

# PREVALENCE OF ESINOPHILIC ESOPHAGITIS AMONG ATOPIC EGYPTIAN POPULATION

By

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## ABSTRACT

**Background:** Eosinophilic esophagitis (EoE) is an atopic inflammatory disease of the esophagus that has become increasingly recognized in children and adults during the last decade. EoE is an atopic inflammatory disease of the esophagus that has become increasingly. Eosinophils are typically present throughout the gastrointestinal tract since it is continuously exposed to foods, environmental allergens, toxins, and pathogens.

**Objective:** To evaluate the prevalence of eosinophilic esophagitis in atopic patients.

**Patients and Methods:** This was a retrospective single center non randomized, observational study, 120 patients with age ranged from 18-60 years were recruited for this study. They were evaluated for esophageal symptoms using the frequency scale for the symptoms of gastro-esophageal reflux disease (GERD). It was conducted at Dermatology, Ear, Nose, and Throat (ENT), Ophthalmology and allergy clinic of Internal Medicine Departments, Al-Husein University Hospital. The study was done during the periods between July 2017 and September 2018.

**Results:** The mean total immunoglobulin E (IgE) of group II was higher than group I with significant statistical difference between both groups. As regards the mean blood eosinophils of group II was higher than group I with significant statistical difference between both groups. Heartburn documented the higher presentations (83%), followed by regurgitation (58.5%), and a combination of other symptoms in patients. Only 6 cases out of 53 examined, endoscopic biopsies have histological features of EoE. The remaining 47 biopsies featured different histological diagnosis which included mild reflux esophagitis in 12 cases, moderate reflux esophagitis in 20 cases, and severe reflux esophagitis in 15 cases.

**Conclusion:** Atopic patients who suffered from esophagitis symptoms were assessed for EoE by endoscopic and histopathological examination especially if there was a high IgE level or increased blood eosinophils.

**Keywords:** Eosinophilic, Atopic Egyptian, Eosinophylic esophagitis.

## INTRODUCTION

Although the typical onset of eosinophilic esophagitis (EoE) in childhood, the disease can be found in all age groups, and the symptoms tend to vary depending on the age of presentation. EOE is defined as clinic-pathologic

disorder characterized by presence of  $> 15$  eosinophils per high power field (HPF) in one or more esophageal biopsy specimens (*Furuta et al., 2011*).

The prevalence of the eosinophylic esophagitis is increasing among Caucasian, Asian and other ethnicities

during the last years (*Syed et al.*, 2012). Actually, it is not clear whether EOE is truly increasing or, if it is becoming more recognized by endoscopist and pathologists (*Prasad et al.*, 2011). Some authors attribute this increase in prevalence rate of esinophilic esophagitis to parallel increases in atopic diseases, and they assume that there is an overlapping spectrum between GORD, allergy and esinophilic esophagitis (*Sealock et al.*, 2010).

Another referred this increase to parallel increasing in routine oesophageal biopsy rates (*Syed et al.*, 2012). Until recently, there are no published reports in literature about the prevalence of eosinophylic esophagitis in Egyptian population.

**The aim of this study was to** evaluate the prevalence of esinophilic esophagitis in atopic patients.

#### PATIENTS AND METHODS

A retrospective single center non randomized, observational study, 120 patients with age ranged from 18-60 years were recruited for this study. They were evaluated for esophageal symptoms using the frequency scale for the symptoms of GERD. It was conducted at Dermatology, ENT, Ophthalmology and Allergy Clinic of Internal Medicine Department, Al-Husein University Hospital. The study was done during the periods between July 2017 and September 2018.

**Inclusion criteria:** Any patients with any type of atopy (Atopic rhinitis 20 patients, atopic eczema 20 patients, atopic conjunctivitis 20 patients, atopic asthma 60 patients) with history of dysphagia,

food impaction and/or history suggestive GORD included in this study.

**Exclusion criteria:** Patients refusing to be enrolled in this study and patients with acute severe asthma.

**The study was divided into two groups:**

**Group (1)** included atopic patients without esophageal symptoms (67), and **Group (2)** included atopic patients with esophageal symptoms (53). An informed written consent was signed by each patient after explaining the purpose and the methods of the study then approved by the local ethics committee.

The selected atopic patients who had one or more of the esophageal symptoms such as reflux (heartburn or regurgitation) or symptoms of esophageal complications (dysphagia or history food impaction) (*Cherian et al.*, 2010) underwent clinical assessment. They were subjected to upper GIT endoscopy under conscious sedation (by Midazolam 5–8 mg intravenously) after written consent for the sedation and the procedure for endoscopic assessment mainly for esophagus with biopsies (*Ndraha, 2010*). Endoscopic assessment of esophageal mucosa and cardia was done for presence of the GERD by presence of mucosal damage as the lower segment erosive esophagitis, esophageal ulcers, benign stenosis, and presence of sliding hiatal hernia with or without gastric contents refluxate. Endoscopic picture of the EoE such as esophageal circular rings (trachization), or whitish plaque were also evaluated (*Rosner and Milton, 2010*). All patients were subjected to multiple esophageal mucosal biopsies (at least four esophageal mucosal biopsies were taken for each patient) for

histopathological examination (*Rawy and Mansour, 2015*).

This study involved 53 cases of esophageal biopsies. The specimens were received from two separate sites in the esophagus mainly proximal and middle with occasional lower esophageal part biopsy. From each paraffin-embedded block, two sections (3–4  $\mu\text{m}$  each) were prepared for routine hematoxylin and eosin stain. All histological staining was performed in accordance with conventional procedures (*Monjur, 2016*). Sections stained by hematoxylin and eosin were examined to detect the number of eosinophils in the esophageal mucosa, abscess formation, associated dysplasia, or reflux esophagitis; all cases having less than 15 eosinophils/HPF were excluded.

The presence of intraepithelial eosinophils, at least 15/HPF in any one field, is considered diagnostic for EoE, while the presence of 6–14/HPF was considered indeterminate; eosinophils may be diffuse or in clusters and may form micro-abscess. The eosinophils should present only in the esophagus and the presence of eosinophils in other parts of the intestine suggest eosinophilic

gastroenteritis (*Asher and Dellon, 2014*). Other less specific histological features that have occurred with EoE included intercellular edema, eosinophilic degranulation, marked basal cell hyperplasia, and fibrosis of the lamina propria if the biopsy contained subepithelial layers. Histopathologic features without clinical correlation cannot diagnose EoE (*Trevisani et al., 2010*).

#### **Statistical Analysis:**

Data were collected, revised, coded and entered to the Statistical Package for the Social Science (IBM SPSS) version 20. The qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges. The comparison between two groups with qualitative data were done by using Chi-square test. The comparison between the two independent groups with quantitative data and parametric distribution were done by using independent t-test or Mann – Whitney U test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. P value < 0.05 was considered significant.

## RESULTS

This study included 120 patients diagnosed with atopy. The mean age was  $52.80 \pm 10.78$ . The study included 52 men and 68 women. Patients were reviewed for GERD symptoms and 53 cases documented one or more positive GERD symptoms. Accordingly, the patients were divided into two groups: group I (67) included atopic patients without GERD

symptoms and group II (53 asthmatic patients with GERD symptoms. The mean age of group II was higher than group I with no significant statistical differences between both groups. As regards sex results, it was found that females of group I was higher than group II with no significant statistical differences between both groups (**Table 1**).

**Table (1): Distribution of the studied cases according to demographic data and demographic results of both groups**

| Parameters |               | Groups | Group I           | Group II          | P-value |
|------------|---------------|--------|-------------------|-------------------|---------|
|            |               |        | No.= 67           | No.= 53           |         |
| Sex        | Female        |        | 39 (58.2%)        | 29 (54.7%)        | 0.701   |
|            | Male          |        | 28 (41.8%)        | 24 (45.3%)        |         |
| Age        | Mean $\pm$ SD |        | $52.44 \pm 10.97$ | $53.26 \pm 10.61$ | 0.679   |
|            | Range         |        | 30 – 75           | 30 – 75           |         |

The Median Total IgE of group II was higher than group I with highly significant statistical differences between both groups. The Median blood esinophils of

group II was higher than group I with significant statistical differences between both groups (**Table 2**).

**Table (2): Comparison between the results of both groups regarding spirometer**

| Parameters       |               | Groups | Group I             | Group II           | P-value |
|------------------|---------------|--------|---------------------|--------------------|---------|
|                  |               |        | No.= 67             | No.= 53            |         |
| Total IgE        | Mean $\pm$ SD |        | $102.43 \pm 105.10$ | $147.15 \pm 41.20$ | 0.001   |
|                  | Range         |        | 24 – 898            | 84 – 190           |         |
| Blood esinophils | Mean $\pm$ SD |        | $10.39 \pm 5.03$    | $17.08 \pm 5.52$   | 0.001   |
|                  | Range         |        | 3 – 29              | 8 – 29             |         |

**Group I:** atopic patients without GERD symptoms.

**Group II:** atopic patients with GERD symptoms.

The number and percentage of different symptoms and signs for all patients. Heartburn documented the higher presentations (83%) followed by regurgitation (58.5%) and a combination of other symptoms in patients. The endoscopic findings, normal esophageal picture in 6 cases, erosive esophagitis different grades in 48 cases, esophageal stenosis in one case, esophageal rings in 6 cases, longitudinal furrows in 5 cases, and

white plaques in 20 cases. Other endoscopic findings showed 7 cases with hiatal hernia, 1 case with antral gastritis, 1 case with pangastritis, 2 cases with gastric ulcer, and 2 cases with biliary reflux. Duodenitis was found in 1 case without any duodenal ulcers. Positive campylobacterlike organism (CLO) test was found in 7 cases for H.pylori screening (Table 3).

**Table (3): Distribution of the studied cases according symptoms, signs and endoscopic findings for all patients**

| Symptoms                                | No.                       | %     |       |
|---|---------------------------|-------|-------|
| Heart burn                              | 44                        | 83.0% |       |
| Regurgitation                           | 31                        | 58.5% |       |
| Dysphagia                               | 11                        | 20.8% |       |
| Heartburn and regurgitation             | 23                        | 43.4% |       |
| Heartburn and dysphagia                 | 4                         | 7.5%  |       |
| Heartburn, regurgitation, and dysphagia | 4                         | 7.5%  |       |
| Esinophilia                             | Positive for eosinophilia | 47    | 88.7% |
|   | Negative for eosinophilia | 6     | 11.3% |
| Normal esophagus                        | 6                         | 11.3% |       |
| Erosive esophagitis (grade la-a)        | 36                        | 67.9% |       |
| Erosive esophagitis (grade la-b)        | 8                         | 15.1% |       |
| Erosive esophagitis (grade la-c)        | 4                         | 7.5%  |       |
| Esophageal stenosis                     | 1                         | 1.9%  |       |
| Hiatus henia                            | 7                         | 13.2% |       |
| Esophageal rings                        | 6                         | 11.3% |       |
| Longitudinal furrow                     | 5                         | 9.4%  |       |
| Antral gastritis                        | 20                        | 37.7% |       |
| White plaque                            | 1                         | 1.9%  |       |
| Pangastritis                            | 1                         | 1.9%  |       |
| Biliary reflux                          | 2                         | 3.8%  |       |
| Gastric ulcer                           | 4                         | 7.5%  |       |
| Duodenitis                              | 1                         | 1.9%  |       |
| Duodenal ulcers                         | 0                         | 0.0%  |       |
| Positive CLO test                       | 7                         | 13.2% |       |
| Negative CLO test                       | 46                        | 86.8% |       |

Only 6 cases out of 53 examined endoscopic biopsies have histological features of EoE. The remaining 47 biopsies feature different histological

diagnosis included mild reflux esophagitis in 12 cases, moderate reflux esophagitis in 20 cases, and severe reflux esophagitis in 15 cases (**Table 4**).

**Table (4): Distribution of the studied cases according to lesion (histopathological diagnosis)**

| Lesion                      | No. | %     |
|-----------------------------|-----|-------|
| Eosinophilic esophagitis    | 6   | 11.3% |
| Mild reflux esophagitis     | 12  | 22.6% |
| Moderate reflux esophagitis | 20  | 37.7% |
| Severe reflux esophagitis   | 15  | 28.3% |

## DISCUSSION

Eosinophilic esophagitis (EoE) is sometimes referred to as “asthma of the esophagus” given that it shares many clinical and pathophysiologic characteristics with asthma (*Dellon, 2014*). It is defined as a clinicopathologic disorder characterized by  $\geq 15$  eosinophils per high power field (HPF) in one or more esophageal biopsy specimens and the absence of pathologic gastrointestinal reflux disease (GERD) (as evidenced by a normal pH monitoring study or lack of response to adequate acid-suppression therapy) (*Dellon, 2011*).

The aim of this study was to evaluate the prevalence of eosinophilic esophagitis in atopic patients. This study was carried out on Egyptian asthmatic patients with esophageal symptoms. It included 120 atopic patients. From those patients, only 53 patients had esophageal symptoms (heartburn, regurgitation, or dysphagia). Upper GIT endoscopy was done to all 53 cases and the findings were recorded. Esophageal biopsy was taken from all cases and examined histopathologically for EoE.

**The study was divided into two groups:** Group (A) included atopic patients

without esophageal symptoms (67 cases) and group (B) that included atopic patients with esophageal symptoms (53 cases). In the current study, asthma as a main atopic respiratory disease was chosen and studied to assess the frequency and incidence of EoE in asthmatic patients. The results showed that about 11% of asthmatic patients who suffered from GERD symptoms had associated EoE confirmed by esophageal biopsy and histologic findings. The incidence of EoE increased in atopic asthmatic patients who had high IgE and this observation was matched with that of Mulder *et al.* (2012). Bronchial asthma is usually associated with esophageal symptoms specially GERD and is considered one of the extraesophageal syndromes of GERD (*Carr et al., 2018*).

Our results showed an increase in the prevalence of EoE in men than women (60% men versus 40% women) which was in agreement with *Veerappan et al. (2012)* who reported that EoE is more prevalent in men than women younger than 50 years. Another study found that the male:female ratio was 4:1. Also, in this study, the most common presenting symptoms of EoE are heartburn, regurgitation, and dysphagia presenting more than 50% of

cases (75, 52, 18%, respectively). These results were similar to previous studies which reported that dysphagia was present in 64.0 and 89% of EoE patient (Veerappan *et al.*, 2012). Endoscopic features of EoE may include mucosal edema, concentric rings, longitudinal furrows, strictures, white exudates or plaques, and pallor or decreased vasculature. One study of histologically confirmed EoE by Sgouros *et al.* (2010) reported that 8.8% of patients had no detectable endoscopic findings of EoE. Mackenzie *et al.* (2012) found that 42% EoE patients did not have typical findings on endoscopy and might have been missed unless biopsies were taken.

In the current study, four esophageal mucosal biopsies were taken from each case and this was matched with Nielsen *et al.* (2014) who document that the recommended least number of biopsies to establish the morphologic diagnosis of EoE are four biopsies and more. The prevalence of EoE in cohort study was 6.5% which is markedly higher than that of an asymptomatic Swedish community by Ronkainen *et al.* (2010) study. The prevalence in patients with dysphagia (10%) was similar to the prevalence described in other dysphagia populations (10%–15%) in Prasad *et al.* (2010) study. The significance of the population studied cannot be overstated because these are the patients whom gastroenterologists evaluate daily.

Another prospective study by Prasad *et al.* (2010) studied dysphagia patients, identified age, food impaction greater than 5 minutes, endoscopic features of EoE, and use of PPI for GERD as independent risk factors. In previous reports, the

prevalence of gastroesophageal reflux disease among asthmatics was reported to be about 30–80% in Balson *et al.* (2010) and Vincent *et al.* (2010) studies, which were much higher than that of general population of 10–17%.

According to the traditional concept, gastroesophageal reflux can cause airway hypersensitivity by direct effect of acid and indirect effect of neural reflex, and also asthma itself can worsen the reflux through intrathoracic negative pressure made by cough and drug-induced lowering of lower esophageal sphincter pressure.

## CONCLUSION

Atopic patients who suffered from esophagitis symptoms should be assessed for EoE by endoscopic and histopathological examination especially if there was a high IgE level or increased blood eosinophils.

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## معدل إنتشار إتهاب المريء الإزینوفیلی فی مرض التحسس بین المرضی المصریین

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**خلفية البحث:** إتهاب المريء العصبي هو مرض إتهاب المريء التأتبي الذي أصبح يتزايد بشكل متزايد. عادة ما توجد الحمضات في جميع أنحاء الجهاز الهضمي لأنها تتعرض باستمرار للأطعمة والمواد المسببة للحساسية البيئية والسموم ومسببات الأمراض.

**الهدف من البحث:** تقييم مدى إنتشار إتهاب المريء الازینوفیلی لدى مرضی التأتبي.

**المرضى وطرق البحث:** شملت هذه الدراسة 120 مریضا بالربو تتراوح أعمارهم بین 18-60 عامًا لهذه الدراسة بأثر رجعي غير معشاة، دراسة قائمة على الملاحظة لمركز واحد بأثر رجعي. وتم تقييمهم لأعراض المريء باستخدام مقياس التردد لأعراض مرض الجزر المعدي المريئي (جيرد). وقد تم إجراؤه في عيادة الأمراض الجلدية والأذن والأنف والحنجرة وطب العيون والحساسية بقسم الطب الباطني بمستشفى الحسين الجامعي خلال الفترة ما بین يوليو 2017 وسبتمبر 2018.

**نتائج البحث:** كان متوسط الهيموجلوبين المناعي الكلي للمجموعة الثانية أعلى من المجموعة الأولى مع وجود فروق ذات دلالة إحصائية بین المجموعتين. وفيما يتعلق بمتوسط عدد كريات الدم من المجموعة الثانية أعلى من المجموعة الأولى مع وجود فروق ذات دلالة إحصائية بین المجموعتين. توثق الحموضة المعوية أعلى الأعراض (83%) يليها قلنس (58.5%) ومجموعة من الأعراض الأخرى لدى المرضى. فقط 6 حالات من أصل 53 خزعة بالمنظار تم فحصها لها سمات نسيجية لإتهاب المريء اليوزيني، والـ 47 خزعة المتبقية تتميز بتشخيص نسيجي مختلف شمل إتهاب المريء الارتجاعي الخفيف في 12 حالة، وإتهاب

المريء الارتجاعي المعتدل في 20 حالة، وإلتهاب المريء الارتجاعي الشديد في 15 حالة.

**الاستنتاج:** مرضى الحساسية الذين عانوا من أعراض التهاب المريء يجب تقييمهم من أجل التهاب المريء الازينوفايلى عن طريق الفحص بالمنظار والفحص التشريحي المرضي خاصة إذا كان هناك إرتفاعاً في مستوى الهيموجلوبين المناعي أو زيادة الحمضات في الدم.

**الكلمات الدالة:** إلهاب المريء العصبي، التأتبي المصري، إلهاب المريء الازينوفايلى.