prevalent symptom (96%) ($p < 0.001$), followed by dysphagia (50%), vomiting (45%), and food impaction (25%). This high prevalence of heartburn underscores its overlap with GERD which can mimic or coexist with EoE. This finding is supported by a study, which emphasize heart burn and food impaction as a hallmark symptoms of EoE due to structural changes like strictures or rings [125].

Dysphagia showed a trend toward significance ($p = 0.056$), these results supported by a prior study in Egypt [126] and corroborated by a previous study, showing dysphagia as a key indicator of EoE [42].

Associated Illnesses

Allergic rhinitis and bronchial asthma were reported in 24% and 23% of patients, respectively, while food allergies were reported in only 14%. Although these conditions are known risk factors for EoE, this study did not find significant associations between them and EoE. This lack of correlation could be attributed to the small sample size of EoE cases (n = 5), these results supported by other two studies conducted in Egypt[127,128]. And conclusion is highlighted by a study showing the strong association between EoE and atopic diseases, suggesting that larger studies may reveal statistically significant relationships.[129] Additionally, the lower prevalence of food allergies in the current study contrasts with findings by a prior study, which demonstrated that dietary triggers play a critical role in EoE pathogenesis [130].

Endoscopic Findings

Endoscopic evaluation revealed erosions in 49% of patients, while rings and linear furrows were observed in 8% and 7%, respectively. Multivariate analysis identified rings and linear furrows as independent predictors of EoE, with odds ratios of 12.6 and 16.4, respectively. These findings are consistent with a study that describes these features as characteristic markers of EoE. [26], Erosions, while significantly associated with EoE ($p = 0.025$), were less predictive, likely due to their non-specificity and overlap with GERD-related changes. The absence of other abnormalities, such as strictures, may reflect the relatively early stage of disease in the current study [126].

Role of Age in EoE Diagnosis

Patients diagnosed with EoE were significantly older (mean age: 57 years vs. 40 years; $p < 0.001$) than those without the condition. This finding aligns with a study that reported an increasing prevalence of EoE with age.[131] Older age may reflect delayed diagnosis or prolonged exposure to environmental triggers, as suggested by a prior study [132]. The differences in gender and smoking status suggests that these factors may influence EoE development in this population, consistent with prior studies [125].

Histologic Confirmation of EoE

Only 5% of our study was diagnosed with EoE based on histological examination. While this prevalence appears low compared to international studies, it reflects the localized epidemiology and potential underdiagnosis of EoE in this Egypt and these results supported by two studies in Egypt with prevalence of 4% EoE[133].

Another study emphasizes the importance of biopsy and histological confirmation in distinguishing EoE from GERD, particularly in populations with overlapping symptoms.[134] The small number of confirmed cases highlights the need for increased awareness and targeted diagnostic strategies.

Remarks regarding the current study:

Small sample size: with only five confirmed EoE cases, the statistical power to detect meaningful associations is constrained.

Single center recruitment: conducting the study at two centers within the same geographic area limits generalizability

Clinical Implications and Future Directions

These findings highlight the importance of considering EoE in patients presenting with heartburn, chronic dysphagia and food impaction, particularly when endoscopic findings include rings and linear furrows. Early recognition and diagnosis can prevent complications such as strictures and improve long-term outcomes. Future research should aim to:

- Expand the sample size and include multicenter participation to enhance statistical robustness.
- Incorporate longitudinal follow-up to assess disease progression and response to therapy.
- Explore genetic and environmental factors contributing to EoE in diverse populations.
- Investigate the role of dietary interventions and emerging therapies in managing EoE.

CONCLUSION

In summary, this study provides valuable insights into the clinical profile and predictors of eosinophilic esophagitis in a cross-sectional study of Egyptian patients. Heartburn and dysphagia, along with endoscopic findings of rings and linear furrows, emerged as key indicators of EoE. These results highlight the need for heightened awareness among clinicians and underscore the importance of targeted diagnostic strategies to optimize patient care.

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