

# Effect of Peripheral Eosinophilia and Total Immunoglobulin E Levels on Severity of Chronic Rhinosinusitis

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**Objectives:** The aim of this work to measure if peripheral eosinophilia and total immunoglobulin E "IgE" levels correlate with the severity of chronic rhinosinusitis (CRS) proved by computed tomography (CT) scans of paranasal sinuses.

Study Design : Retrospective study from 30 patients with chronic rhinosinusitis (CRS).

**Methods:** CT scans were performed for all patients with CRS and peripheral eosinophilia and total IgE levels were measured. The relationship between peripheral eosinophilia and total IgE levels regarding their effect on severity of CRS.

**Results:** There was a significant positive correlation between peripheral eosinophilia and severity CRS. The total IgE levels did not correlate with the severity and mucosal disease of CRS.

**Conclusion:** Peripheral eosinophilia in patients with CRS indicates the severity and degree of mucosal affection guided by CT scans. In contrast, total IgE levels did not correlate with the severity of CRS and C.T scans findings.

**Keywords:** Eosinophilia, Immunoglobulin E "IgE", chronic rhinosinusitis.

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## Introduction

Chronic rhinosinusitis (CRS) is one of the most common health problems, and even with the recent advances, the aetiology, pathogenesis and treatment of CRS is a matter of debate. [1] It is a clinical syndrome associated with persistent inflammation of the mucosa of the nose and paranasal sinuses for 12 weeks or longer. [2] The management of CRS or recurrent rhinosinusitis problems has many aspects and should include consideration of medical and anatomic factors. The relationship between allergy and rhinosinusitis has not been clearly well known. [3]

Diagnosis of CRS depends on the signs, symptoms and objective evidence of mucosal inflammation detected by nasal endoscopy and/or computerized tomography of paranasal sinuses. [4] It is also important to recognize that this is a heterogeneous disease spectrum which is subjected to further subclassifications. [5]

The pathogenesis of CRS remains ill defined and seems to be multifactorial. Altered eosinophil function and IgE - mediated disease processes are two factors that have been implicated in the pathogenesis of CRS. [6]

The eosinophil comprises about 2% to 5% of granulocytes in an individual without allergies. Activated eosinophils have been found to play a role in allergy, asthma, parasitic diseases, granulomatous diseases, fibrotic conditions, and several malignant tumors. Tissue eosinophilia in the upper and lower airway mucosa seems to have an important role in the development of CRS and asthma. [7] Eosinophils contain and release many toxic proinflammatory mediators, as major basic protein, eosinophil cationic protein, lipid mediators and cytokines. Activation of eosinophils and lymphocytes causes inflammation of the sinus mucosa and cause thickening of

the mucosal lining of the sinuses. The thickened mucosa can be detected by a computed tomography (CT) scans. [8]

Eosinophilic chronic hyperplastic rhinosinusitis represents a subtype of CRS that has been related to tissue eosinophilia. [9] The release of many proinflammatory mediators from the activated eosinophils may contribute to mucosal inflammation, edema and tissue injury. This tissue response may lead to secondary bacterial infection with the development of chronic mucosal hyperplasia and airway obstruction. The relationship between IgE - mediated hypersensitivity and CRS remains ill-defined. However, many authors suggest a clinical association between allergic upper airway disease and CRS, the exact mechanism of how allergy predispose to CRS or affect the prognosis of CRS is unclear. [10]

Many inflammatory cells as eosinophils, mast cells and T-lymphocytes play the main role in both allergic rhinitis and CRS. The aim of this study was to assess the relationship between peripheral eosinophilia, total IgE levels, and the severity of CRS which was detected by the presence of mucosal disease on sinus CT imaging. The method of measuring differential leukocyte count (DLC) is simple and noninvasive technique for evaluation of amount of eosinophils and so the severity of CRS.

## Patients and Methods

This study was carried out in October 6 University Hospital and Microbiology & Immunology Department in Ain-Shams University on 30 patients (20 men and 10 women), from April 2015 to October 2017. Written informed consent from all patient was obtained. The study protocol was accepted by the local ethical committee.

All patients were older than 20 years of age and CT scans

were performed for all patients using bone window thin cuts 3mm thickness, axial and coronal cuts, without contrast. All patients in the study were examined by nasal endoscopy and received medical treatment for one month before radiological evaluation in the form of local steroids, mucolytics and nasal decongestant.

Peripheral eosinophil levels and total IgE levels were measured. The scans were graded using the Lund-Mackey scoring system. This system grades each paranasal sinus (maxillary, frontal sphenoid, anterior ethmoids, and posterior ethmoids) as follow:

0, no abnormality; 1, partial opacification; and 2, total opacification. The osteomeatal complex is scored as 0 when there is no opacification and 2 when it is obstructed. The total score possible with this system ranges from 0 to 24. A score higher than 12 is abnormal.

The total serum IgE levels (IU/ml) were measured using an enzyme-linked immunosorbent assay and DLC was measured for each patient for the percentage of peripheral eosinophils greater than 4% were considered abnormal.

Linear regression analysis (using Sigma Plot software Systat Software Inc, San Jose, California) was used to measure the statistical significance. The correlation coefficient,  $r$ , represents the degree to which the two variables correlate:  $r > 0.5$  means a strong correlation;  $r = 0$  means no correlation, and  $r < 0$  means negative correlation.

It was considered that IgE level greater than 100 IU/ml and an eosinophil count higher than 550 cells / $\mu$ L to be abnormal values for these two tests. Therefore, for purpose of calculating positive and negative data, we used the following cut off points: for IgE, 100 IU/ $\mu$ L; for eosinophilia 550 cells/ $\mu$ L; and for CT scans a Lund-Mackey score of 12.

## Results

The mean CT score was 18.8. The mean total IgE level was 186.4 IU/ml with 56.8% of abnormal IgE associated with an abnormal CT score. Nevertheless, the total IgE did not correlate with CT stage of the disease ( $r=0.18$ ,  $P=0.3$ ).

The mean percentage of peripheral eosinophils was 9%. There was a significant positive correlation between CT stage and peripheral eosinophil levels ( $r=0.5$ ,  $P=0.04$ ).

## Discussion

Chronic rhinosinusitis is a disease that affect millions of people every year and trials to establish a clear etiology, pathophysiology and management have frustrated clinicians. [12] The definition of CRS is based on the presence of specific symptoms for at least 12 weeks and does not include objective criteria such as nasal endoscopic findings and computed tomographic "CT" appearance. [13] These symptoms are not disease – specific and may be the result of many subtypes of CRS. Rhinosinusitis symptoms result when the disease affect the viscosity of mucous secretion, mucociliary clearance and ostial patency which is the most important in pathogenesis of CRS. [14]

Recent researchers have concentrated on the eosinophil as the characteristic and predominant cell in CRS. Histopathologic studies of the sinus mucosa of adult patients with CRS showed eosinophilic tissue infiltration in addition to elevated levels of interleukin 5, granulocyte and macrophage colony stimulating factor, and interleukin 3, all of them support the idea of eosinophilic inflammation. [7]

Harlin et al [15] revealed the infiltration of sinus mucosa by

eosinophils in patients with CRS. Eosinophilia was significantly higher in CRS associated with allergic rhinitis or asthma than in CRS as the only manifestation. Bryson et al [16] proved that the amount of eosinophils in diseased tissue from patients with CRS with or without polyps was significantly greater than in nasal mucosa of control group. Newman et al [8] proved the strong relationship between the severity of chronic rhinosinusitis and peripheral eosinophilia. He found in 39% of patients with severe CRS who undergoing functional endoscopic sinus surgery were correlated with the presence of peripheral eosinophilia. Sixty-five percent of patient with extensive mucosal disease and severe CRS had eosinophilia in contrast to only 7% of those with CRS with score lower than 12.

Zadeh et al [17] showed that patients with higher serum eosinophilia had history of allergic fungal sinusitis, asthma and nasal polyps. They also mentioned a significant correlation between eosinophilia and recurrent infection after surgery and higher incidence of revision surgery. Kountakis et al [9] reported a significant correlation between peripheral eosinophilia and nasal polyps, asthma and severity of CRS. They also demonstrated the association between sinus tissue eosinophilia and the clinical condition of these patients. They found increased sinus mucosal eosinophilia to be accompanied by a higher incidence of asthma and severe CRS with higher CT scores. These data confirm the important of the eosinophils in the pathogenesis of CRS.

Our study measured the relationship between peripheral eosinophilia and severity of CRS proved by CT imaging of these patients. Eighty-two percent of our patients showed elevated peripheral eosinophilia had abnormal CT findings. The blood eosinophil count increased with severity of mucosal disease in CRS this means a strong relationship between the severity of CRS and peripheral eosinophilia, and simply this an easy test can be used as a marker for measurement of the disease severity. Our study did not show a correlation between serum total IgE levels and severity of CRS guided by CT imaging. Emanuel and Shah [3] studied allergy testing in 200 patients with CRS who had undergone functional endoscopic sinus surgery. Eighty-four percent of these patients were positive for allergies and 60% of all patients had positive allergic sensitivity, and 52% had multiple allergen sensitivities. Gutman et al [10] demonstrated similar results in their study on 48 patients with CRS and recurrent acute rhinosinusitis and 57% had a positive allergy test. Pelikan and Pelikan – Filipeck [18] demonstrated that 75% of their patients with allergies showed an increase in maxillary sinus mucosal thickening on CT imaging. Naclerio et al [19] showed a 60% prevalence of mild sinus mucosal disease changes on sinus radiographs in symptomatic patients with allergies during ragweed season. These changes did not resolve after treatment. Berrettini et al [20] demonstrated abnormalities on CT imaging in 67.5% of patients with perennial allergic rhinitis compared with 33.4% of controls.

There are many studies regarding IgE total serum levels and its relation to the severity of mucosal disease of CRS. Baroody et al [21] discussed CT imaging and IgE levels in 300 patients. Opposite to our study, they mentioned a positive correlation between severity of CRS based on CT imaging and IgE levels. Newman et al [8] showed a positive correlation between severity of CRS based on CT imaging and both tissue and peripheral eosinophilia, but did not find a correlation between severity of CRS and total IgE levels. Hoover et al [22] did not find any relation between mucosal disease and IgE level. The weak points of our study were limited number of patients with CRS included in this work and the diagnostic criteria for the severity of CRS better to be more clarified and obvious for more accuracy. We need more

data collection from the patients in addition to objective and subjective measurements to reach to the ideal results.

### Conclusion

In this study, the serum eosinophil level is useful as simple and rapid indicator of paranasal sinuses mucosal disease and hence the severity of CRS. Increase level of peripheral eosinophilia in patients with CRS correlate with the extensive disease. In contrast, there is no significant correlation between total IgE levels and CT imaging of mucosal disease of the paranasal sinuses.

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