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RESEARCH ARTICLE

A STUDY ON PREDICTION OF ALLERGIC FUNGAL RHINOSINUSITIS WITH SERUM IgE LEVELS

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Abstract

Background: Allergic fungal rhinosinusitis (AFRS) with IgE mediated allergic pathogenesis is a category of non-invasive fungal sinusitis. In our study, we followed up patients with AFRS who have undergone functional endoscopic sinus surgery and correlated endoscopic appearance (Kupferberg staging) with pre and postoperative total serum IgE levels.

Objectives:

1. To assess preoperative and postoperative endoscopic staging as well as total serum IgE levels in patients with AFRS who underwent functional sinus surgery.
2. To assess the sensitivity of total serum IgE level in predicting the disease status in patients with AFRS on postoperative follow up.

Methodology: A prospective longitudinal cohort study was done on 68 patients diagnosed to have AFRS. Preoperative endoscopic staging was done along with total serum IgE levels and skin allergy test for all patients. Postoperatively the patients underwent repeat endoscopy and serum IgE level testing at 4 to 7 months follow up.

Results: We had 68 patients in the age group of 21-60 years in the study. The majority of the patients in the study group were males (61.8%). In our study, 54 of 68 patients had a fall in postoperative total serum IgE levels when compared to their preoperative values. The sensitivity of total serum IgE levels in this study was, therefore, 84%. The specificity of total serum IgE level was only 33.3% in our study.

Conclusion: In this study on patients with AFRS who underwent total serum IgE estimation and rigid nasal endoscopy both pre and post operatively shows that total serum IgE levels is a fairly good prognostic measure in patients with AFRS. Eventhough the test specificity is low, both total serum IgE levels and clinical findings together may be ideal to asses the prognosis for the individual patients with AFRS.

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Introduction:-

Allergic fungal rhinosinusitis (AFRS) with IgE mediated allergic pathogenesis is a category of non-invasive fungal sinusitis whose diagnosis is based on several welldefined criteria.[1] The fungi associated with the disease are Aspergillus species and dematiaceous fungi like Alternaria, Bipolaris, Curvularia and Drescherella. In the Indian subcontinent, the major species isolated is Aspergillus.[2] AFRS accounts for 6-8% of all chronic sinusitis requiring surgical interventions. A warm and humid climate amplifies the disease prevalence.

Clinically, patients present with nasal obstruction, nasal discharge, facial pain, headache and anosmia. Many authors have described nasal obstruction and polyposis as the main presenting features in AFRS.[3] They can also present with proptosis and telecanthus due to extension of disease into the orbit and periorbital region or pressure on the medial orbital structures. Extension intracranially has also been described.[4] The process of extrasinus extension commences with bony expansion and remodeling, eventually causing bone erosion.

An IgE mediated allergic pathogenesis has been proposed for AFRS.[3] While total serum IgE levels are elevated in the disease, fungal specific IgE levels may also be elevated. The association between IgE levels and endoscopic evidence of disease in patients on follow up after surgical excision of disease has been less well studied. If such an association is found, it would help to avoid unnecessary radiological studies to assess the presence of disease, particularly if endoscopic appearances are equivocal or a complete endoscopic assessment is difficult. The present study, therefore, aims to follow up patients with AFRS who have undergone surgery and correlate endoscopic appearance with serum total IgE levels.

Objectives:-

1. To assess preoperative and postoperative endoscopic staging as well as total serum IgE levels in patients with AFRS who underwent functional sinus surgery.
2. To assess the sensitivity of total serum IgE level in predicting the disease status in patients with AFRS on postoperative follow up.

Materials and method:-

A prospective longitudinal cohort study was done on 68 patients diagnosed to have AFRS based on clinical, radiological and histopathological criteria in the Department of ENT at Gadag Institute of Medical Sciences, Gadag, Karnataka, India during the period of January 2021 to March 2022.

Patients were included in the study if they met the following criteria and if they were willing to participate in the study. The inclusion criteria were patients between 21 to 60 years of age, patients with chronic rhinosinusitis with polyposis, patients with hyperdense areas on CT scan of the paranasal sinuses and patients with histopathological evidences of AFRS.

A detailed history was taken from all patients. History of nasal obstruction, nasal discharge, headache, facial pain, visual disturbance, sneezing and anosmia was documented. Any comorbid illness like diabetes mellitus, hypertension and bronchial asthma along with a history of smoking and alcohol were noted.

A diagnostic rigid nasal endoscopy was done and staging of polyposis was done by Kupferberg staging system. All patients also underwent preoperative skin allergen testing (including fungal allergen testing). Patients also had preoperative total serum IgE level testing. Radiological evaluation of the CT scan was done using Lund and MacKay grading system.

Postoperatively, after a period of 4 to 7 months, rigid nasal endoscopy was performed and staging was done by Kupferberg endoscopic staging system. The total serum IgE levels were reassessed postoperatively after a period of 4 months. The sensitivity, specificity, positive predictive value and negative predictive value of total serum IgE levels were calculated.

Results:-

68 Patients diagnosed with AFRS based on standard criteria were recruited to the study. The mean age of this cohort was 36.5 years (range = 21 - 60 years). The median age was 34.05 years. The majority of patients were seen

to be within the age group of 31 to 40 years of age. The majority of patients in the study group were males. There were 42 (61.8%) males and 26 (38.2%) females.

Most of our patients were from Karnataka (29.4%) followed by Maharashtra (17.6%) and Telangana (17.6%). Of the patients who were recruited initially in the study, 22 patients were excluded later in the final analysis due to inadequate follow up and all these patients were from either Uttar Pradesh or Bihar. In our study population, except for four individuals, the majority of women (32.3%) were housewives. All the male patients were employed with the majority being involved in manual labourers (29.4%). The next most common occupation was either business (14.8%) or that of clerical staff (14.8%).

The majority of patients with AFRS had coexistent allergy (40.1%). Other comorbidities included systemic hypertension (23.5%), bronchial asthma (11.8%) and diabetes mellitus (5.8%). Of a total of 68 patients, 20 (29.4%) patients had a history of previous nasal surgery. The most common surgery that these patients had undergone was functional endoscopic sinus surgery for chronic sinusitis with polyposis.

The most common symptoms among the study population were nasal obstruction (100%) and nasal discharge (100%). 32 (47%) patients had sneezing and 24 (35.2%) had headache. 4 patients who had bilateral disease had unilateral proptosis and 2 among them had diplopia. One of these 2 patients had CT findings with erosion of the left lamina papyracea with extraconal extension and intracranial extension. The second patient had similar features on the right side along with erosion of the optic canal. The majority (82.3%) had bilateral disease. Most of the patients in the study population were found to have a total Lund-Mackay CT score between 11 -15 (47%). The maxillary sinus and the ethmoid sinuses were involved in all our patients (100%). The majority of patients (82.3%) were found to have a positive fungal culture report, most common being Aspergillus flavus.

About 64 patients out of 68 underwent skin allergy testing. Most of our patients [54(84.4%)] were allergic to dust mites like Dermatophagoides pteronyssinus and Dermatophagoides farinae. 34 (53%) patients were allergic to various fungal species, the most common fungal species being Aspergillus fumigatus. 40 (62.5%) were allergic to various food items like egg, milk, orange and guava.

Around 60 patients out of 68 had undergone testing of serum absolute eosinophil count. The majority of the patients (70%) in the study population was found to have an absolute eosinophilic count below 500 cells/ml. 18 patients (26.7%) had absolute eosinophil count more than 500 cells/ml. Preoperatively, about 30 (44.1%) patients had grade 2 polyps and 38 (55.9%) had grade 3 polyps in their nasal endoscopy. 14 patients out of 30 who had grade 2 polyps had a history of previous endoscopic sinus surgery (Figure 1). Most of our patients (94%) had a preoperative serum IgE value in the range of 0- 4000 U/ml. The lowest value noted was 330 ul/ml and highest was 6548.2 U/ml. (Figure 2)

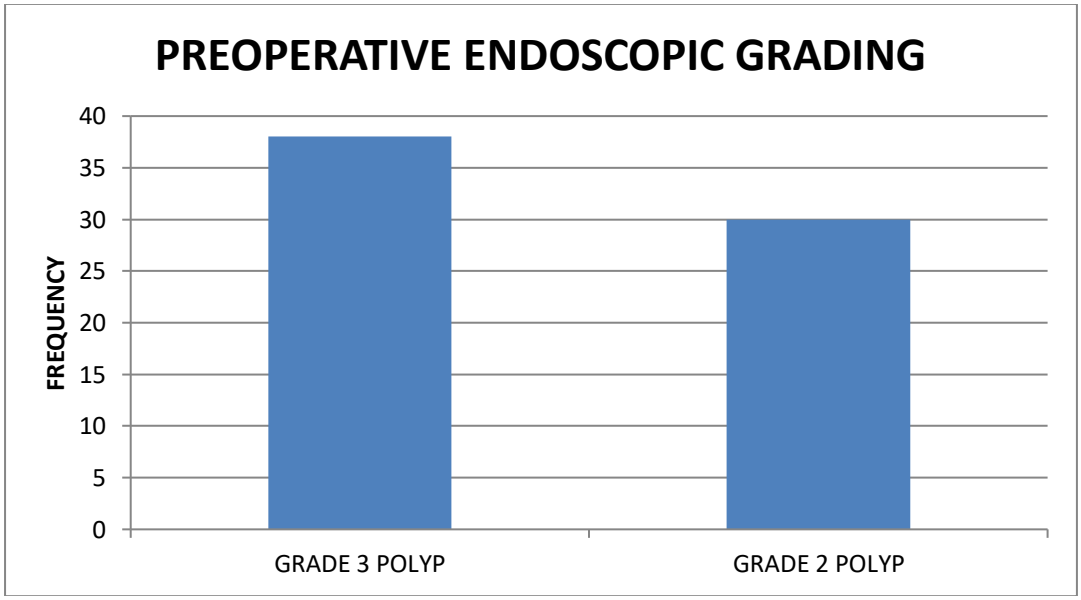

Figure 1:- Distribution of preoperative endoscopic grading in the study group (n=68).

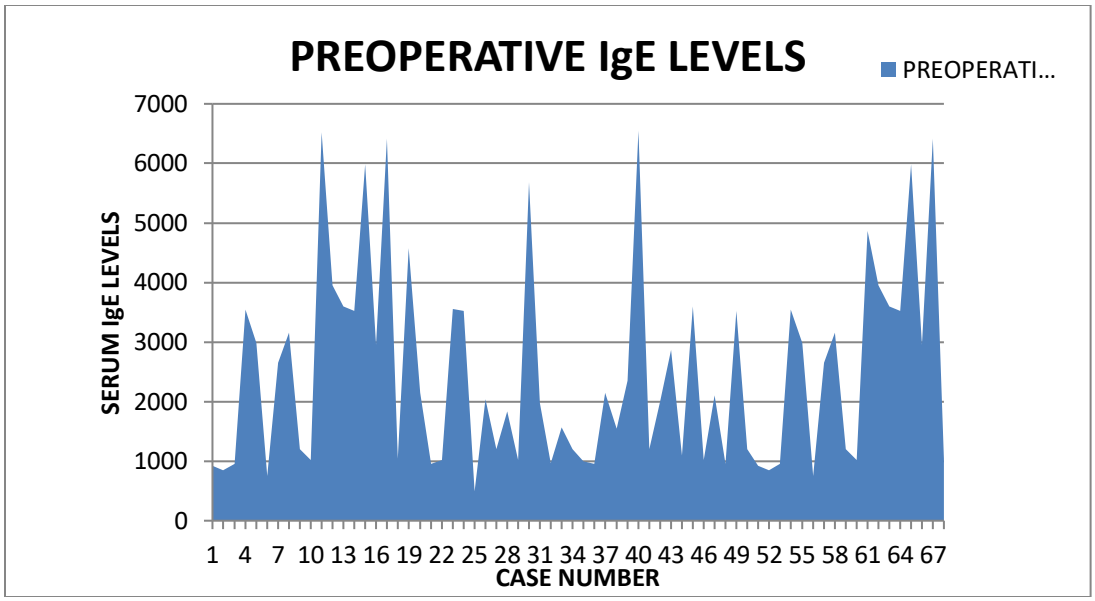

Figure 2:- Distribution of preoperative IgE levels in the study group (n=68).

Postoperatively, a total of 50 (73.5%) patients out of 68, had stage 0 in the rigid nasal endoscopy. 16 (23.6%) patients had stage 1 disease (edematous mucosa) with no evidence of polyps or allergic mucin. 2 patients with polypoidal mucosa (stage 2) had no evidence of allergic mucin (Figure 3).

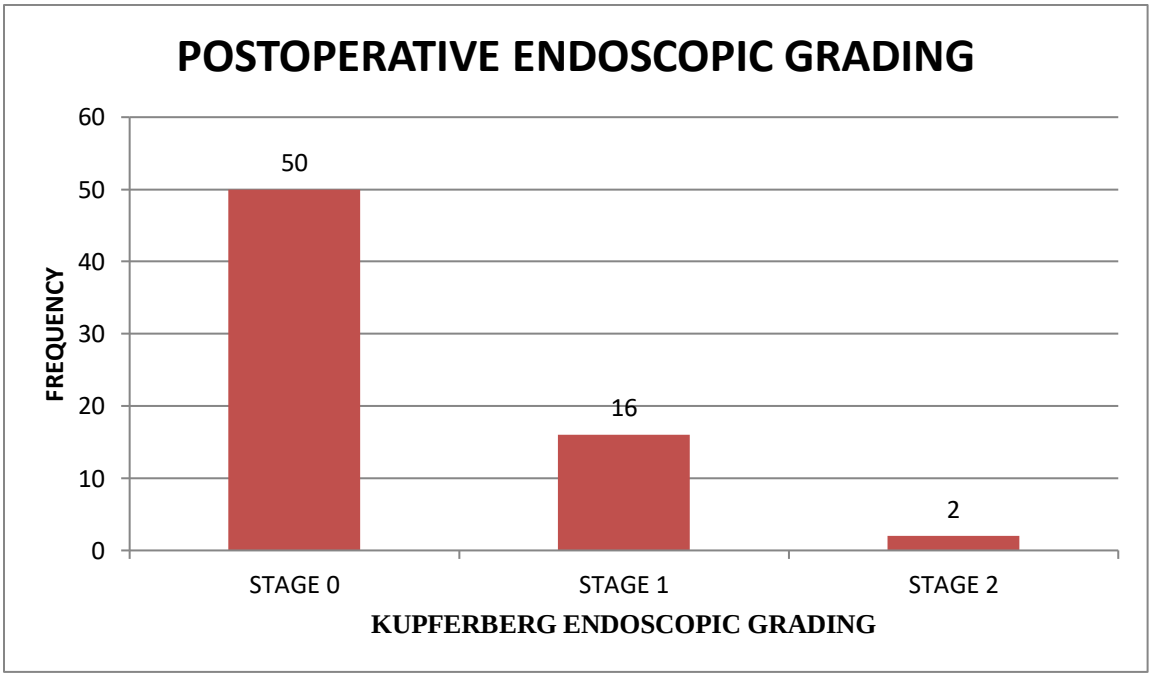

Figure 3:- Distribution of postoperative endoscopic grading (n=68).

Most of our patients (97.1%) had a serum IgE level less than 4000u/l during their first postoperative follow up. These figures reflect the decrease in the antigenic load after surgery. 2 patients had a serum IgE value of 15000 u/ml which was raised following surgery (Figure 4).

Only 8 (16%) who had stage 0 disease postoperatively had elevated post-operative serum IgE levels when compared to their pre-operative values. This included the patient whose post-operative value was15000 U/ml (Figure 4). Six

patients who had stage 1 disease on rigid nasal endoscopy had elevated serum IgE levels when compared to their preoperative values (Figure 5).

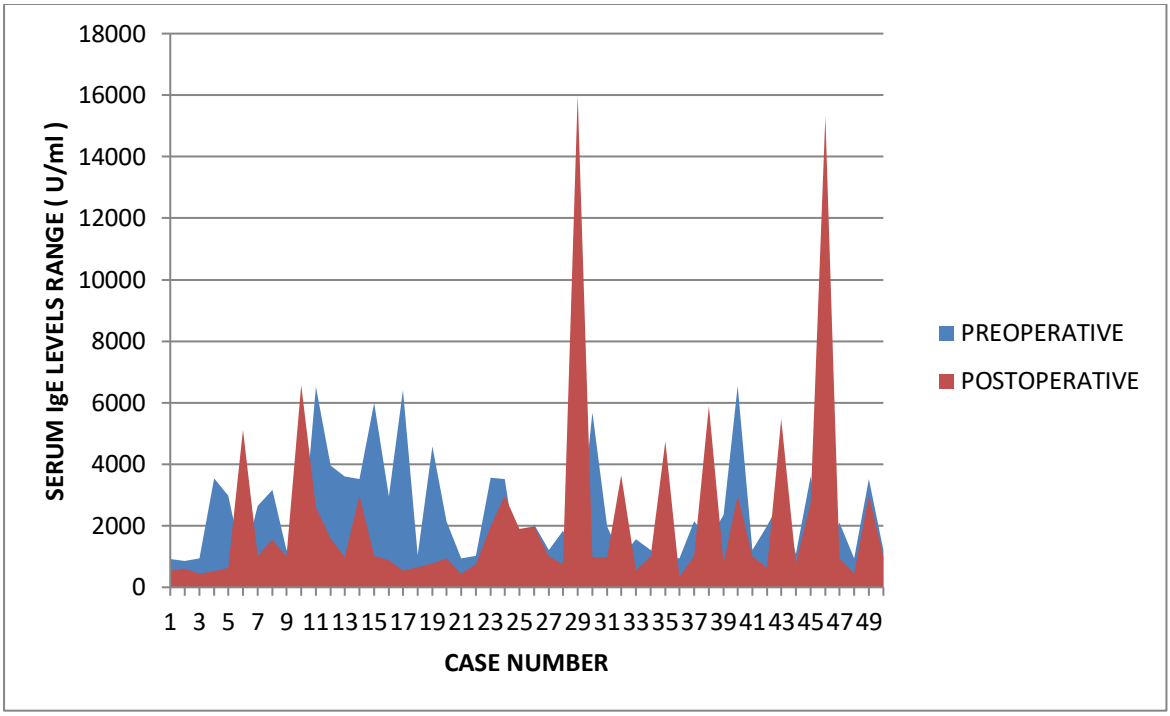

Figure 4:- Comparison of preoperative and postoperative serum IgE levels in patients who were Stage 0 postoperatively (n=50).

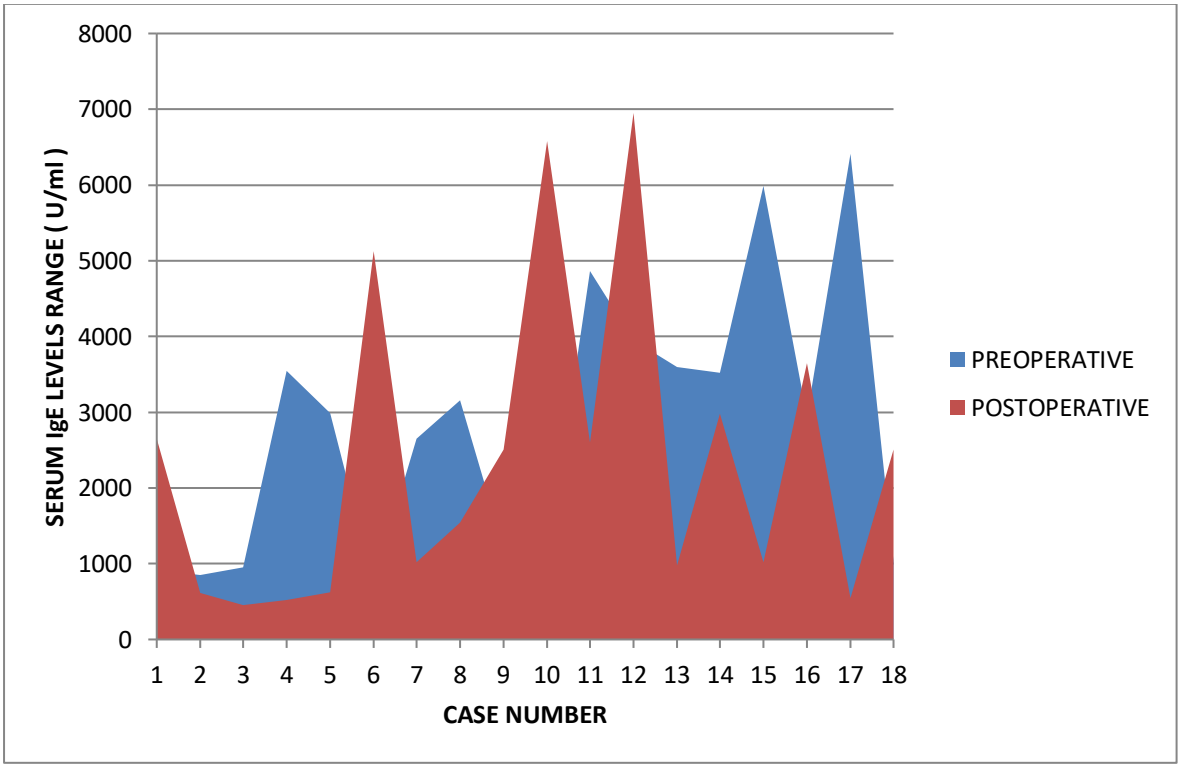

Figure 5:- Comparison of pre-op and post-op serum IgE levels in patients who were Stage1 postoperatively (n=18):

Table 1:- Sensitivity, specificity, positive predictive value of serum IgE in the diagnosis of AFRS.

Statistics	Value	95%confidence interval
Sensitivity	84%	63.92%-95.46%
Specificity	33.33%	7.49 -70.07%
Positive predictive value	77.78%	68.14 -85.14%
Negative predictive value	42.86%	17.13%-73.12%
Accuracy	70.59%	52.52%-84.90%

In our study, 42 of 68 patients had a fall in total serum IgE levels and coincidental stage 0 disease on postoperative rigid nasal endoscopy. Thus, the sensitivity of total serum IgE levels was 84% in our study. Only six of 68 patients had a rise in serum IgE levels despite having stage 1 disease on postoperative rigid nasal endoscopy. Thus, the specificity of total serum IgE level was only 33.3%. The positive predictive value of total serum IgE value was 77.78% in this study. This suggests that the test may not be very accurate in predicting the absence of the disease when screening patients. However, the test may have use in prognostication of the individual patient on long term follow up.

Discussion:-

In our study, we had patients whose age ranged between 21 to 60 years, with a mean of 36.5 years. Similar observations were made by other authors.[1,5] However, Ikram et al[4] who studied a series of patients with AFRS from Pakistan who had intracranial and intraorbital extension found that the average age was only 25 years (range 9 to 46 years). It is possible that since they studied only patient with intraorbital and intracranial extension, the majority of patients were in the younger age groups.

In our study the ratio of male:female was 1.6:1. In comparison with other studies[6,7], we found AFRS typically affects more males than females. Gheganetal[8] showed that patients with bone erosions in AFRS were more likely to be males than females. They found males with AFRS had 18.7 times more chance of bone erosion than males with non AFRS variants of sinusitis.

Allergic rhinitis was a major comorbid pathology in our series, with 32 (47.1%) patients having the disease. All of them had a positive skin allergy test. Drosteet al[9] found that, of a total of 261 patients, 222 (42.2%) patients had sensitivity to indoor and outdoor allergens. Most patients had sensitization to dust mite in their study. Similar results were seen in most patients in our series with 54 (84.4%) being allergic to dust mite. In our study we found that, 34(54%) patients had fungal allergy. Of these 34 patients, 22 (64.8%) patients tested positive for Aspergillus fumigatus. Ten (45.5%) patients were tested positive for multiple fungal species. 24 (76.8%) patients had both fungal and dust mite allergy. In Bent and Kuhn's series, a positive skin allergy test was seen in 100% of patients, whereas in Shazo's series[10] only two-third had a positive skin allergy test. Pantetal[11] showed that 66% of their patients had aeroallergen allergy and 100% had fungal allergy.

All our patients had nasal obstruction and nasal discharge as their primary presenting symptom. Similar observations were seen in many studies[12,13]. This may be because of the presence of nasal polyposis which was seen in all the patients.

58 (85.3%) patients in our study had a positive fungal culture and Aspergillus flavus was identified in majority of the cases. Similar findings were found in the studies by Bent and Kuhn[1] where 11 out of 15 patients had positive fungal culture and Manning et al where[6] all patients had a positive fungal culture. A raised total serum IgE level is not by itself a diagnostic criterion of AFRS. In our study all patients had a raised preoperative total serum IgE level (normal value <85U/ml). In other studies, variable results have been obtained. Bent and Kuhn[1] found that 6 out of 7 patients had raised preoperative IgE levels. Marple et al[14] found that 4 out of 17 (23.5%) had raised total serum IgE levels.

The sensitivity of the total serum IgE level in the prognostication of AFRS is well demonstrated in this study. We found total serum IgE levels to have 84% sensitivity rate in this study. This suggests that, in patients in whom, a longitudinal follow up is possible, total serum IgE levels which show a reduction in the post-operative period are more likely to be associated with Stage 0 disease on rigid nasal endoscopy. However, if total serum IgE levels are

raised, it is possible that patients may have either Stage 0 disease or Stage 1 and 2 diseases. Rigid nasal endoscopy is thus definitely required in these cases to identify residual disease.
The absolute total serum IgE levels do not appear to have any significance in the diagnosis and prognosis of disease in patients with AFRS. However longitudinal follow up of AFRS patients with serum IgE levels and rigid nasal endoscopy will be useful in the majority of patients. The results of our study showed that total serum IgE value may not be a sensitive tool in the screening for the presence of AFRS. However, in a patient who shows a demonstrable fall in total serum IgE level post operatively while on therapy, there is a more than 80% likelihood that this patient has stage 0 disease on rigid nasal endoscopy. To further increase the sensitivity of these parameters, a combination of clinical and total serum IgE values may be studied in these patients.

Conclusion:-

In this study on patients with AFRS who underwent total serum IgE estimation and rigid nasal endoscopy both pre and post operatively shows that total serum IgE levels is a fairly good prognostic measure in patients with AFRS. Eventhough the test specificity is low, both total serum IgE levels and clinical findings together may be ideal to asses the prognosis for the individual patients with AFRS.

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Conflicts of interest:
Nil.

Ethical approval:
IEC approval obtained.

References:-

1. Bent Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg.1994 Nov;111(5):580–8.
2. Rupa V, Jacob M, Mathews M S, Job A, Kurien M, Chandi S M. Clinicopathological and mycological spectrum of allergic fungal sinusitis in South India. Mycoses. 2002, Nov; 45(9–10):364–7.
3. Katzenstein A L, Sale S R, Greenberger P A. Allergic Aspergillus sinusitis: a newly recognized form of sinusitis. J Allergy Clin Immunol. 1983 Jul;72(1):89–93.
4. Ikram M, Akhtar S, Ghaffar S, Enam SA. Management of allergic fungal sinusitis with intracranial spread. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol-Head Neck Surg. 2008 Feb;265(2):179–84.
5. Millar J W. Allergi caspergillosis of the maxillary sinuses. Thorax. 1981;36:710.
6. Manning S C, Mabry R L, Schaefer S D, Close L G. Evidence of IgE-mediated hypersensitivity in allergic fungal sinusitis. The Laryngoscope. 1993 Jul;103(7):717–21.
7. Collins M, Nair S, Smith W, Kette F, Gillis D, Wormald P J. Role of local immunoglobulin E production in the pathophysiology of noninvasive fungal sinusitis. The Laryngoscope. 2004 Jul;114(7):1242–6.
8. Ghegan M D, Lee F-S, Schlosser R J. Incidence of skull base and orbital erosion in allergic fungal rhinosinusitis (AFRS) and non-AFRS. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2006 Apr;134(4):592–5.
9. Droste J H, Kerhof M, de Monchy J G, Schouten J P, Rijcken B. Association of skin test reactivity, specific IgE, total IgE, and eosinophils with nasal symptoms in a community-based population study. The Dutch ECRHS Group. J Allergy Clin Immunol. 1996 Apr; 97(4):922–32.
10. De Shazo R D, Swain R E. Diagnostic criteria for allergic fungal sinusitis. J Allergy Clin Immunol.1995 Jul;96(1):24–35.
11. Pant H, Kette F E, Smith W B, Wormald P J, Macardle P J. Fungal-specific humoral response in eosinophilic mucus chronic rhinosinusitis. The Laryngoscope. 2005 Apr;115(4):601–6.
12. Schubert M S, Goetz D W. Evaluation and treatment of allergic fungal sinusitis. I.Demographics and diagnosis. J Allergy Clin Immunol.1998 Sep;102(3):387–94.
13. Kupferberg S B, Bent J P, Kuhn F A. Prognosis for allergic fungal sinusitis. Otolaryngol—Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg.1997 Jul;117(1):35–41.
14. Marple B F. Allergic fungal rhinosinusitis: current theories and management strategies. TheLaryngoscope. 2001 Jun;111(6):1006–19.