

## **Correlation between fungal antigens and IgE levels in Respiratory allergy patients-An Analysis in a South Indian Otolaryngology center.**

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### **Abstract**

Fungal spores are abundant in nature and much evidence is available to show that fungi can cause atopic clinical illnesses. Many of these fungal spores are lesser than 10microns in diameter and their deposition into lower airways is common. Fungal sensitization is a significant risk factor for developing asthma in later part of life. Present study was intended to explore the clinical profile of the individuals who were sensitized to different type of fungal allergens and find out the relationship between skin tests and laboratory markers (Total Serum IgE, peripheral eosinophils) in different types of allergen sensitivity individuals among various respiratory allergy patients. A retro prospective study was conducted on 570 patients who had visited allergy clinic from Jan 2000-Sep 2009. Patients were selected based on symptoms of allergy. Investigations were done on patients experiencing such patients that included total serum IgE, peripheral eosinophil (%), skin tests; X-ray/CT Scan of paranasal sinuses, nasal endoscopy and spirometry were done wherever it was needed. Based on clinical findings, there were 292 males and 278 females visited hospital. Among skin tests performed, 68.4% were intra dermal and 31.6% were skin prick tests, 84.13% of individuals were found positive and 18.18% were found negative towards allergen sensitivity. From the positive skin tests obtained, numbers of patients sensitized to specific type of allergens were categorized and their demographic characters were discussed in the paper. Total IgE was found to be higher in individuals who were sensitive to fungal and other allergens followed by individuals who were sensitive only to other allergens (except fungi) in all categories of respiratory allergy patients which were discussed in paper.

### **Key Words**

Allergy patients, fungal sensitization, Total serum IgE, Peripheral Eosinophil (%), Skin tests, otolaryngology center.

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### **Introduction**

People are exposed to aeroallergens in various settings, both at home and at work. Fungi are ubiquitous airborne allergens and are important causes of human diseases, especially in the upper and lower respiratory tracts. Allergy is one form of human disease which affects about 20% of the population. A number of allergens associated with various forms of allergy have been reported from all over the world<sup>1, 2</sup>. The concentration of allergens in the environment varies, depending on various factors including climate, vegetation, and air quality. The outdoor allergens are predominantly constituted of plant pollens and fungal spores.

The indoor allergens, on the other hand, are represented by allergens from dust mites, cockroaches and pets. Fungal spores also have been reported from the indoor environment<sup>3</sup>. The concentration and prevalence of the indoor allergens vary substantially and are dependent on moisture content, ventilation, and the presence or absence of pets, carpets, and houseplants<sup>4</sup>. Fungi from human environment or growing in human body may cause allergic reactions. They are associated with number of allergic diseases in humans including allergic rhinitis, conjunctivitis, bronchial asthma and allergic broncho pulmonary mycoses resulting from the exposure to spores<sup>7</sup>. The prevalence of respiratory allergy to fungi is estimated at 20% to 30% among atopic individuals and up to 6% in general population<sup>2, 5, and 6</sup>. The most common fungal

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allergens are *Alternaria*, *Cladosporium*, *Aspergillus*, *Penicillium* and yeasts<sup>8</sup>. Clinically the presenting symptoms associated with allergy are sneezing, nasal discharge, coughing, wheezing, and shortness of breath. Reversible pulmonary airway obstruction, angioedema, urticaria, and even anaphylaxis may manifest in these patients. Although an allergic reaction to fungal allergens is suggested as an important contributing factor in development of respiratory symptoms, other mechanisms, such as increased exposure to fungal metabolites, mycotoxins and other compounds of immunosuppressant's or irritant properties may also be important<sup>9</sup>. Several epidemiological and diagnostic studies reported increasing prevalence of allergic reactivity to fungi assessed with use of skin testing or specific IgE detection<sup>9</sup>. However the exact prevalence of fungal sensitization is not known mainly due to lack of standardized fungal extracts and due to overwhelming number of fungal species that are able to elicit IgE mediated reactions<sup>7</sup>. The effective in vivo and in vitro diagnosis of fungal allergies is based on availability of well-characterized allergen preparation<sup>10</sup>. The present study is aimed at determining the prevalence of IgE mediated allergy to fungi, as well as contribution of sensitization to fungi with respect to allergic manifestations to establish a relationship between the anemophilous fungi isolated in the air and patients with respiratory allergy, and to show the fungal extracts that could provoke skin test reactivity in individuals with respiratory allergy (allergic rhinitis, asthma) in a south Indian clinic.

### **Materials and methods**

A retro prospective study was conducted on 570 patients who visited allergy clinic from Jan 2000-Sep 2009. Among the patients who attended, males were 292 and females were 278, with most common age of 37±11.25 years (Mean ± S.D). All patients were subjected to full ENT examination. Patients were selected based on symptoms of sneezing, watery rhinorrhoea, nasal obstruction, eye symptoms (in the form of redness, watering of eyes and itching), itching of nose, throat and ear and any asthma related symptoms. Investigations were done on patients experiencing such patients that included total serum IgE (by ELFA method), peripheral eosinophil (%), skin tests (done using commercially available antigens); X-ray/CT Scan of paranasal

sinuses, nasal endoscopy and spirometry were done wherever it was needed. Based on clinical findings and investigations done, patients were categorized into three groups, i) Allergic Rhinitis (AR); ii) Allergic Rhinitis with asthma; iii) Allergic Fungal Sinusitis (AFS). Skin tests were performed on 290 individuals, of which 68.4% were intradermal and 31.6% were skin prick tests. Based on positively to skin tests individuals were categorized into three groups based on their difference in sensitivity to antigens in different category of respiratory allergies, a) Positive towards Fungus; b) Positive towards allergens other than fungus (HDM, Pollen, Insects, Food etc...); c) Positive towards other allergens and fungus. Among individuals who were skin test positive towards fungal allergens, individuals sensitized to specific type of fungi were identified through skin tests in different categories of respiratory allergy patients. Patients were excluded from the study if they had clinical features of vasomotor rhinitis, COPD, if they have received treatment of corticosteroid or the other immunosuppressive therapy during preceding 6 months, if they had elevated IgE Level caused by another disease or if they had ever received allergen Immunotherapy. Anterior rhinoscopy was done with sterilized nasal speculum to verify the presence or absence of polyps or hypertrophy of turbinates or any other local pathology. Standard examination of throat and ear was also done. Fungal culture was done on patients' nasal exudation to determine the type of fungi for which the individual was sensitized. Total IgE levels, peripheral Eoisinophil (%) were estimated in 3 groups of patients who were with differing in their sensitivity towards allergens and their means were compared in different categories of respiratory allergy patients. Age group of individuals who visited the allergic clinic and also for the individuals who were sensitized to different allergens among various categories of respiratory allergy patients was calculated through one sample t-test. Mean levels of IgE, peripheral eosinophil (%) were determined and compared in individuals differing in their allergen sensitivity, among various groups of respiratory allergic patients through one sample t-test. The analysis was performed by using SPSS-17.0. Total serum IgE levels, Peripheral Eosinophils (%) were obtained at 95% confidence interval with p value <0.05 considered to be significant.

## **Results and Discussion**

Among skin tests performed, 68.4% were intradermal and 31.6% were skin prick tests were performed, 84.13% of individuals were found positive and 18.18% were found negative towards allergen sensitivity. From the positive skin tests obtained, number of patients sensitized to specific type of allergens was categorized and their demographic characters age and gender (Table 3), (Figure 2). Based on allergen sensitivity, number of individuals who were sensitized to specific allergen among various groups of Respiratory allergy patients is given in Table 4 (Figure 3). Type of specific fungi was identified in all subjects who were found fungal positive is given in Table 5. Individuals on whom fungal culture was conducted, positively towards fungal culture and type of fungi isolated in culture is given in Figure 4. Comparative Mean total IgE and peripheral eosinophil (%) among various groups of respiratory allergic individuals differing in their allergen sensitivity is given in Table 6 & 7. Fungal antigens play an important role in the cause of respiratory allergies. Fungi disseminate their spores in the environment through the atmospheric air, water, insects, man and animals<sup>11</sup>. Air borne fungal spores have been implicated as causative factor in respiratory allergies particularly asthma<sup>7</sup>. Immunoglobulin E specific antigens (allergens) on air borne fungal spores induce type I Hypersensitivity (allergic) respiratory reactions in sensitized subjects causing rhinitis or asthma<sup>12</sup>. Qualitative knowledge of these fungi in a given region is of great importance and concern because they can cause several respiratory diseases in man such as rhinitis and asthma when inhaled<sup>11</sup>. Lowry and Shaffer proposed multiple diagnostic criteria, including eosinophilia, immediate skin reactivity or serum Ig E Antibodies to fungal antigens, nasal mucosal edema or polyposis<sup>13</sup>. Present study was intended to explore the clinical profile of the individuals who were sensitized to different type of fungal allergens and find out the relationship between skin tests and laboratory markers (Total Serum IgE, peripheral eosinophils) in different types of allergen sensitivity individuals among various respiratory allergy patients. Air borne fungal spores occur widely and often in greater concentration than pollens. The prevalence of respiratory fungal allergy was found to be 20-30% of atopic individuals in the study conducted by Horner WE<sup>12</sup>. According to Mc

Clay, et al, Allergic Fungal Sinusitis is most common among adolescents and young adults; the mean age at diagnosis was 21.9 yrs and his study revealed equal incidence in males and females<sup>14</sup>. The group of patients aged 11 to 20 years old had the highest incidence of molds sensitivity<sup>15</sup>. In the present study the most common age group with respiratory allergies was 37.03 yrs and the most common age group for mold sensitivity in present study was 39.25 yrs. The overall incidence of allergy to various allergens in our study was found significant. The incidence of allergy to fungal allergens in the study conducted by Erbek SS<sup>16</sup> was 38.8% in allergic patients. In our study the incidence to fungal allergen sensitivity was found to be quite significant (44%). Skin test was found to be the most reliable method and available method for allergen sensitivity<sup>17</sup>. In studies in which the Skin prick test (SPT) was accepted as the gold standard, in vitro testing has proved less sensitive. Reported sensitivities have ranged from 74%<sup>18</sup> to 92.2%<sup>19</sup>. Present study showed that Skin test positivity was 84.13% in properly selected cases. Among the total skin tests conducted in our study, 68.4% of them were intra dermal, 31.6% were skin prick tests. Our study has demonstrated that if the case has been selected properly after thorough history and preliminary basic investigation, the incidence of positivity of skin tests appears to be quite high (84.13%). Among the individuals who were sensitive to allergens, 55% of the individuals were sensitized to allergens other than fungus, (HDM, Pollen, insects, food, etc), 29.9% of individuals were sensitive to fungus only and 14.7% were sensitive to fungus plus other allergens. Therefore present study has demonstrated that overall sensitivity to fungus was 44%. Among the air borne fungi that spread air spores, important allergens of the world are *Asperigillus*, *Cladosporium*, *Alternaria*, *Pencillium* and *Dechslera*. They have been reported as the predominant organisms in warm, humid and dry climates<sup>20</sup>. A similar study was done by Mezzari, et al.<sup>11</sup> revealed a prevalence of air borne fungi in the city of Porto Alegre; the most predominant fungi found in the air of the city were: *Asperigillus*, *Cladosporium*, *Alternaria*, *Pencillium*, *Curvularia*, *Fusarium* and others. Aerobiological survey done in the city of Bangalore (South India) by Aghase and Vidya (1997) showed predominance of *Cladosporium*, *Alternaria*, *Asperigillus*, *Pencillium*,

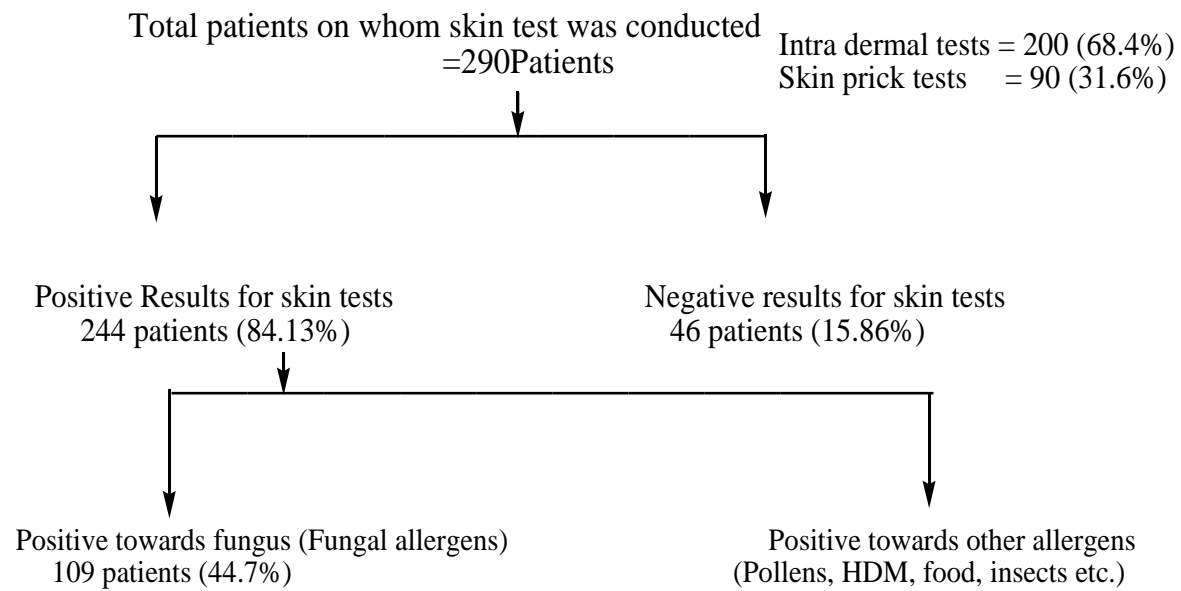
Nigrospora, Helminthosporium, Cercospora and Curvularia<sup>21</sup>.

### **Conclusion**

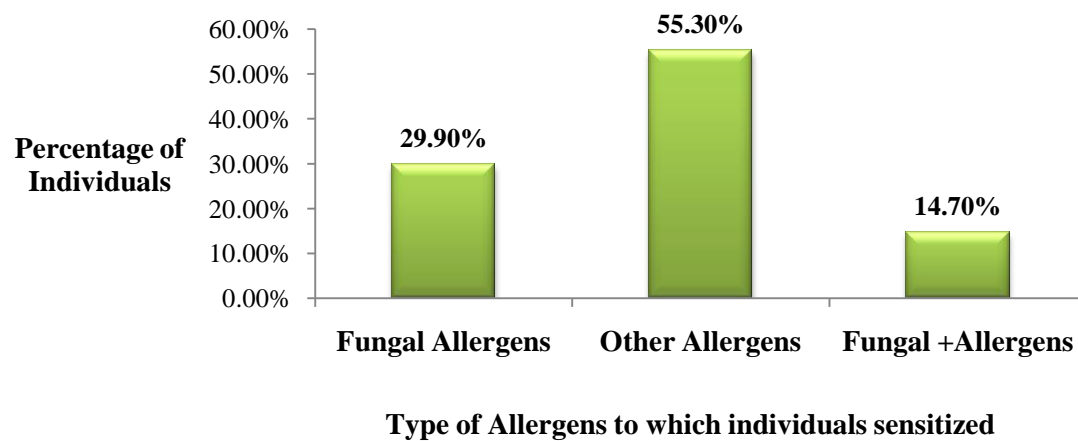
Present study identified the common fungal antigens responsible for rhinitis and asthma in population of south India. Proper history taking followed by Skin tests, Total/Specific IgE in vitro tests, fungal culture in specific cases are helpful in the diagnosis. Fungal sensitivity that was observed in the study population was mainly for Aspergillus, followed by Alternaria.

### **References**

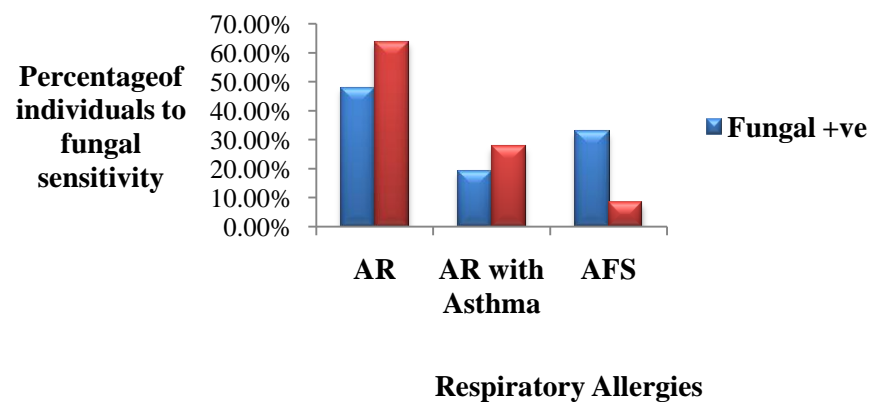
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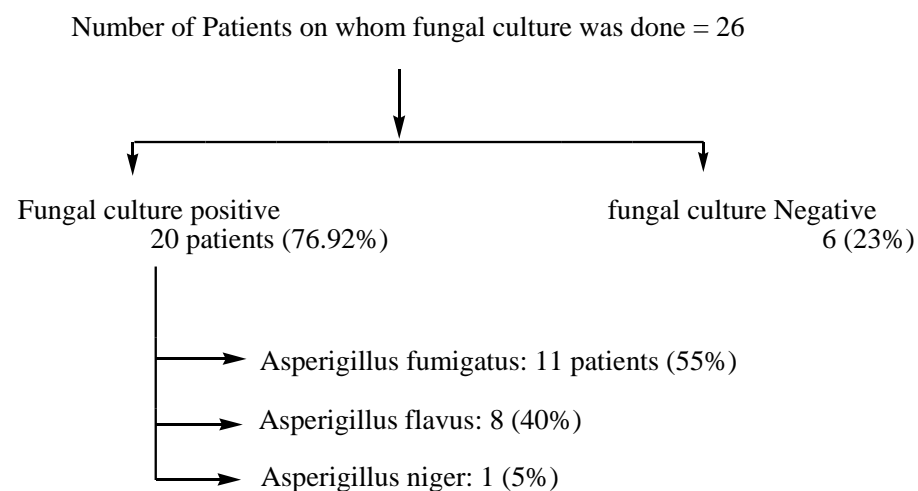
**Figure 1:** Flow chart showing number of individuals on whom Skin tests were conducted.



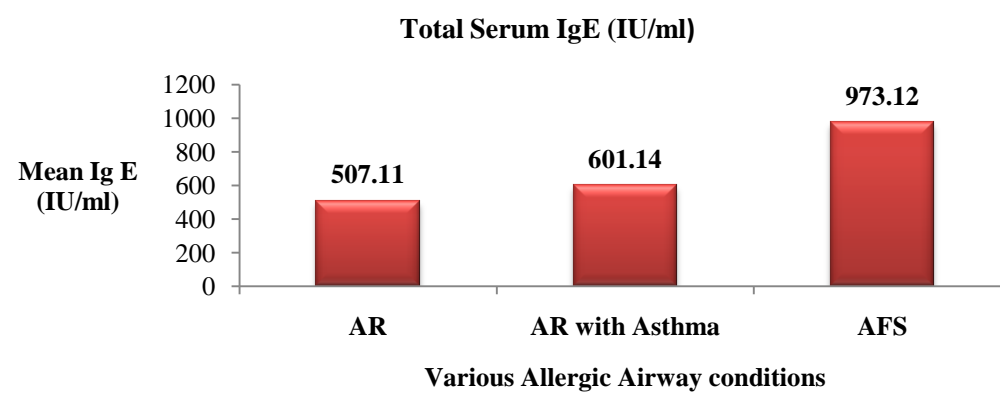
**Figure 2:** Percentage of Individuals sensitive to different allergens.



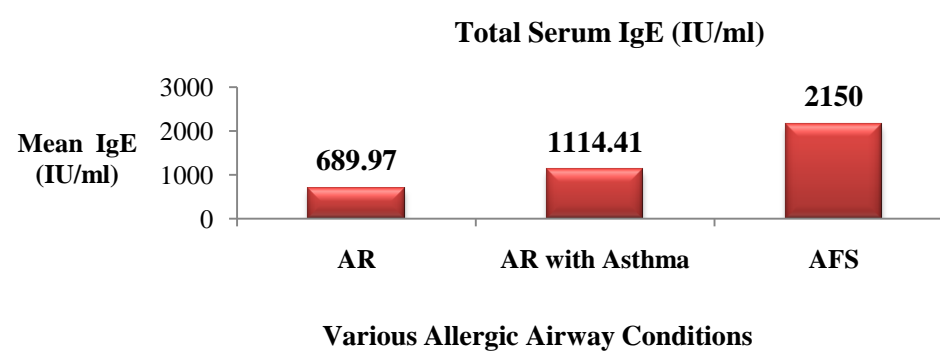
**Figure 3:** Fungal Allergen Sensitivity among Various Respiratory Allergy Individuals.



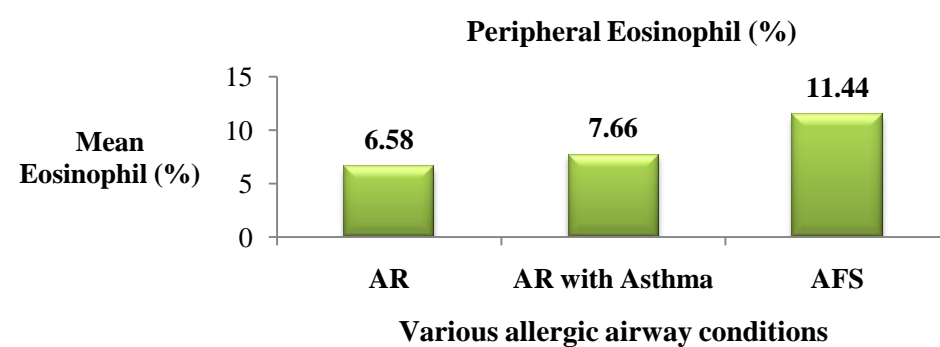
**Figure 4:** Flow chart of fungal culture on patients.



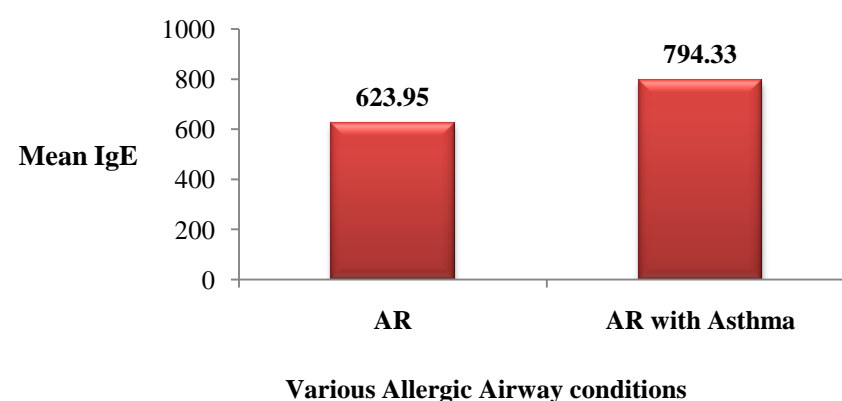
**Figure 5:** Comparative Total IgE among patients with various allergic conditions who were positive to only fungal allergens.



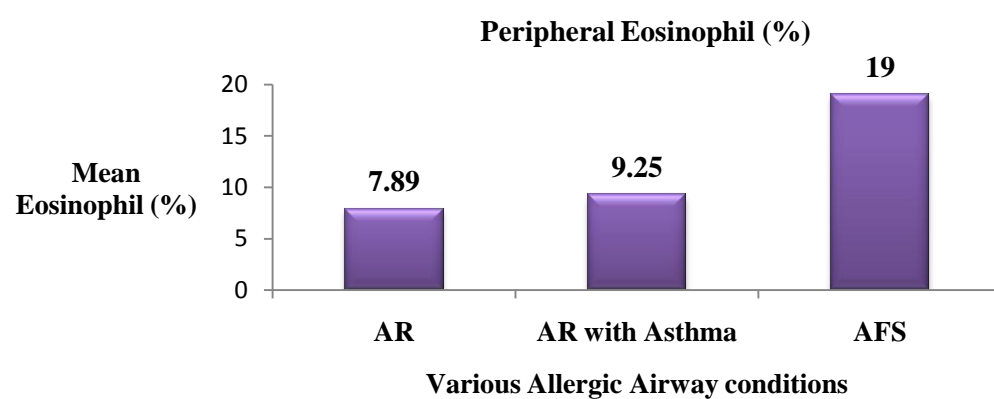
**Figure 6:** Comparative Total IgE among patients with various allergic conditions who were sensitive to fungal plus other allergens.



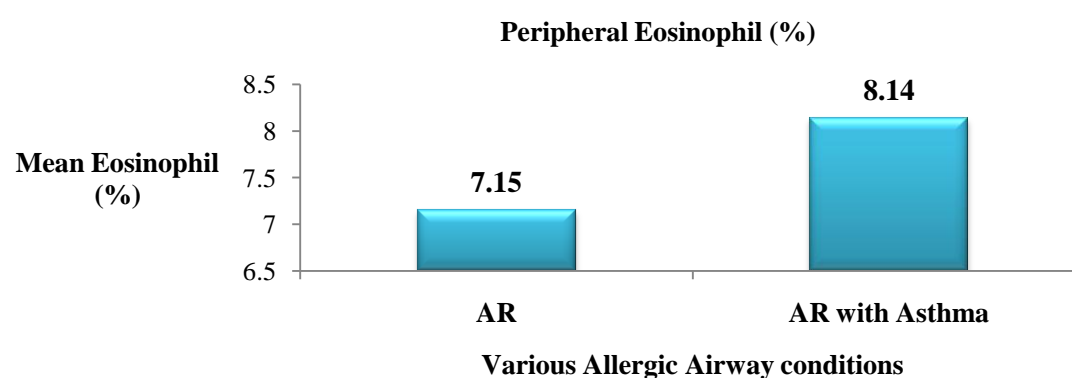
**Figure 7:** Comparative Total IgE among patients with various allergic conditions who were positive to allergens other than fungus.



**Figure 8:** Comparative Peripheral Eosinophil (%) among patients with various allergic conditions who were positive only to fungal allergens.



**Figure 9:** Comparative Peripheral Eosinophil (%) among patients with various allergic patients who were positive to Fungal plus other allergens.



**Figure 10:** Comparative Peripheral Eosinophil (%) among patients with various allergic conditions who were sensitive to allergens other than fungus.

**Table 1:** Descriptive characteristic of patients who visited the allergy clinic.

	Males (%)	Females (%)	Total
Number of Individuals	292 (51.2%)	278 (48.8%)	570 (100%)
Age of Individuals (Mean ± S.D)	38.23±11.03 yrs*	36.10 ± 11.45 yrs*	37.03±11.25 yrs*

\*p<0.01 was considered to be significant.

**Table 2:** Gender and age of Individuals to skin tests were conducted.

	Males (%)	Females (%)	Total
Number of Individuals	148 (51.0%)	142 (48.9%)	570 (100%)
Age of Individuals (Mean ± S.D)	37.23±11.03 yrs*	35.10 ± 11.45 yrs*	36.55±11.75 yrs*

\*p<0.01 was considered to be significant

**Table 3:** Age of individuals sensitive to different allergens.

Type of Allergens to which individuals were sensitized	Number of Patients (%)
Fungal allergens	73 (29.9%)
Age of Individuals (Mean± S.D)	39.25 ± 11.76*
Other allergens (HDM, Pollen, Insects, Food)	135 (55.3%)
Age of Individuals (Mean± S.D)	35.46 ± 12.96*
Fungus + other allergens	36 (14.7%)
Age of Individuals (Mean± S.D)	34.96 ± 10.53*

\*p<0.01 was considered to be significant

**Table 4:** Percentage of Individuals positive for only fungal allergens and fungal plus other allergens among various respiratory allergy patients.

Category	Only fungal allergens	Fungal plus other allergens
Allergic Rhinitis (AR)	35 (47.9%)	23(63.8%)
Allergic Rhinitis with asthma	14 (19.17%)	10 (27.7%)
Allergic Fungal sinusitis (AFS)	24 (32.8%)	3 (8.3%)
Total Individuals (%)	73 (100%)	36 (100%)

**Table 5:** Individuals sensitized to different type of fungi.

Fungi	Allergic Rhinitis	Allergic Rhinitis with Asthma	Allergic fungal Sinusitis	Total
Alternaria Alternata	20	10	10	40
Aspergillus Flavus	17	10	24	51
A. Fumigatus	28	14	25	67
A. Niger	16	6	10	32
A. Tamarii	22	8	21	51
A. Versicolor	14	7	6	27
Cladosporium	7	2	4	13
Candida	10	3	3	16
Mucor	6	2	9	17
Pencillium	11	3	7	21
Rhizopus	14	5	9	28
Trichoderma	6	0	2	8

**Table 6:** Total IgE (IU/ml) in patients with various conditions.

Category	Only Fungal +ve	Both (Fungal+others)	Others
AR	507.11±63.49*	689.97±71.56*	623.95±29.4*
AR with Asthma	601.14±75.88*	1114.41±230.90*	794.33±80.58*
AFS	973.12±46.76*	2150.00±50.00**	

\*p<0.01 was considered to be significant, \*\*p<0.05 was considered to be very significant.

**Table 7:** Comparative Peripheral Eisinophil Count (%) among patients with various allergic conditions who were sensitive to all allergens.

Category	Only Fungal +ve	Both (Fungal+others)	Others
AR	6.58±1.21*	7.89±0.704*	7.15±0.840*
AR with Asthma	7.66±1.22*	9.25±1.63*	8.14±0.47*
AFS	11.44±1.63*	19.00±1.00**	

\*p<0.01 was considered to be significant, \*\*p<0.05 was considered to be very significant.

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