ALLERGEN SENSITIVITY PATTERN AND IT'S CORRELATION WITH TOTAL SERUM IGE LEVELS AND EOSINOPHIL COUNT AMONG PATIENTS WITH ALLERGIC RHINITIS AND /OR ASTHMA IN NORTH KARNATAKA

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Dissertation submitted to

BLDE (Deemed to be University) Vijayapur, Karnataka

In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

RADIOLOGY

Under the guidance of

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PROFESSOR

DEPARTMENTOF RADIOLOGY

BLDE (Deemed to be University)

SHRIB.M.PATILMEDICALCOLLEGE

HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

KARNATAKA

2020

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IN

RESPIRATORY MEDICINE

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LIST OF ABBREVIATIONS

%	:	Percentage
IgE	:	Immunoglobulin- E
IgM	:	Immunoglobulin- M
IgG	:	Immunoglobulin- G
FcRI	:	Fc receptor I
IL-4	:	Interleukin-4
TNF	:	Tumor Necrosis Factor
IL-6	:	Interleukin-6
Th1	:	T- helper 1 cells
Th2	:	T- helper 2 cells
DALY	:	Death and Disability Associated Life Years
ISAAC	:	International Study of Allergy and Asthma in Children
MC	:	Mast Cells
SAR	:	Seasonal Allergic Rhinitis
PAR	:	Perennial Allergic Rhinitis
AR	:	Allergic Rhinitis
CD40	:	Cluster of differentiation 40
IL-1	:	Interleukin-1
IL-3	:	Interleukin-3
IL-5	:	Interleukin-5
IL-8	:	Interleukin-8
IL-13	:	Interleukin-13
MHC	:	Major Histocompatibility Complex
FcεRI	:	Fc epsilon receptor I
ICAM-1	:	Intracellular adhesion molecules-1
ASM	:	Airway Smooth Muscle
GM-CSF	:	Granulocyte- Monocyte Colony Stimulating Factor

VCAM-1	:	Vascular cell adhesion molecule-1
EAR	:	Early Asthmatic Reaction
PGD2	:	Prostaglandin D2
LTC4	:	Leukotriene C4
LTD4	:	Leukotriene D4
BAL	:	Bronchoalveolar Lavage
LAR	:	Late Asthmatic Reaction
IgE-CAI	:	IgE-mediated chronic allergic inflammation
Th17	:	T-helper 17 cells
FcRII	:	Fc receptor I
CD23	:	Cluster of differentiation 23
SNP	:	Single-nucleotide polymorphisms
IL-33	:	Interleukin-33
PTPN22	:	Protein tyrosine phosphatase non-receptor 22
CTLA-4	:	Cytotoxic T-lymphocyte-associated antigen 4
miRNA	:	Micro Ribonucleic acid
BSACI	:	British Society of Allergy and Clinical Immunology
PNIF	:	Peak nasal inspiratory flow
MRI	:	Magnetic Resonance Imaging
NMCC	:	Nasal mucociliary clearance
FeNO	:	Fractional exhaled nitric oxide
WHO	:	World Health Organisation
INS	:	Intra-nasal steroids
SPT	:	Skin Prick Test
RAST	:	Radioallergosorbent test
INCS	:	Intra-nasal corticosteroids
AZE	:	Azelastine
AIT	:	Allergen Immunotherapy
LTRA	:	Leukotriene Receptor Antagonist

VAS	:	Visual Analog Scale
SIT	:	Specific Immunotherapy
SCIT	:	Subcutaneous Immunotherapy
SLIT	:	Sublingual Immunotherapy
OIT	:	Oral Immunotherapy
TDIT	:	Transdermal Immunotherapy
ICS	:	Inhaled Corticosteroids
FEV1	:	Forced Expiratory Volume in 1st second
LAMA	:	Long Acting Muscarinic Antagonist
OCS	:	Oral corticosteroids
ARIA	:	Allergic rhinitis and its impact on asthma
GINA	:	Global Initiative for Asthma
AEC	:	Absolute Eosinophil Counts

ABSTRACT

BACKGROUND:

Respiratory allergy is the most common allergy among all the populations and various age groups throughout the world, thus making it a significant health problem. The types of allergens vary according to the geographic area, climate, location, economic status, ethnic identity, etc. India, being a populous country with different climatic conditions and diverse food habits, the pattern of allergen sensitivity varies from place to place. Skin prick testing remains to be the gold standard for assessment of specific IgE against a particular allergen, but several factors make the test less preferred. Hence total serum IgE levels and eosinophil counts are preferred. This study is undertaken to evaluate the allergen patterns in patients with nasobronchial allergy and to correlate the total serum IgE levels and eosinophil count to the skin prick test so as to determine the possibility of their use as a screening test.

AIMS AND OBJECTIVES:

To determine allergen sensitivity patterns among the patients with allergic rhinitis and/or asthma and correlate the skin prick test reactivity with total serum IgE levels and absolute eosinophil counts.

MATERIALS AND METHODS:

A cross-sectional study on 44 patients with the diagnosis of allergic rhinitis and/or asthma, was carried out in the Department of Respiratory Medicine, B.L.D.E(DEEMED TO BE UNIVERSITY)'s, Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura, Karnataka. Allergen skin prick test was done in each patient 73 allergen extracts, and Total serum IgE levels and eosinophil counts were measured. The most common allergens leading to a positive skin prick test were identified.

RESULTS:

Out of the 44 patients enrolled, females were predominant, with common age group being 41-65 years. Majority of the patients had only allergic rhinitis (38.6%), compared to those with only asthma and both allergic rhinitis and asthma. The most common allergens with skin prick test positivity were House dust Mites, *Blomia* being the commonest (50%). *Aspergillus flavus, Fusarium solanii, Curvularia lunata, Cladosporium herbarum and Candida albicans* were the most common Fungi, whereas sensitisation to Cyanodondactlon was common among Pollens. Wheat dust and Grain dust (rice) were the commonest Dust allergens that the patients were sensitised to, while Mosquito was common amongst Epithelia. Gram kabuli was the Food allergen that most patients were sensitised to. There was a significant association of total serum IgE levels with Mites and Pollens, while the association was significant between absolute eosinophil counts and Dust allergens. The correlation between total serum IgE levels and absolute eosniophil counts was significant ($P<0.05$). There was a moderate correlation between total serum IgE levels and the number of allergens the patients were sensitised to, whereas weak correlation existed between absolute eosinophil counts and the number of allergens the patients were sensitised to, both of which were statistically significant.

CONCLUSION:

House Dust Mites are the common offending allergens in the patients of respiratory allergy in North Karnataka. Total serum IgE levels could be used as a screening tool in asthmatics, although skin prick test remains the gold standard test. Total serum IgE levels and absolute eosinophil counts could be helpful in identifying the extent of allergen sensitivity.

KEY WORDS: Skin prick test, allergen sensitivity, total IgE, eosinophil counts

INTRODUCTION

Respiratory allergy is the most common allergy among all the populations and various age groups throughout the world, thus making it a significant health problem. In both developed and the developing countries, allergic diseases' prevalence is increasing steadily, ranging from 15%-30% throughout the world.[1,2] While allergic rhinitis constitutes more than 50% of all allergies seen in India,[3] more than 15 million people in the country are affected by asthma.[4] Rhinitis and asthma exist together frequently, because of continuing inflammation involving one common airway.[5,6]

Allergic rhinitis is defined as an inflammatory condition of the nasal mucosa characterised by sneezing, nasal itching, and nasal congestion caused by an Immunoglobulin-E (IgE) mediated response.[7] Asthma is a heterogenous disease, characterized by airway inflammation, leading to paroxysmal spasmodic narrowing of the bronchial airway.[8] It is characterized as "allergic" and "non-allergic" asthma, depending upon the triggering factor. Over the years, there has been an increasing prevalence of allergic asthma, rendering it a significant health issue.[9]

The types of allergens vary according to the geographic area, climate, location, economic status, ethnic identity, etc. India, being a populous country with different climatic conditions and diverse food habits, the pattern of allergen sensitivity varies from place to place.[10]

Skin prick testing remains to be the gold standard for assessment of specific IgE against a particular offending allergen,[2,11] but several factors exist that make the test less preferred among people, like higher cost, skin diseases and allergies, younger population, and the risk of complications like anaphylaxis. Consequently, the detection of total serum IgE levels

along with eosinophil counts are used to avoid such problems. Earlier, Total serum IgE was preferred as the screening test for diagnosis of allergy by many physicians.[2] Peripheral blood eosinophil counts are also elevated in atopic individuals. Though these tests are not specific for an allergen, as they increase in diseases like alcoholism, some malignancies, and helminthic infections, they bear the advantage of cheaper cost and better patient compliance as they are easy to perform. Various studies have shown a strong relationship among skin prick test positivity, total serum IgE levels, and eosinophil count, but there is a scarcity of data among patients in the district of Vijayapura, Karnataka.

This study is undertaken to evaluate the allergen sensitivity patterns among patients to facilitate better strategies for management and prevention of Allergic Rhinitis and Extrinsic asthma, targeting immunotherapy and decreasing their economic expanse, and improving the quality of life. The study also aims to study the correlation of total serum IgE levels and the eosinophil counts with the skin prick test so as to determine the possibility of their use as a screening test.

AIMS AND OBJECTIVES OF THE STUDY

AIM:

The study aims to determine allergen sensitivity patterns among the patients with allergic rhinitis and/or asthma and correlate the skin prick test reactivity with total serum IgE levels and absolute eosinophil counts.

PRIMARY OBJECTIVES:

1. To evaluate the possible offending allergens among patients with allergic rhinitis, asthma, and a combination of both in Vijayapura district, to target desensitization.

2. To determine the total serum IgE levels, serum eosinophil counts and study their correlation with skin prick test positivity.

SECONDARY OBJECTIVES:

1. To evaluate the demographic profile of patients with skin prick test positivity.

REVIEW OF LITERATURE

HISTORY:

Clemens von Pirquet, a Viennese pediatrician, in the year 1906, noted patients who were injected with the horse serum or a smallpox vaccine developed severe reactions to the subsequent injections which led him to the introduction of the concept called "allergy".[12] The term "allergy" was derived from the Greek words, allos, which means "other", and ergon means "work".[13]

Earlier, inappropriate immune system activation was thought to be the cause for allergies, that lead to the term "hypersensitivity". All the forms of hypersensitivity were classified as allergies, until 1963, when Philip Gell and Robin Coombs classified hypersensitivity reactions into four types, based on the identification of several different disease mechanisms that had a unifying factor to the aberrant activation of the immune system.[14] With this, allergy was classified under type I hypersensitivity, characterized by rapidly developing reactions that involve IgE antibodies.[15]

There are 4 types of hypersensitivity reactions:

Type I: Immunoglobulin E-mediated reaction (immediate)

Type II: IgM or IgG Antibody-mediated reaction (immediate)

Type III: Immune complex-mediated reaction (immediate)

Type IV: Cytotoxic, cell-mediated, hypersensitivity reaction (delayed)

Immediate hypersensitivity reactions occur within 24 hours whereas, delayed hypersensitivity reactions usually occur 12 hours after exposure to allergen. The maximal reaction time is from 48 to 72 hours in a delayed hypersensitivity reaction.[16]

For any IgE-mediated reaction, many physicians and scientists used the term "atopy", coined by Coca and Cooke in 1923.[17,18] But the word "atopy" was reserved by the pediatricians for a genetically mediated predisposition to an excessive IgE reaction.[19] The term was derived from Greek meaning "absurdity".[20]

Gell and Coombs IgE– Mediated Reaction:

Type I hypersensitivity is characterised by immediate responses to allergens and involves the release of mast cell or basophils. When presented to the allergen, IgE cross-links with the FcRI on mast cells. This sets off a reaction of signals intracellularly that results in the synthesis of prostaglandins and cysteinyl leukotrienes, as well as the transcription of Interleukin 4&6 and TNF genes. It also causes mediators such as histamines, proteases, and proteoglycans to be released, resulting in edoema of the tissues, vasodilation, mucus production, and constriction of smooth muscle. This immediate reaction may be followed by a late phase response in 8-24 hours, which is characterised by respiratory, as well as cardiovascular, gastrointestinal, and cutaneous symptoms.[21] The IgE mediated hypersensitivity reaction is depicted in Figure 1.

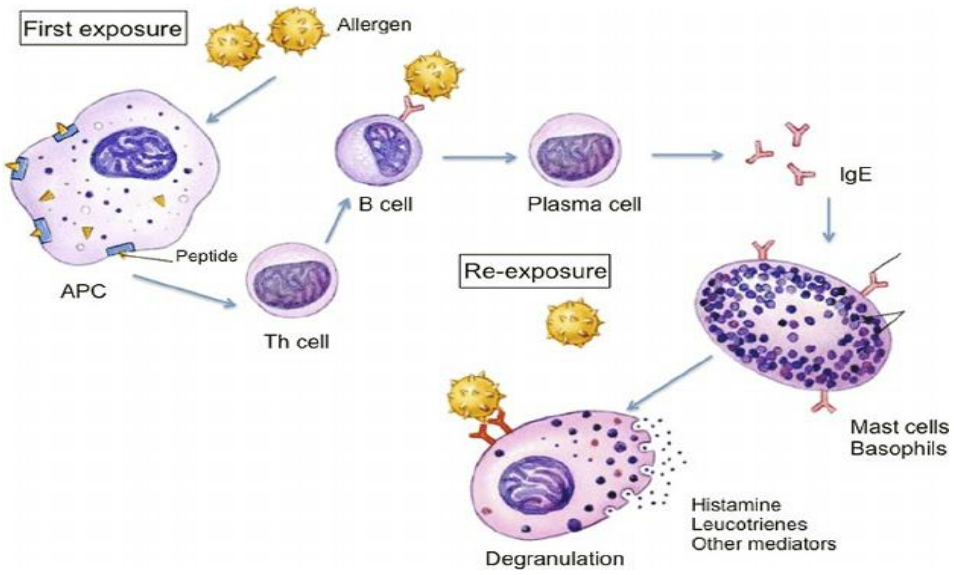


Figure 1: Type I: IgE mediated hypersensitivity reaction[22]

ALLERGIC DISEASES:

Allergic diseases include food allergies, hay fever, atopic dermatitis, allergic rhinitis, asthma, and anaphylaxis. Respiratory allergy that consists of allergic rhinitis and asthma, are the most common allergies amongst all populations and various age groups throughout the world, thus making it a significant health issue. Proteins in the air that are inhaled, trigger airway inflammation, leading to respiratory allergies.

RISK FACTORS:

Risk factors causing allergy could be caused by two different factors, namely host and environmental factors as depicted in Figure 2.[23] Host factors include sex, race, age, heredity etc. Heredity is identified to be the most significant host factor contributing to allergy.

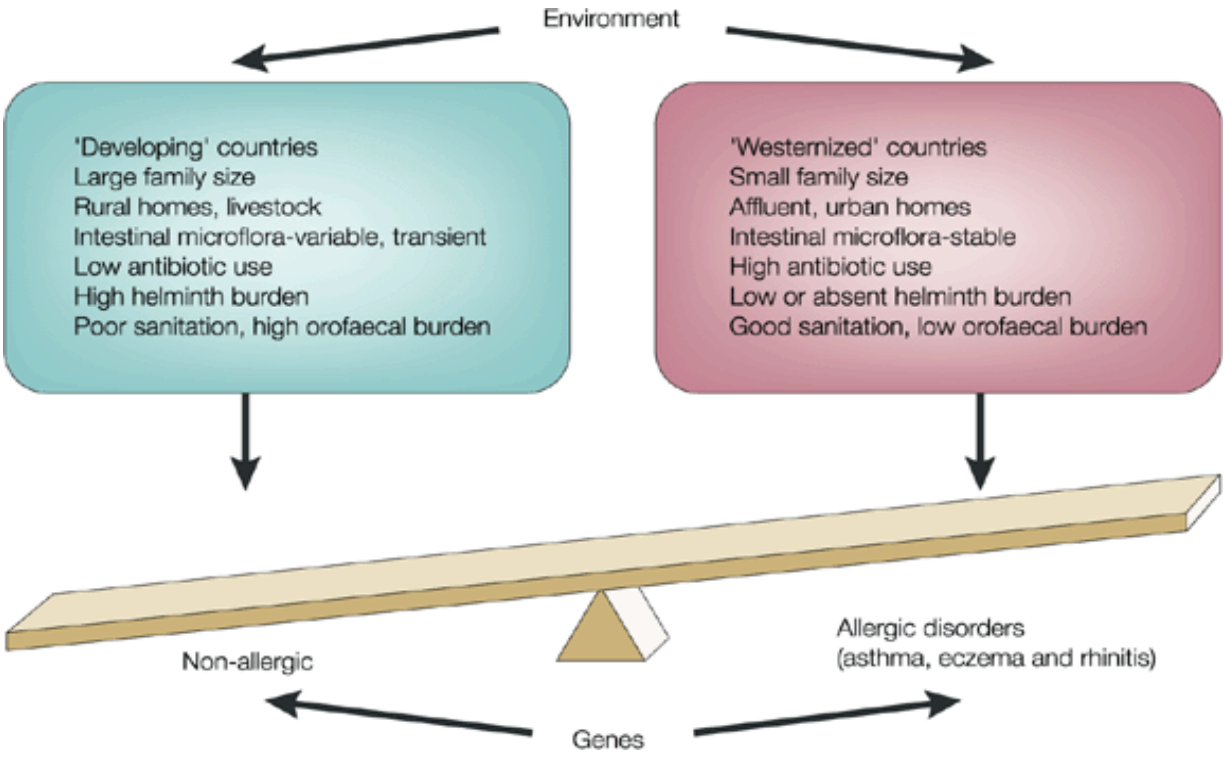


Figure 2: Risk factors for allergy[24]

CAUSES OF ALLERGY:

1. Dust mites:

   Dust mite allergy is a common allergic condition leading to rhinitis, asthma, or eczema.

2. Food:

   Most of the allergic responses occur to a wide variety of foods, the commonest being cow's milk, eggs, fish, wheat, peanuts.[25]

   In India, the population is sensitized to most commonly eggs and fish. Although peanuts are notorious to cause severe allergic reactions, they are not commonly reported amongst adults or children. The reaction are very severe and more common when combined with asthma.

3. Latex:

   The incidence of sensitivity to latex amongst healthcare workers is very high (7-10%), although the prevalence in general population is <1%.[26]

   Contact dermatitis is the most common response to latex which usually lasts 48–96 hours. Latex is also found to cross-react with banana, kiwifruit, etc, because of its similarity with other plant proteins.[26]

4. Medications:

   Certain medications like penicillin, tetracyclins, cephalosporins, sulfonamides etc., cause allergic reactions in susceptible individuals.[27]

5. Insect stings:

   Wasps, bees, ants, mosquitoes, ticks typically cause allergic reactions.

6. Stress:

During chronic stress, both the hypothalamic–pituitary–adrenal axis and the autonomic nervous system cause suppression of interleukin 12, leading to a TH2-predominant response, thus aggravating the allergic conditions.[28] Stress per se does not lead to the development of allergy, but exaggerates the allergic response.

7. Genetics:

The identical twins generally have the same allergic conditions in 70% of the time, non- identical twins tend to exhibit the same allergy in about 40% of the time.[29] Children born to allergic parents commonly suffer from allergies and their allergies are comparatively severe to that of those allergic children born to non-allergic parents.[30,31]

8. Hygiene hypothesis:

Introduced by Strachan in 1989.[32] As proposed by Riedler et al., 2001[33], the immunological explanation behind hygiene hypothesis, is that, the influence of exposure to pathogens on the changing of the predominately Th2 biased environment during infancy led to modifying the Th2-like immune responses or by boosting Th1-like cytokine responses. Hence a decreased exposure to pathogens weaken the Th1 type immune responses and thus allow pro-allergic Th2 responses to become dominant. This phenomenon was referred to as the "biodiversity hypothesis," because of the environmental microflora's potential protective effect of colonization of mucosa.[34]

According to the literature, there is an association between changes in human microbiota and allergy. Microbes in gastrointestinal tract, skin, and airway demonstrate variations amongst different individuals than within an individual. During the first year of life, there is a greater variability in these microbial colonisation with increased susceptibility to outside insults, emphasising that these microbes influence the immune system at an early phase in life.[34]

Th2 responses are down-regulated and Th1-mediated immune response is elicited when the human body interacts with many bacteria and viruses. Allergic diseases are caused when there is inadequate stimulation of Th1 leading to overactive Th2, which has been the first proposed mechanism for hygiene hypothesis.[35] In individuals living in a sterile environment, immune system is not exposed to enough pathogens to get sensitised to various allergens. Since the body is not exposed to a certain level of pathogens, immune system acts on the harmless antigens, triggering an immune response even to the benign allergens.[36]

The incidence of autoimmune diseases is less in the developing world than in the developed countries.[37] Immunological disorders appear to be on the rise as a country becomes cleaner and wealthier. Antibiotic use during the first year of life, as well as antibacterial cleaning products, has been linked to allergic diseases, including an increased incidence of asthma.[38,39] The hygiene hypothesis is summarised in Figure 3.

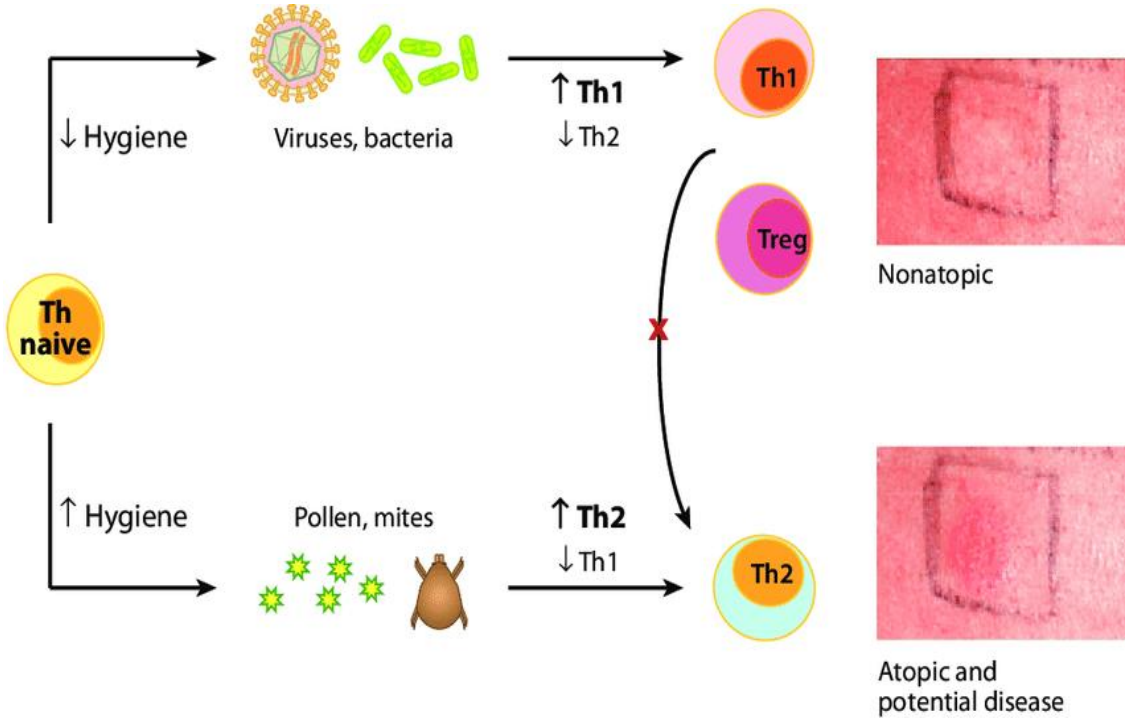


Figure 3: The Hygiene Hypothesis[40]

EPIDEMIOLOGY:

The increase in allergic diseases is seen since 1920s. Though genetic factors determine the susceptibility to atopic disease, atopy has increased in a very short span of time that is unexplainable by genetically associated changes in the population, which gives rise to the probability of environmental or lifestyle changes governing the susceptibility to atopic diseases.[41]

Several hypotheses have been drawn for the increased rate of allergic diseases. Lifestyle changes like increased cleanliness or hygiene, decline in physical activity, associated with dietary changes leading to obesity along with environmental factors like elevated exposure to perennial allergens because of changes in housing and more indoor time have led to the reduced activation of immune defence mechanism, leading to reactivity of body immune system to self antigens.

Recently, studies have focussed on the importance of the gastrointestinal microbiota to identify the reason for rapid increase in allergic diseases in the recent times. The exposure to food and feco-oral pathogens is more in the developing countries,[42] hence the incidence of allergy being less in those countries. It has also been observed that the rise in exposure to parasitic infections is directly proportional to decrease in prevalence of asthma, effect because of alteration of Th1/Th2 regulation.[43,44]

The prevalence of allergic diseases, is increasing steadily, ranging from 15%-30%.[1,2] Rhinitis and asthma are known to co-exist frequently in 70–80% of Indian patients and are considered as continuum of inflammation of a single common airway.[5,6]

There has been a steady increase in the prevalence of allergic rhinitis amongst Indians in the past 20 years.[45] Allergic rhinitis has reported to be significantly impacting the quality of life adversely among the patients.

Frequent aeroallergens in India to cause allergic rhinitis are, house dust mite, pollen, cockroach, and moulds.[46] A study by Saha GK, concluded that majority of the patients with respiratory allergy exhibited sensitisation to house dust mites with commonest being *D-Farinae*, *D- Pteronyssinus and Blomia tropicalis* at 63.72%, 75.06%, and 72% respectively.[47]

Similar studies by Mahesh PA et al.,[48] and Doshi A et al.,[49] from other parts of India also showed *D- Pteronyssinus* as the commonest offending allergen. In another study done by Dey D et al.,[50] the increased frequency of *D- Pteronyssinus* sensitisation was further validated. A study conducted amongst children with asthma aged ≥5 years, by Raj D et al.,[51] showed the common sensitisers to be housefly antigen in 36.7% of the study subjects, rice grain dust in 31%, cockroach in 18%, and house dust mite in 8% of patients.

Allergic rhinitis patients can present as "sneezers and runners" or "blockers". The blockers are mostly sensitised to house dust mites while sneezers and runners have higher pollen sensitisation.

Among two different pollen seasons in India, tree pollens are common during February to April, and grass pollen during September to December.[46] The common pollen in a particular region depends on the local vegetation of that region.[52]

Asthma is the other allergic disease with an increasing prevalence in India over the last two decades, impairing quality of life. The Death and Disability Associated Life Years (DALY), in India, per case of asthma, was identified to be twice higher than the global average.[53] The prevalence was more in Indian states with low economic status, with lower rates in North Eastern states.[54]

In a study conducted by Kumar P et al.,[54], a huge burden of 80%, 52%, and 78% was found to be due to use of firewood, cow dung cakes and kerosene as fuels, respectively.

International Study of Allergy and Asthma in Children (ISAAC) studies provides data on prevalence of asthma among children, which is lower in India compared to developed countries.[55,56] In a study by Paramesh H,[57] a rising prevalence of asthma had been reported. Over a 20-year period, the prevalence rate increased from 9% to 29.5%, influenced by demographic changes. The common triggers amongst asthmatics in India were found to be dust (49%). Female gender, advanced age, urban areas, socially deprived groups, atopy, family history, and exposure to Environmental Tobacco Smoke were identified as risk factors for asthma by Aggarwal et al.[58]

Among Indians with acute severe asthma, sensitisation to *Aspergillus* (51%) and allergic bronchopulmonary aspergillosis (38%) was common.[59] Similar results were obtained in children too.[60]

PATHOPHYSIOLOGY OF ALLERGIC DISEASES:

Acute response:

In allergy, initially, against the allergen, a type I hypersensitivity reaction is produced by the body's immune system. The allergen is presented by antigen-presenting cell causing response in a Th2 lymphocyte. The Th2 lymphocyte produces interleukin-4. Th2 cells interact with B cells, which are involved in production of antibodies. This interaction promotes the release of huge amounts of IgE antibodies by the B cell. IgE secreted binds to the receptor, FcRI. The IgE-coated cells become sensitized to the allergen at this stage.[61] After reexposure, the allergen binds to IgE molecules on the surface of mast cells or basophils. Cross linking of IgE and Fc receptors activates the sensitised cell.

Further, histamine, cytokines, leukotrienes, interleukins, and prostaglandins are released into the surrounding tissue by activated mast cells and basophils by degranulation,

leading to systemic effects and hence resulting in the symptoms of rhinorrhea, itching, dyspnoea, and anaphylaxis.[61]

Late-phase response:

The allergic reaction generally progresses to a late phase in usually 50% of the individuals with a previous history of an allergic reaction. Late phase responses occur after acute response subsides, due to the migration of lymphocytes, neutrophils, eosinophils and macrophages, to initial site. Late phase reaction occurs normally 2-24 hours after the initial reaction.[62] This late phase reaction, if occurs in repeated episodes, leads to development of chronic allergic symptoms. This eventually leads to sensitisation of tissues to subsequent exposure. Cytokines released by mast cells are the reason for long-term effects. In asthma, the late-phase responses differ from those of other allergic responses, despite the immune mechanism involved being the same.[63] The acute and late phase responses are summarised in Figure 4.

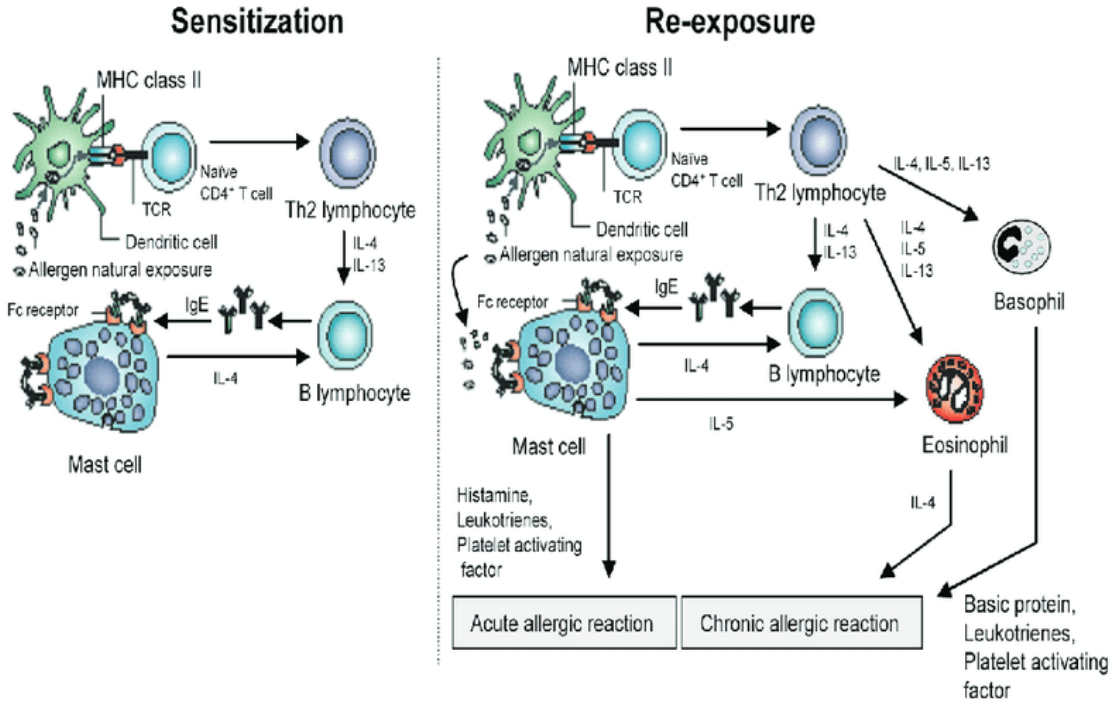


Figure 4: Pathophysiology of acute and late phase responses[64]

MAST CELLS IN ALLERGIES:

Mast cells (MC) secrete several autacoids, proteases, and cytokines, leading to symptoms like rhinitis, bronchospasm, conjunctivitis, erythema, urticaria, angioedema, vomiting, diarrhoea, and hypotension.

MCs express class II MHC antigens that present soluble antigens to T cells, thus leading to T cell proliferation. Dendritic cell development and activation of T cells are also influenced by MCs.

Mast cells in Allergic Rhinitis:

Allergic rhinitis involves a mucosal inflammatory response. In both Seasonal Allergic Rhinitis (SAR) and Perennial Allergic Rhinitis (PAR), there are more MCs in the epithelium and more Th2 cytokines expressed by MCs.

MCs in allergic rhinitis patients were identified to induce plasma cell IgE synthesis, as well as the interaction of CD40 with its ligand implying that MCs help to produce IgE in nasal mucosa.[65] These findings are further supported with the fact that allergic nasal mucosa contains an increased number of IgE-secreting plasma cells.[66]

The biological effects of mast cell derived cytokines are tabulated in Table 1.

Cytokines	**Target cells**	**Biological Effects**
IL-4	B cells	↑ IgE production, ↑ IL-6
	T cells	differentiation to Th2 phenotype
	Eosinophils	Transendothelial migration
	Mast cells	↑ FcεRI, ↑ ICAM-1
	Airway Smooth Muscle cells	Bronchial hyperresponsiveness
IL-3, IL-5, GM-CSF	Eosinophils	Growth, adhesion, transendothelial migration, chemotaxis, activation, and prolonged survival
IL-6	B cells	↑ immunoglobulin secretion including IgE
	T cells	Growth, differentiation
IL-13	B cells	IgE synthesis
	Eosinophils	Activation, ↑ survival
	Endothelial cells	↑ VCAM-1

Table 1: Biological effects of Mast Cell–Derived Cytokines in Vitro[67]

Mast cells in Asthma:

Asthma is a complicated disease characterised by airway obstruction. The presence of ASM hyper-responsiveness to bronchoconstricting stimuli in asthma is the highest contributor to airflow obstruction. The mediators released by MCs, and their infiltration in airways, suggest that MCs are central effector cells in asthma pathophysiology.

The early asthmatic reaction (EAR):

Various mediators are released by MCs in the mucosa of airway during the EAR. In vitro, the relative rate of release of mediators is, Histamine > PGD2 (Prostaglandin D2) > LTC4 (Leukotriene-C4).[68] These mediators are recovered in bronchoalveolar lavage fluid (BAL) within five to ten minutes following a bronchial allergen challenge.[69] Bronchoconstriction, mucosal edoema, and mucus secretion are all caused by histamine, PGD2, and LTC4/LTD4.

The late asthmatic reaction (LAR):

LAR is linked to the accumulation and activation of inflammatory cells. During the LAR, the MC's function as a source of bronchospastic mediators is less evident than it is during the EAR. The LAR has higher levels of histamine, PGD2, and LTC4.[70,71]

During the LAR, tryptase levels decrease, which could indicate a lack of MC activity.[70] GM-CSF inhibits tryptase expression and may increases IgE-dependent histamine release.[72] The LAR is also reduced by omalizumab therapy. Mast cells and their progenitors in Asthma are depicted in Figure 5.

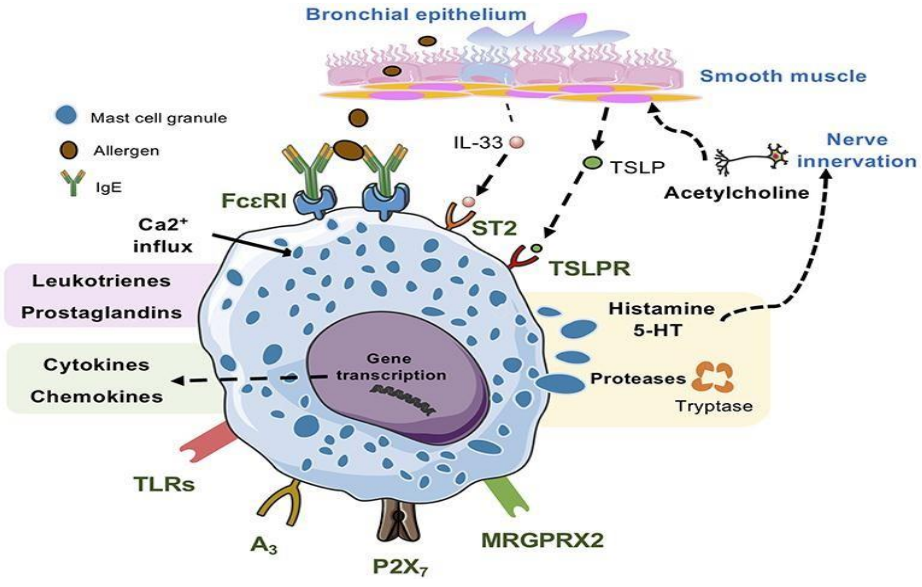


Figure 5: Mast Cells and Their Progenitors in Allergic Asthma[73]

Chronic allergic asthma:

MCs in the bronchial mucosa are activated in chronic allergic "Th2 high" asthma. Morphologic examination revealed that in "stable" atopic asthma, airway epithelium, submucosa, and airway smooth muscle are constantly degranulating.[74]

Several studies have also discovered a rise in the amount of mast cells in BAL from stable asthmatics when compared to healthy controls, in addition to elevated histamine and tryptase concentrations.[75]

MCs in the bronchial mucosa of asthma patients express a variety of cytokines. Correlations have been established between eosinophil counts and MC densities. Hence MC derived cytokines have significant contribution in asthma pathophysiology.[76] MCs were found to be conditioned and stimulated in patients with steroid-free symptomatic asthma. They have increased IgE-dependent histamine release as well as increased spontaneous histamine release.[77]

In symptomatic asthmatics, activation of MCs, although IgE dependent, did not lead to comparative increase in histamine release. However, in asymptomatic asthmatics, there was a high spontaneous release of histamine, emphasising that the release could be due to IgE-dependent activation.[78]

Non-allergic (“Intrinsic”) Asthma:

Numerous asthmatics, especially those with late-onset asthma, show no signs of sensitization towards common allergens. They have "intrinsic" asthma, or non-allergic asthma. This type of disease has a onset at later age, more severe and persistent, and commonly associated with nasal polyposis and aspirin sensitivity.

Like in extrinsic asthma, the inflammatory pattern is similar, implying that a common mechanism may contribute to both the phenotypes of asthma.[79] In both atopic and non-atopic asthmatic subjects, MC FcRI+ is highly expressed in the bronchial mucosa.[80]

Epsilon germline gene and mature epsilon heavy chain mRNA+ B cells are elevated in the bronchial mucosa in both asthma phenotypes, indicating local IgE synthesis,[76] which accounts for the raise in MC FcRI+ expression.[81] IL-4 plays a vital role in promoting the synthesis of IgE.[82]

BASOPHILS IN ALLERGIC DISEASES:

Basophils are the smallest granulocytes, accounting for <1 percent of leukocytes in peripheral blood of human beings.[83]

Basophils and MCs differ in a number of ways, including their location and lifespan.[83,84] Mast cells are rarely detected in blood and reside in peripheral tissues, whereas basophils tend to circulate in peripheral blood and only during inflammation, they migrate to site of inflammation. Furthermore, basophils have a much shorter life span (60 h) than mast cells (2–3 weeks).

Non-redundant functions of basophils have also been observed in chronic allergic inflammation and parasite protection.[85,86]

<u>IgE-dependent airway inflammation – asthma and allergic rhinitis:</u>

Whenever an allergen binds to FcRI receptors on the surface of basophils with specific IgE, cell mediators and cytokines are secreted. The overall response to antigen-

induced mediator release is determined by cell sensitivity or the amount of receptors needed to accomplish 50% of maximum release for aggregation.[83]

Depleting basophils improves rhinitis symptoms, according to recent research.[87,88] Mast cells are also significant in the formation of allergic rhinitis,[89,90] in one model, and it is assumed that basophils must be engaged sequentially to elicit nasal immune responses.

The role of basophils in allergic asthma is unknown. It has been found in one study that mast cells are responsible for airway inflammation in asthma, and not basophils,[91] whereas there are evidences from other studies citing basophils as important in airway inflammation.[92,93] According to these findings, the importance of these cells in asthma varies depending on the experimental conditions. They also play critical roles in IgE-mediated chronic allergic inflammation (IgE-CAI).

Basophil-derived molecules inducing allergic inflammation:

Chemokines and cytokines:

In response to various stimuli, human basophils have been fouund to produce large amounts of IL-4. Several lines of evidence suggest that basophil-derived IL-4 stimulates eosinophil infiltration by acting on a variety of cell types. Indeed, in several allergy models, basophil depletion reduces eosinophil recruitment to the site of inflammation.[94,95,96]

Basophils produce IL-6, IL-13, TNF.[97] Basophil-derived IL-6 has lately been linked to Th17 cell differentiation and humoral memory responses.[98]

Possible roles of basophils in allergy are described in Figure 6.[99]

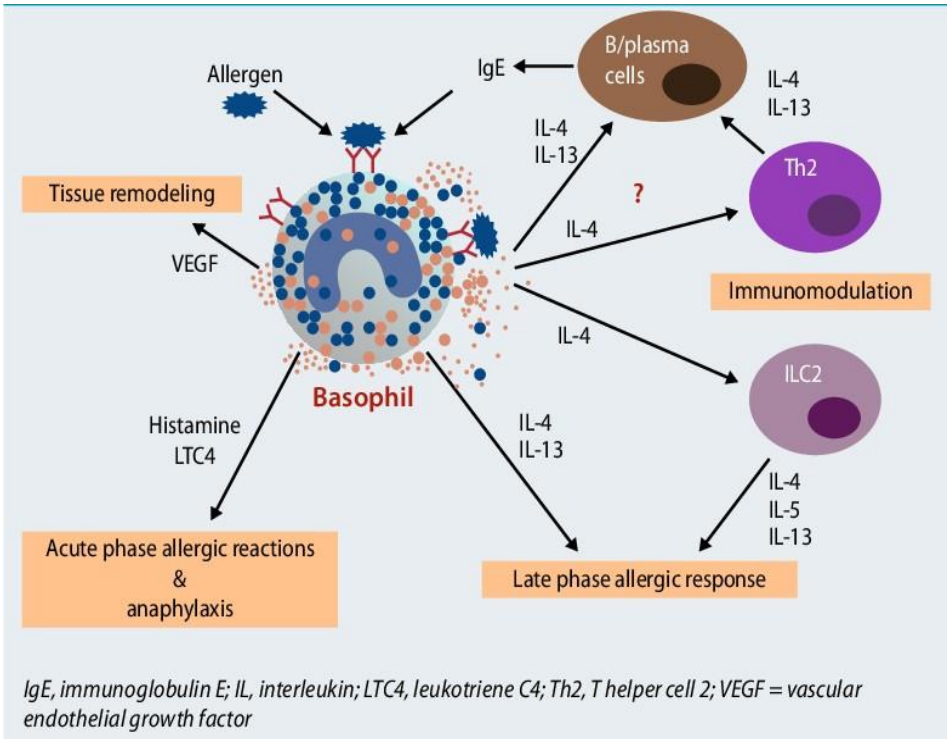


Figure 6: Possible roles of basophils in allergy[99]

Recent researches on basophils, helped to recognise them as vital players in several IgE- mediated allergic mechanisms. They have the ability to initiate and spread inflammation by producing specific cytokines and proteases. Basophils, in collaboration with Dendritic cells, can also induce Th2 differentiation.[100]

EOSINOPHILS IN ALLERGIC DISEASES:

Allergies, drug reactions, helminth infections, Churg-Strauss syndrome, some malignancies and metabolic disorders, eosinophilic gastrointestinal disorders, and hypereosinophilic syndrome are all associated with eosinophilia.

Eosinophils are bone marrow-derived leukocytes that make up less than 5% of blood leukocytes but can be found in higher numbers in tissues such as the bone marrow and the gastrointestinal tract. Activated eosinophils from the bloodstream can be recruited into tissues under a variety of conditions, thus releasing preformed and newly synthesised products such

as cytokines, chemokines, lipid mediators, and cytotoxic granule proteins that can initiate, rapidly escalate, and sustain local inflammatory and remodelling responses.

Eosinophil-rich inflammation has long been associated with parasitic infestation and allergic inflammation. The biologic effects of eosinophils are shown in Figure 7. The proof for eosinophil involvement in rhinosinusitis is circumstantial.[101,102] Anti-eosinophil therapies in asthma are being tried recently, since sputum eosinophils responded well to inhaled steroids.[103] Biologics have been introduced to treat moderate to severe asthma.[104]

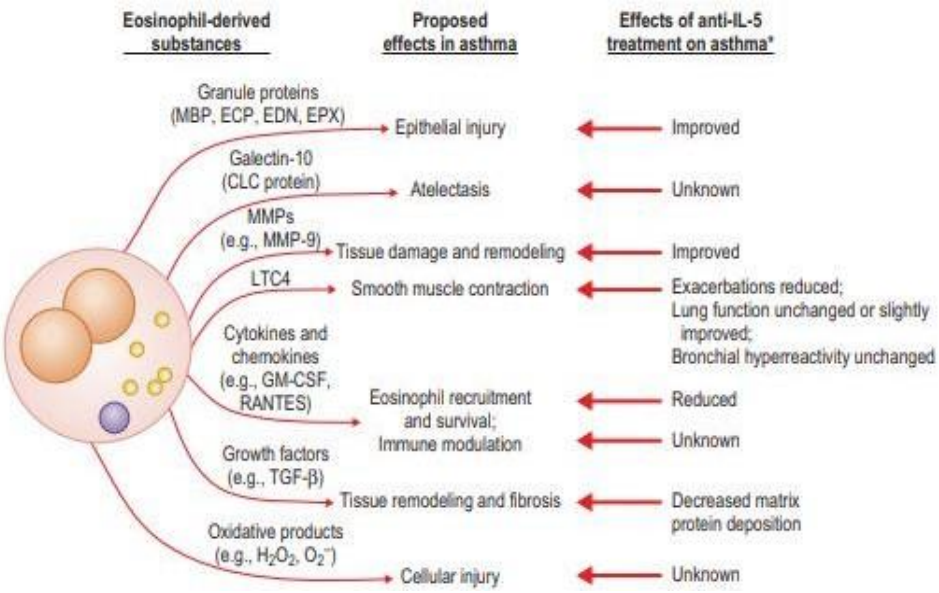


Figure 7: Eosinophil's biologic effects in asthma[105]

IMMUNOGLOBULIN-E:

IgE was the last immunoglobulin to be identified, because of its very low serum levels. IgE is released as a monomer and plays an important role in parasitic infection responses. It is elevated in atopic persons usually. Helminths stimulate the production of IgE antibodies, including parasite-specific IgE antibodies.

They possess "gate keeper function"- recognising the foreign antigens early. IgE-mediated allergy also might aid the host because allergic mucus secretion reactions such as coughing, bronchoconstriction, sneezing, itching, tear production, vomiting, inflammation, and diarrhoea are the mechanisms that expel allergenic proteins from the body. A humanised monoclonal anti-IgE antibody can play an important role in the treatment of IgE sensitised individuals.

Fcε receptors:

Two types of IgE receptors exist. A high affinity IgE receptor, FcRI, whereas FcRII (CD23) is a low-affinity receptor. FcRI is expressed in the skin by mast cells and basophils, as well as dendritic cells and Langerhans cells and FcRII is expressed on monocytes, B cells, and dendritic cells. In people who have very low levels of specific IgE antibodies, FcRI-expressing cells can bind a wide range of IgE antibodies, each with a potentially distinct specificity. Allergic individuals have higher levels of specific IgE antibodies. Hence the FcRIs are more heavily armed with specific IgE, reaching a density that allows for cross-linking of the FcRIs upon exposure to allergens. CD23 is thought to have both positive and negative regulatory functions. It acts as a buffer against excessive IgE accumulation, and in its soluble form, it can prevent IgE binding to the FcRI.

Detection of IgE levels in circulation:

The levels of circulating IgE can be measured either as total serum IgE or levels of specific IgE directed against a particular allergen. There are several methods to measure the IgE levels, namely, radioallergosorbent test (RAST), enzyme-linked immunosorbent assays (ELISA), fluorescent enzyme immunoassays (FEIA), and chemiluminescent immunoassays (CLIA). However, the latter mentioned methods have superseded the RAST method. While

the total serum IgE levels can generally help in diagnosing and monitoring patients with allergic conditions, the specific IgE levels could help determine whether the patient is allergic to a specific allergen. The values of upper limit of normal total serum IgE have been reported variedly in several studies, ranging from 150 to 1,000 UI/ml, however, the usually accepted upper limit is between 150 and 300 UI/ml.[106] According to several studies in literature, sensitivity and specificity of total IgE testing varied from 65% to 89% approximately, citing that the total serum IgE levels could be possibly used for diagnosis of allergic diseases, although specific IgE to an allergen had proved better sensitivity and specificity to determine the offending allergen.[106]

Specific IgE levels can be used to detect sensitisation to several indoor and outdoor allergens, including House dust mites, mould, fungal spores, dander, pollens, etc., and also to food allergens, medicines, latex, venoms, cosmetics, household chemicals etc. Specific IgE testing can also be done to test different mixes of allergens, like food mix, nut mix, grass mix, mould mix, fruit mix etc.

On reviewing the literature, the total IgE levels were found to be highest among patients with asthma alone, when compared to those with only allergic rhinitis. Also, it has also been reported that overlaps of elevated IgE levels with normal values were highest for allergic rhinitis and least for patients with asthma. In a study by Sandeep T et al., mean IgE levels ranged from 151.95 IU/ml in normal subjects to 1045.32 IU/ml in severe asthmatics.[107] Another study reported the mean serum IgE level in moderate-severe allergic rhinitis patients to be 383.69±154.86 IU/mL.[108] Total serum IgE levels were observed to be elevated amongst asthmatics compared to those suffering from allergic rhinitis, although both the groups have showed elevated total IgE levels, overall, making it a reliable marker for diagnosing allergic asthma.

In a study from China, the mean total serum IgE levels among the patients sensitised to house dust mites, were 608.90±529.98 KU/L, while to pollens, the value of total IgE ranged from 63-251 KU/L, whereas 18.8 to 2000 KU/L was the range for fungal sensitisation.[109]

Omalizumab therapy (anti-IgE antibody therapy) could be initiated in patients with allergic rhinitis and/or asthma, based on the body weight and baseline total serum IgE levels, using a dosing table. It is administered as a subcutaneous injection every 2 or 4 weeks.

It is a treatment option included in step 5 of treatment for asthma according to GINA. It is approved for patients with allergic asthma with pre-treatment IgE levels within the range of 30-1500 KU/L. The use of omalizumab has shown to reduce the use of rescue medication, asymptomatic period and better quality of life among asthmatics.

It has also been observed, in several randomised control trials, that omalizumab decreased the total serum IgE levels and provided a symptom free period for patients with seasonal allergic rhinitis.

Hence, total IgE levels could be helpful in, apart from diagnosing or screening for allergic diseases, monitoring the response to therapy, and also to administer the correct doses of biologics directed against IgE as a part of therapy.

ALLERGIC RHINITIS:

Allergic rhinitis (AR) is a significant health burden and one of the most common conditions in otolaryngology practice.[109] It is estimated to affect the lives of >500 million people worldwide.

Allergic rhinitis worldwide:

The global prevalence of AR has been shown to vary up to 40% in adults and 25% in children.[107] The Allergies in Asia Pacific survey reported adult prevalence of 9% across the region, 63% of patients having seasonal or intermittent allergies.[110]

Allergic rhinitis in India:

Reported incidence of allergic rhinitis in India, ranges between 20% and 30%.[111] 30% of the Indian population suffers from AR, and 15% develop asthma.[112]

AR is an inflammatory, IgE-mediated disease characterized by nasal congestion, rhinorrhea, sneezing, and/or nasal itching.[113]

Allergic rhinitis classification:

(1) Based on the temporal pattern of exposure:

- Seasonal
- Perennial- round the year or episodic

(2) Based on the frequency of symptoms:[114]

- Intermittent
- Persistent

(3) Based on the severity of symptoms:[115]

- Mild
- Moderate- severe

History of allergic rhinitis:

10th century physician Rhazes gave the first accurate description of Allergic Rhinitis.[116] Charles Blackley recognised pollen as the cause in 1859.[117] There has been a link with hay because of an old and incorrect theory that symptoms of allergic rhinitis were brought about by the smell of new hay.[118]

Symptoms	**Sneezers and Runners**	**Blockers**
Sneezing	Especially paroxysmal	Little or none
Rhinorrhea	Watery anterior and posterior	Thick mucus more posterior
Nasal itching	Yes	No
Nasal blockage	Variable	Often severe
Diurnal rhythm	Worse during day, improving at night	Constant, day and night, may be worse at night
Conjunctivitis	Often present	

Table 2: Comparison of sneezers/ runners with blockers[119]

Plants causing hay fever:

- Trees: like as pine, mulberry, cedar, hazel, willow, olive etc.
- "Allergy friendly" trees: female ash, red maple, yellow poplar, dogwood, magnolia, double-flowered cherry, fir, spruce and flowering plum.[120]
- Grasses: ryegrass and timothy.
- Weeds: ragweed, plantain, Fat hen, and sorrel/dock.
- Allergy to Balsam of Peru.

Genetic factors contributing to allergic rhinitis:

Numerous latest studies have concentrated on specific loci that may be treatment targets for allergic rhinitis. Single-nucleotide polymorphisms (SNPs) in the interleukin-33 (IL-33) gene have yielded some of the most successful results.[121-123] It has been found that,

following pollen and other allergen exposure, allergic rhinitis patients had higher levels of IL-33 in their nasal epithelium.[124]

Another study discovered that certain SNPs in the protein tyrosine phosphatase non-receptor 22 (PTPN22) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) genes are linked to allergic rhinitis and asthma in children.[125] Many different researchers have identified miRNAs as potential therapeutic targets for treatment of allergic rhinitis.[122,126-128]

DIAGNOSIS OF ALLERGIC RHINITIS:

A history and physical examination can be used to make a presumptive diagnosis of AR. The presence of a specific IgE antibody to an inhalant allergen(s) can help confirm the diagnosis of AR.

Many AR patients can be treated empirically without IgE allergy confirmation. However, in certain situations, like no response to empiric treatment, uncertain diagnosis, confirmatory testing is required.

British Society of Allergy and Clinical Immunology (BSACI) Guideline for Diagnosis of Allergic Rhinitis:[129]

ROUTINE TESTS:

- Nasal airway assessment
- Peak nasal inspiratory flow (PNIF)
- Allergy tests
- Skin
- Serum-specific IgE

ADDITIONAL TESTS:

- Endoscopy
- Rigid

- Flexible
- Radiology
- CT scan

OPTIONAL TESTS:

- Nasal challenge: Allergen, Lysine aspirin
- Nasal samples: Cytology/nasal secretions, Nasal biopsy, Nasal swab
- Radiology: MRI
- Mucociliary function: Nasal mucociliary clearance (NMCC), Ciliary beat frequency, Electron microscopy
- Nasal airway assessment – Rhinomanometry (anterior, posterior), Acoustic rhinometry
- Exhaled nitric oxide (FeNO=fractional exhaled nitric oxide) : Normal levels are <20 ppb, elevated in eosinophilic lower respiratory tract inflammation

According to WHO guidelines, allergy testing, and immunotherapy, can be considered in patients whose symptoms are not adequately controlled by antihistamines and moderate-dose intranasal steroids (INS), with trial of medications for at least two to four weeks. Total serum IgE measurement has limited value in diagnosis of AR.[130]

IgE specific tests are of two types: skin testing and blood testing.

Skin testing:

A bioassay involving introduction of specific allergen into the patient's skin. It allows for direct observation of body's reaction to a specific antigen. By interacting with IgE antibodies on the surface of cutaneous mast cells, the antigen quickly activates them. This causes mast cell granules to release chemical substances such as histamine, resulting in a wheal and flare reaction within a period of 15 to 20 minutes.[131,132]

The skin prick/puncture technique or the intradermal/intracutaneous technique are the most commonly used methods for skin testing. Skin prick testing has high sensitivity and specificity.[133,134]

Skin testing is appropriate for patients of all ages. Albeit, the prevalence of skin prick test (SPT) positivity declining after the age of 50, significantly positive tests can be detected in the elderly.[130,134-136]

Advantages of SPT:

- Immediate results.
- Simple to use, less costly.

Disadvantages of SPT:

- Withhold medications with antihistamine properties for minimum 7 days.
- If active eczema on the test site, cannot be performed.

Contraindications of SPT:

- Diffuse cutaneous condition.
- Severe dermatographism.
- Inability to stop drugs that the patient is using which interfere with SPT results.

Puncture technique, the Scratch testing, is rarely used nowadays because of lower sensitivity and specificity with poor reproducibility.[130,137] Other types of skin tests to identify IgE-specific allergens are intradermal and intradermal dilutional tests, especially when the prick test is negative but high index of suspicion for allergy remians.[138, 139]

Blood testing:

An in vitro test can be used to determine allergen-specific IgE levels in a patient's serum. Radioallergosorbent tests, aka RAST are rarely used nowadays.[137]

One of the benefits of immunoassays is, there is no fear of adverse events. Antihistamines and other medications need not be discontinued. Blood allergy testing may be preferred over skin testing in case of dermatographism or severe eczema are present.[130]

SPT is thought to be more sensitive than blood test as well as less costly.[130,140-142]

Other tests:

Acoustic rhinometry, olfactory testing, food allergy testing, microarray testing, nasal nitric oxide measurements, and nasal allergen challenges are among the other diagnostic tests available. Some clinicians have used nasal smears to evaluate nasal eosinophilia, but there is no general agreement on their usefulness.[143-145] There is not enough evidence for or against using these tests.

In patients who already meet clinical criteria for AR, radiographic imaging is unnecessary. Any benefits of routine imaging are negated by the possibility of significant adverse events and unnecessary costs.[146,147] Iodinated contrast has the potential to cause allergic anaphylactic reactions as well as nephrotoxicity.[148]

TREATMENT OF ALLERGIC RHINITIS (Figure 8):

- ✓ Allergen avoidance
- ✓ Isotonic saline irrigation in both adults and children.
- ✓ Oral H1-antihistamines: on neurally mediated symptoms of itch, sneeze and rhinorrhoea and only a modest effect on nasal congestion.
- ✓ Intranasal corticosteroids
- ✓ Intranasal corticosteroids + oral antihistamine or plus a leukotriene receptor antagonist
- ✓ Systemic glucocorticoids

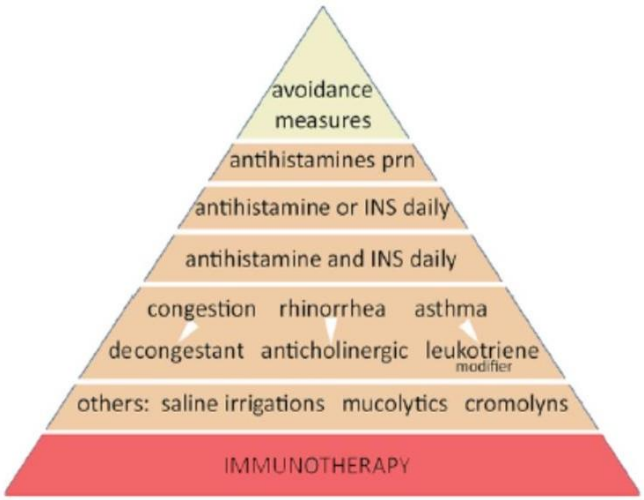


Figure 8: Allergy treatment pyramid[149]

Recommendations for pharmacotherapy for allergic rhinitis (according to ARIA guidelines):[102]

- ✓ Intranasal corticosteroids (INCSs) are more effective in controlling symptoms.[150-153]
- ✓ The first choice of treatment are INCSs.
- ✓ The combined use of an oral H1-antihistamine and INCS does not provide better efficacy than INCSs alone.[154,155]
- ✓ The fixed combination of intranasal Fluticasone Propionate and azelastine in a nasal spray, is more effective than INCS or H1-antihistamine monotherapy and is indicated for patients in whom INCS monotherapy is considered inadequate,[113,156-158] with severe AR or for patients who want a quick relief of symptoms.[154,155]
- ✓ Oral H1-antihistamines of the first generation are sedating and should be avoided,[159] as well as the prolonged use of nasal alpha-sympathomimetics (in vasoconstrictive nasal sprays).
- ✓ Depot corticosteroids i.m. are not indicated in allergic rhinitis.

The latest guidelines for Allergic Rhinitis (MASK algorithm),[102] includes Visual Analogue Scale for Global Rhinitis symptoms (Figure 9), for selecting pharmacological treatment and step-up or step-down of treatment based on symptom control. The step up algorithms of untreated and treated allergic rhinitis are represented in Figure 10 and Figure 11, respectively. The effects of pharmacotherapy on individual rhinitis symptoms are summarised in Table 3.

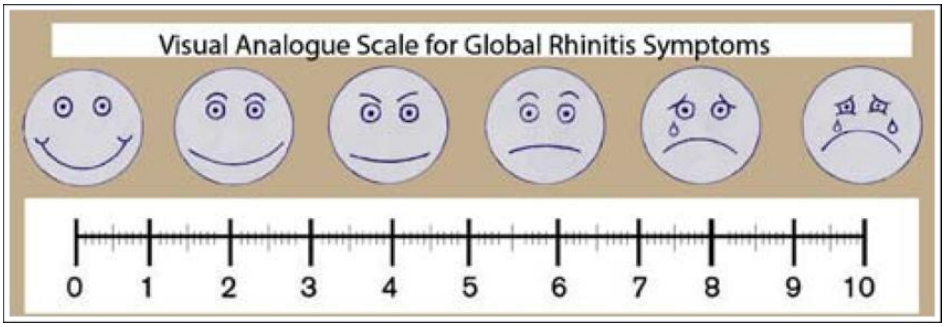


Figure 9: Visual analogue scale for Global Rhinitis Symptoms

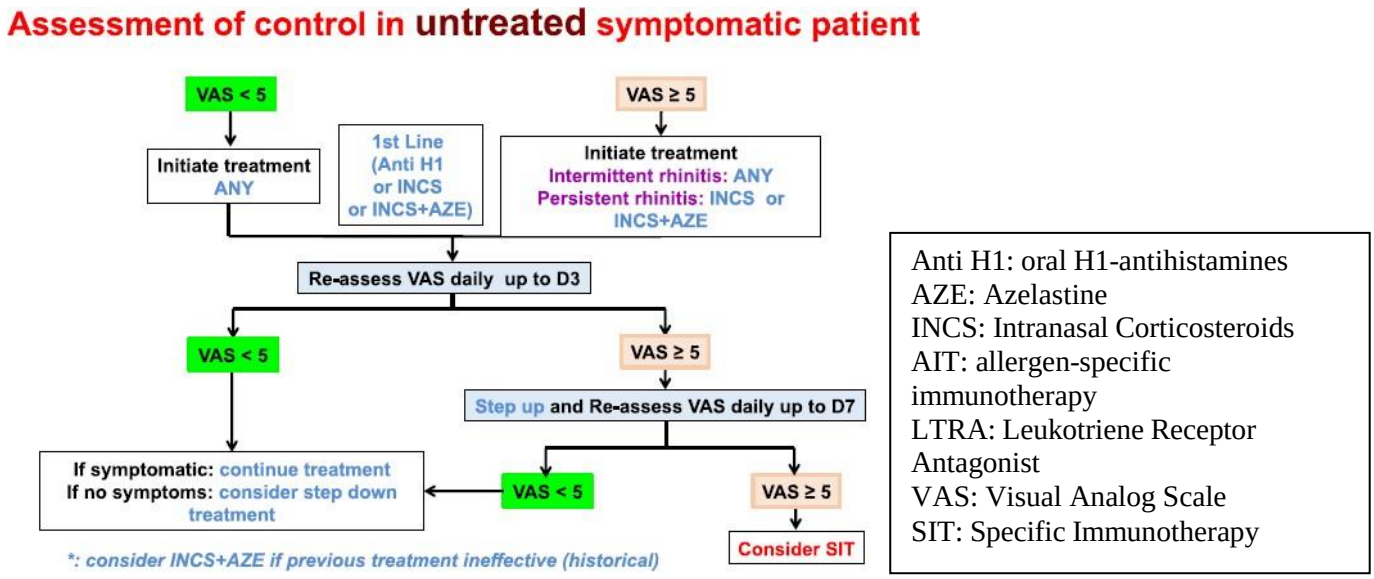


Figure 10: Step up algorithm in untreated allergic rhinitis according to ARIA guidelines[102]

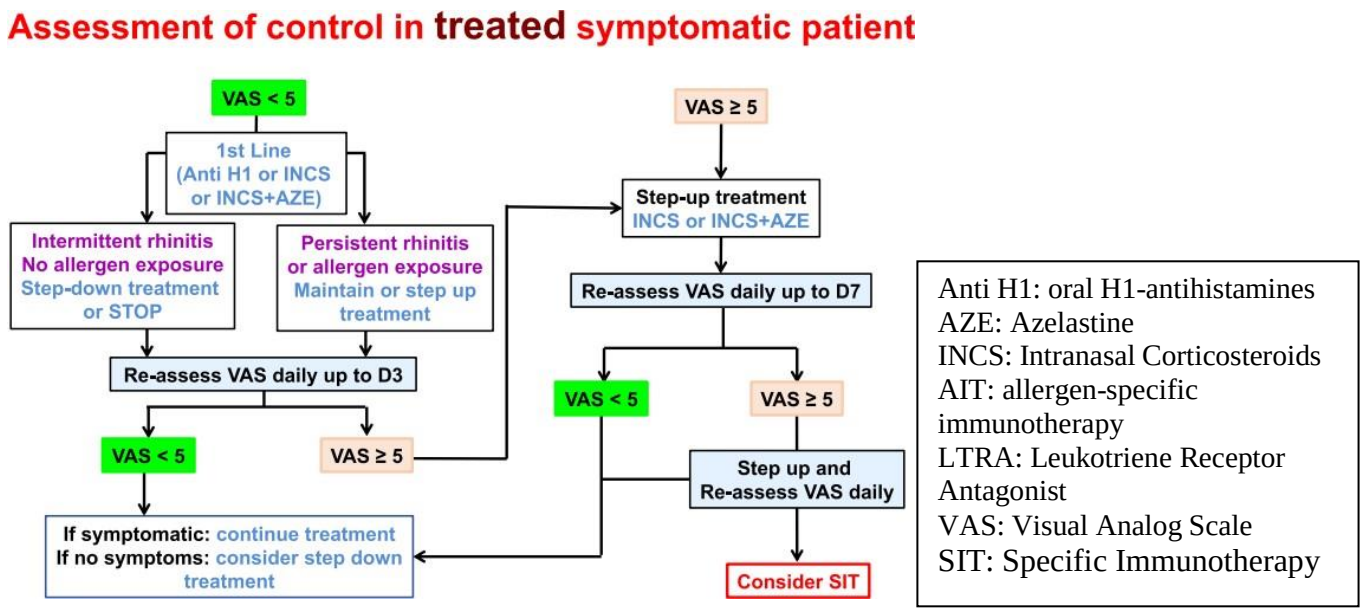


Figure 11: Step up algorithm in treated allergic rhinitis according to ARIA guidelines[102]

	Sneezing	Rhinorrhea	Nasal obstruction	Nasal itch	Eye symptoms
H1 antihistamines • Oral • Intranasal • Eye drops	 ++ ++ 0	 ++ ++ 0	 + + 0	 +++ ++ 0	 ++ 0 +++
Corticosteroids • Intranasal	+++	+++	++	++	++
Chromones • Intranasal • Eye drops	 + 0	 + 0	 + 0	 + 0	 0 ++
Decongestants • Intranasal • Oral	 0 0	 0 0	 ++++ +	 0 0	 0 0
Anti-cholinergics	0	++	0	0	0
Anti-leukotrienes	0	+	++	0	++
Intranasal steroids and intranasal antihistamine	+++	+++	+++	+++	+++

Table 3: Pharmacotherapy effects on individual rhinitis symptoms[129]

ALLERGEN IMMUNOTHERAPY:

Pollen allergen immunotherapy was first tested by the British physicians Noon and Freeman in London.[160,161] Noon stated a hypothesis that a person can achieve a state of immunity by injecting pollen toxin in patients with hay fever. [162]

In the 1930s, allergen immunotherapy was widely used in the treatment of hay fever. Larger amounts of allergen are introduced into the body to change the body's immune system response.[163]

The goal of desensitisation immunotherapy is to induce tolerance to allergen by decreasing its proclivity to induce IgE production. Desensitization is achieved by administering increasing doses of allergen, that slowly reduces IgE-dominated response. There is a shift of immune response from humoral immunity to cellular immunity.

Types of Allergen Immunotherapy:

1. Subcutaneous:

   Subcutaneous immunotherapy (SCIT) involve two phases of injections- build up phase (3-6 months) and maintenance phase. Build up phase is weekly injections and maintenance phase is monthly injections lasting for three to five years.[164] After reaching the effective dose, the maintenance phase begins, which depends on an individual's response to the build-up phase.[165]

   A fatal anaphylactic reaction with SCIT is rare. The adverse effects vary depending on the allergen extract used and the schedule of allergen immunotherapy.[166]

   SCIT schedules can be given as cluster approach, conventional approach or rush approach.

2. Sublingual:

Sublingual immunotherapy(SLIT) involves placing of tablets or drops of allergen extracts sublingually, which would be absorbed through the lining of the mouth.

SLIT is usually given in several doses over a period of 12 weeks.[167] The best time to start the therapy is twelve weeks before the start of pollen season.[167] The first dose, when given to the patient, should be monitored by a physician for any reactions or anaphylaxis. The subsequent doses can be self administered by the patients, thus making it a convenient approach when compared to SCIT.

With SLIT, the occurrence of serious adverse effects is very rare, though there have been a few reports of anaphylaxis reported.[168] The side effects are usually local, like swelling of mouth, lip, tongue, nausea, vomiting, throat irritation, uvular edema, and resolve in few days. It is better tolerated than SCIT.

3. Oral:

Oral immunotherapy (OIT) involves fedding increasing amounts of food allergen in an allergic individual, so as to raise the threshold that is required to cause an allergic reaction. It has been observed that the patients on OIT have increased risk of needing epinephrine.[169]

4. Transdermal:

Transdermal immunotherapy (TDIT) involves epicutaneous application of an antigen to raise the threshold for reaction trigger.

Indications for Allergen Immunotherapy (AIT):[154]

1. Allergic rhinitis/conjunctivitis and/or allergic asthma.

2. A particular allergen exposure must cause symptoms of allergy.

3. Poor symptom control despite adequate pharmacotherapy.

4. Consent of the patient.

The step by step approach for consideration of AIT is highlighted in Figure 12.

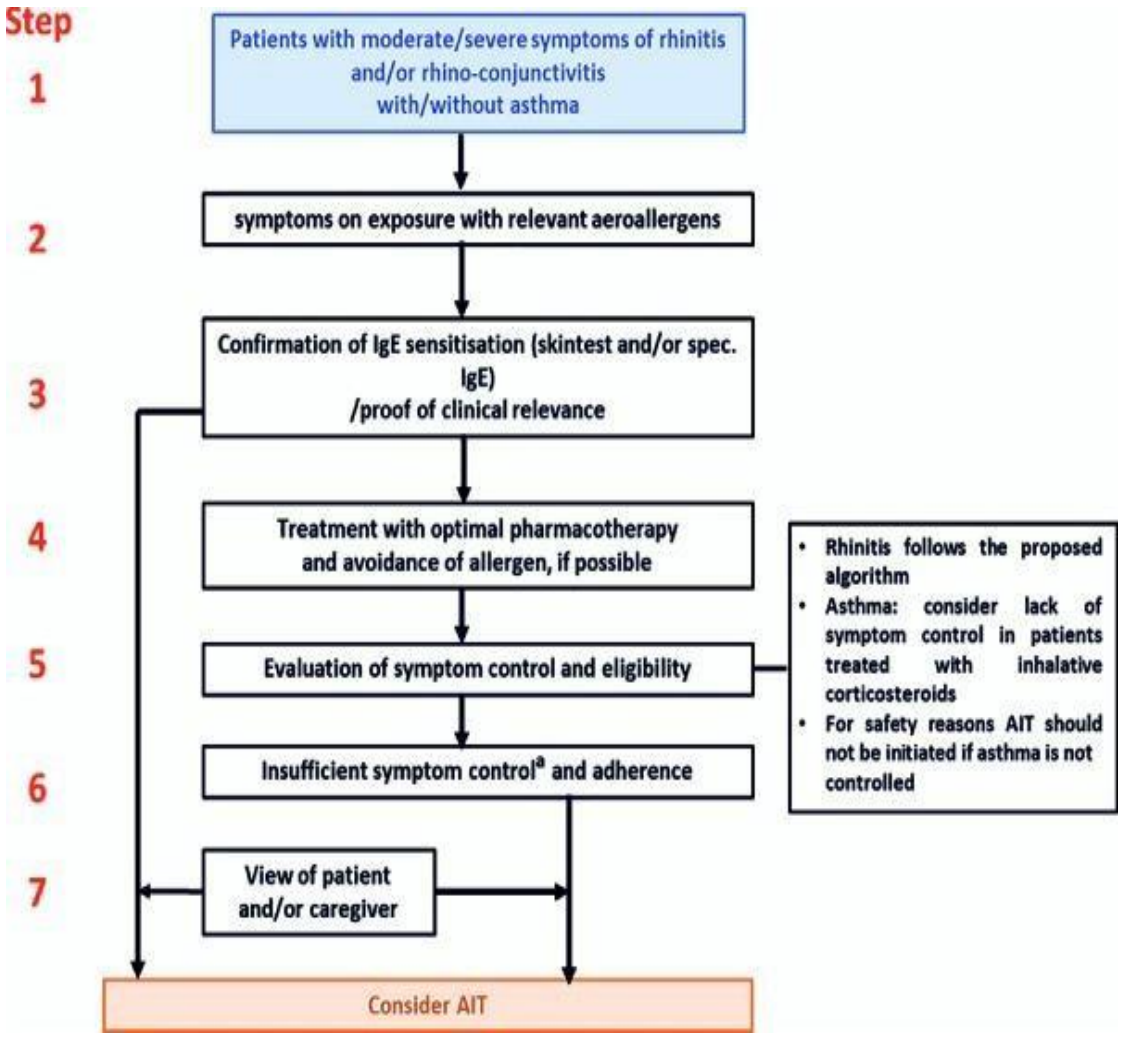
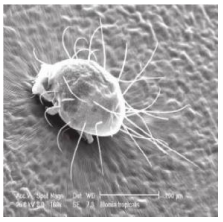
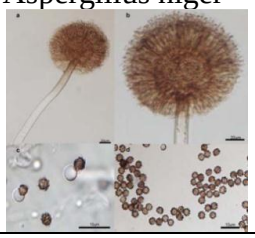
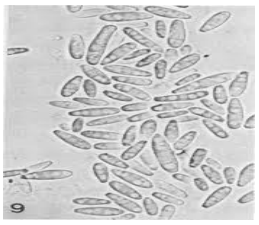
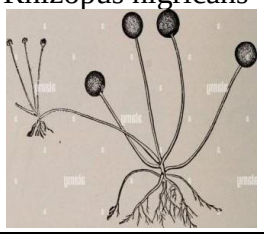
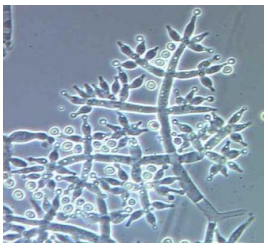


Figure 12: Step by step approach for the indication of AIT[102]

D-Farinae 	D-Pteronyssinus) 	Blomia 	Aspergillus fumigatus 
Aspergillus niger 	Aspergillus flavus 	Fusarium solanii 	Rhizopus nigricans 
Curvularia lunata 	Cladosporium herbarum 	Candida albicans 	Trichoderma 
Cynodondactylon 	Parthenium hysterophorus 	Xanthium strumarium 	Ageratum conyzoides 
Ricinus communis 	Zea mays 	Ipomoea 	Cocos nucifera 
Peltophorum pterocarpum 	Wheat dust	Cotton dust	House dust

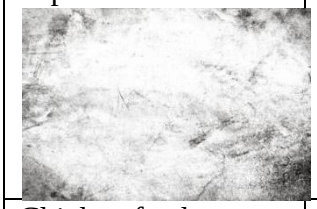
Paper dust 	Hay dust 	Grain dust (rice) 	Sheep's wool 
Chicken feather 	Ant black 	Cockroach 	Honey bee 
Cricket 	Mosquito 	House fly 	Rice weevil 
Moth 	Wasp 	Grasshopper 	Ant red 
Potato 	Maize 	Dal urad 	Tomato 
Lemon 	Cashew 	Peanut (groundnut) 	Milk 

Figure 13: Some of the allergens whose extracts are used for skin prick testing

ASTHMA:

DEFINITION:[170]

- Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.

PHENOTYPES OF ASTHMA:

- **Allergic asthma:**
  - It is the most easily recognized asthma phenotype, which often commences in childhood and is associated with a past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy. Induced sputum analysis shows predominance of eosinophils.
  - Good response to inhaled corticosteroid (ICS) treatment.
- **Non-allergic asthma:**
  - Asthma not associated with allergy.
  - Sputum may be neutrophilic or eosinophilic
  - Patients with this phenotype show short-term response to ICS.
- **Adult-onset (late-onset) asthma:**
  - Some adults, particularly women, present with asthma for the first time in adult life.
  - These patients tend to be non-allergic, and often require higher doses of ICS or are relatively refractory to corticosteroid treatment.

- **Asthma with persistent airflow limitation:**
  - Some patients with long-standing asthma develop airflow limitation that is persistent or incompletely reversible, due to airway wall remodeling.
- **Asthma with obesity:** obese patients with asthma have prominent respiratory symptoms but little eosinophilic airway inflammation.

DIAGNOSIS OF ASTHMA:

Depends on the following:

1. History of variable respiratory symptoms

2. Confirmed variable expiratory airflow limitation- an increase in FEV1 of >12% and >200ml post bronchodilator in adults is confirmatory of asthma (greater confidence if increase is >14% and >400ml in FEV1 post bronchodilator.[171]

Other tests:

i. Bronchial provocation test

ii. Allergy tests- Skin prick test, Total IgE and serum specific IgE

iii. Fractional concentration of exhaled nitric oxide (FeNO)

TREATMENT OF ASTHMA:[171]

Steps 1 and 2:

As needed Low dose Inhaled Corticosteroids (ICS) - Formoterol as controller and reliever medication.

Step 3:

Controller- Low dose maintenance ICS - Formoterol

Reliever- As needed low dose ICS-Formoterol.

Step 4:

Controller- Medium dose maintenance ICS - Formoterol

Reliever As needed low dose ICS-Formoterol.

Step 5:

Controller- High dose maintenance ICS - Formoterol, Add on LAMA, Phenotypic assessment +/- biologics

Reliever- As needed low dose ICS-Formoterol.

If the patient's symptoms do not subside with Step 5 treatment, the following add on therapies can be considered:

- ✓ Add on azithromycin- found to reduce the severity of exacerbations.
- ✓ Add on bronchial thermoplasty- if patient is resistant to therapy
- ✓ Add on low dose oral corticosteroids

Other therapies:

- Allergen immunotherapy
- Vaccinations- for prevention of Influenza and Pneumococcal infections
- Vitamin D

<u>Non-pharmacological strategies:</u>

- Cessation of Smoking and tobacco smoke exposure
- Physical activity and healthy diet
- Cessation of occupational exposure
- Breathing exercise
- Avoidance of medications that aggravate asthma
- Avoidance of indoor and outdoor allergens

OTHER TESTS PERFORMED FOR ALLERGIC DISEASES:

- ✓ Patch testing
- ✓ Challenge testing
- ✓ Provocative and neutralization testing
- ✓ Skin titration (Rinkel method)
- ✓ Applied kinesiology

STUDIES THAT SHOWED CORRELATION BETWEEN SKIN PRICK TEST AND IMMUNOLOGICAL TESTS TO DIAGNOSE ALLERGY AMONG PATIENTS:

Yong Gi Jung et al. conducted a study to compare the SPT and immunological tests as a tool to diagnose house dust mite allergy and concluded that the skin prick test was useful in the population <30 years old, while total serum IgE levels were helpful in diagnosing allergy among the people >30 years.[12]

In 2013, Raj Kumar et al. studied the pattern of skin prick test sensitivity to various aeroallergens in patients with asthma and/or allergic rhinitis in Vallabhai Patel Chest Institute, Delhi. Out of the 918 patients enrolled, the most affected age group was 20-29 years (28.43%), with male predominance(59.69%). The most common offending allergens were identified to be insects(43.90%), followed by pollens, dust mites, and fungal spores.[6]

In the year 2014, Gabriele de Vos reviewed the better test for diagnosing aeroallergen sensitization and predicting clinical allergy. He concluded that some patients with high total serum IgE did not have a skin prick test reactivity and hence the two tests complemented each other and should not be interpreted interchangeably.[13]

In a study conducted by Dr. Suaad Mohammad H. Rasheed et al., in the year 2016, 128 patients with symptoms of allergic asthma and/or allergic rhinitis were enrolled to study the

association between elevated total IgE levels and skin test reactivity. Skin test was positive in 112 (87.5%) patients, and 72 (64%) had high total IgE levels. The study concluded that the results of the skin prick test and total serum IgE levels correlated significantly, and total serum IgE could be used as a diagnostic marker to identify respiratory allergy.[2]

Manuprita Sharma, Tanya Khaitan, Santosh Raman, Ritika Jain, Arpita Kabiraj conducted a retrospective study in the year 2017 to determine serum IgE levels and eosinophil counts in patients with allergic rhinitis and healthy controls and to establish a correlation between them. A total of 155 subjects were selected, with male predominance seen among those with higher total serum IgE levels, while female predominance was seen among those with higher eosinophil counts. They established a weakly positive correlation between total serum IgE and eosinophil levels.[14]

A study on the pattern of skin sensitivity to aeroallergens by skin prick test in patients with respiratory allergy in South-Western Maharashtra was conducted in the year 2020 by C.D.S Katoch et al. It was a cross-sectional hospital-based study, which included a total of 327 patients. 271(82.27%) subjects had a positive skin prick test to more than one aeroallergen, and dust mite was identified to be the most common allergen causing the respiratory allergy.[15]

In 2020, Dr. Naresh Kumar Rao P, Dr. Shahzad Hussain Arastu, in agreement with the previously conducted studies, concluded that total serum IgE levels were elevated in 70% of asthmatics, while eosinophil count was increased in 65% among them, establishing a positive correlation between the two diagnostic tests. They also stated that blood eosinophilia is related to the severity of the nasal disease.[8]

In another study by Muddaiah D, Venkatarangaiah S, in the year 2020, there was a significant association between total serum IgE levels and eosinophil counts, and their values correlating with clinical severity in patients of allergic rhinitis and asthma.[16]

MATERIALS AND METHODS

SOURCE OF DATA:

This study was carried out in the Department of Respiratory Medicine, B.L.D.E(DEEMED TO BE UNIVERSITY)'s, Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura, Karnataka. Study was conducted from January 2021 to June 2022 on 44 patients attending the out-patient and in-patient department of Respiratory Medicine with diagnosis of allergic rhinitis as per ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines 2019 and Asthma diagnosed according to GINA guidelines (2020). This study was conducted after obtaining approval from the institutional ethical committee. Patients were explained about the procedure in detail and consent was obtained for the same.

Study design: Cross-sectional study.

Study Period: One and half years.

Sample size calculation:

With the anticipated Proportion of positivity to skin prick test 87% [2] , the study would require a sample size of 44 patients with 95% level of confidence and 10% absolute precision**.**

Formula used:

$$n=\frac{z^2\ p*q}{d^2}$$

Where Z= Z statistic at α level of significance

d^2= Absolute error

P= Proportion rate

q= 100-p

Statistical Analysis:

The data obtained was entered in a Microsoft Excel sheet, and statistical analysis was performed using a statistical package for the social sciences (Version 20). Categorical variables were compared using the Chi-square test. The formula for the chi-square statistic used in the chi square test is:

$\chi_c^2 = \sum(Oi – Ei)2/Ei$

The subscript "c" are the degrees of freedom. "O" is observed value and E is expected value.

C= (number of rows-1) *(number of columns-1).

Continuous variables were compared using the Pearson correlation tests. $p<0.05$ was considered statistically significant. All statistical tests were performed two-tailed.

INCLUSION CRITERIA:

- Patients suffering from allergic rhinitis and/or asthma of age above 18 years and less than 60 years.
- Patients not on any anti-histamines for seven days.
- Patients ready to give informed consent for inclusion in the study and skin-prick testing.

EXCLUSION CRITERIA:

- Patients with exacerbation of asthma.
- Patients with associated pulmonary diseases, including tuberculosis and chronic obstructive pulmonary disease.
- Patients on anti-IgE and steroid therapy.

- Patients of dermographism.
- Pregnant and lactating women.
- Patients unwilling to take part in the study or to give written consent for the study.

METHODOLOGY :

Patients with allergic rhinitis assessed as per ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines 2019, i.e. if they had two or more symptoms out of watery runny nose, nasal itching, nasal obstruction or sneezing, lasting for at least more than 4 days per week and also for more than 4 weeks in past 12 months, and Asthma patients diagnosed according to GINA guidelines (2020), attending the out-patient and in-patient department of Respiratory Medicine in Shri B. M. Patil Hospital, Vijayapura, from January 2021 to June 2022, were enrolled in the study and subjected to a detailed history, involving the collection of demographic data, with skin prick testing, and blood examination for total serum IgE levels and eosinophil counts.

SKIN- PRICK TEST PROCEDURE:

Skin prick test was done with 73 different types of allergens, which included 3 types of mites, 9 types of fungi, 9 types of pollens, 6 types of dust, 15 types of epithelia, and 31 types of food allergens. A drop of antigen was applied on the healthy skin on the upper back in the identical order and immediately pricked at a 45° angle using a lancet. Saline was used as a negative control, while histamine was used as a positive control. The wheal diameter was measured after 15-20 minutes and considered positive if it was 3mm greater than the negative control.

IMMUNOLOGICAL TEST:

Under aseptic precautions, using a disposable needle and syringe, three milliliters (ml) of venous blood was collected from each patient. Samples were allowed to clot at room temperature, and after centrifugation for 5 minutes, stored immediately at -20°C until testing for total IgE. Total serum IgE levels were measured using Enzyme Linked Fluorescent Assay. IgE concentrations were expressed in KU/L. High total serum IgE levels were defined as >150 KU/L.

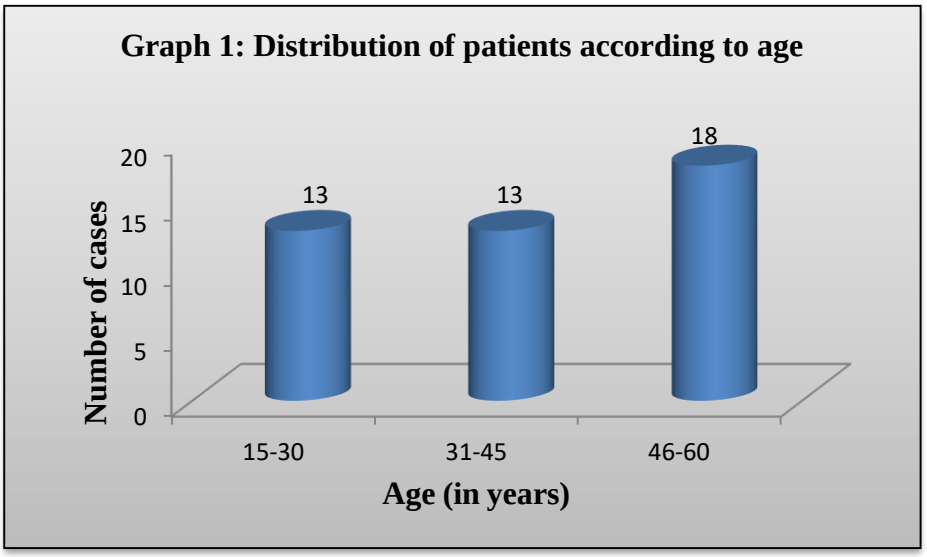
PERIPHERAL BLOOD EXAMINATION FOR EOSINOPHIL COUNT:

Venous blood was drawn into collection tubes containing ethylene diamine tetraacetic acid anticoagulant. Eosinophil counts were performed in the hospital laboratory in automated hematology analyzers. These were measured as the number of cells per milliliter and recalculated as the number of cells per cubic millimeter. High eosinophil counts were defined as >500 cells per cubic millimeter.

RESULTS

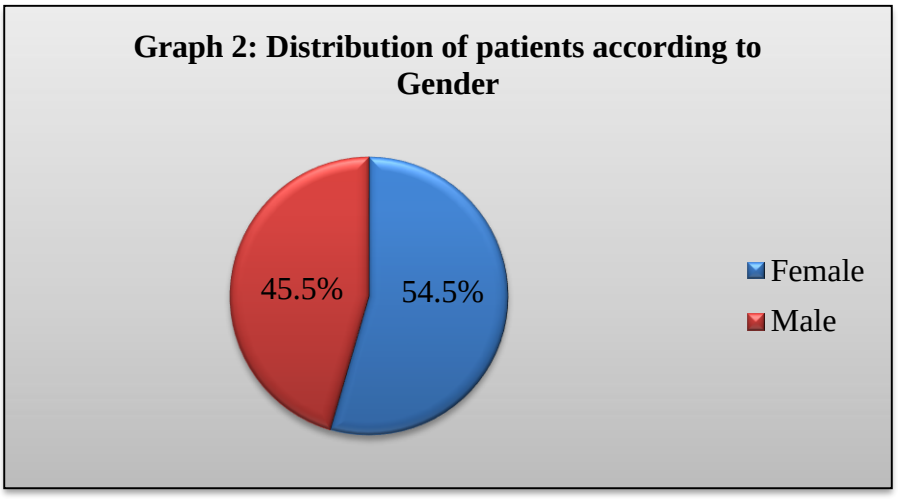
AGE DISTRIBUTION

The distribution of patients according to different age groups is depicted in Graph 1. The mean age was 39.63 years.



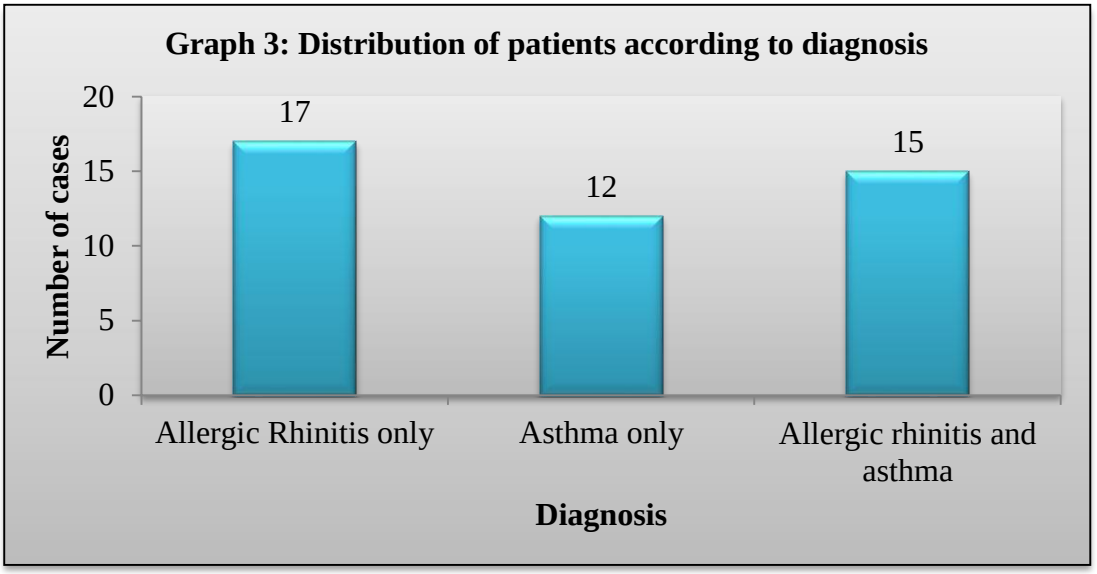
GENDER DISTRIBUTION

It was observed that the gender inclination was towards females with 54.5% of patients (24 in number) while 45.5% of patients were males (20 in number) (Graph 2).



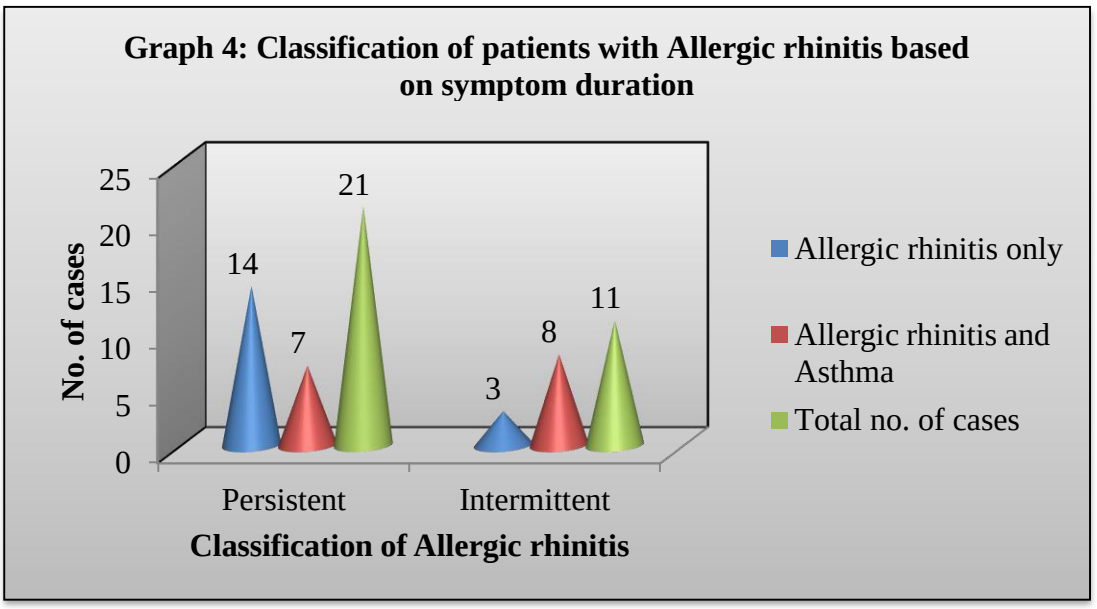
DIAGNOSIS DISTRIBUTION

The distribution of patients into the categories of allergic rhinitis only, asthma only and asthma and allergic rhinitis is shown in Graph 3.



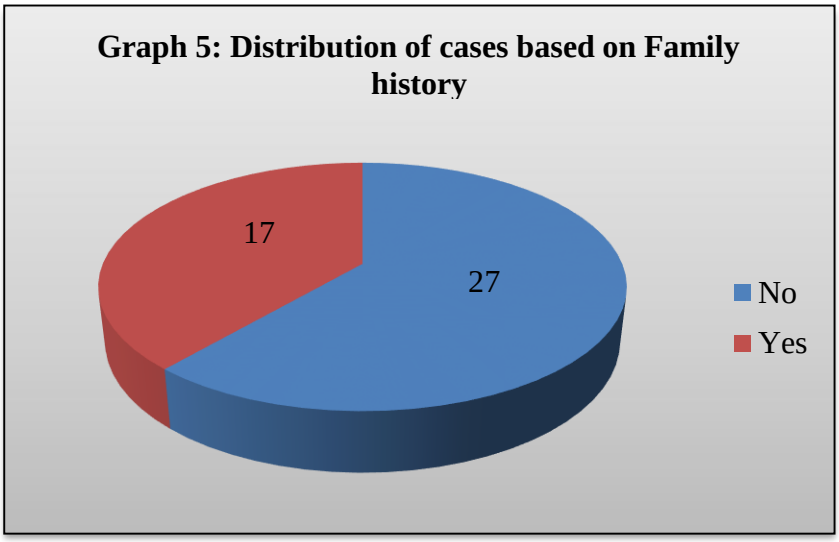
DISTRIBUTION OF PATIENTS WITH ALLERGIC RHINITIS

Out of the 32 patients suffering from Allergic rhinitis, 21 patients (65.6%) had Persistent Allergic rhinitis whereas 11 patients (34.4%) had Intermittent Allergic rhinitis (Graph 4).



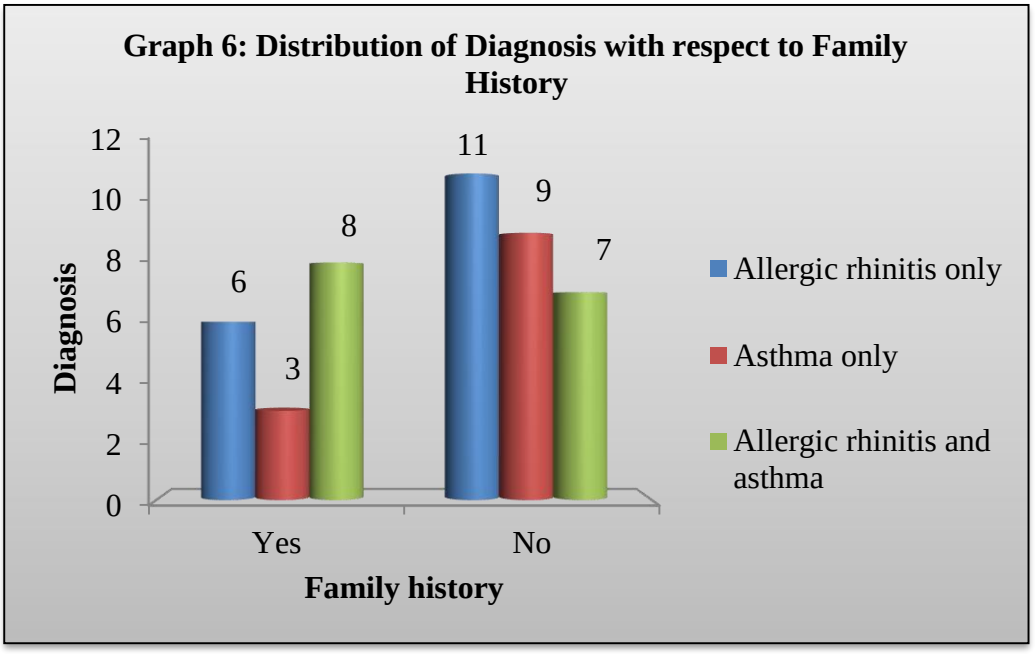
DISTRIBUTION BASED ON FAMILY HISTORY

17 out of 44 patients had family history of allergic diseases. The distribution of cases based on family history is shown in Graph 5.



DIAGNOSIS DISTRIBUTION WITH RESPECT TO FAMILY HISTORY:

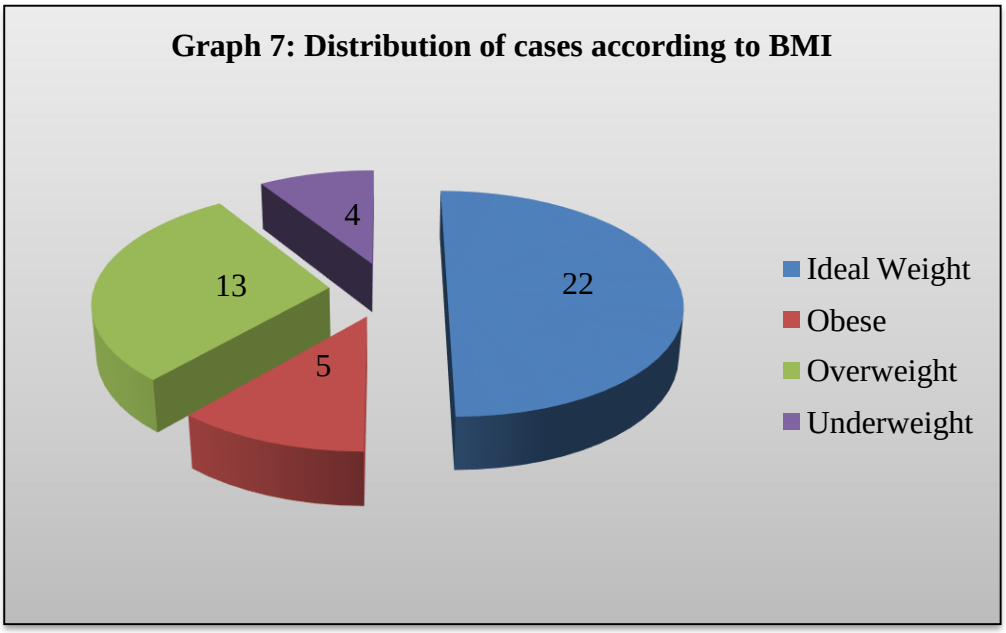
35.3% with only allergic rhinitis, 25% with asthma only and 53.3% of patients with both allergic rhinitis and asthma had family history of allergic diseases, as depicted in Graph 6.



BMI DISTRIBUTION

Of the 44 patients, 50% were of Ideal body weight, whereas 29.5% were overweight, 11.4% were Obese and 9.1% Underweight. The distribution of cases is shown in Graph 7.

Graph 7: Distribution of cases according to BMI



DISTRIBUTION BASED ON DIET

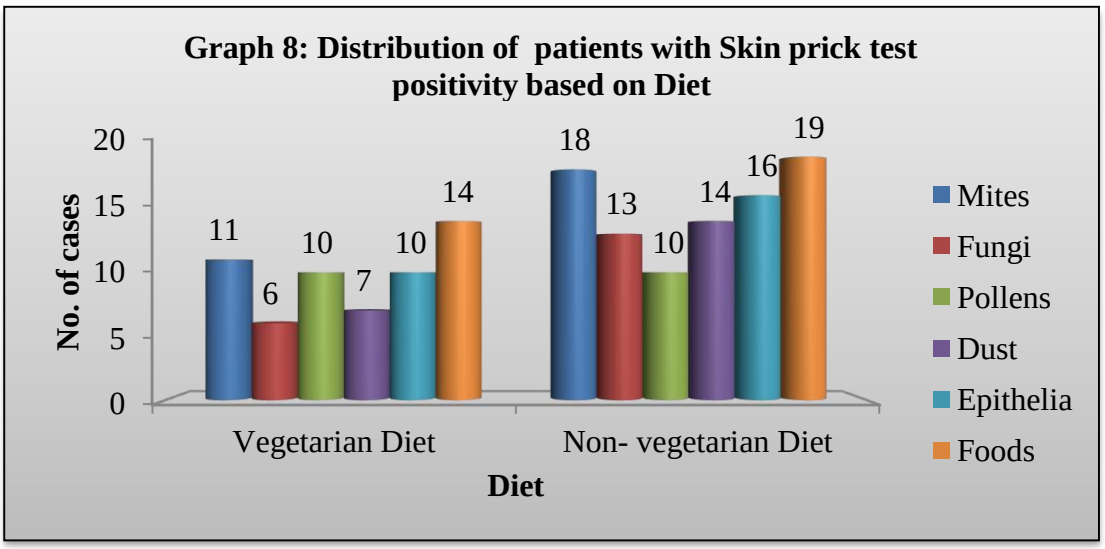
Out of the 44 patients enrolled in the study, 25 patients (56.8%) were Non- vegetarians while 43.2% were vegetarians, the distribution depicted in Table 4.

Table 4: Distribution of cases based on Diet:

Diet	Number of cases	Percentage of cases
Vegetarian Diet	19	43.2
Non- vegetarian Diet	25	56.8

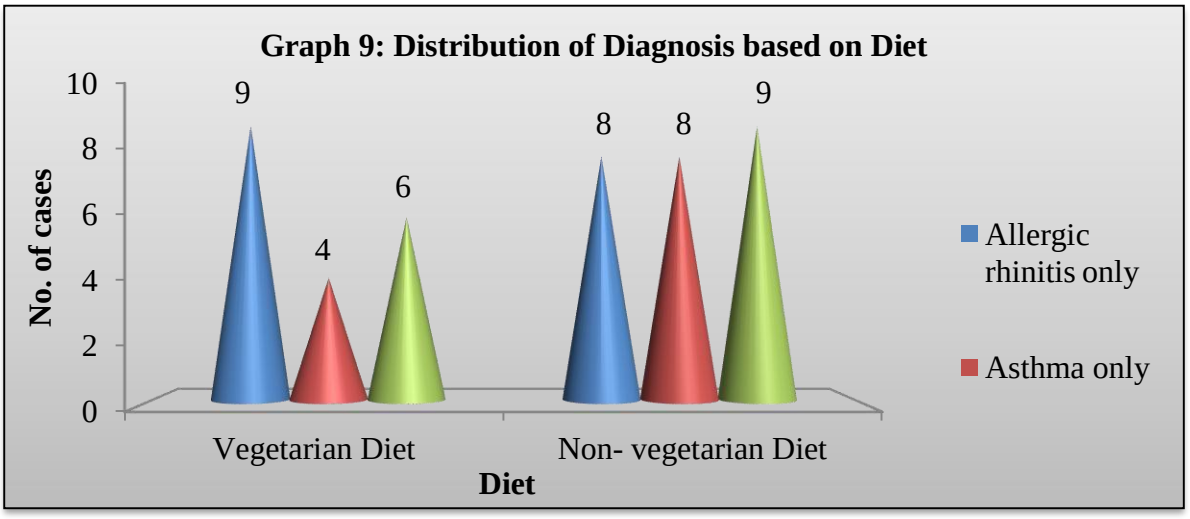
Distribution of patients with Skin prick test positivity based on Diet:

Maximum number of patients among Vegetarians and Non- Vegetarians showed Skin prick test positivity to Food allergens, 14 and 19 patients respectively. The distribution of cases to each group of allergens is represented in Graph 8.



Distribution of patients with Skin prick test positivity based on Diet with respect to Diagnosis:

Among the 19 Vegetarians, majority (47.3%) of cases had only Allergic rhinitis. Out of 25 Non- vegetarians, maximum number of patients (36%) had both Allergic rhinitis and Asthma, the distribution of diagnosis based on diet is depicted in Graph 9.



DISTRIBUTION OF CASES BASED ON THE CLASSIFICATION OF ALLERGENS

The distribution of patients into the categories of sensitisation to only indoor allergens, only outdoor allergens and both indoor and outdoor allergens, and based on the diagnosis is represented in Graph 10 and Table 5, respectively.

Graph 10: Distribution of cases based on the classification of allergens

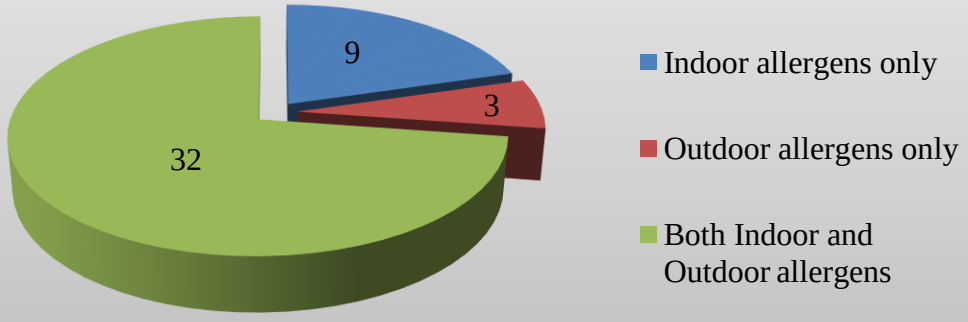
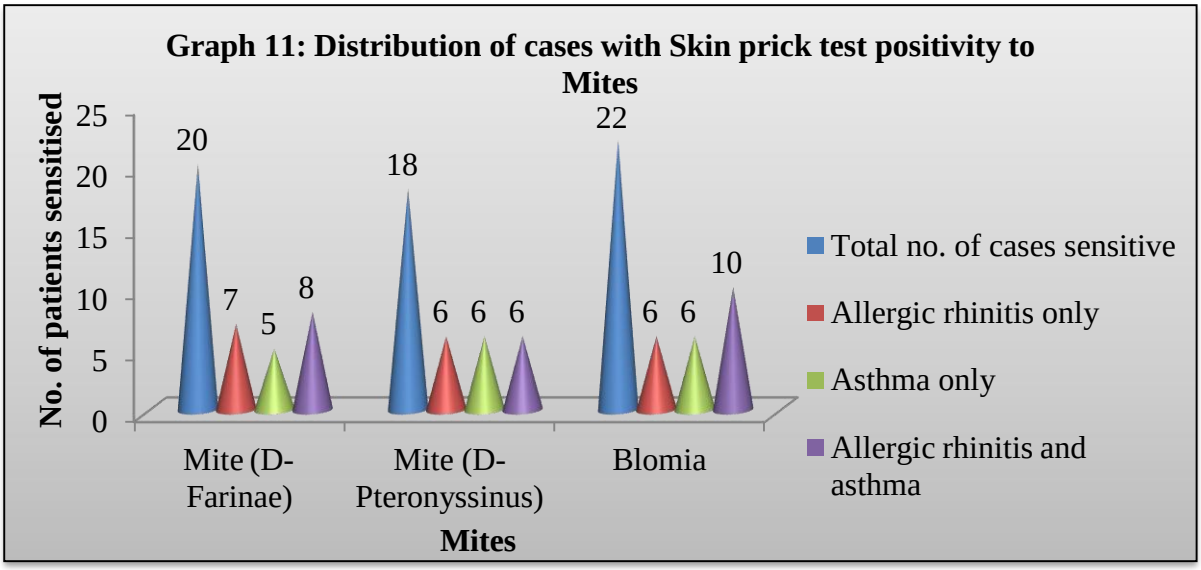


Table 5: Distribution of Diagnosis based on the classification of allergens:

Classification of Allergens	Allergic rhinitis only		Asthma only		Allergic rhinitis and Asthma	
	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases
Indoor allergens only	2	11.8	2	16.7	5	33.3
Outdoor allergens only	1	5.9	1	8.3	1	6.7
Both Indoor and Outdoor allergens	14	82.3	9	75	9	60

SKIN PRICK TEST POSITIVITY TO MITES

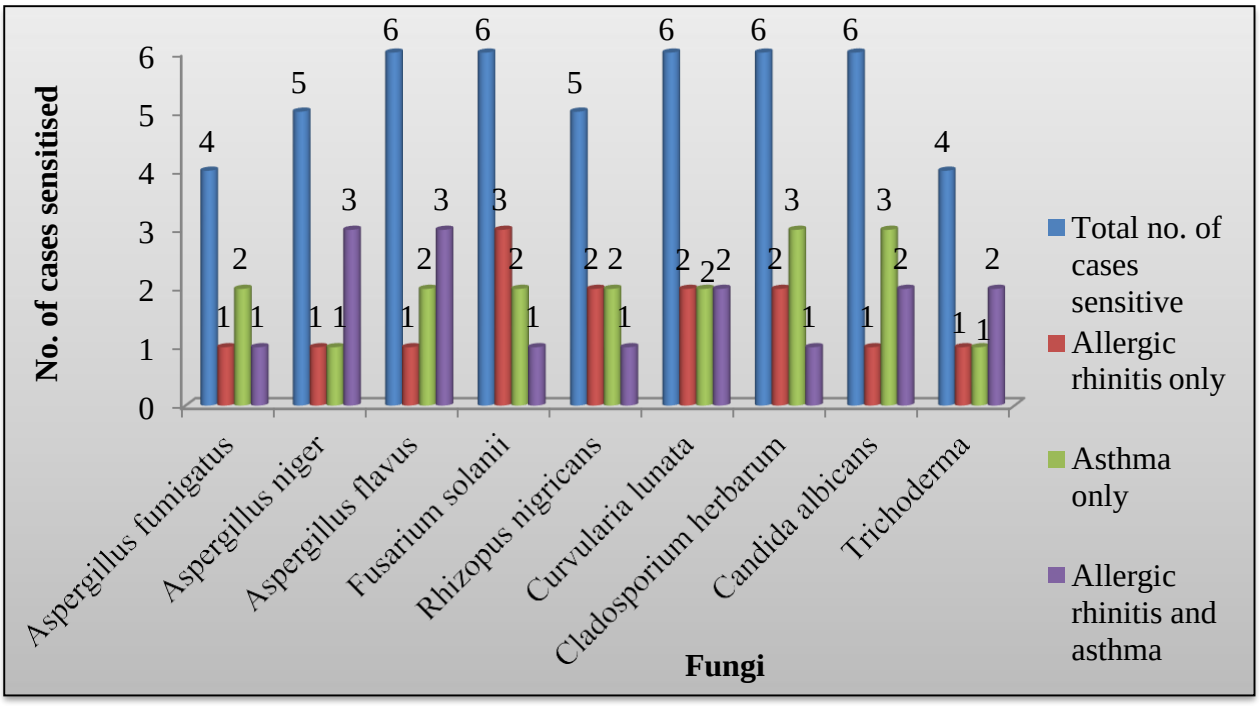
The distribution of cases with sensitisation to Mites with respect to diagnosis is represented in Graph 11. Among the house dust mites, sensitivity to *Blomia* was found to be commonest.



SKIN PRICK TEST POSITIVITY TO FUNGI

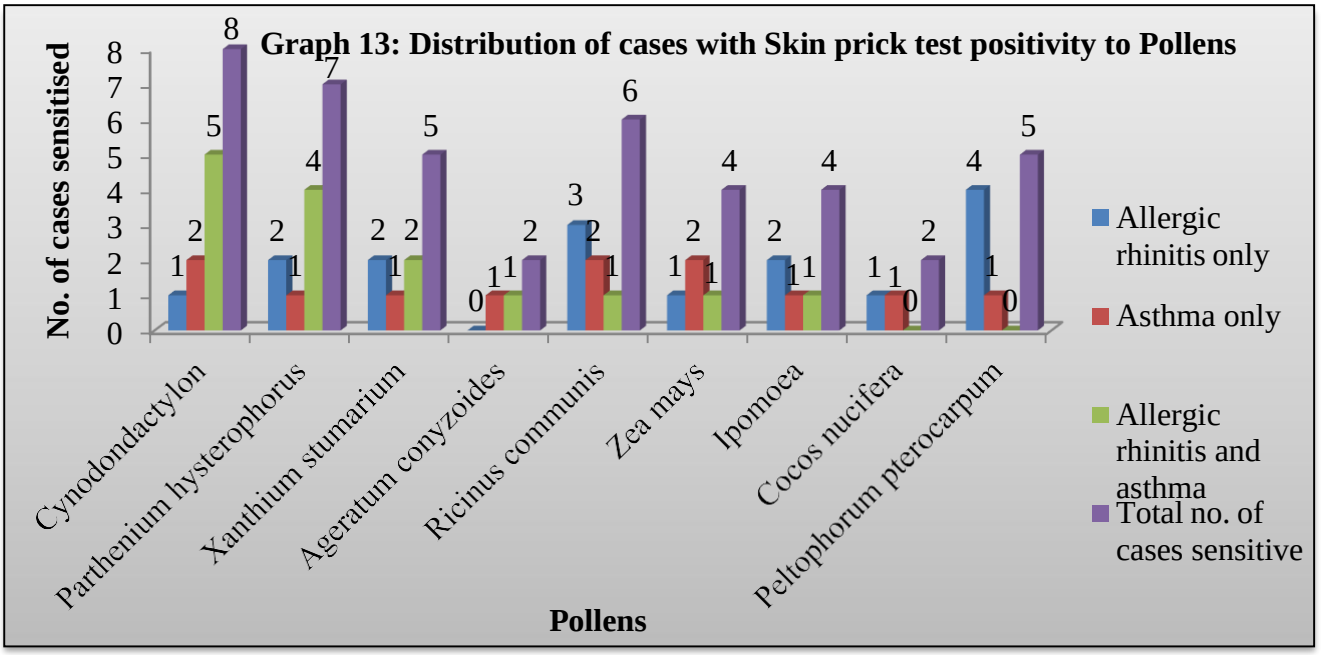
The distribution of cases with sensitisation to fungi with respect to diagnosis is represented in Graph 12.

Graph 12: Distribution of cases with Skin prick test positivity to Fungi



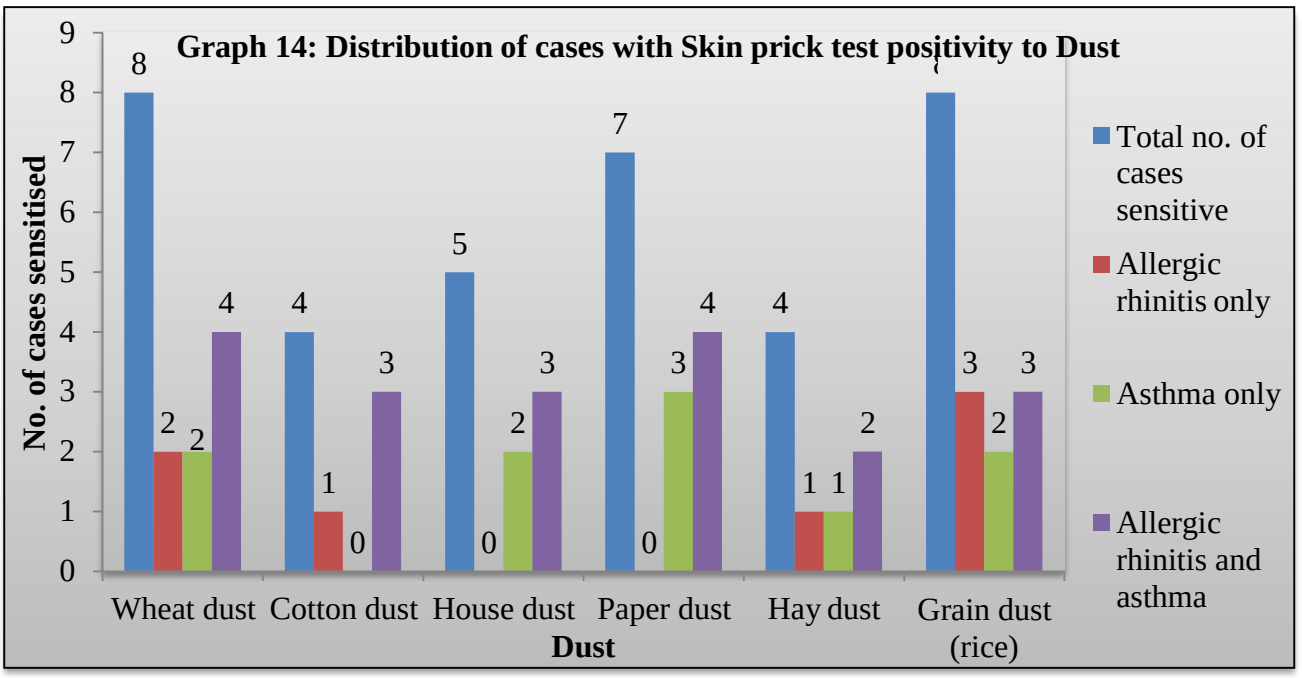
SKIN PRICK TEST POSITIVITY TO POLLENS

Out of Pollens, the most common offending allergen was *Cyanodondactylon* (18.2%), the distribution depicted in Graph 13.



SKIN PRICK TEST POSITIVITY TO DUST

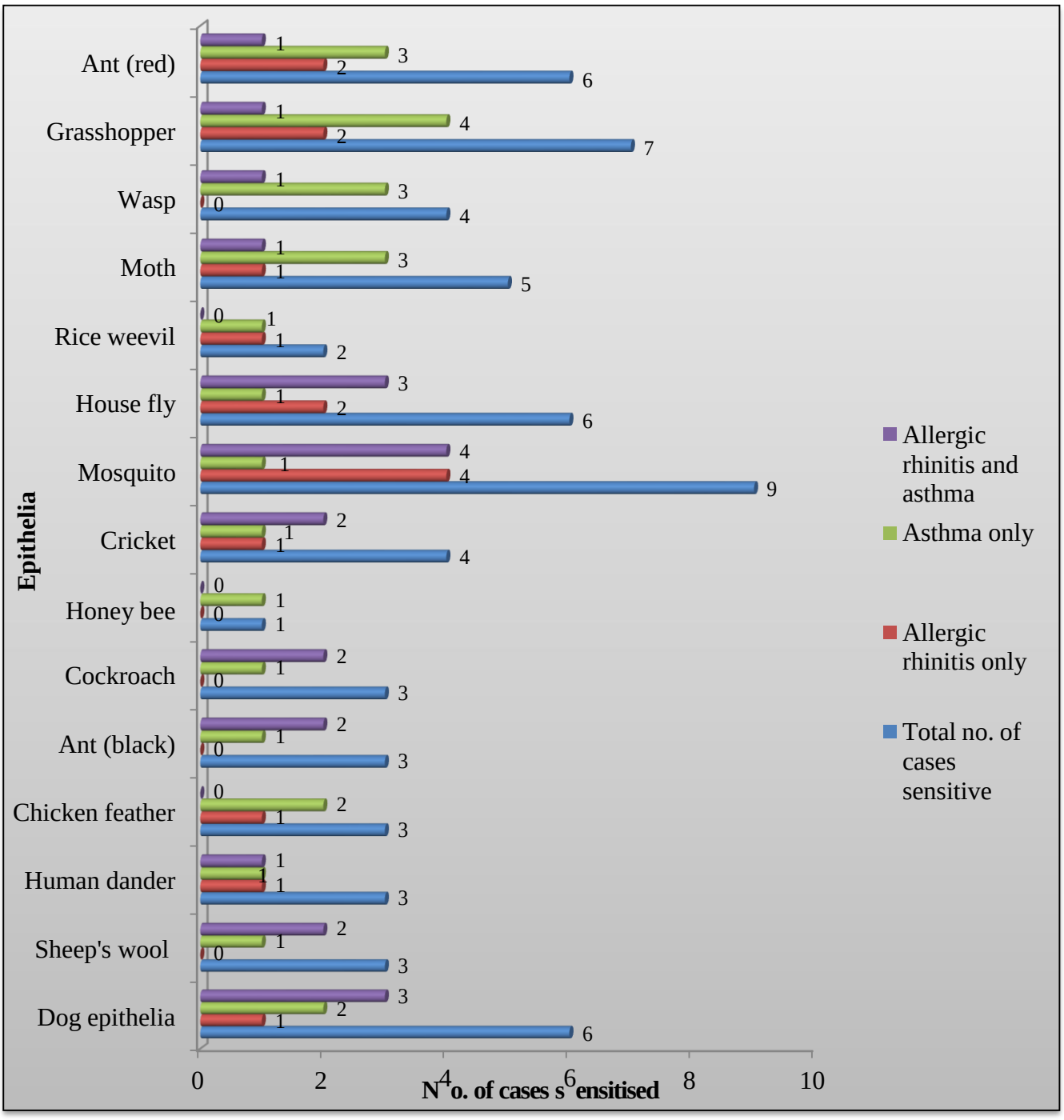
Skin prick test positivity to Wheat dust and Grain dust (rice) was observed in 8 patients (18.2%) commonly, the distribution represented in Graph 14.



SKIN PRICK TEST POSITIVITY TO EPITHELIA (INSECTS AND ANIMALS)

Mosquito was the commonest allergen (20.5%) among epithelia, followed by Grasshopper in 7 patients (15.9%). Allergen sensitivity pattern amongst epithelia with respect to diagnosis are shown in Graph 15.

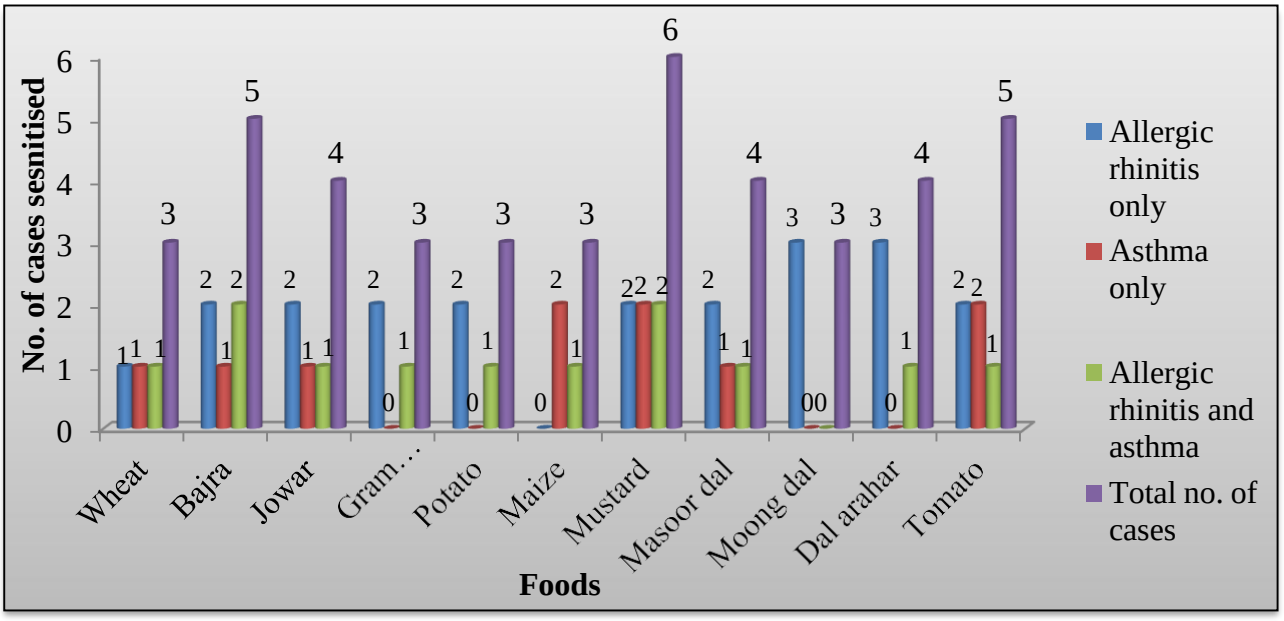
Graph 15: Distribution of cases with Skin prick test positivity to Epithelia (Insects and Animals)



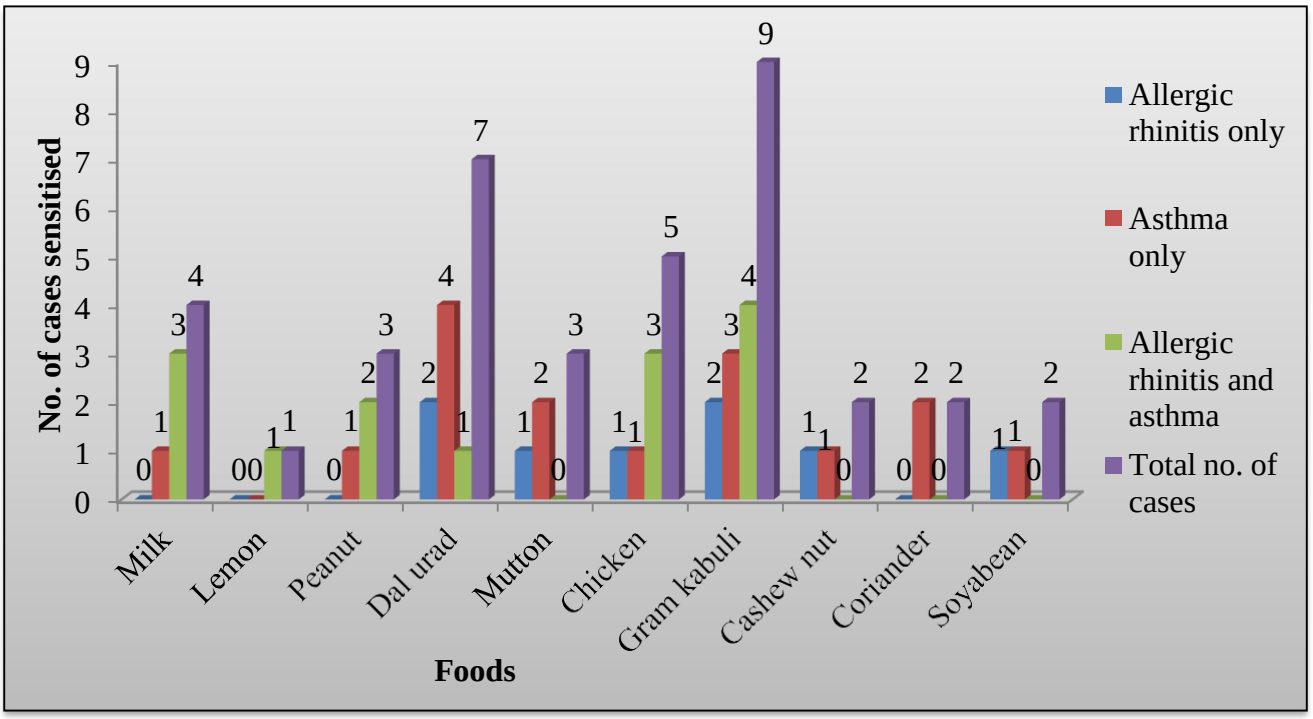
SKIN PRICK TEST POSITIVITY TO FOODS

Out of 44 patients, 9 patients (20.5%) showed sensitivity to Gram kabuli, the commonest allergen among foods, followed by Dal urad in 7 patients (15.9%), while none of the patients were sensitive to Brinjal. Distribution of cases with sensitisation to foods with respect to diagnosis are depicted in Graphs 16(i), 16(ii) and 16(iii).

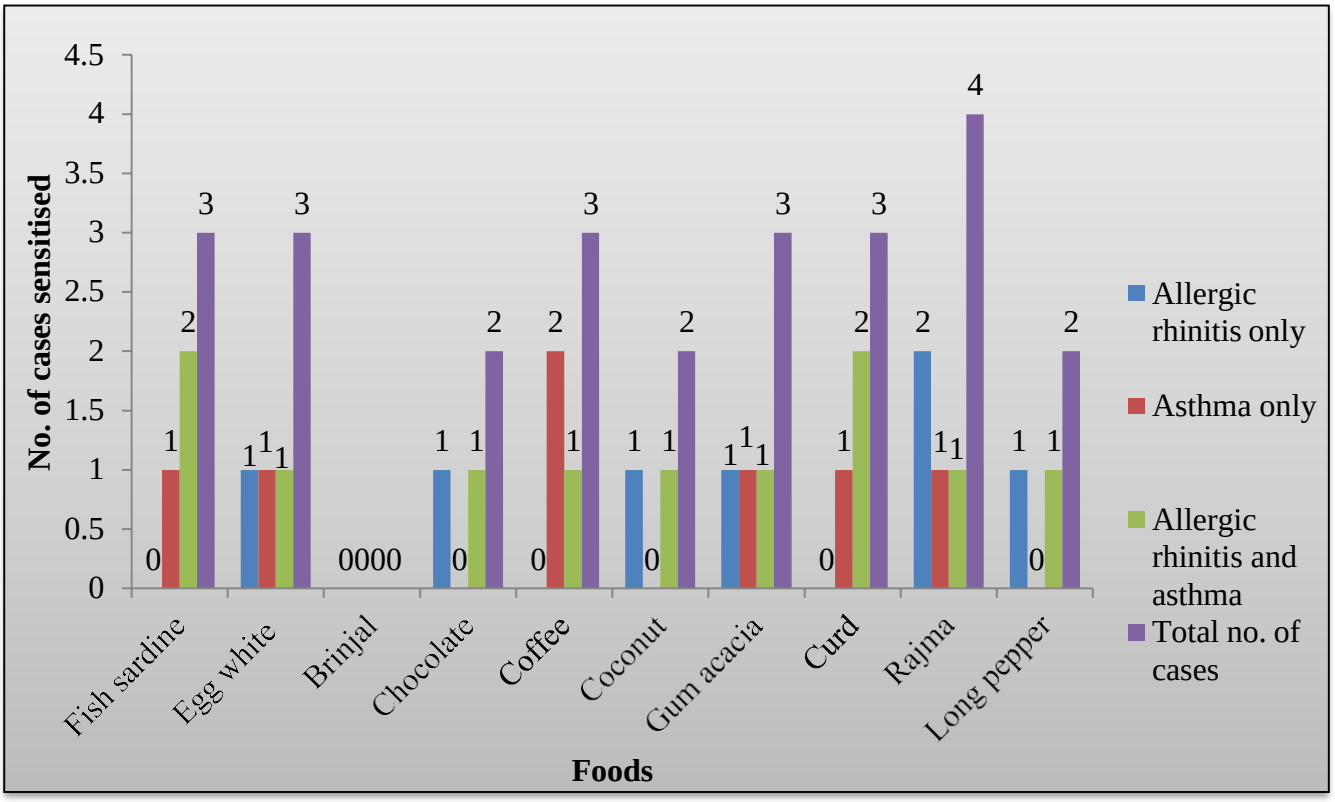
Graph 16(i): Distribution of cases with Skin prick test positivity to Foods:



Graph 16(ii): Distribution of cases with Skin prick test positivity to Foods:

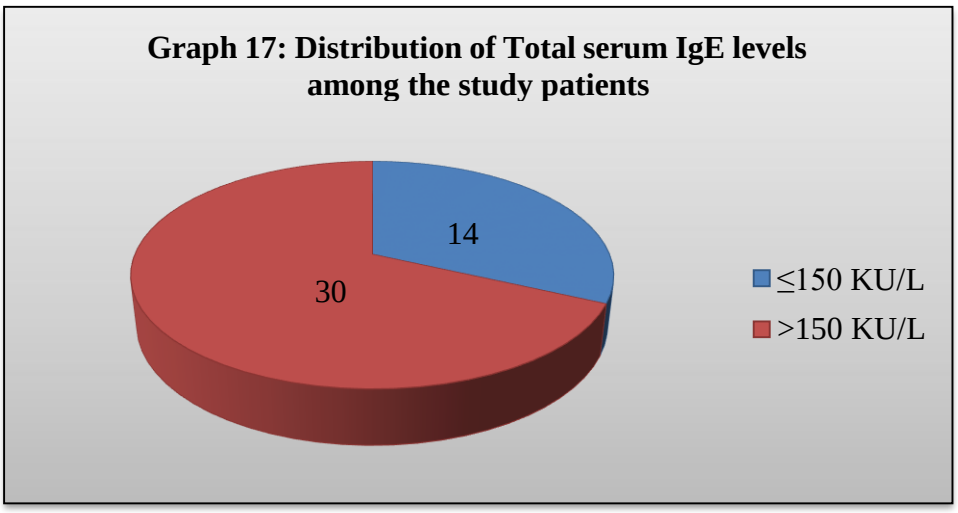


Graph 16(iii): Distribution of cases with Skin prick test positivity to Foods:



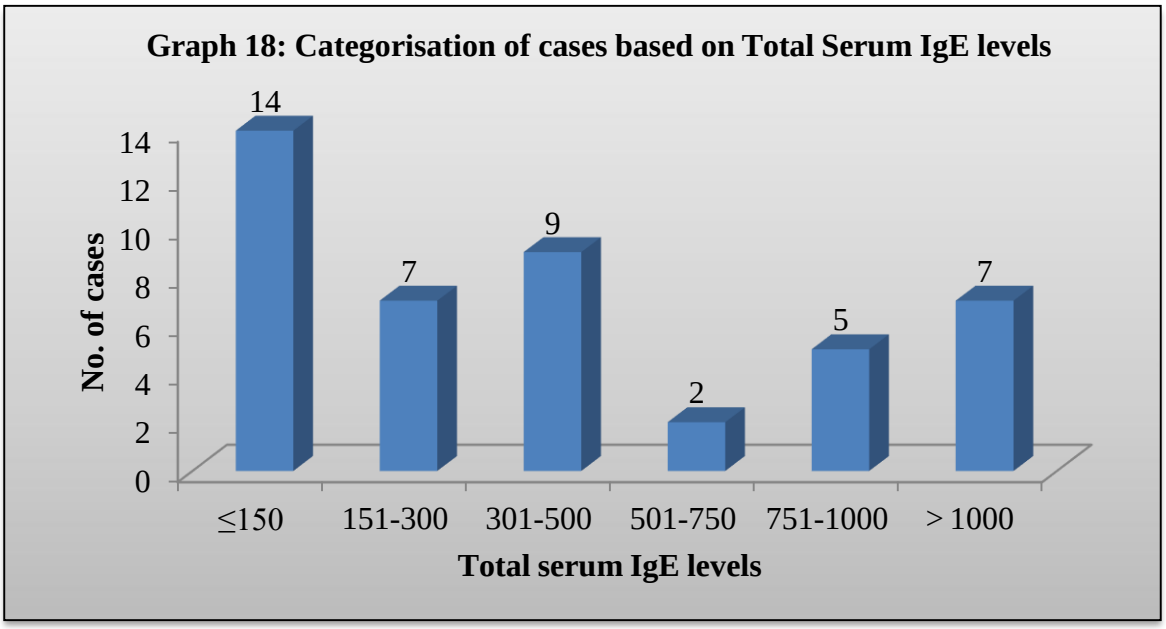
DISTRIBUTION BASED ON TOTAL SERUM IgE LEVELS

The distribution of total serum IgE levels among the study patients is depicted in Graph 17. Out of 44 patients, 14 patients had normal Total Serum IgE levels, while 30 patients had elevated Total Serum IgE levels.



Categorisation of cases based on Total Serum IgE levels:

The total number of patients in the study are categorised according to Total serum IgE levels as in Graph 18.



DISTRIBUTION OF DIAGNOSIS ACCORDING TO TOTAL SERUM IgE LEVELS

Diagnosis distribution with respect to the total serum IgE levels are represented in Table 6. All the patients (12 out of 12) with only asthma had elevated total serum IgE levels.

Table 6: Distribution of Diagnosis with respect to Total Serum IgE levels:

Total Serum IgE	Allergic rhinitis only		Asthma only		Allergic rhinitis and asthma	
	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases
≤150 KU/L	8	47.1	0	0	6	40
>150 KU/L	9	52.9	12	100	9	60
Total	17	100	12	100	15	100

DISTRIBUTION OF TOTAL SERUM IgE LEVELS AMONG ALLERGENS

Distribution of Total serum IgE levels among Mites:

Overall, total serum IgE was increased in the maximum number of patients who showed sensitisation to House dust mites, commonest among them being *Blomia* in 17 patients. The association between total serum IgE levels and skin prick test positivity to Mites is positive and statistically significant (P<0.05) as shown in Table 7.

Table 7: Distribution of Total serum IgE levels among Mites:

			Mites		Total	Chi square value	P value
			Negative	Positive			
Total Serum IgE	≤150	Count	8	6	14	4.856	0.028*
		% within IgE	57.1%	42.9%	100.0%		
	>150	Count	7	23	30		
		% within IgE	23.3%	76.7%	100.0%		
Total		Count	15	29	44		
		% within IgE	34.1%	65.9%	100.0%		
*Statistically significant							

Distribution of Total serum IgE levels among Fungi:

Among the fungi, total serum IgE levels were elevated among patients sensitised to *Fusarium solanii*. All the patients sensitised to *Fusarium solanii* and *Rhizopus nigricans* had elevated total serum IgE levels, and the association was not statistically significant (P>0.05) (Table 8).

Table 8: Distribution of Total serum IgE levels among Fungi:

			Fungi		Total	Chi square value	P value
			Negative	Positive			
Total Serum IgE	≤150	Count	9	5	14	0.467	.495
		% within IgE	64.3%	35.7%	100.0%		
	>150	Count	16	14	30		
		% within IgE	53.3%	46.7%	100.0%		
Total		Count	25	19	44		
		% within IgE	56.8%	43.2%	100.0%		
Statistically not significant							

Distribution of Total serum IgE levels among Pollens:

Association of total serum IgE levels with sensitisation to Pollens is depicted in Table 9. There was a statistically significant association between skin prick test reactivity to Pollens with total serum IgE levels (P<0.05).

Table 9: Distribution of Total serum IgE levels among Pollens:

			Pollens		Total	Chi square value	P value
			Negative	Positive			
Total Serum IgE	≤150	Count	11	3	14	4.781	0.029*
		% within IgE	78.6%	21.4%	100.0%		
	>150	Count	13	17	30		
		% within IgE	43.3%	56.7%	100.0%		
Total		Count	24	20	44		
		% within IgE	54.5%	45.5%	100.0%		
* Statistically significant							

Distribution of Total serum IgE levels among Dust:

All patients with skin prick test positivity to Cotton dust and House dust had elevated total serum IgE levels. The association between skin prick test positivity to Dust and total serum IgE levels, as depicted in Table 10, was found to be statistically not significant (P>0.05).

Table 10: Distribution of Total serum IgE levels among Dust:

			Dust		Total	Chi square value	P value
			Negative	Positive			
Total Serum IgE	≤150	Count	9	5	14	1.188	0.276
		% within IgE	64.3%	35.7%	100.0%		
	>150	Count	14	16	30		
		% within IgE	46.7%	53.3%	100.0%		
Total		Count	23	21	44		
		% within IgE	52.3%	47.7%	100.0%		
Statistically not significant							

Distribution of Total serum IgE levels among Epithelia (Insects and animals):

The association between Total serum IgE levels and sensitivity to Epithelia was statistically not significant (P>0.05) (Table 11).

Table 11: Distribution of Total serum IgE levels among Epithelia (Insects and animals):

			Epithelia		Total	Chi square value	P value
			Negative	Positive			
Total Serum IgE	≤150	Count	7	7	14	0.702	0.402
		% within IgE	50.0%	50.0%	100.0%		
	>150	Count	11	19	30		
		% within IgE	36.7%	63.3%	100.0%		
Total		Count	18	26	44		
		% within IgE	40.9%	59.1%	100.0%		
Statistically not significant							

Distribution of Total serum IgE levels among Foods:

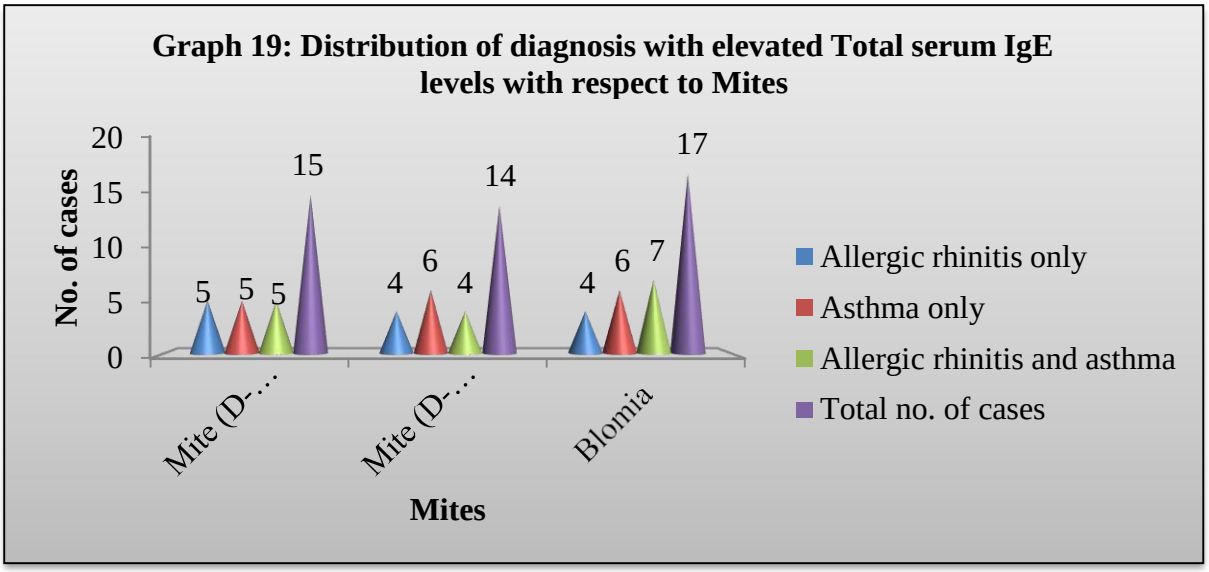
Patients sensitised to food allergens showed variable total serum IgE levels, and the association was not statistically significant (P>0.05) (Table 12).

Table 12: Distribution of Total serum IgE levels among Foods:

			Foods		Total	Chi square value	P value
			Negative	Positive			
Total Serum IgE	≤150	Count	4	10	14	0.140	0.709
		% within IgE	28.6%	71.4%	100.0%		
	>150	Count	7	23	30		
		% within IgE	23.3%	76.7%	100.0%		
Total		Count	11	33	44		
		% within IgE	25.0%	75.0%	100.0%		
Statistically not significant							

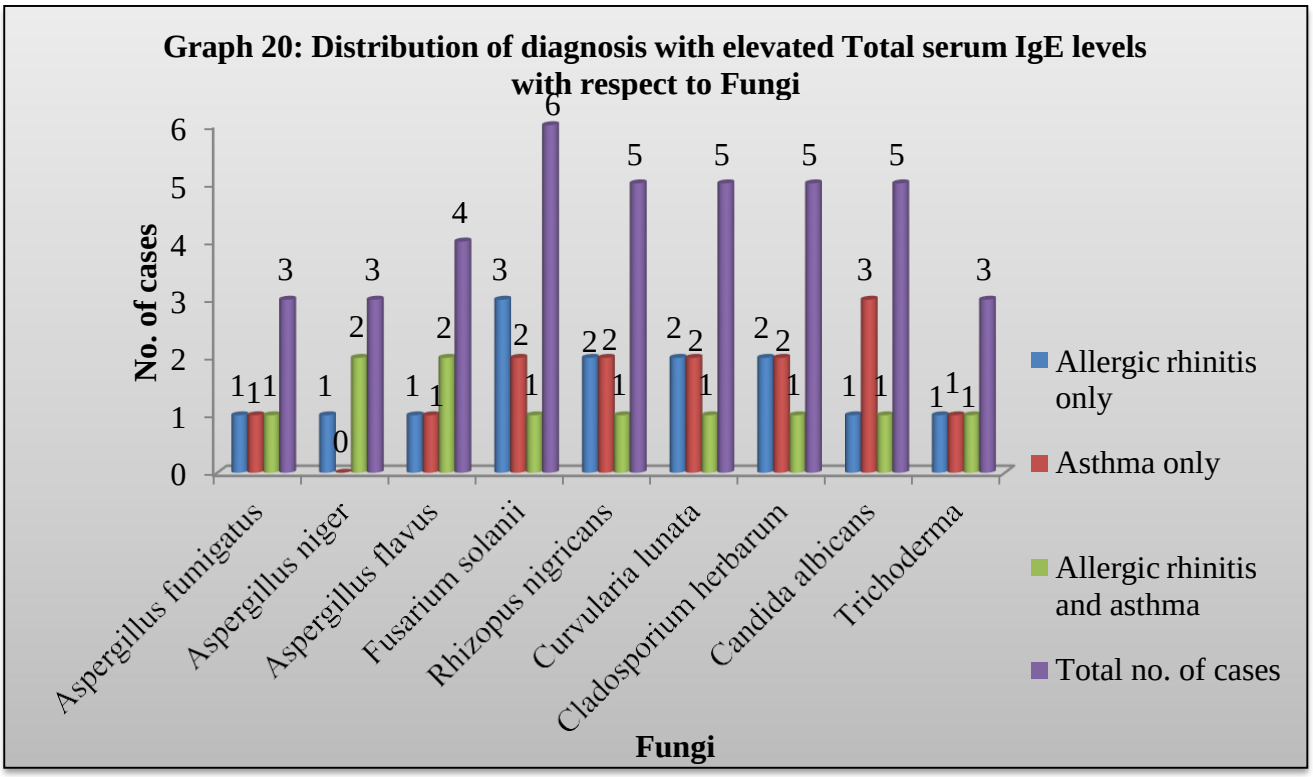
Distribution of diagnosis with elevated Total serum IgE levels with respect to Mites (Graph 19):

Of the Mite sensitised patients with elevated Total serum IgE levels, most had Asthma only.



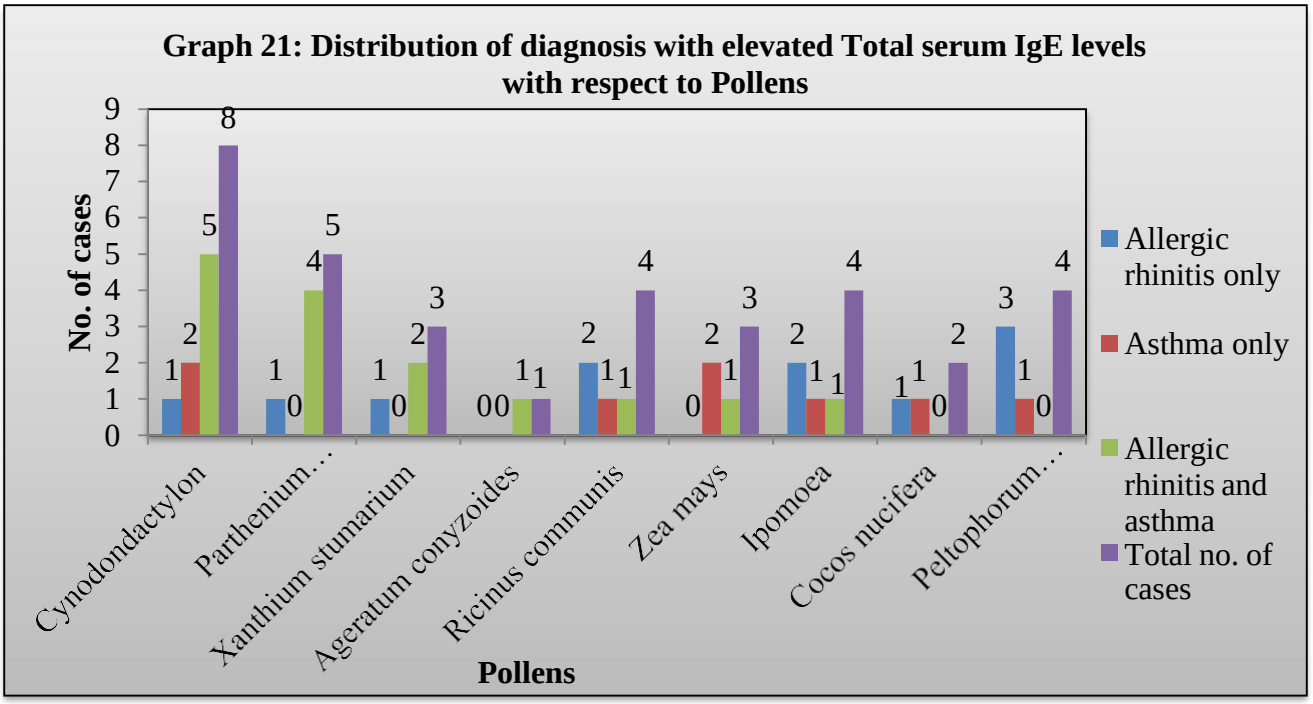
Distribution of diagnosis with elevated Total serum IgE levels with respect to Fungi:

Majority with Asthma only had sensitisation to *Candida albicans* (25%), while *Fusarium solanii* was the common amongst those with only Allergic rhinitis (17.7%) (Graph 20).



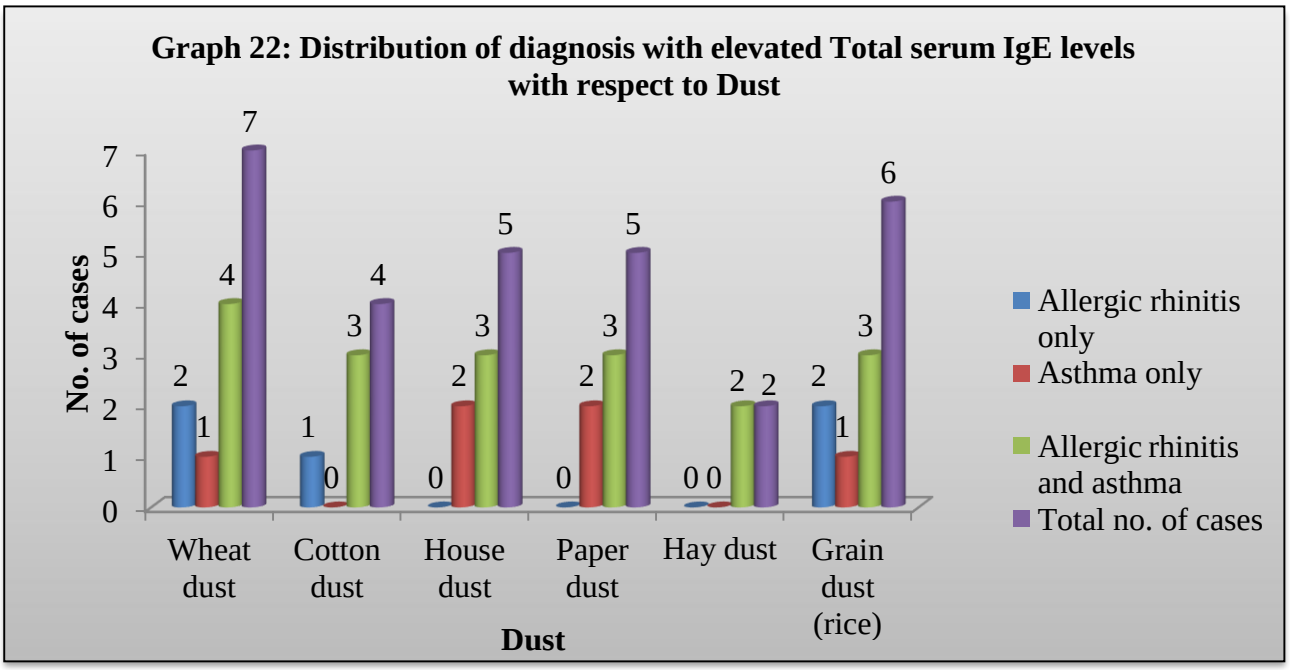
Distribution of diagnosis with elevated Total serum IgE levels with respect to Pollens:

The distribution of cases with elevated total serum IgE levels with sensitivity to Pollens based on diagnosis is represented in Graph 21.



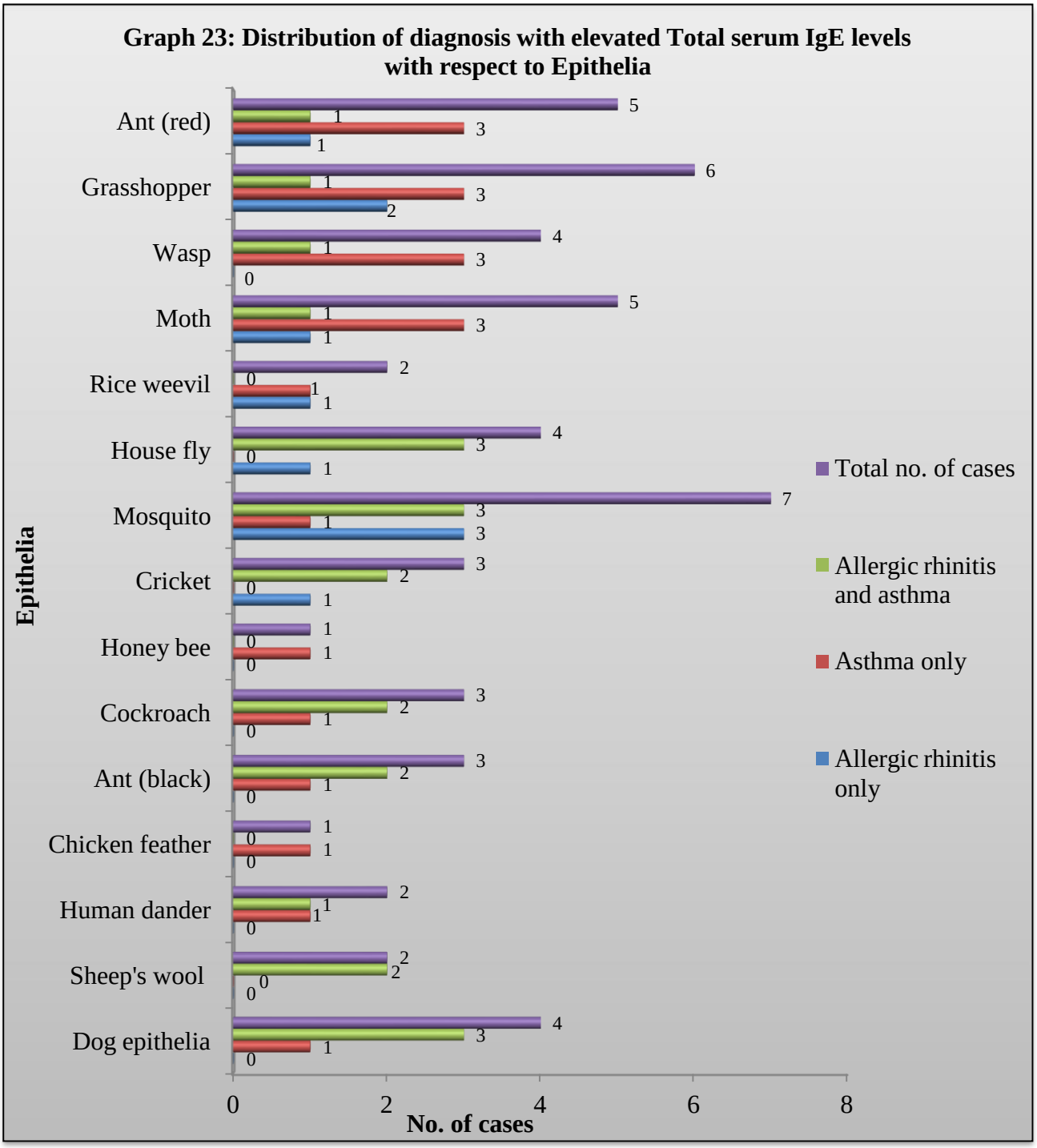
Distribution of diagnosis with elevated Total serum IgE levels with respect to Dust:

The distribution of cases with elevated total serum IgE levels with sensitivity to Dust based on diagnosis is represented in Graph 22.



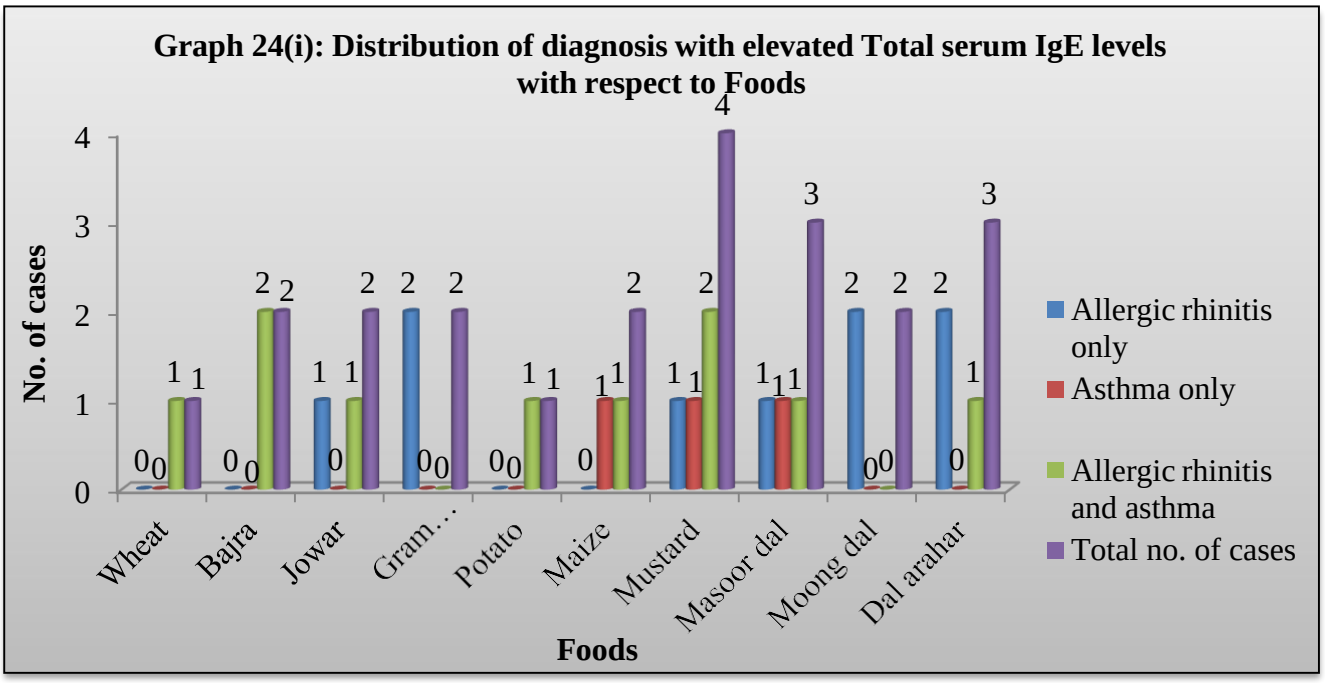
Distribution of diagnosis with elevated Total serum IgE levels with respect to Epithelia (Insects and animals):

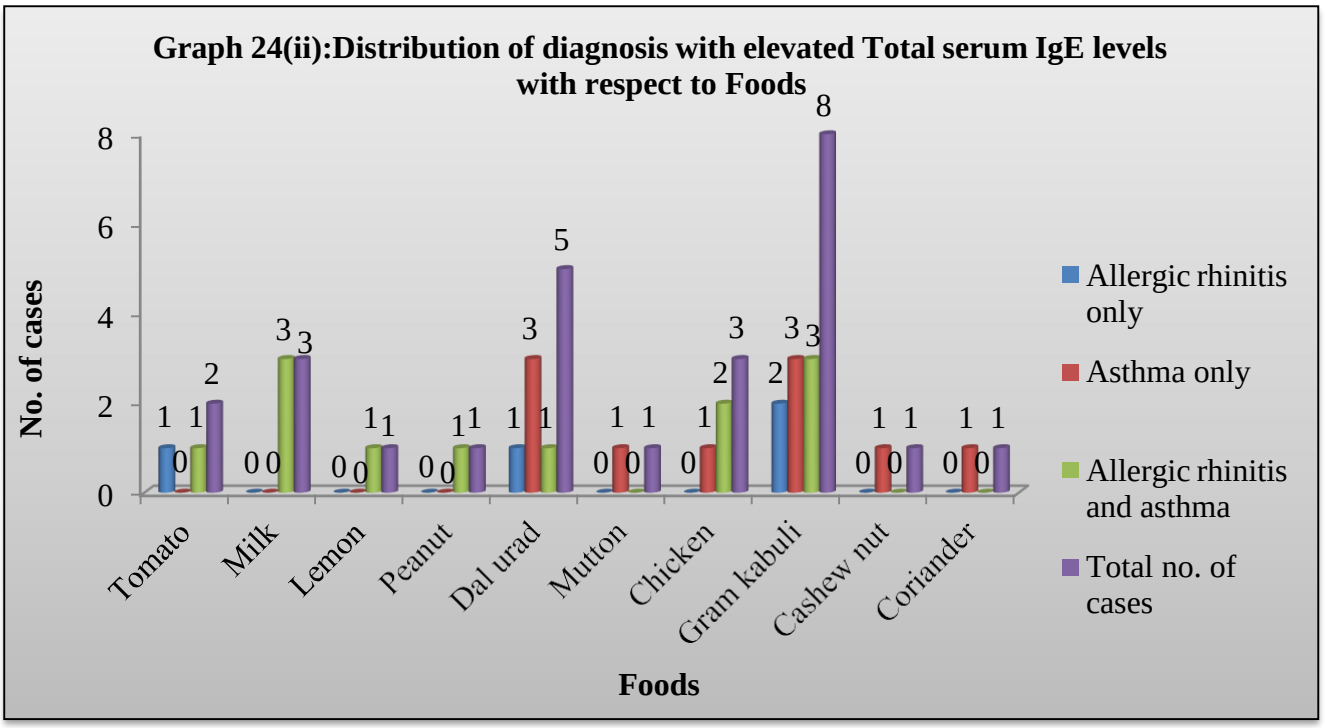
The distribution of cases with elevated total serum IgE levels with sensitivity to Epithelia based on diagnosis is represented in Graph 23.

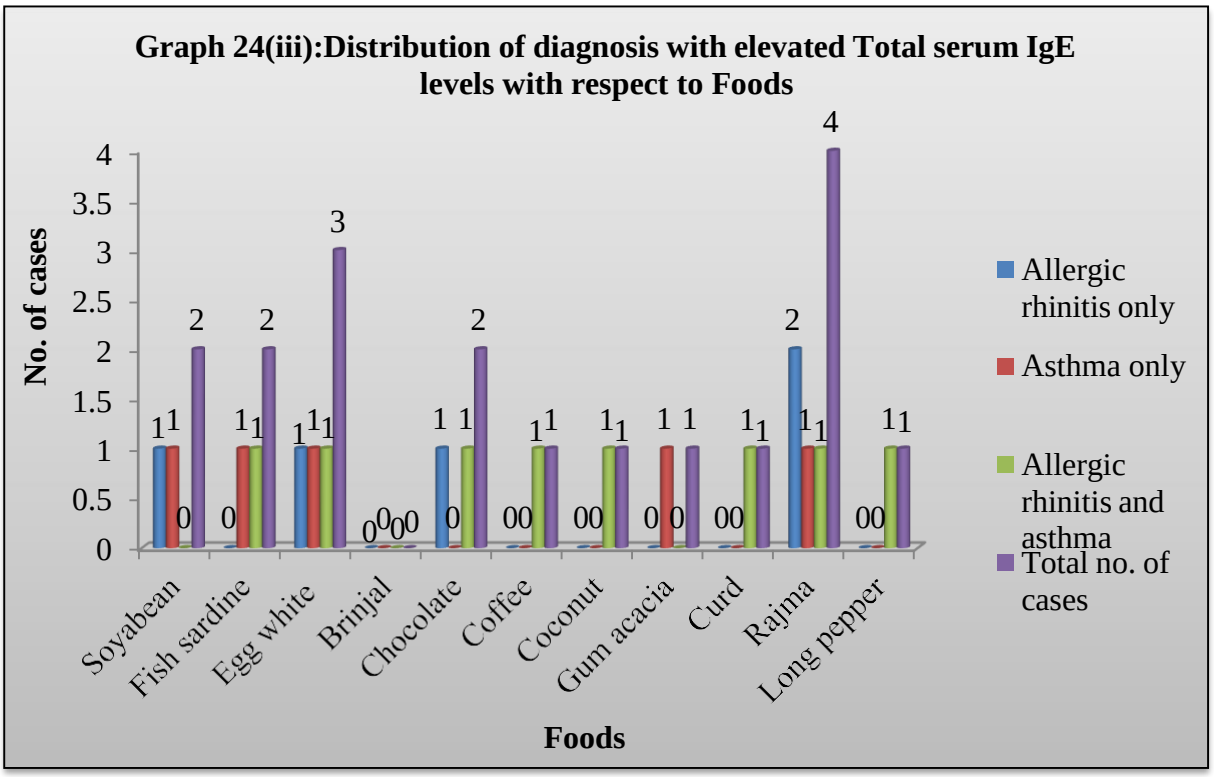


Distribution of diagnosis with elevated Total serum IgE levels with respect to Foods:

Patients with elevated Total serum IgE levels and sensitised to Food allergens, most of them with Asthma only showed no sensitivity to majority of the food allergens. The distribution of diagnosis with sensitisation towards food allergens with elevated total serum IgE levels, is represented in Graphs 24(i), 24(ii) and 24(iii).

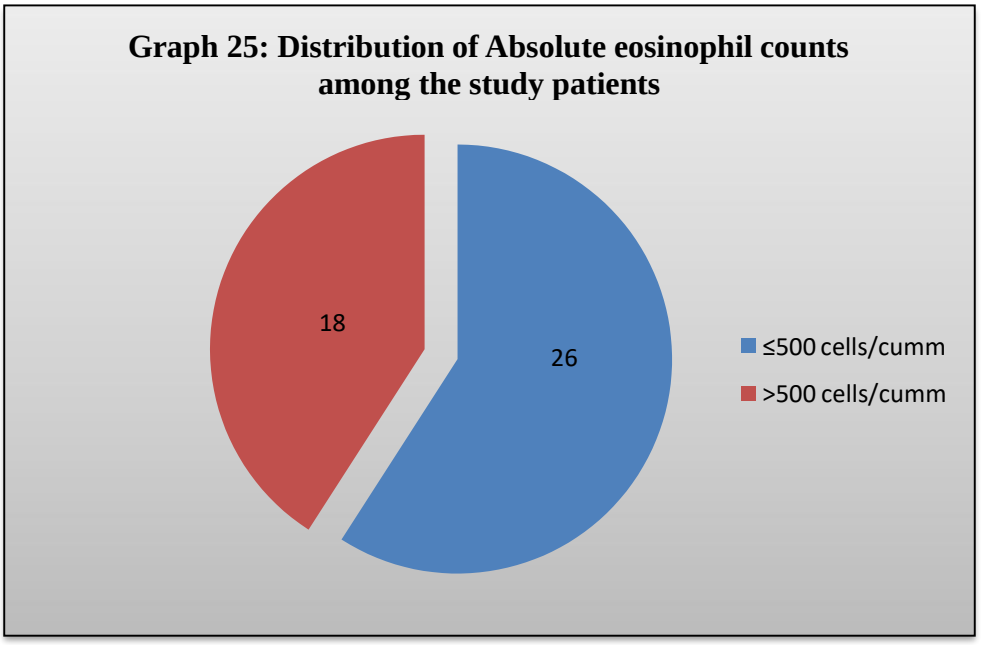






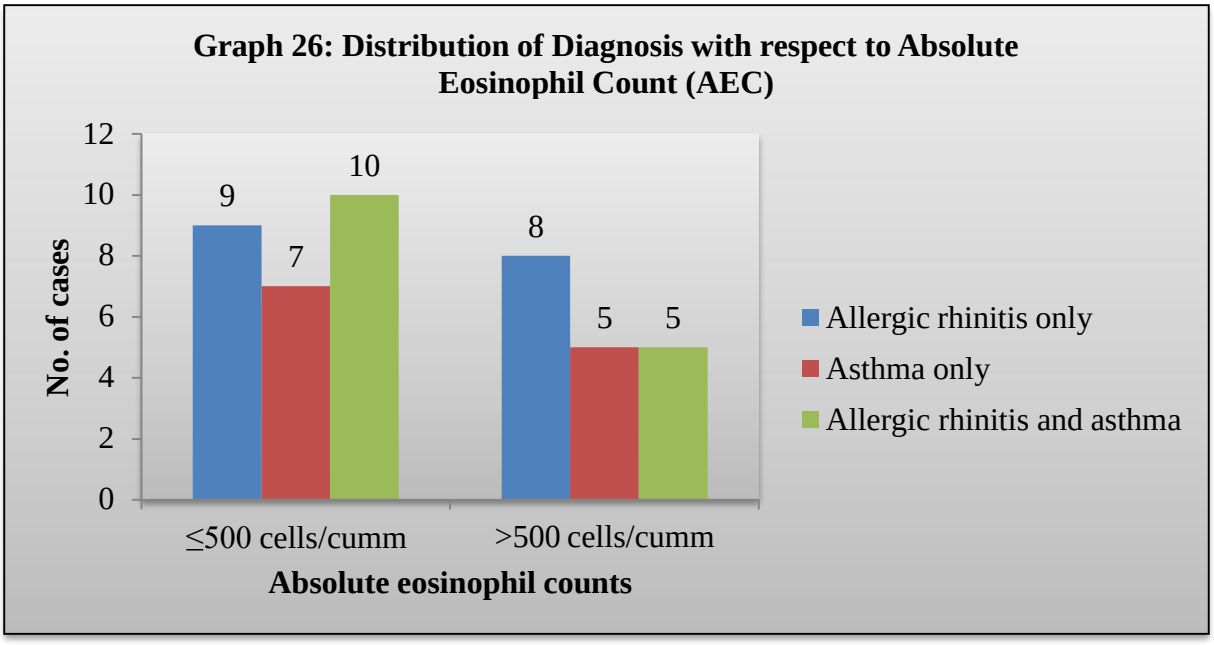
DISTRIBUTION BASED ON ABSOLUTE EOSINOPHIL COUNTS

Out of 44 patients, 26 patients (59%) had normal eosinophil counts, while 18 patients had elevated eosinophil counts, the distribution depicted in Graph 25.



Distribution of Diagnosis with respect to Absolute Eosinophil Count (AEC):

Based on the eosinophil counts, the distribution of patients according to the diagnosis is shown in Graph 26.



Distribution of Absolute Eosinophil Counts (AEC) among Mites:

The association between sensitivity to Mites with AEC, as shown in Table 13, was statistically not significant (P>0.05). Absolute eosinophil counts were elevated among majority of patients sensitised to House dust Mites, especially *Blomia* (55.6%).

Table 13: Distribution of Absolute Eosinophil Counts (AEC) among Mites:

			Mites		Total	Chi square value	P value
			Negative	Positive			
AEC	≤500	Count	11	15	26	1.910	0.167
		% within AEC	42.3%	57.7%	100.0%		
	>500	Count	4	14	18		
		% within AEC	22.2%	77.8%	100.0%		
Total		Count	15	29	44		
		% within AEC	34.1%	65.9%	100.0%		
Statistically not significant							

Distribution of Absolute Eosinophil Counts (AEC) among Fungi:

The distribution of AEC among patients with sensitisation to Fungi is depicted in Table 14, and the association was not statistically significant (P>0.05). Among Fungi, most of the patients with elevated Absolute eosinophil counts were sensitised to *Candida albicans* (5 patients).

Table 14: Distribution of Absolute Eosinophil Counts (AEC) among Fungi:

			Fungi		Total	Chi square value	P value
			Negative	Positive			
AEC	≤500	Count	14	12	26	0.229	0.632
		% within AEC	53.8%	46.2%	100.0%		
	>500	Count	11	7	18		
		% within AEC	61.1%	38.9%	100.0%		
Total		Count	25	19	44		
		% within AEC	56.8%	43.2%	100.0%		
Statistically not significant							

Distribution of Absolute Eosinophil Counts (AEC) among Pollens:

The association between AEC and sensitivity to Pollens was statistically not significant (P>0.05) (Table 15). *Cynodondactylon* was the most common allergen among pollens that the patients were sensitised to, who had elevated Absolute eosinophil counts.

Table 15: Distribution of Absolute Eosinophil Counts (AEC) among Pollens:

			Pollens		Total	Chi square value	P value
			Negative	Positive			
AEC	≤500	Count	16	10	26	1.254	0.263
		% within AEC	61.5%	38.5%	100.0%		
	>500	Count	8	10	18		
		% within AEC	44.4%	55.6%	100.0%		
Total		Count	24	20	44		
		% within AEC	54.5%	45.5%	100.0%		
Statistically not significant							

Distribution of Absolute Eosinophil Counts (AEC) among Dust:

Among Dust, majority of the patients with elevated Absolute eosinophil counts were sensitised to Paper dust (33.3%), and there was a positive and significant association between skin prick test positivity to Dust allergens and AEC (P<0.05), as represented in Table 16.

Table 16: Distribution of Absolute Eosinophil Counts (AEC) among Dust:

			Dust		Total	Chi square value	P value
			Negative	Positive			
AEC	≤500	Count	18	8	26	7.326	0.007*
		% within AEC	69.2%	30.8%	100.0%		
	>500	Count	5	13	18		
		% within AEC	27.8%	72.2%	100.0%		
Total		Count	23	21	44		
		% within aec	52.3%	47.7%	100.0%		
*Statistically significant							

Distribution of Absolute Eosinophil Counts (AEC) among Epithelia (Insects and animals):

The patients who had normal AEC levels, showed more sensitivity to Epithelia than those with elevated AEC, the association being statistically not significant (P>0.05) (Table 17).

Table 17: Distribution of Absolute Eosinophil Counts (AEC) among Epithelia:

			Epithelia		Total	Chi square value	P value
			Negative	Positive			
AEC	≤500	Count	9	17	26	1.041	.307
		% within AEC	34.6%	65.4%	100.0%		
	>500	Count	9	9	18		
		% within AEC	50.0%	50.0%	100.0%		
Total		Count	18	26	44		
		% within AEC	40.9%	59.1%	100.0%		
Statistically not significant							

Distribution of Absolute Eosinophil Counts (AEC) among Foods:

The association between AEC and skin prick test sensitivity towards food allergens was found to be statistically not significant (P>0.05) (Table 18).

Table 18: Distribution of Absolute Eosinophil Counts (AEC) among Foods:

			Foods		Total	Chi square value	P value
			Negative	Positive			
AEC	≤500	Count	5	21	26	1.128	0.288
		% within AEC	19.2%	80.8%	100.0%		
	>500	Count	6	12	18		
		% within AEC	33.3%	66.7%	100.0%		
Total		Count	11	33	44		
		% within AEC	25.0%	75.0%	100.0%		
Statistically not significant							

Distribution of cases with elevated absolute eosinophil counts with respect to allergens:

Among the patients with elevated Absolute eosinophil counts sensitised to Mites, majority of them had only Asthma. Among Fungi, the patients with Asthma only showed more sensitivity to the allergens compared to those with Allergic rhinitis only and both Allergic rhinitis and Asthma. Among Pollens, 3 out of 5 patients with sensitivity to *Cynodondactylon* and associated elevated Absolute eosinophil counts had both Allergic rhinitis and Asthma. Among patients sensitised to Dust, majority had both Allergic rhinitis and Asthma compared to those with only Asthma or Allergic rhinitis. Mosquito was the most common allergen among patients with elevated Absolute eosinophil counts (4 in number). Patients with both Allergic rhinitis and Asthma showed more skin prick test positivity to Food allergens when compared to those with only Allergic rhinitis or only Asthma. The distribution of cases with elevated AEC with respect to allergens is depicted in Table 19.

Table 19: Distribution of cases with elevated absolute eosinophil counts with respect to allergens:

Allergens		Absolute eosinophil counts >500 cells/cu.mm						Total	
		Allergic rhinitis only		Asthma only		Allergic rhinitis and asthma			
		No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases	No. of cases	% of cases
Mites	Mite *(D-Farinae)*	3	17.6	**4**	33.3	1	6.6	8	44.4
	Mite *(D- Pteronyssinus)*	3	17.6	**4**	33.3	2	13.3	9	50
	Blomia	3	17.6	**4**	33.3	3	20	10	55.6
Fungi	*Aspergillus fumigatus*	1	5.8	1	8.3	0	0	2	11.1
	Aspergillus niger	1	5.8	0	0	1	6.6	2	11.1
	Aspergillus flavus	1	5.8	2	16.6	1	6.6	4	22.2
	Fusarium solanii	1	5.8	1	8.3	1	6.6	3	16.7
	Rhizopus nigricans	1	5.8	2	16.6	1	6.6	4	22.2
	Curvularia lunata	0	0	2	16.6	1	6.6	3	16.7
	Cladosporium herbarum	0	0	**3**	25	1	6.6	4	22.2
	Candida albicans	1	5.8	**3**	25	1	6.6	5	27.8
	Trichoderma	0	0	0	0	1	6.6	1	5.5
Pollens	*Cynodondactylon*	1	5.8	1	8.3	**3**	20	5	27.8
	Parthenium hysterophorus	1	5.8	0	0	2	13.3	3	16.7
	Xanthium stumarium	1	5.8	0	0	0	0	1	5.5
	Ageratum conyzoides	0	0	0	0	0	0	0	0
	Ricinus communis	**2**	11.7	1	8.3	1	6.6	4	22.2
	Zea mays	0	0	**2**	16.6	0	0	2	11.1
	Ipomoea	**2**	11.7	1	8.3	1	6.6	4	22.2
	Cocos nucifera	0	0	0	0	0	0	0	0
	Peltophorum pterocarpum	**2**	11.7	1	8.3	0	0	3	16.7
Dust	Wheat dust	2	11.7	1	8.3	2	13.3	5	27.8
	Cotton dust	1	5.8	0	0	3	20	4	22.2
	House dust	0	0	1	8.3	3	20	4	22.2
	Paper dust	0	0	2	16.6	**4**	26.6	6	33.3
	Hay dust	0	0	0	0	1	6.6	1	5.5
	Grain dust (rice)	2	11.7	1	8.3	2	13.3	5	27.8
Epithelia	Dog epithelia	0	0	0	0	2	13.3	2	11.1
	Sheep's wool	0	0	0	0	1	6.6	1	5.5
	Human dander	0	0	1	8.3	1	6.6	2	11.1
	Chicken feather	0	0	1	8.3	0	0	1	5.5
	Ant (black)	0	0	1	8.3	0	0	1	5.5
	Cockroach	0	0	1	8.3	0	0	1	5.5
	Honey bee	0	0	1	8.3	0	0	1	5.5
	Cricket	1	5.8	0	0	1	6.6	2	11.1
	Mosquito	2	11.7	1	8.3	1	6.6	4	22.2

	House fly	1	5.8	0	0	2	13.3	3	16.7
	Rice weevil	0	0	1	8.3	0	0	1	5.5
	Moth	1	5.8	2	16.6	0	0	3	16.7
	Wasp	0	0	2	16.6	0	0	2	11.1
	Grasshopper	2	11.7	0	0	0	0	2	11.1
	Ant (red)	0	0	2	16.6	0	0	2	11.1
Foods	Wheat	0	0	0	0	1	6.6	1	5.5
	Bajra	0	0	0	0	0	0	0	0
	Jowar	0	0	0	0	0	0	0	0
	Gram Bengali	2	11.7	0	0	1	6.6	3	16.7
	Potato	0	0	0	0	1	6.6	1	5.5
	Maize	0	0	1	8.3	0	0	1	5.5
	Mustard	1	5.8	1	8.3	0	0	2	11.1
	Masoor dal	1	5.8	1	8.3	0	0	2	11.1
	Moong dal	1	5.8	0	0	0	0	1	5.5
	Dal arahar	1	5.8	0	0	1	6.6	2	11.1
	Tomato	0	0	0	0	1	6.6	1	5.5
	Milk	0	0	0	0	2	13.3	2	11.1
	Lemon	0	0	0	0	1	6.6	1	5.5
	Peanut	0	0	0	0	0	0	0	0
	Dal urad	0	0	2	16.6	0	0	2	11.1
	Mutton	0	0	1	8.3	0	0	1	5.5
	Chicken	0	0	1	8.3	0	0	1	5.5
	Gram kabuli	2	11.7	**3**	25	1	6.6	6	33.3
	Cashew nut	0	0	1	8.3	0	0	1	5.5
	Coriander	0	0	1	8.3	0	0	1	5.5
	Soyabean	0	0	1	8.3	0	0	1	5.5
	Fish sardine	0	0	1	8.3	0	0	1	5.5
	Egg white	0	0	0	0	0	0	0	0
	Brinjal	0	0	0	0	0	0	0	0
	Chocolate	1	5.8	0	0	1	6.6	2	11.1
	Coffee	0	0	0	0	0	0	0	0
	Coconut	0	0	0	0	0	0	0	0
	Gum acacia	0	0	0	0	0	0	0	0
	Curd	0	0	0	0	2	13.3	2	11.1
	Rajma	1	5.8	0	0	0	0	1	5.5
	Long pepper	0	0	0	0	0	0	0	0

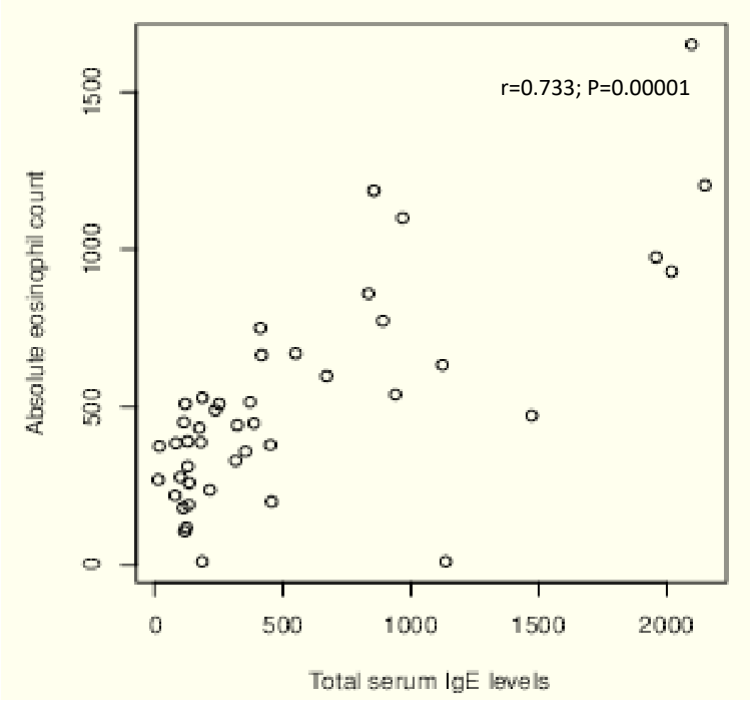
Correlation of Total Serum IgE levels with Absolute Eosinophil Counts:

Table 20 and Graph 27 represent the positive and significant correlation between total serum IgE levels and absolute eosinophil counts, implying that with higher total IgE levels, eosinophil counts raise.

Table 20: Correlation between total serum IgE levels and Absolute eosinophil counts:

			AEC		Total	Pearson correlation co-efficient	P value
			≤500	>500			
Total Serum IgE	**≤150**	Count	13	1	14	0.733	0.00001*
		% within IgE	92.9%	7.1%	100.0%		
	>150	Count	13	17	30		
		% within IgE	43.3%	56.7%	100.0%		
Total		Count	26	18	44		
		% within IgE	59.1%	40.9%	100.0%		
*Statistically significant							

Graph 27: Correlation graph between total serum IgE levels with absolute eosinophil counts:



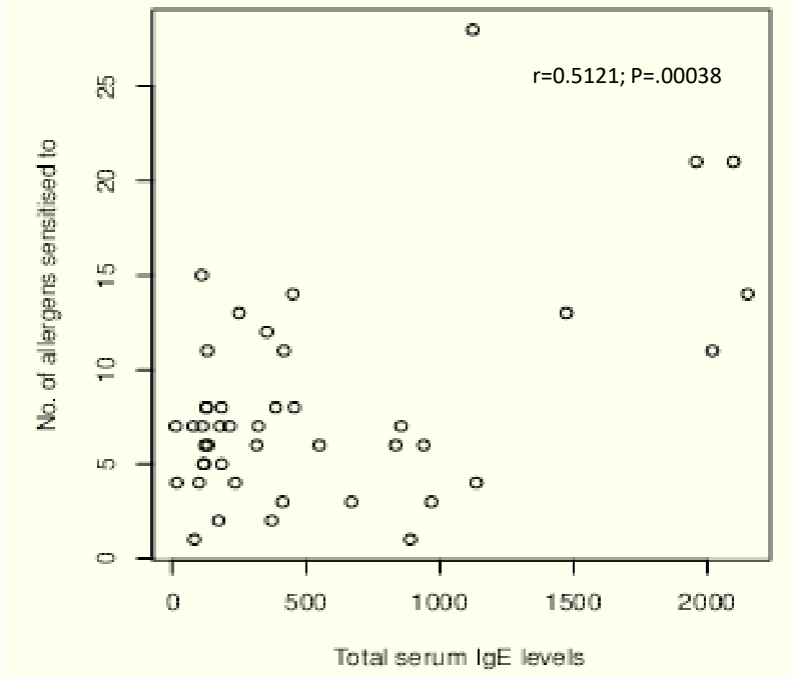
Correlation between Total Serum IgE levels and Skin prick test positivity to allergens:

66.7% with elevated total serum IgE levels were sensitised to less than 10 allergens. There was a moderate positive and significant correlation between the number of allergens the patients were sensitised to and the total serum IgE levels(Table 21 and Graph 28), indicating the extent of allergen sensitivity is more with higher IgE levels.

Table 21: Correlation between Total Serum IgE levels and Skin prick test positivity to allergens:

			No. of allergens patients were sensitised to			**Total**	**Pearson correlation coefficient**	**P value**
			0-10	**11-20**	**21-30**			
Total Serum IgE	**≤150**	Count	12	2	0	14	0.5121	.00038*
		% within IgE	85.7%	14.3%	0	100.0%		
	>150	Count	20	7	3	30		
		% within IgE	66.7%	23.3%	10%	100.0%		
Total		Count	32	9	3	44		
		% within IgE	72.7%	20.5%	6.81%	100.0%		
*Statistically significant								

Graph 28: Correlation graph between total serum IgE levels and skin prick test positivity to allergens



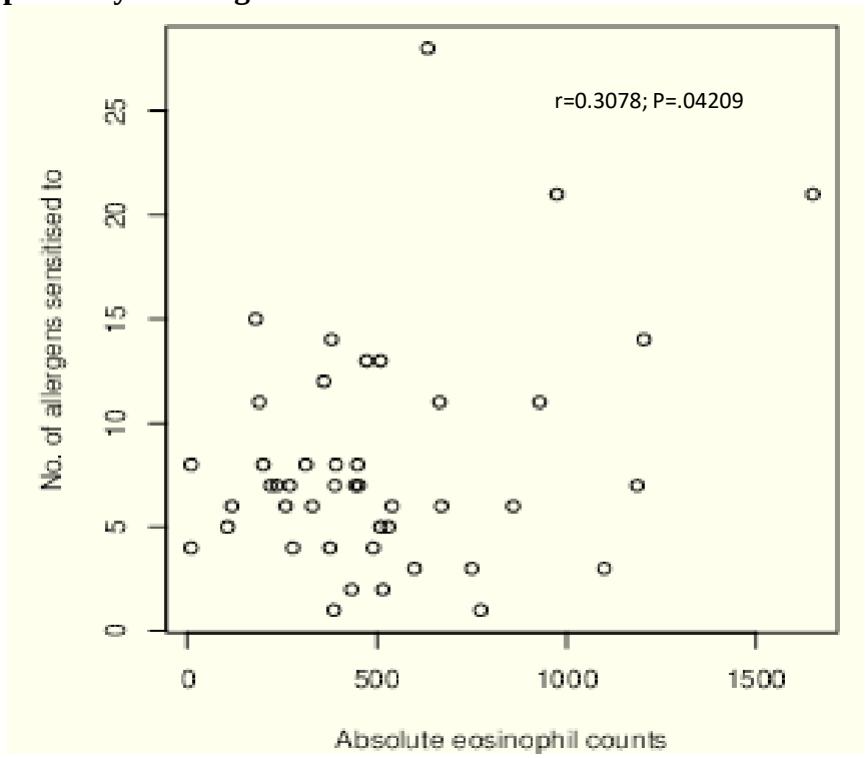
Correlation between Absolute eosinophil counts and Skin prick test positivity to allergens:

The correlation, although weak, is positive and statistically significant between absolute eosinophil counts and number of allergens the patients were sensitised to, as represented in Table 22 and Graph 29. With the increase in the number of allergens the patients were sensitised to, there was a rise in the eosinophil counts.

Table 22: Correlation between Absolute eosinophil counts and Skin prick test positivity to allergens:

			No. of allergens patients were sensitised to			**Total**	**Pearson correlation coefficient**	**P value**
			0-10	**11-20**	**21-30**			
AEC	**≤500**	Count	21	5	0	26	0.3078	.042095*
		% within IgE	80.8%	19.2%	0	100.0%		
	>500	Count	11	4	3	18		
		% within IgE	61.1%	22.2%	16.7%	100.0%		
Total		Count	32	9	3	44		
		% within IgE	72.7%	20.5%	6.81%	100.0%		
*Statistically significant								

Graph 29: Correlation graph between absolute eosinophil counts and skin prick test positivity to allergens



DISCUSSION

Among patients with respiratory allergy, the allergens are the main cause of triggering symptoms. Defining the most prevalent allergens in a particular geographic area plays a pivotal role and has been the subject of many studies carried out in different parts of the world. Avoidance of allergens forms the most important part of management and specific immunotherapy could be selected based on the prevalent allergens causing allergies in that area. In this study, 44 patients were tested for skin prick test sensitivity against 73 allergen extracts.

Out of the 44 patients enrolled, 18 patients (40.9%) belonged to the age group of 46-60 years, and 13 patients each (29.5%) in the age groups of 15-30 years and 31-45 years, the mean age being 39.63 years. This is comparable to the study conducted in Udupi district of Karnataka[171], the mean age of the patients being 41.47 (±14 years). A study by Arbat A et al. in Central India[172], where skin prick test sensitivity was studied among 143 patients, showed that 46% of patients belonged to the age group of 30-49 years compared to 29.5% in this study.

In the present study, it was observed that the gender inclination was towards females with 54.5% of patients (24 in number) while 45.5% of patients were males (20 in number) which is in accordance with the study conducted by Katoch CD et al.[173] which also consisted majorly of female population, while another study by Kumar R et al.,[6] conducted in Delhi, showed a male preponderance. Studies from Western parts of the world by Farrokhi S et al.[174] and Moghtaderi M et al.[175] in Southwestern parts of Iran also consisted majorly of female population. The female preponderance in our study could be attributed to the hormonal variations in female sex, environmental or genetic conditions.

Among 44 patients enrolled with allergic diseases, 12 patients (27.3%) had only asthma, while 17 patients (38.6%) had allergic rhinitis alone, and 15 patients (34.1%) were diagnosed with both allergic rhinitis and asthma (Graph 3). These results are similar to a study conducted in Rajasthan, India, by Sharma RK et al.,[176] where patients with only Allergic rhinitis were predominant (44.78%) followed by those with both allergic rhinitis and asthma (29.1%), while patients with only asthma were least in number (26.12%), though the percentages of distribution of cases differed. Another study by Moghtaderi M et al.[175] conducted in Southwestern Iran, showed similar distribution. Although similar results were seen in few studies, several studies conducted in different parts of India, showed wide variation in the above mentioned conditions. In a study by Arastu SH,[8] amongst the enrolled patients, majority had only asthma (60%), followed by only allergic rhinitis (24%) and 16% had both allergic rhinitis and asthma. Another study by Kumar V et al.[177] showed predominant population of patients suffering from both allergic rhinitis and asthma (54.09%) followed by only asthma in 30.6% of patients while only allergic rhinitis was present in 15.3% of patients, which is in contrast to our study.

In our study, based on the ARIA classification, out of the 32 patients suffering from Allergic rhinitis, 21 patients (65.6%) had Persistent Allergic rhinitis whereas 11 patients (34.4%) had Intermittent Allergic rhinitis. Majority of the patients (82.4%) with only Allergic rhinitis had Persistent symptoms, whereas majority of the patients (53.3%) with both Allergic rhinitis and Asthma had Intermittent symptoms. The higher incidence of patients with Persistent Allergic rhinitis could be attributed to the sensitisation of majority of the patients in our study to both indoor and outdoor allergens. A study by Singh D et al.[178] in Rajasthan, India, showed similar results with Persistent Allergic rhinitis reported in 64.3%, while Intermittent Allergic rhinitis was reported in 35.6%. The percentage of patients with

Persistent Allergic rhinitis in another study by Farrokhi S et al.,[174] conducted in Southwestern part of Iran, was found to be 86.3% which is higher when compared to our study.

Family history of asthma and allergic diseases are strong determinants of asthma, but the magnitude of effect varies according to the hereditary group so that some subtypes have a stronger hereditary component, and others may be more strongly related to environmental exposures. Among the patients enrolled in our study, 38.63% had family history of allergic diseases. 35.9% of patients with only allergic rhinitis had positive family history of allergy, while 25% with only asthma and 53.3% of patients with both allergic rhinitis and asthma had a positive family history of allergy. A study by Dey D et al.[50] showed 37.6% of patients with a positive family history, which is comparable to our study, whilst studies by Gowda G et al.[4] and Assarehzadegan MA et al.[179] showed a positive family history in 43.16% and 59.5% of patients which is higher when compared to our study group.

Though the real association between obesity and allergic disorders is unclear, there is evidence that obesity and overweight are linked with allergic diseases probably because of the immunological effects of adipose tissue on the development of allergies.[180] Out of the 44 patients in the study, majority of the patients (50%) had Ideal body weight, whereas 40.9% were overweight and obese, while 9.1% of the patients were Underweight. The association of obesity with asthma has been gaining attention, but there are a few studies conducted to identify the association between BMI and allergic rhinitis. Bist SS et al.[181] conducted a study in Uttarakhand, India to identify the relationship of BMI with allergic rhinitis, and it has been observed that there was a significant association between increasing BMI and allergic rhinitis.

Most of the patients in our study were Non- vegetarians (56.8%). Both the Vegetarians as well as Non- Vegetarians were predominantly sensitised to Food allergens followed by Mites. While the Vegetarians were least sensitised to Fungi (31.5%), Non-vegetarians showed least Skin prick test positivity towards Pollens (40%). Amongst the Vegetarians, majority (47.3%) had only Allergic rhinitis, whilst 36% among Non- vegetarians had both Allergic rhinitis and Asthma. Western diet (such as saturated fatty acids and cholesterol) has been shown to aggravate and Mediterranean diet (such as unsaturated fatty acids, vitamins, and fiber) is known to protect against allergic diseases. Specific receptors are involved in their mechanisms of action.[182] In studies from Sweden, Greece, and Mexico, children with diet inclusive of vegetables and fruits has proved to be a protective factor for atopic diseases.[183,184,185] Agrawal et al. in a study, concluded consumption of a Non-vegetarian diet, daily or occasionally, suffered more from asthma than those who were strictly vegetarian.[186] The finding of this study in which asthma was diagnosed significantly higher among Non-vegetarians contributes to the growing evidence of protective effects of vegetarian diet in asthma.

In our study, 72.7% of the patients were sensitised to both indoor and outdoor allergens, while 20.5% of the patients showed skin prick test positivity to only indoor allergens and 6.8% were sensitised to only outdoor allergens. Among the patients sensitised to both indoor and outdoor allergens, 43.8% had only allergic rhinitis, whereas 28.1% of patients were suffering from only asthma and both allergic rhinitis and asthma, respectively. In a study by Katel P et al.,[187] it has been observed that both indoor and outdoor allergens are the cause of allergic rhinitis in Thai population, which is in accordance with our study. Another study supporting the results of our study, was conducted by Kerkhof M et al.,[188] that

concluded that sensitisation to both indoor and outdoor allergens was associated with increased bronchial hyperresponsiveness.

With respect to the regional geography with high humidity, sensitisation to indoor allergens was expected. As expected, patients sensitised only to indoor allergens were higher compared to those sensitised to only outdoor allergens in our study.

ALLERGEN SENSITIVITY PATTERN AMONG PATIENTS WITH ALLERGIC RHINITIS AND/OR ASTHMA

The aeroallergen sensitisation patterns vary with the difference in geographical locations, altitudes and climate. Hence it is important to determine the allergen sensitivity pattern in a defined geographical area to help direct treatment and avoidance measures for patients suffering from allergic diseases. The pattern of sensitisation to allergens was carried out using a predetermined panel of 73 allergen extracts.

In our study, it was observed that the most common allergens that the patients were sensitised to were the House dust mites. Overall, 65.9% of the patients showed skin prick test positivity to atleast one house dust mite. Following the house dust mites, the next common allergens were Mosquito and Gram kabuli, each in 9 patients (20.5%) out of the 44 patients. 8 patients (18.2%) showed sensitivity to *Cynodondactylon* and Wheat dust. The least common allergens that showed skin prick test positivity in only one patient (2.3%) were Honey bee and Lemon, while none of the patients were sensitive to Brinjal. The results of our study are consistent with other studies conducted in several parts of India. House dust mite was identified as the commonest allergen to cause nasobronchial allergy in 24.21%, in a study by Chogtu et al.[171] In the western part of India, Mumbai, 77.13%, 60% in Northern part of India- Allahabad, and 70% in southern part of India- North Kerala, were sensitised to House dust mites, which were the commonest in the respective geographical areas.[189,190,191]

Though most of the studies in India, identified house dust mites to be the most common allergens, a few studies stated other allergens as the cause of nasobronchial allergy. Prasad R et al.'s[192] and Kumar R et al.'s[193] study in Uttar Pradesh and New Delhi, respectively, cited insects as the common offending allergens, whilst another study by Jain S et al.[194] found pollens to be the most common offending allergens.

SKIN PRICK TEST POSITIVITY TO MITES

House dust mites were the common allergens the patients were sensitised to, commonest among them being *Blomia*, with skin prick test positivity observed in 50% of the patients, followed by sensitisation to Mite (*D- Farinae*) in 45.5% and Mite (*D-Pteronyssinus*) in 40.9% of the patients. The results from a study by Shikha G et al.,[195] conducted in Bangalore, India, showed that Mite (*D- Pteronyssinus*) was the most common allergen amongst the house dust mites, which are in contrast to our study, although *Blomia* was not present in their allergen panel. Sensitisation to *Blomia* was commonly tested in Western population and in a study by Stanaland BE et al.,[196] sensitisation to *Blomia* was the least common(38%) when compared with Mite (*D- Pteronyssinus*) (62%) and Mite (*D-Farinae*) (60%). In contradiction to our study, another study in West Bengal by Podder S et al.[197] identified *D- pteronyssinus* (75.06%) to be the common allergen among patients with nasobronchial allergy, followed by *Blomia* (72%), and *D. Farinae* (63.72%)

22.7% of the patients with only allergic rhinitis, 18.2% with only asthma and 25% with both allergic rhinitis and asthma were sensitised to house dust mites. This is in accordance to the study by Moghtaderi M et al.[175] where the maximum number of patients with both allergic rhinitis and asthma were sensitised to house dust mites, followed by those with only allergic rhinitis and then those with only asthma.

Out of 17 patients with Allergic rhinitis only, the most common allergen was found to be Mite (*D- Farinae*) in 7 patients (41.1%), followed by Mite (*D- Pteronyssinus*) and *Blomia* in 6 patients (35.2%) each. In support to our study, a study by Aydin S et al.[198] showed that majority (29.3%) of patients were sensitive to Mite (*D- Farinae*) and 25.3% were sensitive to Mite (*D- Pteronyssinus*).

In a study conducted amongst asthmatics, by Ferrandiz R et al.,[199] *D-Pteronyssinus* (87%), *Blomia* (85%) were the commonest allergens followed by *D-Farinae* (83%), which is in accordance to our study, where 50% of patients with Asthma only had sensitisation to Mite (*D- Pteronyssinus*) and *Blomia* (6 patients each) followed by Mite (*D- Farinae*) in 5 patients (41.6%). The association of house dust mite allergy and asthma has been reported from several parts of the world based on avoidance studies and population surveys, which reported that exposure of allergic patients to mite allergens are the major cause non specific bronchial hyper-reactivity.[200]

In our study, majority of patients with both allergic rhinitis and asthma were sensitive to *Blomia* (66.7%) followed by Mite (*D- Farinae*) in 8 patients (53.3%). and Mite (*D-Pteronyssinus*) in 40% of the patients. Supporting the results of our study, Liu X et al.[201] have also cited *Blomia* as the commonest allergen amongst those suffering from both allergic rhinitis and asthma.

SKIN PRICK TEST POSITIVITY TO FUNGI

Among the Fungi, the common allergens were identified to be *Aspergillus flavus, Fusarium solanii, Curvularia lunata, Cladosporium herbarum and Candida albicans* with 6 patients (13.6% each) showing skin prick test positivity. 11.4% of patients were sensitive to *Aspergillus niger* and *Rhizopus nigricans* and 9.1% (least common allergens) showed skin prick test positivity towards *Aspergillus fumigatus* and *Trichoderma*. These results are in

accordance to the study conducted by Chogtu B et al.,[171] conducted in Udipi district of Karnataka, where *Aspergillus flavus* was the most common allergen. Study from Punjab by Jerath VP et al.,[202] reported *Cladosporium herbarum* as the most common allergen. Differing from our study, several studies have shown *Aspergillus fumigatus* as the common allergen. Karmakar S et al.,[203] in his study to identify the skin prick test sensitivity among patients with nasobronchial allergy in Uttar Pradesh, identified *Aspergillus fumigatus* (16%) to be the most common allergen amongst fungi, followed by *Aspergillus niger* (12%), *Cladosporium herbarum* (6%) and *Fusarium solanii* (4%), whereas study from Jabalpur on poultry workers by Verma KS et al.[204] reported *Aspergillus niger* as the most common allergen. This difference in various studies regarding the sensitivity pattern also highlights the regional variation of allergens.

Majority of the patients with allergic rhinitis only (17.6%) were sensitised to *Fusarium solanii* in our study. On the contrary, in a study from Bangalore by Gowda G et al.,[205] the commonest fungus amongst the patients with only allergic rhinitis was *Aspergillus flavus*(3.5%).

In our study, *Cladosporium herbarum* and *Candida albicans* were common (25%) among patients with asthma only. In contradiction to our results, a study conducted in Delhi by Kumar M et al.[206] among asthmatics, reported *Aspergillus fumigatus* as the most common offending allergen. Another study by Assarehzadegan MA et al.[179] in Iran reported similar results as our study, where *Cladosporium herbarum* and *Alternaria* were identified as the common allergens, although Alternaria was not included in our allergen panel.

Of the 15 patients with both allergic rhinitis and asthma, *Aspergillus niger* and *Aspergillus flavus* were the common allergens found in 20% of the patients. These results are

similar to a study by Kunoor AK et al.[207] in Central Kerala, which reported *Aspergillus flavus* as the most common allergen among patients with both allergic rhinitis and asthma.

SKIN PRICK TEST POSITIVITY TO POLLENS

Among Pollens, sensitivity to *Cyanodondactylon* was commonly observed in 8 patients (18.2%) followed by *Parthenium hysterophorus* in 7 patients (15.9%). *Ricinus communis* was positive in 13.6% of patients, *Xanthium strumarium* and *Peltophorum pterocarpum* in 11.4%, *Zea mays* and *Ipomoea* in 9.1%, and *Ageratum conyzoides* and *Cocos nucifera* in 4.5% of patients. Comparable to our study, Kumar R et al.[6] in Delhi, also reported *Cyanodondactylon* to be the most common allergen showing positive skin prick test. In West Bengal, *Cocos nucifera* was the commonest pollen causing sensitisation, followed by *Cynodondactylon*,[50] whereas *Cocos nucifera* was the least common in our study. Sensitisation to different pollens in different regions could be attributed to the varied climatic conditions pertaining to the geographical area.

In our study, *Peltophorum pterocarpum* was the common allergen amongst patients with allergic rhinitis only, skin prick test being positive in 4 patients (23.5%). These results are in discordance with another study conducted to identify sensitisation patterns among patients with allergic rhinitis in Central India,[172] which reported *Parthenium hysterophorus* as the most common offending pollen.

Among the patients with asthma only, *Cyanodondactylon, Ricinus communis and Zea mays* were the common allergens that the patients were sensitive to. This is in accordance with a study from Delhi by Kumar M et al.,[206] which also reported *Cynodondactylon* as the common pollen, whereas in contrast, other studies from South India reported *Parthenium hysterophorus* as the dominant pollen (20.86%) (12).

Out of the 15 patients who had both allergic rhinitis and asthma, 5 patients (33.3%) showed sensitivity to *Cyanodondactylon* while none of them showed sensitivity to *Peltophorum pterocarpum* and *Cocos nucifera*.

SKIN PRICK TEST POSITIVITY TO DUST

Overall, in our study, skin prick test positivity to Wheat dust and Grain dust (rice) was observed in 8 patients (18.2%) commonly. These results are comparable to the study by Kumar R et al.[6] in Delhi, which also identified Wheat dust (8.28%) to be the most common allergen followed by House dust (7.08%). Another study by Chogtu et al.[171] from Udipi, Karnataka, also reported Grain dust (rice) to be the commonest allergen (33%), but Wheat dust was the least common (15.8%).

While Grain dust (rice) was the most common allergen, showing skin prick test positivity in 3 out of 17 patients (17.6%) of allergic rhinitis only in our study, Paper dust was found to be the most common allergen among asthma only patients, whereas wheat dust and paper dust were common among patients with both allergic rhinitis and asthma. Clinical profile of allergic rhinitis in Central India[194] also showed that Grain dust (rice) was the common allergen with patients showing positivity to skin prick test. A study from Kerala also reported Grain dust (rice) to be common amongst those with only asthma, which is in contradiction to the results of our study.[207]

Sensitivity to cotton dust was observed in the patients with Allergic rhinitis only and those with both allergic rhinitis and asthma, but none who had asthma only, showed sensitivity to cotton dust. None of the patients with allergic rhinitis only showed sensitivity to house dust and paper dust in our study.

SKIN PRICK TEST POSITIVITY TO EPITHELIA (INSECTS AND ANIMALS)

Overall, Mosquito was the commonest allergen, with 9 patients (20.5%) showing sensitivity, among epithelia, followed by Grasshopper in 7 patients (15.9%). The least common allergen was Honey bee, which showed skin prick test positivity in only one patient with asthma only, while patients with allergic rhinitis only and those who had both allergic rhinitis and asthma showed no sensitivity to Honey bee. A study by Chogtu et al.[171] also demonstrated grasshopper as the common allergen among patients with nasobronchial allergy in the region of Udipi, which is comparable to the results of our study. Studies from other parts of the country reported varying results as cockroach was the most offending allergen in Uttar Pradesh, while moth was the commonest in Gujarat.[208,209]

Mosquito was the common allergen found among the patients with allergic rhinitis, positive in 4 out of 17 patients (23.5%) and also among patients with both allergic rhinitis and asthma, while Grasshopper was the commonest in 4 patients (33.3%) among the 12 patients with asthma only. A study from Bangalore reported Cricket (22.3%) as the commonest among insects and epithelia followed by Mosquito (10.07%) among asthmatics, and another study by Jain S et al.[194] reported cockroach as the commonest amongst those with only allergic rhinitis, which are inconsistent with the results of our study.

Whilst all the 12 patients with asthma only showed sensitivity to at least one allergen, none of the patients with allergic rhinitis only showed sensitivity to sheep's wool, ant (black), cockroach, wasp and honey bee. Patients with both allergic rhinitis and asthma were not sensitised to Chicken feather, Honey bee and Rice weevil.

SKIN PRICK TEST POSITIVITY TO FOODS

Out of 44 patients, 9 patients (20.5%) showed sensitivity to Gram kabuli, the commonest allergen among foods, followed by Dal urad in 7 patients (15.9%), while none of

the patients were sensitive to Brinjal. In contrast to our study, split red gram, split green gram, glycine max, coriander and pearl millet showed maximum sensitivity among patients with nasobronchial allergy in Udipi district of Karnataka.[171] In a study by Moghtaderi M et al. in Iran, 59% of the patients with clinical history of allergy to brinjal showed skin prick test positivity.[210]

Among patients with allergic rhinitis only, Moong dal and Dal arahar were most common allergens, positive in 3 patients (17.6%), while Dal urad was the most common in 4 out of 12 patients (33.3%) among patients with asthma only. Gram kabuli was the most common allergen found among patients who had both allergic rhinitis and asthma. Sensitivity to Moong Dal was shown by patients with Allergic rhinitis only, whereas sensitivity to Coriander was shown by patients with asthma only.

According to Jain S et al.,[194] in contrary to the results of our study, sensitisation to milk (5%) was the most significant trigger for allergic rhinitis patients, and maximum intolerance to cow milk was elicited in patients with bronchial asthma in Delhi by Kumar R et al.[193] In a study by Kunoor AK et al.,[207] prawn was the commonest allergen amongst patients with only allergic rhinitis (72.4%) with only asthma (82.7%), while wheat and potato were the next commonest, respectively. The variant results of food allergen sensitivity in different regions might be due to the different food habits in each region. More studies on food allergen sensitivity pattern are required or further elucidation of commonest allergens pertaining to a specific geographical area.

DISTRIBUTION BASED ON TOTAL SERUM IgE LEVELS

Out of 44 patients, 14 patients (31.8%) had normal Total Serum IgE levels, while 30 patients (68.2%) had elevated Total Serum IgE levels. These results are comparable to a study by Arastu SH[8] that reported 67% patients with elevated total serum IgE levels. Another

study by Kathuria PC et al.,[211] stated that high titres of total serum IgE levels (58.6%) were associated with respiratory allergy among Indian patients. Another study by Kumar V et al.[177] reported that 94% of the study population had elevated total serum IgE levels, which was higher compared to our study. Overall, the results could elucidate the central role of total IgE in development of allergic disorders and also confirm the diagnostic accuracy of total serum IgE to detect allergic conditions.

In our study, of the 30 patients with elevated Total serum IgE levels, 9 patients (20.5%) had IgE levels in the range of 301-500 KU/L, whereas 15.9 % had values within 151-300 KU/L and >1000 KU/L each. Only 2 patients had IgE levels within the range of 501-750 KU/L. These results are inconsistent with a study from Bihar that showed 51.36% of the patients with total serum IgE levels >1000KU/L [177] while another study by Tegnoor MS et al.[212] in Hyderabad reported 57% of patients with IgE levels between 300-500 KU/L.

All the patients (12 out of 12) with only asthma had elevated total serum IgE levels, whereas 9 out of 17 patients (52.9%) with only allergic rhinitis had elevated total serum IgE levels. 9 out of 15 patients (60%) with both allergic rhinitis and asthma had elevated total serum IgE levels. In contrast to our study, Rasheed SM et al.[2] reported majority of patients (63.1%) with both allergic rhinitis and asthma with elevated total serum IgE levels, followed by 58.1% with only allergic rhinitis and 55.3% with only asthma. There is evidence that total serum IgE levels among atopics correlate with the size of the target organ, being lowest among rhinitis, intermediate in asthmatics and highest in atopic eczema,[213] which correlates to the results of our study. None of the patients with only asthma had normal total serum IgE levels, while 47.1% of patients with only allergic rhinitis and 40% with both allergic rhinitis and asthma had normal total serum IgE levels in our study.

ASSOCIATION OF TOTAL SERUM IgE LEVELS WITH MITES

Overall, total serum IgE was found to be elevated in the maximum number of patients who were sensitised to House dust mites (76.7%), commonest among them being *Blomia* in 17 patients. These results are in contrast to a study from Bihar by Kumar V et al.,[177] where elevated total serum IgE levels were common amongst patients sensitised to molds. Out of 14 patients with normal Total serum IgE levels in our study, 6 patients were sensitised for Mites. There was a positive and statistically significant ($P<0.05$) association between Total serum IgE levels and Skin prick test positivity for Mites. Supporting the results of our study, Kim HS et al.'s study from Korea[214] also established a positive and significant correlation between skin prick test sensitivity to mites and total serum IgE levels.

Among the patients with elevated Total serum IgE levels, most of the patients with Asthma only were sensitised to Mites, compared to those with Allergic rhinitis only or both Allergic rhinitis and asthma. While sensitivity to Mite (*D- Pteronyssinus*) was majorly observed among patients with Asthma only (42.9%), sensitivity to *Blomia* was higher among those with both Allergic rhinitis and Asthma (41.2%).

ASSOCIATION OF TOTAL SERUM IgE LEVELS AMONG FUNGI

Out of 19 patients who showed skin prick test positivity to Fungi, 14 patients (46.7%) had elevated Total serum IgE levels. Total serum IgE levels were elevated among all the patients sensitised to *Fusarium solanii* and *Rhizopus nigricans*. 16 out of 30 patients were not sensitised to Fungi but had elevated Total serum IgE levels. Of the 14 patients with normal Total serum IgE levels, 5 patients (35.7%) were sensitised to Fungi. The association between Total serum IgE levels and Skin prick test positivity to Fungi was not statistically significant ($P>0.05$). This is in accordance to the study by Salama LA et al.,[215] where majority of

patients (71.1%) sensitised to *Fusarium solanii* had elevated total serum IgE levels, and the association was also not statistically significant.

Among the fungi, none of the patients with Asthma only who had elevated Total serum IgE levels showed Skin prick test positivity to *Aspergillus niger*. Sensitivity to *Aspergillus fumigatus* and *Trichoderma* was present in one patient in each group of Asthma only, Allergic rhinitis only and both Allergic rhinitis and Asthma, with elevated Total serum IgE levels. Majority of the patients with Asthma only had skin prick test positivity to *Candida albicans* (25%), while *Fusarium solanii* was the common allergen that patients with only Allergic rhinitis were sensitised to (17.7%). In patients with both allergic rhinitis and asthma, sensitisation to *Aspergillus niger* and *Aspergillus flavus* was predominant (13.3% each).

ASSOCIATION OF TOTAL SERUM IgE LEVELS WITH POLLENS

Out of the pollens, all the patients sensitised to *Cynodondactylon* had elevated total serum IgE levels (8 out of 8). Elevated total serum IgE levels were also found in all patients sensitised to *Cocos nucifera* and *Ipomoea*. Among the 20 patients who were sensitised to Pollens, 17 patients (85%) had elevated Total serum IgE levels. Among the 24 patients without sensitisation to Pollens, 11 patients had normal Total serum IgE levels (45.8%). There is a positive and statistically significant ($P<0.05$) association between Total serum IgE levels and Skin prick test positivity for Pollens. The results of our study were in contrast to the results by Salama LA et al.,[215] where most of the patients (71.4%) had skin prick test positivity to weed pollens compared to grass pollen in our study, and the association between pollens and total serum IgE levels was not statistically significant in their study.

Patients with both Allergic rhinitis and asthma and elevated Total serum IgE levels showed maximum sensitivity to *Cynodondactylon* compared to other pollens, with none of

them sensitive to *Cocos nucifera* and *Peltophorum pterocarpum*. Majority of patients with Alergic rhinitis only (17.6%) showed sensitivity to *Peltophorum pterocarpum*, whereas *Zea mays* and *Cynodondactylon* were the common allergens among pollens in Asthma only patients (16.6%) with elevated Total serum IgE levels.

ASSOCIATION OF TOTAL SERUM IgE LEVELS WITH DUST

All patients with skin prick test positivity to Cotton dust and House dust had elevated total serum IgE levels. Among Dust allergens, 16 patients (53.3%) were sensitised who had elevated Total serum IgE levels. Out of the 14 patients with normal Total serum IgE levels, 9 patients (64.3%) showed no skin prick test positivity to Dust allergens. Salama LA et al.[215] reported 92.9% sensitivity to cotton dust with elevated IgE levels, and the association between dust allergens and total serum IgE levels was significant, compared to our study where the association was statistically not significant (P>0.05).

Out of the patients with elevated Total serum IgE levels, sensitivity to Wheat dust was commonest (26.7%) in patients with both allergic rhinitis and asthma. Amongst patients with only asthma, sensitivity to House dust and Paper dust was the commonest (16.6% each), and sensitivity to Wheat dust and Grain dust (rice) was present in 11.7% of the patients with only allergic rhinitis. None of the patients with only Allergic rhinitis and elevated Total serum IgE levels showed sensitivity to House dust, Paper dust and Hay dust.

ASSOCIATION OF TOTAL SERUM IgE LEVELS WITH EPITHELIA

Elevated total serum IgE levels were found in all the patients with sensitivity to Ant (black), Cockrach, Honey bee, Rice weevil, Moth and Wasp. Out of 26 patients sensitised to Epithelia, 19 patients had elevated Total serum IgE levels. Among the 14 patients with normal Total serum IgE levels, 50% were sensitive to Epithelia whereas 50% showed no skin

prick test positivity to Epithelia. There is a positive association between Total serum IgE levels and Skin prick test sensitivity to Epithelia but not statistically significant (P>0.05). 71.6% of the patients with sensitivity to cockroach had elevated total serum IgE levels and the association was not significant in a study by Salama LA et al.[215]

Among the patients with elevated Total serum IgE levels, majority of them with both Allergic rhinitis and Asthma showed sensitivity to all the allergens amongst Epithelia, commonest being Dog epithelia, Mosquito and House fly (20% each), whereas patients with only Allergic rhinitis showed no sensitivity to almost 50% allergens among Epithelia. 17.6% of patients with only allergic rhinitis showed sensitivity to Mosquito, whilst Moth, Wasp, Grasshopper, Ant (red) were the common allergens that the patients with only asthma were sensitised to.

ASSOCIATION OF TOTAL SERUM IgE LEVELS WITH FOODS

Patients sensitised to food allergens showed variable total serum IgE levels, although all the patients with sensitivity to Lemon, Soyabean, Egg white, Chocolate and Rajma showed only elevated IgE levels. Among patients sensitised to Food allergens, 23 out of 33 patients had elevated Total serum IgE levels. Amongst the patients with normal Total serum IgE levels, 10 patients (71.4%) were sensitised to Food allergens whereas only 4 patients (28.6%) showed no skin prick test positivity. There is a positive association between Total serum IgE levels and Skin prick test sensitivity to Food allergens but association is not statistically significant (P>0.05). Salama LA et al.[215] tested skin prick test positivity for only corn and wheat, and 69% and 67.9% had elevated total serum IgE levels, respectively and the association was not statistically significant.

Patients with only allergic rhinitis with elevated Total serum IgE levels showed maximum sensitivity to Moong dal, Dal arahar, Gram bengali, Gram kabuli and Rajma

(11.7% each). While skin prick test to Dal urad and Gram kabuli was positive in 25% of the patients with only asthma and with elevated total serum IgE levels, 20% of patients with both allergic rhinitis and asthma showed sensitisation to Milk and Gram kabuli.

DISTRIBUTION BASED ON ABSOLUTE EOSINOPHIL COUNTS

Out of 44 patients, 26 patients (59%) had normal eosinophil counts, while 18 patients (41%) had elevated eosinophil counts as opposed to the results of the studies by Arastu SH[8] and Muddaiah D et al.[216] where the majority of the patients (59%) had elevated eosinophil counts. Another study by Tegnoor MS et al.[212] reported only 14% of patients with elevated eosinophil counts among allergic rhinitis patients. The discrepancy in the percentage of patients with elevated eosinophil counts could be attributed to the notion that blood eosinophilia is associated with more severe asthma, increased rate of exacerbations and resistance to treatment.

In our study, majority of the patients with only allergic rhinitis had elevated eosinophil counts. 5 patients out of 12 patients (41.7%) with only asthma, 8 out of 17 patients (47.1%) with only allergic rhinitis and 5 out of 15 patients (33.3%) with both allergic rhinitis and asthma had elevated eosinophil counts. In agreement to our study, Brakhas SA et al.[217] also reported elevated eosinophil counts among most of the patients with only allergic rhinitis compared to those with only asthma. Chen Y et al.[218] also reported that elevated eosinophils in peripheral blood were observed amongst patients with moderate to severe allergic rhinitis. Majority of the patients in all three groups in our study (i.e. 9 with only allergic rhinitis, 7 with only asthma, 10 with both allergic rhinitis and asthma) had normal eosinophil counts when compared with those with elevated eosinophil counts. Altaii HA et al.,[219] in their study, reported contradicting results where 31.58% of patients with elevated eosinophil counts had asthma, 18.52% of patients had allergic rhinitis. Another study with inconsistent results was

by Arastu SH,[8] where majority (68.75%) with raised eosinophil counts had both allergic rhinitis and asthma, followed by only asthma (65%) and only allergic rhinitis (37.5%).

ASSOCIATION OF EOSINOPHIL COUNTS WITH MITES

Out of the 18 patients with elevated Absolute eosinophil counts, 14 patients (77.8%) showed skin prick test positivity to Mites, commonest being *Blomia* (55.6%). Among the 29 patients sensitised to Mites, only 48.2% had associated elevation of Absolute eosinophil counts. There exists a positive association between Absolute eosinophil counts and Skin prick test sensitivity to Mites, but the association is not statistically significant (P>0.05), although Sacco O et al.[220] found statistically significant association between sensitisation to mites and elevated eosinophil counts. Min HJ e al.[221] identified a significant correlation between house dust mite sensitivity and eosinophil counts among patients with allergic rhinitis.

Among the patients with elevated Absolute eosinophil counts sensitised to Mites, in our study, majority of them had only Asthma (33.3%).

ASSOCIATION OF EOSINOPHIL COUNTS WITH FUNGI

Among Fungi, most of the patients with elevated Absolute eosinophil counts were sensitised to *Candida albicans* (27.8%), followed by *Rhizopus nigricans*, *Aspergillus flavus* and *Cladosporium herbarum* (22.2%). Among the 19 patients with sensitisation to Fungi, only 7 patients (36.8%) had elevated Absolute eosinophil counts whereas majority of patients' Absolute eosinophil counts were within normal limits. Out of 25 patients with no sensitivity to Fungi, 11 patients had elevated Absolute eosinophil counts. There was a positive association between Skin prick test sensitivity to Fungi and Absolute eosinophil counts, and not a statistically significant association (P>0.05).

Among Fungi, the patients with Asthma only showed more sensitivity to the allergens (25%) compared to those with Allergic rhinitis only and both Allergic rhinitis and Asthma, who had associated elevated Absolute eosinophil counts.

ASSOCIATION OF EOSINOPHIL COUNTS WITH POLLENS

55.6% of the patients with elevated Absolute eosinophil counts had skin prick test positivity to Pollens, whereas 38.5% of patients having sensitisation to Pollens had normal Absolute eosinophil counts. *Cynodondactylon* was the most common allergen among pollens that the patients were sensitised to, who had elevated Absolute eosinophil counts (27.8%). None of the patients with elevated Absolute eosinophil counts were sensitised to *Ageratum conyzoides* and *Cocos nucifera*. There was a positive but statistically not significant association (P>0.05) between Absolute eosinophil counts and Skin prick test sensitivity to Pollens. In contrary to the results of our study, Min HJ e al.[221] identified a significant correlation between pollens sensitivity and eosinophil counts among patients with allergic rhinitis.

Among Pollens, 20% of patients with sensitivity to *Cynodondactylon* and associated elevated Absolute eosinophil counts had both Allergic rhinitis and Asthma. None of the patients with elevated Absolute eosinophil counts who had Asthma only were sensitised to *Xanthium stumarium* and *Parthenium hysterophorus*.

ASSOCIATION OF EOSINOPHIL COUNTS WITH DUST

Of the 18 patients with elevated Absolute eosinophil counts, 13 patients (72.2%) had skin prick test positivity to Dust allergens. Among the 26 patients with normal Absolute eosinophil counts, only 30.8% had sensitisation to Dust, while 69.2% had no sensitivity to Dust allergens. Majority of the patients in our study with elevated Absolute eosinophil counts

were sensitised to Paper dust (33.3%) among the dust allergens. There was a positive and statistically significant association ($P<0.05$) between Absolute eosinophil counts and Skin prick test sensitivity to Dust allergens.

Among patients sensitised to Dust, majority had both Allergic rhinitis and Asthma compared to those with only Asthma or Allergic rhinitis. None of the patients with only allergic rhinitis showed skin prick test positivity towards House dust, Paper dust and Hay dust, whereas sensitisation to Hay dust and Cotton dust was observed in none of the patients with only asthma.

ASSOCIATION OF EOSINOPHIL COUNTS WITH EPITHELIA (INSECTS AND ANIMALS)

In comparison to the patients with elevated Absolute eosinophil counts, those who had Absolute eosinophil counts within normal limits, showed more sensitivity to Epithelia. Among the 26 patients with normal Absolute eosinophil counts, 65.4% had sensitivity to Epithelia, whereas 50% of the patients with elevated Absolute eosinophil counts had skin prick test positivity to Epithelia. Mosquito was the most common allergen among patients with elevated Absolute eosinophil counts (22.2%). There was a positive but statistically insignificant association ($P>0.05$) between skin prick test positivity to Epithelia and Absolute eosinophil counts.

Out of the patients with only allergic rhinitis, Mosquito and Grasshopper (11.7% each) were the allergens that the patients were most sensitised to. Moth, Wasp and ant (red) were common among those with only asthma, and Dog epithelia and Housefly were the common offending allergens among patients with both allergic rhinitis and asthma with elevated eosinophil counts.

ASSOCIATION OF EOSINOPHIL COUNTS WITH FOODS

6 out of 9 patients (33.3%) sensitive to Gram kabuli had elevated Absolute eosinophil counts among the food allergens, while all those sensitised to Bajra, Jowar, Peanut, Egg white, Coffee, Coconut, Gum acacia and Long pepper had normal Absolute eosinophil counts. 80.8% of patients with skin prick test positivity to Food allergens had normal Absolute eosinophil counts, and 12 out of 18 patients (66.7%) with skin prick test positivity to Food allergens had elevated Absolute eosinophil counts. Of the 33 patients with skin prick test positivity to Food allergens, only 12 patients (33%) had elevated Absolute eosinophil counts, whereas 21 patients (67%) had normal Absolute eosinophil counts. There was a positive but statistically not significant association ($P>0.05$) between Absolute eosinophil counts and skin prick test positivity to Food allergens.

While Gram kabuli was the common allergen among patients with elevated Absolute eosinophil counts, patients with both Allergic rhinitis and Asthma showed more skin prick test positivity to Food allergens when compared to those with only Allergic rhinitis or only Asthma.

CORRELATION

Out of the 14 patients whose Total Serum IgE levels were within normal limits, 13 patients had associated normal Absolute eosinophil counts and only one patient with elevated Absolute eosinophil counts. Of the 30 patients with elevated Total Serum IgE levels, 17 patients had associated elevated absolute eosinophil counts. There was a positive and statistically significant ($P<0.05$) correlation between Total serum IgE levels and Absolute eosinophil counts. Consistent with the results of our study, Altaii HA et al.[219] and Muddaiah D et al.,[216] also reported significant positive correlation between total serum IgE levels and eosinophil counts.

Among the 44 patients enrolled in our study, only 2 patients (4.5%) were monosensitised, whereas the rest were sensitive to at least 2 allergens. Most of the patients (66.7%) with elevated total serum IgE levels were sensitised to at least 10 allergens, while 23.3% were sensitised to 10-20 allergens and 10% to 21-30 allergens. 61.1% of patients with elevated absolute eosinophil counts were sensitised to less than 10 allergens, 22.2% to 10-20 allergens and 16.7% to 20-30 allergens. Polysensitisation might be the result of genetic or environmental factors that favour growth and vegetation of specific plant species with similar survival conditions.

There was a positive correlation between total serum IgE levels and skin prick test positivity, as well as between absolute eosniophil counts and skin prick test positivity, and the correlation was statistically significant ($P<0.05$). This implies that higher levels of total serum IgE, and higher eosinophil counts correspond to the number of allergens the patients are sensitised to. A study by Rasheed SM et al. showed 25.5% of patients with monosensitisation, which differ from the results of our study, although a significant correlation was established between total serum IgE levels and skin prick test positivity. Also, IgE values were significantly associated with skin prick test reactivity in another study by Baldacci S et al.[222] However, another study by Gharagozlou M et al.[223] found no correlation between total serum IgE levels and skin prick test positivity.

LIMITATIONS

1. All the patients in our study were tested with a predetermined allergen panel.
2. The study was hospital based, referral bias being the limitation.
3. The study incorporated 44 patients. A study of larger magnitude would have had better statistical significance.
4. Not all the patients who visited the hospital agreed for skin prick testing, nor fulfilled the inclusion criteria, hence generalising the results might not be appropriate unless all consecutive patients are enrolled.
5. Most of the patients belonged to the age group of above 45 years, who had longer duration of the disease, which might have lead to high total serum IgE levels.
6. The other conditions leading to high total serum IgE, like parasitic infection or viral infection, were not assessed.
7. The other causes of high eosinophil counts were not ruled out.
8. The results of this study could not be extrapolated to a larger population and different parts of the state, because of the varied geography in different regions.

CONCLUSION

In this study, most of the patients belonged to the age group of 45-60 years, with female predominance. The majority of the patients included in the study, were found to be suffering from only allergic rhinitis. The study population predominantly constituted of Non-Vegetarians and patients with Ideal body weight, with maximum sensitisation to both indoor and outdoor allergens. Most of the patients with both allergic rhinitis and asthma had family history of allergies.

The results of this study gave a comprehensive knowledge of locally prevalent allergens in North Karnataka amongst patients with allergic rhinitis and/or asthma. Overall, House dust mites were the most common offending allergens, majority to *Blomia*. *Aspergillus flavus, Fusarium solanii, Curvularia lunata, Cladosporium herbarum* and *Candida albicans* were the common fungi, whereas *Cyanodondactylon* was commonest among Pollens. Most of the patients showed skin prick test positivity to Wheat dust and Grain dust (rice) among Dust allergens, while Mosquito was the common offending allergen in Insects and Animals. Among the food allergens, most of the patients were sensitised to Gram kabuli.

Majority of the study population had elevated total serum IgE levels (68.2%). All the patients with only asthma had elevated total serum IgE levels. The association of total serum IgE levels with House dust mites and Pollens was statistically significant. Absolute eosinophil counts were within normal levels in most of the study patients. Among those with elevated eosinophil counts, majority had only allergic rhinitis. The association of absolute eosinophil counts with Dust allergens alone was significant.

There was a positive correlation between total serum IgE levels with eosinophil counts. Although the total serum IgE levels and eosinophil counts was positively correlated

with the number of allergens the patients were sensitised to, the correlation was weak with that of eosinophil counts.

The basis of allergic diseases is the allergen sensitisation mediated by IgE and eosinophils, total serum IgE levels could be used as a diagnostic criterion, especially among asthmatics, according to this study. The possibility of sensitisation to multiple allergens increases with increase in levels of total serum IgE above the normal range.

Albeit the positive correlation among total serum IgE, eosinophil counts and skin prick test positivity, the use of only IgE as a screening tool might not be sufficient, as it might be elevated in several other conditions. Hence, skin prick test remains the gold standard for diagnosis of particular allergens, so as to direct treatment, like avoidance measures and immunotherapy, appropriately.

In conclusion, the common offending allergens in each groups were:

- Mites- *Blomia* > *D- Farinae*.
- Fungi- *Aspergillus flavus*, *Fusarium solanii*, *Curvularia lunata*, *Cladosporium herbarum* and *Candida albicans*
- Pollens- *Cynodondactylon* > *Parthenium hysterophorus*
- Dust- Wheat and Grain dust (rice) > Paper dust
- Epithelia (Insects and animals)- Mosquito > Grasshopper
- Foods- Gram kabuli > Dal urad

SUMMARY

Forty-four patients diagnosed with either allergic rhinitis or asthma or both, attending the out-patient and in-patient department of Respiratory Medicine, BLDE (Deemed to be University), Shri. B. M. Patil Medical College, Hospital and Research Centre, Vijayapura, between January 2021 and June 2022 were studied. The study was conducted to evaluate the allergen patterns in patients with nasobronchial allergy and to correlate total serum IgE levels and eosinophil count to the skin prick test so as to evaluate the possibility of their use as a screening test.

1. In this study, female patients (54.5%) were more than males (45.5%).
2. The most common age group was 45-60 years with 40.9%, followed by 29.5% in 15-30 years and 31-45 years each.
3. In this study, most of them had only allergic rhinitis (38.6%) followed by those with both allergic rhinitis and asthma (34.1%) and only asthma (27.3%). Among the patients suffering from Allergic rhinitis, majority had persistent allergic rhinitis (65.6%), while 34.4% had Intermittent allergic rhinitis.
4. Out of the 38.63% of the patients with positive family history in our study, 53.3% had both allergic rhinitis and asthma, whilst 35.9% had only allergic rhinitis and 25% had only asthma.
5. 50% of the patients enrolled had ideal body weight, whereas 40.9% were overweight.
6. This study consisted majorly of Non- Vegetarians (56.8%) compared to Vegetarians (43.2%). Sensitisation to food allergens followed by mites was common among both the groups. Only allergic rhinitis was the common diagnosis among Vegetarians, while both allergic rhinitis and asthma was predominant in Non- Vegetarians.

7. Sensitisation to both indoor and outdoor allergens was common in the study population (72.7%), among whom, majority (43.8%) had only allergic rhinitis.
8. The most common allergens that the patients were sensitised to were House dust mites (65.9%). Individually, the most common allergens next to the House dust mites were Mosquito and Gram kabuli (20.5% each). The least common allergens that showed skin prick test positivity were Honey bee and Lemon (2.3%), while none of the patients were sensitised to Brinjal.
9. The commonest house dust mite was *Blomia*, with skin prick test positivity in 50% of the patients, followed by Mite (*D- Farinae*) in 45.5% and Mite (*D- Pteronyssinus*) in 40.9%. Mite (*D- Farinae*) was common (41.1%) amongst patients with only allergic rhinitis, whereas Mite (*D- Pteronyssinus*) and *Blomia* were common among only asthmatics, and Blomia being the common allergen in patients with both allergic rhinitis and asthma.
10. *Aspergillus flavus, Fusarium solanii, Curvularia lunata, Cladosporium herbarum* and *Candida albicans* were the common allergens among Fungi (sensitisation in 13.6% of the patients, each), the least common sensitisation observed towards *Aspergillus fumigatus* and *Trichoderma*. *Fusarium solanii* was common amongst patients with only allergic rhinitis, whereas *Cladosporium herbarum* and *Candida albicans* were common among only asthmatics, and *Aspergillus niger* and *Aspergillus flavus* being the common allergens in patients with both allergic rhinitis and asthma.
11. Among Pollens, overall, sensitivity to *Cyanodondactylon* was commonly observed (18.2%) and *Cocos nucifera* was the least common. Among those with only allergic rhinitis, sensitisation to *Peltophorum pterocarpum* was common, and amongst only asthmatics and those with both allergic rhinitis and asthma, *Cyanodondactylon* was the frequent allergen.

12. Wheat dust and Grain dust (rice) were the common dust allergens in this study, with predominant sensitisation to Grain dust (rice) among those with only allergic rhinitis, Paper dust among only asthma patients, Wheat dust and Paper dust in both allergic rhinitis and asthma patients.
13. Mosquito was the commonest allergen overall as well as among patients with only allergic rhinitis and both allergic rhinitis and asthma, while Grasshopper being the frequent allergen among only asthmatics.
14. Gram kabuli was the most frequent allergen with skin prick test positivity, overall as well as in those with both allergic rhinitis and asthma, while Moong dal and Dal urad were sensitised commonly amongst only allergic rhinitis patients and only asthma patients, respectively.
15. Majority of the study population had elevated total serum IgE levels (68.2%) while 31.8% of the patients had normal total serum IgE levels. All the patients with only asthma, 60% with both allergic rhinitis and asthma, and 52.9% with only allergic rhinitis had elevated total serum IgE levels.
16. There was a positive and statistically significant association between Total serum IgE levels and Skin prick test positivity for Mites and Pollens, whereas the association was not statistically significant with Fungi, Dust, Epithelia and Food allergens.
17. 59% of the patients enrolled in the study had normal eosinophil counts, while only 41% had elevated eosinophil counts. 41.7% with only asthma, 47.1% with only allergic rhinitis and 33.3% with both allergic rhinitis and asthma had elevated eosinophil counts.
18. The association between eosinophil counts and skin prick test sensitivity to Dust allergens was alone statistically significant, whereas association to Mites, Fungi, Pollens, Epithelia and Food allergens was not statistically significant.

19. There was a positive and statistically significant correlation between Total serum IgE levels and Absolute eosinophil counts (p=0.00001).
20. The correlation between total serum IgE levels and the number of allergens the patients were sensitised to, showed a moderate and statistically significant correlation (p=0.00038).
21. There was a weak but statistically significant positive correlation between absolute eosinophil counts and the number of allergens the patients were sensitised to (p=0.042095).

RECOMMENDATIONS

1. It is recommended to conduct this type of study time to time to assess the sensitisation patterns in different parts of the country for identification of newer allergens, that aid the clinicians to streamline the treatment options and allergen avoidance measures.
2. A multicenter study from different parts of Southern India, comprising of different populations, would be helpful in proposing an optimal panel of allergens that the patients could be tested for, uniformly.
3. Total serum IgE and absolute eosinophil counts to be performed along with Pulmonary function testing to be performed in cases of allergic rhinitis and/or asthma.
4. Study of pollens (Palynology) to identify local medically relevant pollens will help in Allergic rhinitis and/or asthma.
5. Skin prick testing to be uniformly performed in all allergic diseases to improve the health related quality of life of the patients.

BIBLIOGRAPHY

1. Singh AB, Kumar P. Aeroallergens in clinical practice of allergy in India. An overview. Annals of Agricultural and Environmental Medicine. 2003 Jan 1;10(2):131-6.
2. Hameed HG, AL-Fatlawi SN, Khudhair SA, Rasheed SM. Relationship between Total Serum IgE Level and Skin Prick Test in Patients with Symptoms of Respiratory Allergy. kufa Journal for Nursing sciences. 2016;6(3):53-9.
3. Shaikh WA. Allergies in India: An analysis of 1,619 patients attending an allergy clinic in Bombay. International Review of Allergy and Clinical Immunology. 1997;3(2):101.
4. Gowda G, Nagaraj C, Parasuramalu BG, Huliraj N. Aeroallergen sensitivity among patients suffering from bronchial asthma in Bangalore. International Journal of Health & Allied Sciences. 2013 Oct 1;2(4):237.
5. Pedersen PA, Weeke ER. Asthma and allergic rhinitis in the same patients. Allergy. 1983 Jan;38(1):25-9.
6. Kumar R, Sharan N, Kumar M, Bisht I, Gaur SN. Pattern of skin sensitivity to various aeroallergens in patients of bronchial asthma and/or allergic rhinitis in India. Indian Journal of Allergy, Asthma and Immunology. 2012 Jul 1;26(2):66.
7. Howarth PH, von Mutius E, Martinez FD. Allergic and non allergic rhinitis. Natural history, development and prevention of allergic disease in childhood. In: Middleton's allergy principles and practice. USA: Mosbey; 2003. p. 1391-407.
8. Arastu SH. Prospective Study on Assessment of Atopy by Serum IgE in Asthma & Rhinosinusitis. JMSCR. 2020 Apr 04;08(04):285-91.
9. Backman H, Räisänen P, Hedman L, Stridsman C, Andersson M, Lindberg A, Lundbäck B, Rönmark E. Increased prevalence of allergic asthma from 1996 to 2006 and further to

2016-results from three population surveys. Clin Exp Allergy. 2017 Nov;47(11):1426-1435. doi: 10.1111/cea.12963. Epub 2017 Jul 12. PMID: 28608416.

10. Prasad R, Verma SK, Dua R, Kant S, Kushwaha RA, Agarwal SP. A study of skin sensitivity to various allergens by skin prick test in patients of nasobronchial allergy. Lung India. 2009 Jul;26(3):70-3. doi: 10.4103/0970-2113.53228. PMID: 20442839; PMCID: PMC2862509.
11. Heinzerling,L.,Mari,A.,Bergmann,K.,Bresciani,M., Burbach,G., Darsow, U. and et al. (2013).The skin prick test - European standards. ClinTransl Allergy; 3(1):3.
12. Kay AB. Overview of 'allergy and allergic diseases: with a view to the future'. British medical bulletin. 2000 Jan 1;56(4):843-64.
13. Von Pirquet C. Allergie. Ann Allergy. 1946 Sep 1;4(5):388-90.
14. Gell PG, Coombs RR. 1968. Clinical aspects of immunology.
15. Szebeni J, editor. The complement system: Novel roles in health and disease. Springer Science & Business Media; 2007 May 8.
16. Marwa K, Kondamudi NP. Type IV hypersensitivity reaction. InStatPearls [Internet] 2021 Aug 14. StatPearls Publishing.
17. Coca AF, Cooke RA. On the classification of the phenomena of hypersensitiveness. The journal of immunology. 1923 May 1;8(3):163-82.
18. Atopic Dermatitis A, Leung AK, Ellis KL. DOWNLOAD http://archbd. net/1cESKQP Dermatological Diseases and Cumulative Life Course Impairment, Alexa Boer Kimball, M. Dennis Linder, 2013, Medical, 161 pages.. Handbook of Atopic Eczema, Johannes Ring, Bernhard Przybilla, Thomas Ruzicka, Feb 23, 2006, Medical, 635 pages. Atopic eczema (atopic dermatitis, neurodermitis diffusa, endogenous eczema).
19. Pawankar R, Holgate ST, Rosenwasser LJ, editors. Allergy Frontiers: Classification and Pathomechanisms. Springer Science & Business Media; 2009 Mar 13.

20. Harper D. Online etymology dictionary. 2001. Availabe from: www. etymonline. com/index. php. 2001.
21. Oettgen HC. Fifty years later: Emerging functions of IgE antibodies in host defense, immune regulation, and allergic diseases. Journal of Allergy and Clinical Immunology. 2016 Jun 1;137(6):1631-45.
22. Pedrosa M, Prieto-García A, Sala-Cunill A, Spanish Group for the Study of Bradykinin-Mediated Angioedema (SGBA) and the Spanish Committee of Cutaneous Allergy (CCA), Spanish Group for the Study of Bradykinin-Mediated Angioedema (SGBA):, Caballero T, Baeza ML, Cabañas R, Campos A, Cimbollek S, Gómez-Traseira C. Management of angioedema without urticaria in the emergency department. Annals of Medicine. 2014 Dec 1;46(8):607-18.
23. Grammatikos AP. The genetic and environmental basis of atopic diseases. Annals of medicine. 2008 Jan 1;40(7):482-95.
24. Wills-Karp M, Santeliz J, Karp CL. The germless theory of allergic disease: revisiting the hygiene hypothesis. Nature Reviews Immunology. 2001 Oct;1(1):69-75.
25. Aafa.org. 2022. Asthma and Allergy Foundation of America | AAFA | Home. [online] Available at: <http://aafa.org/display.cfm?id=9&sub=20&cont=286> [Accessed 1 May 2022].
26. Sussman GL, Beezhold DH. Allergy to latex rubber. Annals of Internal Medicine. 1995 Jan 1;122(1):43-6.
27. Gonzalez-Estrada A, Radojicic C. Penicillin allergy: a practical guide for clinicians. Cleve Clin J Med. 2015 May 1;82(5):295-300.
28. Dave ND, Xiang L, Rehm KE, Marshall GD. Stress and allergic diseases. Immunology and Allergy Clinics. 2011 Feb 1;31(1):55-68.

29. Galli SJ (February 2000). "Allergy". Current Biology. 10 (3): R93-5. doi:10.1016/S0960-9822(00)00322-5. PMID 10679332. S2CID 215506771.
30. De Swert LF. Risk factors for allergy. European journal of pediatrics. 1999 Jan;158(2):89-94.
31. Croner S. Prediction and detection of allergy development: influence of genetic and environmental factors. The Journal of pediatrics. 1992 Nov 1;121(5):S58-63.
32. Andreae D, Nowak-Węgrzyn A. The effect of infant allergen/immunogen exposure on long-term health. InEarly Nutrition and Long-Term Health 2017 Jan 1 (pp. 131-173). Woodhead Publishing.
33. Riedler J, Braun-Fahrländer C, Eder W, Schreuer M, Waser M, Maisch S, Carr D, Schierl R, Nowak D, Von Mutius E, ALEX Study Team. Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. The Lancet. 2001 Oct 6;358(9288):1129-33.
34. Daniel R. Cox, Sarah K. Wise and Fuad M. Baroody.Cummings Otolaryngology: Head and Neck Surgery, 35, 558-585.e9
35. Folkerts G, Walzl G, Openshaw PJ. Do common childhood infections 'teach'the immune system not to be allergic?. Immunology today. 2000 Mar 1;21(3):118-20.
36. Willett, E., 2022. The Hygiene Hypothesis. [online] Edward Willett. Available at: <https://edwardwillett.com/2000/05/the-hygiene-hypothesis/> [Accessed 1 May 2022].
37. Gibson PG, Henry RL, Shah S, Powell H, Wang H. Migration to a western country increases asthma symptoms but not eosinophilic airway inflammation. Pediatric pulmonology. 2003 Sep;36(3):209-15.
38. Thavagnanam S, Fleming J, Bromley A, Shields MD, Cardwell CR. A meta- analysis of the association between Caesarean section and childhood asthma. Clinical & Experimental Allergy. 2008 Apr;38(4):629-33.

39. Zock JP, Plana E, Jarvis D, Antó JM, Kromhout H, Kennedy SM, Künzli N, Villani S, Olivieri M, Torén K, Radon K. The use of household cleaning sprays and adult asthma: an international longitudinal study. American journal of respiratory and critical care medicine. 2007 Oct 15;176(8):735-41.
40. Hamid Q, Tulic M. Immunobiology of asthma. Annual review of physiology. 2009 Mar 17;71:489-507.
41. Bloomfield SF, Stanwell- Smith R, Crevel RW, Pickup J. Too clean, or not too clean: the hygiene hypothesis and home hygiene. Clinical & Experimental Allergy. 2006 Apr;36(4):402-25.
42. Matricardi PM, Rosmini F, Riondino S, Fortini M, Ferrigno L, Rapicetta M, Bonini S. Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study. Bmj. 2000 Feb 12;320(7232):412-7.
43. Masters ST, Barrett-Connor EL. Parasites and asthma--predictive or protective?. Epidemiologic reviews. 1985 Jan 1;7:49-58.
44. Sheikh A, Strachan DP. The hygiene theory: fact or fiction?. Current opinion in otolaryngology & head and neck surgery. 2004 Jun 1;12(3):232-6.
45. Chandrika D. Allergic rhinitis in India: an overview. International Journal of Otorhinolaryngology and Head and Neck Surgery. 2017;**3**(1):1–6.
46. Shah A, Pawankar R. Allergic rhinitis and co-morbid asthma: perspective from India-ARIA Asia-Pacific Workshop report. Asian pacific journal of allergy and immunology. 2009 Mar 1;27(1):71.
47. Saha GK. House dust mite allergy in Calcutta, India: evaluation by RAST. Annals of allergy. 1993 Apr 1;70(4):305-9.

48. Mahesh PA, Kummeling I, Amrutha DH, Vedanthan PK. Effect of area of residence on patterns of aeroallergen sensitization in atopic patients. American Journal of Rhinology & Allergy. 2010 Sep;24(5):e98-103.

49. Doshi A, Tripathi DM. Early house dust mite sensitivity in Mumbai children. The Indian Journal of Pediatrics. 2016 May;83(5):386-90.

50. Dey D, Mondal P, Laha A, Sarkar T, Moitra S, Bhattacharyya S, Saha GK, Podder S. Sensitization to common aeroallergens in the atopic population of West Bengal, India: an investigation by skin prick test. International archives of allergy and immunology. 2019;178(1):60-5.

51. Raj D, Lodha R, Pandey A, Mukherjee A, Agrawal A, Kabra SK. Aeroallergen sensitization in childhood asthmatics in northern India. Indian pediatrics. 2013 Dec;50(12):1113-8.

52. Singh AB, Mathur C. An aerobiological perspective in allergy and asthma. Asia Pacific Allergy. 2012 Jul 1;2(3):210-22.

53. Salvi S, Kumar GA, Dhaliwal RS, Paulson K, Agrawal A, Koul PA, Mahesh PA, Nair S, Singh V, Aggarwal AN, Christopher DJ. The burden of chronic respiratory diseases and their heterogeneity across the states of India: the Global Burden of Disease Study 1990–2016. The Lancet Global Health. 2018 Dec 1;6(12):e1363-74.

54. Kumar P, Ram U. Patterns, factors associated and morbidity burden of asthma in India. PloS one. 2017 Oct 26;12(10):e0185938..

55. Hassenbach M, Albus M. 23. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Lancet 1998; 351: 1225-32. 24. Kruse S, Japha T, Tedner M, Sparholt SH, Forster J, Kuehr J, et al. The. Lancet. 1998;351:1225-32.

56. Lai CK, Beasley R, Crane J, Foliaki S, Shah J, Weiland S. International Study of Asthma and Allergies in Childhood Phase Three Study Group. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax. 2009 Jun;64(6):476-83.
57. Paramesh H. Epidemiology of asthma in India. The Indian Journal of Pediatrics. 2002 Apr;69(4):309-12.
58. Aggarwal AN, Chaudhry K, Chhabra SK, D Souza GA, Gupta D, Jindal SK, Katiyar SK, Kumar R, Shah B, Vijayan VK. Prevalence and risk factors for bronchial asthma in Indian adults: a multicentre study. Indian Journal of Chest Diseases and Allied Sciences. 2006 Jan 18;48(1):13.
59. Agarwal R, Nath A, Aggarwal AN, Gupta D, Chakrabarti A. Aspergillus hypersensitivity and allergic bronchopulmonary aspergillosis in patients with acute severe asthma in a respiratory intensive care unit in North India. Mycoses. 2010 Mar;53(2):138-43.
60. Gupta A, Singh M, Chakrabarti A, Mathew JL, Rawat A. Correlation between fungal sensitisation in childhood persistent asthma and disease severity. Mycoses. 2018 Mar;61(3):195-200.
61. Janeway C, Travers P, Walport M, Shlomchik M. Immunobiology. Garland Science. New York. 2004.
62. Grimbaldeston MA, Metz M, Yu M, Tsai M, Galli SJ. Effector and potential immunoregulatory roles of mast cells in IgE-associated acquired immune responses. Current opinion in immunology. 2006 Dec 1;18(6):751-60.
63. Holt PG, Sly PD. Th2 cytokines in the asthma late-phase response. The Lancet. 2007 Oct 20;370(9596):1396-8.

64. Taher YA. Allergen specific immunotherapy: The future cure for allergic asthma. Mechanisms and improvement in a mouse model (Doctoral dissertation, Utrecht University).

65. Bentley AM, Jacobson MR, Cumberworth V, Barkans JR, Moqbel R, Schwartz LB, Irani AM, Kay AB, Durham SR. Immunohistology of the nasal mucosa in seasonal allergic rhinitis: increases in activated eosinophils and epithelial mast cells. Journal of allergy and clinical immunology. 1992 Apr 1;89(4):877-83.

66. Ying S, Durham SR, Corrigan CJ, Hamid Q, Kay AB. Phenotype of cells expressing mRNA for TH2-type (interleukin 4 and interleukin 5) and TH1-type (interleukin 2 and interferon gamma) cytokines in bronchoalveolar lavage and bronchial biopsies from atopic asthmatic and normal control subjects. American journal of respiratory cell and molecular biology. 1995 May;12(5):477-87.

67. Mukai K, Tsai M, Saito H, Galli SJ. Mast cells as sources of cytokines, chemokines, and growth factors. Immunological reviews. 2018 Mar;282(1):121-50.

68. Cai Y, Bjermer L, Halstensen TS. Bronchial mast cells are the dominating LTC4S-expressing cells in aspirin-tolerant asthma. American journal of respiratory cell and molecular biology. 2003 Dec;29(6):683-93.

69. Nasser SM, Pulimood TB. Allergens and thunderstorm asthma. Current allergy and asthma reports. 2009 Sep;9(5):384-90.

70. Green RM, Custovic A, Sanderson G, Hunter J, Johnston SL, Woodcock A. Synergism between allergens and viruses and risk of hospital admission with asthma: case-control study. Bmj. 2002 Mar 30;324(7340):763.

71. Calhoun WJ, Dick EC, Schwartz LB, Busse WW. A common cold virus, rhinovirus 16, potentiates airway inflammation after segmental antigen bronchoprovocation in allergic subjects. The Journal of clinical investigation. 1994 Dec 1;94(6):2200-8.

72. Dakhama A, Park JW, Taube C, Chayama K, Balhorn A, Joetham A, Wei XD, Fan RH, Swasey C, Miyahara N, Kodama T. The role of virus-specific immunoglobulin E in airway hyperresponsiveness. American journal of respiratory and critical care medicine. 2004 Nov 1;170(9):952-9.

73. Méndez-Enríquez E, Hallgren J. Mast cells and their progenitors in allergic asthma. Frontiers in immunology. 2019 May 29;10:821.

74. Begueret H, Berger P, Vernejoux JM, Dubuisson L, Marthan R, Tunon-de-Lara JM. Inflammation of bronchial smooth muscle in allergic asthma. Thorax. 2007 Jan 1;62(1):8-15.

75. Casale TB, Wood D, Richerson HB, Zehr B, Zavala D, Hunninghake GW. Direct evidence of a role for mast cells in the pathogenesis of antigen-induced bronchoconstriction. The Journal of clinical investigation. 1987 Nov 1;80(5):1507-11.

76. Ying S, Humbert M, Barkans J, Corrigan CJ, Pfister R, Menz G, Larché M, Robinson DS, Durham SR, Kay AB. Expression of IL-4 and IL-5 mRNA and protein product by CD4+ and CD8+ T cells, eosinophils, and mast cells in bronchial biopsies obtained from atopic and nonatopic (intrinsic) asthmatics. The Journal of Immunology. 1997 Apr 1;158(7):3539-44.

77. Flint KC, Leung KB, Hudspith BN, Brostoff J, Pearce FL, Johnson NM. Bronchoalveolar mast cells in extrinsic asthma: a mechanism for the initiation of antigen specific bronchoconstriction. Br Med J (Clin Res Ed). 1985 Oct 5;291(6500):923-6.

78. Broide DH, Gleich GJ, Cuomo AJ, Coburn DA, Federman EC, Schwarte LB, Wasserman SI. Evidence of ongoing mast cell and eosinophil degranulation in symptomatic asthma airway. Journal of Allergy and Clinical Immunology. 1991 Oct 1;88(4):637-48.

79. Bentley AM, Menz G, Storz CH, Robinson DS, Bradley B, Jeffery PK, Durham SR, Kay AB. Identification of T lymphocytes, macrophages, and activated eosinophils in the bronchial mucosa in intrinsic asthma. Am Rev Respir Dis. 1992;146(2):500.

80. Humbert M, Grant JA, Taborda-Barata L, et al. High-affinity IgE receptor (FcepsilonRI)-bearing cells in bronchial biopsies from atopic and nonatopic asthma. Am J Respir Crit Care Med 1996;153:1931–7.

81. Humbert M, Durham SR, Ying S, et al. IL-4 and IL-5 mRNA and protein in bronchial biopsies from patients with atopic and nonatopic asthma: evidence against "intrinsic" asthma being a distinct immunopathologic entity. Am J Respir Crit Care Med 1996;154:1497–504.

82. Del Prete G, Maggi E, Parronchi P, et al. IL-4 is an essential factor for the IgE synthesis induced in vitro by human T cell clones and their supernatants. J Immunol 1988;140:4193–8.

83. Galli SJ, Gordon JR, Wershil BK. Cytokine production by mast cells and basophils. Current opinion in immunology. 1991 Dec 1;3(6):865-73.

84. Stone KD, Prussin C, Metcalfe DD. IgE, mast cells, basophils, and eosinophils. Journal of Allergy and Clinical Immunology. 2010 Feb 1;125(2):S73-80.

85. Sokol CL, Medzhitov R. Emerging functions of basophils in protective and allergic immune responses. Mucosal immunology. 2010 Mar;3(2):129-37.

86. Karasuyama H, Mukai K, Obata K, Tsujimura Y, Wada T. Nonredundant roles of basophils in immunity. Annual review of immunology. 2011 Apr 23;29:45-69.

87. Haenuki Y, Matsushita K, Futatsugi-Yumikura S, Ishii KJ, Kawagoe T, Imoto Y, Fujieda S, Yasuda M, Hisa Y, Akira S, Nakanishi K. A critical role of IL-33 in experimental allergic rhinitis. Journal of Allergy and clinical immunology. 2012 Jul 1;130(1):184-94.

88. Daeron M, Malbec O, Latour S, Arock M, Fridman WH. Regulation of high-affinity IgE receptor-mediated mast cell activation by murine low-affinity IgG receptors. The Journal of clinical investigation. 1995 Feb 1;95(2):577-85.

89. Miyahara S, Miyahara N, Takeda K, Joetham A, Gelfand EW. Physiologic assessment of allergic rhinitis in mice: Role of the high-affinity IgE receptor (FcεRI). Journal of allergy and clinical immunology. 2005 Nov 1;116(5):1020-7.

90. Miyahara S, Miyahara N, Lucas JJ, Joetham A, Matsubara S, Ohnishi H, Dakhama A, Gelfand EW. Contribution of allergen-specific and nonspecific nasal responses to early-phase and late-phase nasal responses. Journal of allergy and clinical immunology. 2008 Mar 1;121(3):718-24.

91. Sawaguchi M, Tanaka S, Nakatani Y, Harada Y, Mukai K, Matsunaga Y, Ishiwata K, Oboki K, Kambayashi T, Watanabe N, Karasuyama H. Role of mast cells and basophils in IgE responses and in allergic airway hyperresponsiveness. The Journal of Immunology. 2012 Feb 15;188(4):1809-18.

92. Wakahara K, Van VQ, Baba N, Bégin P, Rubio M, Delespesse G, Sarfati M. Basophils are recruited to inflamed lungs and exacerbate memory T h2 responses in mice and humans. Allergy. 2013 Feb;68(2):180-9.

93. Zhong W, Su W, Zhang Y, Liu Q, Wu J, Di C, Zhang Z, Xia Z. Basophils as a primary inducer of the T helper type 2 immunity in ovalbumin- induced allergic airway inflammation. Immunology. 2014 Jun;142(2):202-15.

94. Cheng LE, Sullivan BM, Retana LE, Allen CD, Liang HE, Locksley RM. IgE-activated basophils regulate eosinophil tissue entry by modulating endothelial function. Journal of Experimental Medicine. 2015 Apr 6;212(4):513-24.

95. Motomura Y, Morita H, Moro K, Nakae S, Artis D, Endo TA, Kuroki Y, Ohara O, Koyasu S, Kubo M. Basophil-derived interleukin-4 controls the function of natural

helper cells, a member of ILC2s, in lung inflammation. Immunity. 2014 May 15;40(5):758-71.

96. Nakashima C, Otsuka A, Kitoh A, Honda T, Egawa G, Nakajima S, Nakamizo S, Arita M, Kubo M, Miyachi Y, Kabashima K. Basophils regulate the recruitment of eosinophils in a murine model of irritant contact dermatitis. Journal of Allergy and Clinical Immunology. 2014 Jul 1;134(1):100-7.
97. Schroeder JT. Basophils: emerging roles in the pathogenesis of allergic disease. Immunological reviews. 2011 Jul;242(1):144-60.
98. Yuk CM, Park HJ, Kwon BI, Lah SJ, Chang J, Kim JY, Lee KM, Park SH, Hong S, Lee SH. Basophil-derived IL-6 regulates TH17 cell differentiation and CD4 T cell immunity. Scientific reports. 2017 Jan 30;7(1):1-4.
99. Raap U, Sumbayev VV, Gibbs BF. The role of basophils in allergic inflammation. Allergo Journal. 2015 Aug;24(5):28-33.
100. Miyake K, Karasuyama H. Emerging roles of basophils in allergic inflammation. Allergology International. 2017;66(3):382-91.
101. Stevens WW, Ocampo CJ, Berdnikovs S, et al. Cytokines in chronic rhinosinusitis. Role in eosinophilia and aspirin-exacerbated respiratory disease. Am J Respir Crit Care Med 2015;192:682–94.
102. Schleimer RP. Immunopathogenesis of chronic rhinosinusitis and nasal polyposis. Annu Rev Pathol 2017;12:331–57.
103. Wechsler ME, Fulkerson PC, Bochner BS, et al. Novel targeted therapies for eosinophilic disorders. J Allergy Clin Immunol 2012;130:563–71.
104. O'Sullivan JA, Bochner BS. Eosinophils and eosinophil-associated diseases: an update. J Allergy Clin Immunol 2018;141:505–17.

105. Burks AW, Holgate ST, O'Hehir RE, Bacharier LB, Broide DH, Hershey GK, Peebles RS, editors. Middleton's allergy E-Book: principles and practice. Elsevier Health Sciences; 2019 Sep 25.

106. Laurent J, Noirot C, Ansquer JC, Laurent G, Kestenbaum S, Lagrue G. How to define the normal level of serum IgE in adults?. InAnnales de medecine interne 1985 Jan 1 (Vol. 136, No. 5, pp. 419-422).

107. Sandeep T, Roopakala MS, Silvia CR, Chandrashekara S, Rao M. Evaluation of serum immunoglobulin E levels in bronchial asthma. Lung India: official organ of Indian Chest Society. 2010 Jul;27(3):138.

108. Awan NU, Sohail SK, Naumeri F, Niazi S, Cheema K, Qamar S, Rizvi SF. Association of serum Vitamin D and immunoglobulin E levels with severity of allergic rhinitis. Cureus. 2021 Jan 25;13(1).

109. Xu-De Z, Bei-Bei G, Xi-Juan W, Hai-Bo L, Li-Li Z, Feng-Xia L. Serum IgE Predicts Difference of Population and Allergens in Allergic Diseases: Data from Weifang City, China. Mediators of Inflammation. 2021 Jun 25;2021.

110. Huang Y, Wang C, Cao F, Zhao Y, Lou H, Zhang L. Comparison of long-term efficacy of subcutaneous immunotherapy in pediatric and adult patients with allergic rhinitis. Allergy, asthma & immunology research. 2019 Jan 1;11(1):68-78.

111. Chandrika D. Allergic rhinitis in India: an overview. Int J Otorhinolaryngol Head Neck Surg. 2017 Jan;3(1):1-6.

112. Jaggi V, Dalal A, Ramesh BR, Tikkiwal S, Chaudhry A, Kothari N, Lopez M, Gogtay J. Coexistence of allergic rhinitis and asthma in Indian patients: The CARAS survey. Lung India: Official Organ of Indian Chest Society. 2019 Sep;36(5):411.

113. Seidman MD, Gurgel RK, Lin SY, Schwartz SR, Baroody FM, Bonner JR, Dawson DE, Dykewicz MS, Hackell JM, Han JK, Ishman SL. Clinical practice guideline: allergic rhinitis. Otolaryngology–Head and Neck Surgery. 2015 Feb;152(1_suppl):S1-43.

114. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy. 2008;63(suppl 86):8-160.

115. Wallace DV, Dykewicz MS. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008;122:S1-S84

116. Colgan R. Advice to the young physician: on the art of medicine. New York: Springer; 2009 Sep 19.

117. Hurwitz SH. The lure of medical history: JOHN BOSTOCK (1773-1846): Author of the first clinical description of hay fever. California and Western Medicine. 1929 Aug;31(2):137.

118. Hall M. Lectures on the theory and practice of medicine;: now in course of delivery at the thratre of anatomy and medicine, webb-street, southwark. The Lancet. 1838 May 19;30(768):241-7.

119. Varshney J, Varshney H. Allergic rhinitis: an overview. Indian J. Otolaryngol Head Neck Surg. 67(2):143-149(2015).

120. "Allergy Friendly Trees". Forestry.about.com. March 5, 2014. Archived from the original on April 14, 2014. Retrieved April 25, 2014.

121. Kamekura R, Kojima T, Takano K, Go M, Sawada N, Himi T (2012). "The Role of IL-33 and Its Receptor ST2 in Human Nasal Epithelium with Allergic Rhinitis". Clin Exp Allergy. 42 (2): 218–228.

122. Zhang XH, Zhang YN, Liu Z (2014). "MicroRNA in Chronic Rhinosinusitis and Allergic Rhinitis". Curr Allergy Asthma Rep. 14 (2): 415.

123. Baumann R, Rabaszowski M, Stenin I, Tilgner L, Gaertner-Akerboom M, Scheckenbach K, Wiltfang J, Chaker A, Schipper J, Wagenmann M (2013). "Nasal Levels of Soluble IL-33R ST2 and IL-16 in Allergic Rhinitis: Inverse Correlation Trends with Disease Severity". Clin Exp Allergy. 43 (10): 1134–1143.

124. Ran H, Xiao H, Zhou X, Guo L, Lu S. Single-nucleotide polymorphisms and haplotypes in the interleukin-33 gene are associated with a risk of allergic rhinitis in the Chinese population. Experimental and therapeutic medicine. 2020 Nov 1;20(5):1-.

125. Song SH, Wang XQ, Shen Y, Hong SL, Ke, X. "Association between PTPN22/CTLA-4 Gene Polymorphism and Allergic Rhinitis with Asthma in Children". Iranian Journal of Allergy, Asthma and Immunology: 413–419.

126. Suojalehto H, Toskala E, Kilpeläinen M, Majuri ML, Mitts C, Lindström I, Puustinen A, Plosila T, Sipilä J, Wolff H, Alenius H (2013). "MicroRNA Profiles in Nasal Mucosa of Patients with Allergic and Nonallergic Rhinitis and Asthma". International Forum of Allergy and Rhinology. 3 (8): 612–620.

127. Sastre B, Cañas JA, Rodrigo-Muñoz JM, Del Pozo V. Novel modulators of asthma and allergy: exosomes and microRNAs. Frontiers in immunology. 2017 Jul 21;8:826.

128. Xiao L, Jiang L, Hu Q, Li Y. "MicroRNA-133b Ameliorates Allergic Inflammation and Symptom in Murine Model of Allergic Rhinitis by Targeting NIrp3". CPB. 42 (3): 901–912.

129. Scadding GK, Kariyawasam HH, Scadding G, Mirakian R, Buckley RJ, Dixon T, Durham SR, Farooque S, Jones N, Leech S, Nasser SM. BSACI guideline for the diagnosis and management of allergic and non- allergic rhinitis (Revised Edition 2017; 2007). Clinical & Experimental Allergy. 2017 Jul;47(7):856-89.

130. Bernstein IL, Li JT, Bernstein DI, Hamilton R, Spector SL, Tan R, Sicherer S, Golden DB, Khan DA, Nicklas RA, Portnoy JM. Allergy diagnostic testing: an updated practice parameter. Annals of allergy, asthma & immunology. 2008 Mar 1;100(3):S1-48.

131. Anon JB. Introduction to in vivo allergy testing. Otolaryngology--head and Neck Surgery: Official Journal of American Academy of Otolaryngology-head and Neck Surgery. 1993 Sep 1;109(3 Pt 2):593-600.

132. Kim BJ, Mun SK. Objective measurements using the skin prick test in allergic rhinitis. Archives of Otolaryngology–Head & Neck Surgery. 2010 Nov 15;136(11):1104-6.

133. Oppenheimer J, Nelson HS. Skin testing: a survey of allergists. Ann Allergy Asthma Immunol. 2006;96(1):19-23.

134. Bousquet J, Heinzerling L, Bachert C, Papadopoulos NG, Bousquet PJ, Burney PG, Canonica GW, Carlsen KH, Cox L, Haahtela T, Lodrup Carlsen KC. Practical guide to skin prick tests in allergy to aeroallergens. Allergy. 2012 Jan;67(1):18-24.

135. Ménardo JL, Bousquet J, Rodière M, Astruc J, Michel FB. Skin test reactivity in infancy. Journal of allergy and clinical immunology. 1985 Jun 1;75(6):646-51.

136. Scichilone N, Callari A, Augugliaro G, Marchese M, Togias A, Bellia V. The impact of age on prevalence of positive skin prick tests and specific IgE tests. Respiratory medicine. 2011 May 1;105(5):651-8.

137. Fornadley JA, Corey JP, Osguthorpe JD, Powell JP, Emanuel IA, Boyles JH, Watson TA, Hurst DS, Bryant JL, Pershall KE, Renfro BL. Allergic rhinitis: clinical practice guideline. Otolaryngology–Head and Neck Surgery. 1996 Jul;115(1):115-22.

138. Krouse JH, Mabry RL. Skin testing for inhalant allergy 2003: current strategies. Otolaryngology--Head and Neck Surgery. 2003 Oct;129(4_suppl):S33-49.

139. Sicherer SH, Wood RA. Allergy testing in childhood: using allergen-specific IgE tests. Pediatrics. 2012;129(1):193-197.

140. Shah KM, Rank MA, Davé SA, et al. Predicting which medication classes interfere with allergy skin testing. Allergy Asthma Proc. 2010;31(6):477-482.

141. Chafen JJ, Newberry SJ, Riedl MA, et al. Diagnosing and managing common food allergies: a systematic review. JAMA. 2010;303(18):1848-1856.

142. Tschopp J, Sistek D, Schindler C, et al. Current allergic asthma and rhinitis: diagnostic efficiency of three commonly used atopic markers (IgE, skin prick tests, and Phadiatop). Results from 8329 randomized adults from the SAPALDIA Study. Swiss Study on Air Pollution and Lung Diseases in Adults. Allergy. 1998;53(6):608-613.

143. Ahmadiafshar A, Taghiloo D, Esmailzadeh A, et al. Nasal eosinophilia as a marker for allergic rhinitis: a controlled study of 50 patients. Ear Nose Throat J. 2012;91(3):122-124.

144. Ciprandi G, Vizzaccaro A, Cirillo I, et al. Nasal eosinophils display the best correlation with symptoms, pulmonary function and inflammation in allergic rhinitis. Int Arch Allergy Immunol. 2005;136(3):266-272.

145. Romero JN, Scadding G. Eosinophilia in nasal secretions compared to skin prick test and nasal challenge test in the diagnosis of nasal allergy. Rhinology. 1992;30(3):169-175.

146. American College of Radiology. ACR statement on recent studies regarding CT scans and increased cancer risk.

147. Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours. Lancet. 2012;380(9840):499-505.

148. Katayama H, Yamaguchi K, Kozuka T, et al. Adverse reactions to ionic and nonionic contrast media. Radiology. 1990;175:621- 628.

149. Wise SK, Lin SY, Toskala E, Orlandi RR, Akdis CA, Alt JA, Azar A, Baroody FM, Bachert C, Canonica GW, Chacko T. International consensus statement on allergy and

rhinology: allergic rhinitis. International forum of allergy & rhinology 2018 Feb (Vol. 8, No. 2, pp. 108-352).

150. Larenas-Linnemann D, Mayorga-Butrón JL, Sánchez-González A, Ramírez-García A, Medina-Ávalos M, Figueroa-Morales MA, Montaño-Velázquez B, Montes-Narváez G, Romero-Tapia S, Stone-Aguilar H, Xochihua-Díaz L. ARIA México 2014 adaptación de la guía de práctica clínica ARIA 2010 para México. Metodología ADAPTE. Revista Alergia México. 2014;61(1):S3-116.

151. Roberts G, Xatzipsalti M, Borrego LM, Custovic A, Halken S, Hellings PW, Papadopoulos NG, Rotiroti G, Scadding G, Timmermans F, Valovirta E. Paediatric rhinitis: position paper of the E uropean A cademy of Allergy and C linical I mmunology. Allergy. 2013 Sep;68(9):1102-16.

152. Brozek JL, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, van Wijk RG, Ohta K, Zuberbier T, Schuenemann HJ. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy clin immunol. 2010 Sep 1;126(3):466-76.

153. Wallace DV, Dykewicz MS, Bernstein DI, Blessing-Moore J, Cox L, Khan DA, Lang DM, Nicklas RA, Oppenheimer J, Portnoy JM, Randolph CC. The diagnosis and management of rhinitis: an updated practice parameter. Journal of allergy and clinical immunology. 2008 Aug 1;122(2):S1-84.

154. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, Brignardello-Petersen R, Canonica GW, Casale T, Chavannes NH, de Sousa JC. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines—2016 revision. Journal of Allergy and Clinical Immunology. 2017 Oct 1;140(4):950-8.

155. Dykewicz MS, Wallace DV, Baroody F, Bernstein J, Craig T, Finegold I, Huang F, Larenas-Linnemann D, Meltzer E, Steven G, Bernstein DI. Treatment of seasonal

allergic rhinitis: an evidence-based focused 2017 guideline update. Annals of Allergy, Asthma & Immunology. 2017 Dec 1;119(6):489-511.

156. Carr WW, Ratner P, Munzel U, Murray R, Price D, Canonica GW, Mullol J, Virchow JC, Lieberman P, Meltzer E, Bachert C. Comparison of intranasal azelastine to intranasal fluticasone propionate for symptom control in moderate-to-severe seasonal allergic rhinitis. InAllergy & Asthma Proceedings 2012 Nov 1 (Vol. 33, No. 6).
157. Hampel FC, Ratner PH, Van Bavel J, Amar NJ, Daftary P, Wheeler W, Sacks H. Double-blind, placebo-controlled study of azelastine and fluticasone in a single nasal spray delivery device. Annals of Allergy, Asthma & Immunology. 2010 Aug 1;105(2):168-73.
158. Meltzer EO. Pharmacotherapeutic strategies for allergic rhinitis: matching treatment to symptoms, disease progression, and associated conditions. InAllergy & Asthma Proceedings 2013 Jul 1 (Vol. 34, No. 4).
159. Church MK, Maurer M, Simons FE, Bindslev- Jensen C, Van Cauwenberge P, Bousquet J, Holgate ST, Zuberbier T. Risk of first- generation H1- antihistamines: a GA2LEN position paper. Allergy. 2010 Apr;65(4):459-66.
160. Noon L. Prophylactic inoculation against hay fever. The Lancet. 1911 Jun 10;177(4580):1572-3.
161. Freeman J. Further observations on the treatment of hay fever by hypodermic inoculations of pollen vaccine. The Lancet. 1911 Sep 16;178(4594):814-7.
162. Bostock J. Case of a periodical affection of the eyes and chest. Medico-chirurgical transactions. 1819;10(Pt 1):161.
163. Frew AJ. Allergen immunotherapy. Journal of Allergy and Clinical Immunology. 2010 Feb 1;125(2):S306-13.

164. Van Cauwenberge P. Consensus statement on the treatment of allergic rhinitis (European Academy of Allergology and Clinical Immunology). Clinical Otolaryngology & Allied Sciences. 2001 Aug;26(4):340-1.

165. “Allergy Shots (Immunotherapy) | AAAAI.” The American Academy of Allergy, Asthma & Immunology, 2019

166. Caminati M, Dama AR, Djuric I, Montagni M, Schiappoli M, Ridolo E, Senna G, Canonica GW (February 2015). "Incidence and risk factors for subcutaneous immunotherapy anaphylaxis: the optimization of safety". Expert Review of Clinical Immunology. **11** (2): 233–45.

167. Pepper, Amber N.; Calderón, Moisés A.; Casale, Thomas B. (January 2017). "Sublingual Immunotherapy for the Polyallergic Patient". The Journal of Allergy and Clinical Immunology: In Practice. **5** (1): 41–45. doi:10.1016/j.jaip.2016.06.019. ISSN 2213-2198. PMID 27452888.

168. Canonica GW, Cox L, Pawankar R, Baena-Cagnani CE, Blaiss M, Bonini S, Bousquet J, Calderón M, Compalati E, Durham SR, van Wijk RG. Sublingual immunotherapy: World Allergy Organization position paper 2013 update. World Allergy Organization Journal. 2014 Jan 1;7:6.Couzin-Frankel, Jennifer (September 13, 2019). "First peanut allergy treatment gains backing from FDA advisory panel". Science. doi:10.1126/science.aaz5008.

169. Reddel HK, Bacharier LB, Bateman ED, et al. Global Initiative for Asthma (GINA) Strategy 2021 - Executive summary and rationale for key changes. Eur Respir J 2021; in press (https://doi.org/10.1183/13993003.02730-2021).

170. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2022. Available from: www.ginasthma.org.

171. Chogtu B, Magaji N, Magazine R, Acharya PR. Pattern of allergen sensitivity among patients with bronchial asthma and/or allergic rhinosinusitis in a tertiary care centre of southern India. Journal of Clinical and Diagnostic Research: JCDR. 2017 Aug;11(8):OC01.

172. Arbat A, Tirpude S, Dave MK, Bagdia S, Arbat S. Purview of allergens through skin test in Central India. Environmental Disease. 2016 Jul 1;1(3):99.

173. Katoch CD, Kumar K, Marwah V, Bhatti G. Pattern of skin sensitivity to various aeroallergens by skin prick test in patients of allergic airway disease in South Western Maharashtra. Medical Journal Armed Forces India. 2020 Aug 14.

174. Farrokhi S, Gheybi MK, Movahed A, Tahmasebi R, Iranpour D, Fatemi A, Etemadan R, Gooya M, Zandi S, Ashourinejad H, Alavizadeh S. Common aeroallergens in patients with asthma and allergic rhinitis living in southwestern part of Iran: based on skin prick test reactivity. Iranian Journal of Allergy, Asthma and Immunology. 2015:133-8.

175. Moghtaderi M, Hejrati Z, Kolahi N, Heidari B. Sensitization to aeroallergens in patients with allergic rhinitis, asthma, and atopic dermatitis in Shiraz, Southwestern Iran. Indian Journal of Allergy, Asthma and Immunology. 2015 Jul 1;29(2):79.

176. Sharma RK, Mathur Y, Chhabra G, Luhadia A, Luhadia SK, Dhandoria G. A study of skin sensitivity to various allergens by skin prick test in patients of bronchial asthma and allergic rhinitis. Indian Journal of Allergy, Asthma and Immunology. 2018 Jul 1;32(2):47.

177. Kumar V, Rai DK, Shekhar H. Allergic sensitization in nasobronchial allergy patients and its correlation with total immunoglobulin E level. Indian Journal of Allergy, Asthma and Immunology. 2020 Jul 1;34(2):63.

178. Singh D, Dubey W, Singh UV. Prevalence of airborne pollen in the atmosphere of the city of Jaipur in 2011.

179. Assarehzadegan MA, Shakurnia AH, Amini A. Sensitization to common aeroallergens among asthmatic patients in a tropical region affected by dust storm. J Med Sci. 2013 Oct 1;13(7):592-7.

180. Hersoug LG, Linneberg A. The link between the epidemics of obesity and allergic diseases: does obesity induce decreased immune tolerance?. Allergy. 2007 Oct;62(10):1205-13.

181. Bist SS, Bhagat S, Kala H. A Clinical Study of Relationship of Body Mass Index with Allergic Rhinitis. An International Journal Clinical Rhinology. 2016 Apr 1;9(1):33-6.

182. Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: Systematic review and meta-analysis. J Allergy Clin Immunol 2011;127:724-33.e1-30.

183. de Batlle J, Garcia-Aymerich J, Barraza-Villarreal A, Antó JM, Romieu I. Mediterranean diet is associated with reduced asthma and rhinitis in Mexican children. Allergy 2008;63:1310-6.

184. Nagel G, Weinmayr G, Kleiner A, Garcia-Marcos L, Strachan DP; ISAAC Phase Two Study Group. Effect of diet on asthma and allergic sensitisation in the International Study on Allergies and Asthma in Childhood (ISAAC) phase two.Thorax.2010;65:516-22.

185. Arvaniti F, Priftis KN, Papadimitriou A, Papadopoulos M, Roma E, Kapsokefalou M, et al. Adherence to the Mediterranean type of diet is associated with lower prevalence of asthma symptoms, among 10-12 years old children: The PANACEA study. Pediatr Allergy Immunol 2011;22:283-9.

186. Agrawal S, Pearce N, Ebrahim S. Prevalence and risk factors for self-reported asthma in an adult Indian population: A cross-sectional survey. Int J Tuberc Lung Dis2013;17:275-82.

187. Katel P, Pinkaew B, Talek K, Tantilipikorn P. Pattern of Aeroallergen Sensitization and Quality of Life in Adult Thai Patients With Allergic Rhinitis. Frontiers in Allergy. 2021;2.

188. Kerkhof M, Postma DS, Schouten JP, De Monchy JG. Allergic sensitization to indoor and outdoor allergens and relevance to bronchial hyperresponsiveness in younger and older subjects. Allergy. 2003 Dec;58(12):1261-7.

189. Dreborg S. Diagnosis of food allergy: tests in vivo and in vitro. Pediatr Allergy Immunol. 2001;12(suppl 14):24e30.

190. Tham EH, Lee AJ, Bever HV. Aeroallergen sensitization and allergic disease phenotypes in Asia. Asian Pac J Allergy Immunol. 2016 Sep;34(3):181e189.

191. Shyna KP, Veena Kumari M, Divya Krishnan K, Abdul Azeez VK. Clinical profile and skin prick test analysis in children with allergic rhinitis of North Kerala, India. Int J Comtemp Pediatr. 2018. https://doi.org/10.18203/2349- 3291.ijcp20180436.

192. Prasad R, Verma SK, Dua R, Kant S, Kushwaha RA, Agarwal SP. A study of skin sensitivity to various allergens by skin prick test in patients of nasobronchial allergy. Lung India: official organ of Indian Chest Society. 2009 Jul;26(3):70.

193. Kumar R, Kumar M, Bisht I, Singh K. Prevalence of aeroallergens in patients of bronchial asthma and/or allergic rhinitis in India based on skin prick test reactivity. Indian Journal of Allergy, Asthma and Immunology. 2017 Jul 1;31(2):45.

194. Jain S, Gupta SK. Study of allergen patterns in patients of severe persistent allergic rhinitis in Central India based on Modified Skin Prick Test reactivity. IOSR J Dent Med Sci (IOSR-JDMS). 2018;17:16-20.

195. Shikha G, Swami H. Trends of sensitization pattern to aeroallergens among the patients with allergic rhinitis and/or bronchial asthma in Bangalore: A cross sectional study. Medical Journal Armed Forces India. 2022 Oct 1;78(4):430-6.

196. Stanaland BE, Fernández-Caldas E, Jacinto CM, Trudeau WL, Lockey RF. Sensitization to Blomia tropicalis: skin test and cross-reactivity studies. Journal of allergy and clinical immunology. 1994 Sep 1;94(3):452-7.

197. Podder S, Gupta SK, Saha GK. Incrimination of Blomia tropicalis as a potent allergen in house dust and its role in allergic asthma in Kolkata Metropolis, India. World Allergy Organization Journal. 2010 Jan 1;3(5):182-7.

198. Aydin S, Hardal U, Atli H. An analysis of skin prick test reactions in allergic rhinitis patients in Istanbul, Turkey. Asian Pacific journal of allergy and immunology. 2009 Mar 1;27(1):19.

199. Ferrandiz R, Casas R, Dreborg S. Sensitization to Dermatophagoides siboney, Blomia tropicalis, and other domestic mites in asthmatic patients. Allergy. 1996 Jul;51(7):501-5.

200. Dust mite allergens and asthma: A worldwide problem. International Workshop report. Bull World Health Organ 1988;66:769-80.

201. Liu X, Zheng P, Cai C, Wei N, Huang Z, Zou X, Sun B. The sensitization pattern of Blomia tropicalis in allergic respiratory disease in Guangzhou. The Journal of Practical Medicine. 2018:1720-4.

202. Jerath VP, Sood M, Nishchal R. Prevalance of skin reactivity to fungal antigens in patients of nasobronchial allergy of Jalandhar and neighbouring area in Punjab. Indian Journal of Allergy, Asthma and Immunology. 2012 Jul 1;26(2):73.

203. Karmakar S, Raza K, Prasad R. A study of skin prick test sensitivity to common allergens in patients of nasobronchial allergy. Indian Journal of Allergy, Asthma and Immunology. 2019 Jul 1;33(2):91.

204. Verma KS, Shrivastava P, Dey M. Skin prick test to common air borne fungi on poultry workers. Indian J Allergy Asthma Immunol. 2011;25(2):79-83.

205. Gowda G, Lakshmi S, Parasuramalu BG, Nagaraj C, Gowda BV, Somashekara KG. A study on allergen sensitivity in patients with allergic rhinitis in Bangalore, India. The Journal of Laryngology & Otology. 2014 Oct;128(10):892-6.

206. Kumar M, Gupta RK, Spalgais S, Kumar R. Sensitivity to common aeroallergens in asthma patients in Delhi-National Capital Region. Indian Journal of Allergy, Asthma and Immunology. 2020 Jul 1;34(2):68.

207. Kunoor AK, Harilakshmanan P, James PT, Rakesh PS. Allergen profile of patients from Central Kerala, India. Int J Pharm Bio Sci. 2017;8(1):588-92.

208. Agrawal RL, Chandra A, Jain S, Agrawal G Snehlata. Identification of common allergens by skin prick test associated with united airway disease in Allahabad, Uttar Pradesh, India. Indian J Allergy Asthma Immunol. 2008;22(1):7–13.

209. Patel A, Choudhary S. Prevalence of allergen sensitivity in nasobronchial allergy in Gujarat, India. National Journal of Medical Research. 2012 Dec 31;2(04):431-4.

210. Moghtaderi M, Farjadian S, Reihani I. Sensitization to plant food allergens in patients with asthma. Indian Journal of Allergy, Asthma and Immunology. 2015 Jan 1;29(1):24.

211. Kathuria PC, Rai M. Diagnostic accuracy of skin prick test and specific IgE and their association with Total IgE, AEC and serum cortisol in Indian patients with respiratory allergy. Global Journal of Allergy. 2021 Aug 16;7(1):001-6.

212. Tegnoor MS, Jabri OB, Kumar MV, Kurle V. Assessment of serum IgE levels in patients of allergic rhinitis. Al Ameen J Med Sci. 2017;10(2):136-40.

213. Baldacci S, Omenaas E, Oryszczyn MP. Allergy markers in respiratory epidemiology. European Respiratory Journal. 2001 Apr 1;17(4):773-90.

214. Kim HS, Kang SH, Won S, Lee EK, Chun YH, Yoon JS, Kim HH, Kim JT. Immunoglobulin E to allergen components of house dust mite in Korean children with allergic disease. Asia Pacific Allergy. 2015 Jul 1;5(3):156-62.

215. Salama LA, Mahfouz TA, Sileem AE, Said MW. Skin Prick Test Results and Total IgE Levels of Asthma Patients in Zagazig University Hospital (2015-2019). The Egyptian Journal of Hospital Medicine. 2022 Jan 1;86(1):707-13.

216. Muddaiah D, Venkatarangaiah S. A Study on Total Serum IgE Levels and Absolute Eosinophil Count in Allergic Rhinitis Patients. Journal of Evolution of Medical and Dental Sciences. 2020 Jan 13;9(2):76-81.

217. Brakhas SA, Hassan AJ, Jassim AN. Study of total Immunoglobulin E and Eosinophil count in allergic disease. Baghdad Science Journal. 2016;13(2).

218. Chen Y, Yang M, Deng J, Wang K, Shi J, Sun Y. Elevated levels of activated and pathogenic eosinophils characterize moderate-severe house dust mite allergic rhinitis. Journal of immunology research. 2020 Aug 13;2020.

219. Altaii HA, Al-Tae FM. Investigation of serum total IgE and eosinophil levels in different allergic diseases together with the study of their correlations with various possible allergens in Mosul City. Immunological Investigations. 2022 Apr 3;51(3):567-87.

220. Sacco O, Sale R, Silvestri M, Serpero L, Sabatini F, Raynal ME, Biraghi M, Rossi GA. Total and allergen- specific IgE levels in serum reflect blood eosinophilia and fractional exhaled nitric oxide concentrations but not pulmonary functions in allergic asthmatic children sensitized to house dust mites. Pediatric allergy and immunology. 2003 Dec;14(6):475-81.

221. Min HJ, Hong YH, Yang HS, Kim KS. The correlation of serum eosinophil cationic protein level with eosinophil count, and total IgE level in Korean adult allergic rhinitis patients. Asian Pac J Allergy Immunol. 2016 Dec 1;34:290-4.

222. Baldacci S, Modena P, Carrozzi L, Pedreschi M, Vellutini M, Biavati P, Simoni M, Sapigni T, Viegi G, Paoletti P, Giuntini C. Skin prick test reactivity to common

aeroallergens in relation to total IgE, respiratory symptoms, and smoking in a general population sample of northern Italy. Allergy. 1996 Mar;51(3):149-56.

223. Gharagozlou M, Rastegari V, Movahed M, Moein M, Bemanian MH. Total serum IgE and skin tests in children with respiratory allergy.

ANNEXURE I

B.L.D.E. (DEEMED TO BE UNIVERSITY) IEC/NO-09/2021 Date-22/01/2021

(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)

The Constituent College

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: Allergen sensitivity pattern & its correlation with total serum 1gE levels & Eosinophil count among patients with allergic rhinitis and/or asthama in North Karanataka.

Name of PG student: Dr Pranavi, Department of Respiratory Medicine

Name of Guide/Co-investigator: Dr Ramesh.S.Babar, Professor & HOD of Respiratory Medicine

DR .S.V.PATIL
CHAIRMAN, IEC

Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

2

ANNEXURE II

INFORMED CONSENT FORM

B.L.D.E(DEEMED TO BE UNIVERSITY) SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA – 586103, KARNATAKA

TITLE OF THE PROJECT: "ALLERGEN SENSITIVITY PATTERN AND IT'S CORRELATION WITH TOTAL SERUM IgE LEVELS AND EOSINOPHIL COUNT AMONG PATIENTS WITH ALLERGIC RHINITIS AND/OR ASTHMA IN NORTH KARNATAKA".

PRINCIPAL INVESTIGATOR: Dr. PRANAVI. V
Department of Respiratory Medicine

PG GUIDE: Dr. RAMESH .S. BABAR,
Professor and Head,
Department of Respiratory Medicine,
B.L.D.E (Deemed to be University)'s
Shri B.M.Patil Medical College, Hospital and
Research Centre, Sholapur Road,
Vijayapura- 586103

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to assess "ALLERGEN SENSITIVITY PATTERN AND IT'S CORRELATION WITH TOTAL SERUM IgE LEVELS AND EOSINOPHIL COUNT AMONG PATIENTS WITH ALLERGIC RHINITIS AND/OR ASTHMA IN NORTH KARNATAKA".

I have been explained the reason for conducting this study and selecting me/my ward as a subject for this study. I have also been given a free choice for either being included or not in the study.

PROCEDURE:

I understand that I will undergo a detailed history and clinical examination and investigations.

RISKS AND DISCOMFORTS:

I understand that I/my ward may experience hypersensitivity or anaphylaxis while doing the procedure. I understand that necessary measures will be taken to reduce these complications as and when they arise.

BENEFITS:

I understand that I/my ward's participation in this study will help find out ALLERGEN SENSITIVITY PATTERN AND IT'S CORRELATION WITH TOTAL SERUM IgE LEVELS AND EOSINOPHIL COUNT AMONG PATIENTS WITH ALLERGIC RHINITIS AND/OR ASTHMA IN NORTH KARNATAKA.

CONFIDENTIALITY:

I understand that this study's medical information will become a part of this hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records but will be stored in the investigator's research file and identified only by a code number. The code key connecting the name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purposes, no names will be used, and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may request more questions about the study at any time. Dr. PRANAVI. V is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. And that a copy of this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary, and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. PRANAVI. V will terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my physician or therapist if this is appropriate.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly in my participation in this study, if such injury were reported promptly, medical treatment would be available to me, but no further compensation will be provided.

I understand that I am not waiving any of my legal rights by my agreement to participate in this study.

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. PRANAVI. V has explained the purpose of this research, the study procedure that I will undergo, and the possible discomforts and benefits that I may experience in my own language.

I have been explained all the above in detail in my own language, and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

_____ _____

(Participant) Date

_____ _____

(Witness to above signature) Date

I have explained to_____, the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date: Dr. RAMESH. S. BABAR Dr. PRANAVI. V

(Guide) (Investigator)

ANNEXURE III

PROFORMA

Name of the patient: Age:

Address: Sex:

IP no/OP no:

Occupation:

Presenting Complaints:

History of Present Illness:

Past history:

Personal history:

1. Diet- Veg/Mixed:
2. Appetite:
3. Sleep:
4. Bowel and bladder habits:

Family history:

Menstrual History:

GENERAL PHYSICAL EXAMINATION:

Conscious/ oriented/ co-operative:

Built:

Nourishment:

Ht (cm):

Wt (kg):

BMI:

Pallor

Icterus

Clubbing

Cyanosis

Lymphadenopathy

Edema

6. Vital parameters:

a. Temperature:

b. Pulse:

c. Respiratory rate:

d. BP:

e. SpO2:

SYSTEMIC EXAMINATION:

RESPIRATORY SYSTEM

ABDOMEN EXAMINATION

CARDIOVASCULAR SYSTEM

CENTRAL NERVOUS SYSTEM

INVESTIGATIONS:

Complete blood count:

Total Count	
Neutrophils %	
Lymphocytes %	
Monocytes %	
Eosinophils %	
Basophils %	
Hemoglobin (gm/dl)	
Platelet count (per cu.mm)	
ABSOLUTE EOSINOPHIL COUNT	

Total Serum IgE:

Allergen Skin prick test:

Chest X-ray:

ECG:

Pulmonary Function Test:

FINAL DIAGNOSIS:

DATE SIGNATURE

ANNEXURE IV

KEY TO MASTERCHART

S. No.	Serial Number
AR	Allergic Rhinitis
BMI	Body Mass Index
AEC	Absolute Eosinophil Counts
IgE	Immunoglobulin-E
V	Vegetarian
NV	Non Vegetarian
A	Absent
P	Present
N	No
Y	Yes

S. No	Name	Age	Sex	Diet	AR	Asthma	Both	AR Classification	Family history	BMI	AEC	Total IgE	No. of allergens sensitised to									
													Mites	Fungi	Pollens	Dust	Epithelia	Foods	Total	indoor	outdoor	both
1	Ashok Patil	57	male	V	A	A	P	Intermittent	N	20.7	540	940	1	0	2	0	1	2	6	A	A	P
2	vaibhavi loni	24	female	NV	P	A	A	Persistent	N	23.6	452	113.1	1	0	0	2	1	3	7	A	A	P
3	Genaram choudari	44	male	NV	A	P	A		N	20.8	10	185	3	1	0	0	0	4	8	P	A	A
4	Kalashri kadalskar	20	female	V	P	A	A	Persistent	Y	19.6	1100	968.7	1	0	0	2	0	0	3	A	A	P
5	Shrushti shastri	18	female	V	A	A	P	Intermittent	N	18.3	180	110.7	3	0	1	0	3	8	15	A	A	P
6	Daneshwari rajput	36	female	NV	A	A	P	Intermittent	N	22.9	774	890.34	0	0	0	1	0	0	1	A	P	A
7	Tukaram sangogi	48	male	NV	A	A	P	Intermittent	Y	25.7	860	835.6	3	0	0	2	1	0	6	A	A	P
8	shakuntala patil	50	female	NV	A	A	P	Persistent	Y	30.7	106	117.3	3	2	0	0	0	0	5	P	A	A
9	sharanappa balaganur	38	male	NV	A	A	P	Persistent	Y	22.5	510	250.7	1	0	4	0	1	7	13	A	A	P
10	sanket kulkarni	26	male	V	P	A	A	Persistent	N	22.7	443	322.4	3	0	0	0	2	2	7	P	A	A
11	shivayogi biradar	45	male	V	A	P	A		N	20.8	599	671	0	0	3	0	0	0	3	A	P	A
12	parvati lindi	48	female	NV	P	A	A	Persistent	N	19.9	670	550	1	0	0	0	4	1	6	A	A	P
13	akhila khadekhade	21	female	NV	A	A	P	Persistent	Y	17.3	220	79.6	0	0	4	0	0	3	7	A	A	P
14	vishal patil	23	male	NV	A	A	P	Intermittent	Y	23.9	190	132	2	2	0	0	2	5	11	P	A	A
15	shakuntala jain	60	female	V	A	P	A		Y	26	330	316.4	1	0	2	0	1	2	6	A	A	P
16	anil gaundi	39	male	V	A	A	P	Intermittent	Y	21.1	434	173.8	2	0	0	0	0	0	2	P	A	A
17	laxmi dyaberi	42	female	V	P	A	A	Persistent	N	26.7	386	83.2	0	0	0	0	0	1	1	P	A	A
18	devendra mehta	31	male	V	P	A	A	Intermittent	N	24.8	1650	2097.3	3	2	0	2	6	8	21	A	A	P
19	shivamma honakatti	30	female	NV	P	A	A	Persistent	N	20.3	118	123.1	3	1	0	2	0	0	6	A	A	P
20	Asma riyaz mangalwade	19	female	NV	A	P	A		N	22.4	930	2018.9	3	4	1	2	0	1	11	A	A	P
21	Bhimashankar kumbar	22	male	V	P	A	A	Persistent	Y	21.6	200	456.4	1	2	1	0	2	2	8	A	A	P
22	Rahul kenaganal	22	male	NV	A	P	A		Y	18.4	490	236	1	0	1	0	1	1	4	A	A	P
23	Muttana Hosakoti	40	male	V	P	A	A	Persistent	N	20.9	376	17.6	0	0	4	0	0	0	4	A	P	A
24	drakshayani jangamshetty	56	female	V	P	A	A	Persistent	N	29.1	392	128.4	3	0	0	1	2	2	8	A	A	P
25	saranappa bagdevi	42	male	NV	P	A	A	Persistent	N	27.3	278	100.7	0	1	0	0	1	2	4	A	A	P
26	prema guggari	45	female	V	P	A	A	Persistent	N	24.5	312	128	0	0	0	0	3	5	8	A	A	P
27	basanagouda biradar	46	male	NV	A	P	A		N	23	237	215	0	1	0	1	4	1	7	A	A	P
28	shruti raichur	32	female	NV	P	A	A	Intermittent	Y	24.4	975	1958.3	1	2	5	1	7	5	21	A	A	P
29	mahadevi kantigond	59	female	V	A	A	P	Persistent	N	29.8	260	133.6	0	0	0	1	0	5	6	A	A	P
30	seema vaidya	41	female	NV	P	A	A	Persistent	N	30.7	751	412.9	0	0	1	1	0	1	3	A	A	P
31	Rajini sharma	29	female	V	P	A	A	Intermittent	Y	26.8	510	119.1	0	2	0	1	0	2	5	A	A	P
32	N Goswami	50	male	V	A	A	P	Persistent	N	24.8	270	13.2	0	1	0	0	1	5	7	P	A	A
33	sridevi biradar	27	female	NV	P	A	A	Persistent	Y	29.4	389	179.7	0	1	3	1	1	1	7	A	A	P
34	Rajendra prasad	60	male	V	A	P	A		N	24.2	665	417.7	3	4	2	1	0	1	11	A	A	P
35	Padmavathi Gangireddi	50	female	NV	A	P	A		N	18.1	1187	856	2	0	0	3	0	2	7	A	A	P
36	Geeta Hanchate	48	female	V	A	P	A		Y	26.2	449	387.1	0	1	1	1	2	3	8	A	A	P
37	Sheela prasad	59	female	V	A	A	P	Intermittent	N	31.5	473	1472.9	2	3	2	0	0	6	13	A	A	P
38	Devaki ningappa rogi	55	female	NV	A	P	A		N	25.8	516	372.6	1	0	0	0	0	1	2	P	A	A
39	Kalpana Kanchyani	59	female	NV	A	P	A		N	28.1	10	1136.7	0	0	0	0	1	3	4	A	A	P
40	Kamalabai hiremath	60	female	NV	A	P	A		N	30.3	634	1123.7	3	8	3	4	5	5	28	A	A	P
41	Dastagir kaladgi	34	male	NV	A	A	P	Intermittent	N	21.2	360	354.3	3	1	0	0	3	5	12	P	A	A
42	Prashant kumar rai	24	male	NV	A	A	P	Persistent	Y	27.8	1204	2150	1	6	1	4	2	0	14	A	A	P
43	Ajit kumar	36	male	NV	A	A	P	Persistent	Y	25.1	380	451.3	3	3	2	2	7	2	14	A	A	P
44	Shankargouda patil	29	male	NV	P	A	A	Persistent	Y	30	530	185.5	3	0	0	1	1	0	5	A	A	P

		Sensitisation to allergens																																																																								
S. No	Name	Blomia	D-Farinae	D-Pteronyssinus	Aspergillus fumigatu	Aspergillus niger	Aspergillus flavus	Fusarium solanii	Rhizopus nigricans	Curvularia lunata	Cladosporium herbar	Candida albicans	Trichoderma	Cynodondactylon	Parthenium hysterop	Xanthium strumarium	Ageratum conyzoide	Ricinus communis	Zea mays	Ipomoea	Cocos nucifera	Peltophorum pteroca	Wheat dust	Cotton dust	House dust	Paper dust	Hay dust	Grain dust (rice)	Dog epithelia	Sheep's wool	Human dander	Chicken feather	Ant (black)	Cockroach	Honeybee	Cricket	Mosquito	House fly	Rice weevil	Moth	Wasp	Grass hopper	Ant (red)	Wheat	Bajra	Jowar	Gram bengali	Potato	Maize	Mustard	Masoor dal	Moong dal	Dal arhar	Tomato	Milk	Lemon	Peanut (groundnut)	Dal urad	Mutton	Chicken	Gram kabuli	Cashewnut	Coriander	Soyabean	Fish (sardine)	Egg white	Brinjal	Chocolate	Coffee	Coconut	Gum acacia	Curd	Rajma	Long pepper
1	Ashok Patil	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A
2	vaibhavi loni	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	P	P	A	A	A
3	Genaram choudari	P	P	P	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A	A	P	A
4	Kalashri kadalskar	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
5	Shrushti shastri	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	P	P	P	A	P	A	A	A	P	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A
6	Daneshwari rajput	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
7	Tukaram sangogi	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
8	shakuntala patil	P	P	P	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
9	sharanappa balagar	P	A	A	A	A	A	A	A	A	A	A	A	P	A	P	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	P	A	A	P	P	P	P	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A
10	sanket kulkarni	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A
11	shivayogi biradar	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
12	parvati lindi	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A
13	akhila khadekhade	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
14	vishal patil	P	P	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	P	A	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P
15	shakuntala jain	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
16	anil gaundi	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
17	laxmi dyaberi	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
18	devendra mehta	P	P	P	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	P	P	A	A	A	A	P	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	P	P	P	P	P	A	A	A	A	A	A	A	A	A
19	shivamma honakatti	P	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
20	Asma riyaz mangalw	P	P	P	P	P	P	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A
21	Bhimashankar kumb	A	P	A	A	P	P	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A
22	Rahul kenaganal	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A

Sensitisation to allergens

S. No	Name	Blomia	D-Farinae	D-Pteronyssinus	Aspergillus fumigatu	Aspergillus niger	Aspergillus flavus	Fusarium solanii	Rhizopus nigricans	Curvularia lunata	Cladosporium herbar	Candida albicans	Trichoderma	Cynodondactylon	Parthenium hysterop	Xanthium strumarium	Ageratum conyzoide	Ricinus communis	Zea mays	Ipomoea	Cocos nucifera	Peltophorum pteroca	Wheat dust	Cotton dust	House dust	Paper dust	Hay dust	Grain dust (rice)	Dog epithelia	Sheep's wool	Human dander	Chicken feather	Ant (black)	Cockroach	Honeybee	Cricket	Mosquito	House fly	Rice weevil	Moth	Wasp	Grass hopper	Ant (red)	Wheat	Bajra	Jowar	Gram bengali	Potato	Maize	Mustard	Masoor dal	Moong dal	Dal arhar	Tomato	Milk	Lemon	Peanut (groundnut)	Dal urad	Mutton	Chicken	Gram kabuli	Cashewnut	Coriander	Soyabean	Fish (sardine)	Egg white	Brinjal	Chocolate	Coffee	Coconut	Gum acacia	Curd	Rajma	Long pepper
23	Muttana Hosakoti	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
24	drakshayani jangamsl	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	P	A	A	A	A	A	A	A	P	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
25	saranappa bagdevi	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
26	prema guggari	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	P	A	A	A	P	A	A	A	A	A	A	A	A	P	A	A	A	P	A	A	A	A	P	A	A	A	A	A	A	A	A	P	A	A	A	A	A	P	A	A	A	A	A
27	basanagouda biradar	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A
28	shruti raichur	P	A	A	P	A	A	A	A	A	A	P	A	P	A	A	A	P	P	P	A	P	A	A	A	P	A	A	A	A	P	P	A	A	P	A	P	A	A	P	P	A	P	A	A	A	A	A	P	P	P	A	A	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A
29	mahadevi kantigond	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	P	A	A	P	A	A
30	seema vaidya	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
31	Rajini sharma	A	A	A	A	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A
32	N Goswami	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	P	P	A	A	A	P	A	A	A	A	A	P	A	A	A
33	sridevi biradar	A	A	A	A	A	A	A	A	P	A	A	A	A	P	P	A	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A
34	Rajendra prasad	P	P	P	A	A	A	A	P	P	P	P	A	A	P	A	A	P	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A
35	Padmavathi Gangirec	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A
36	Geeta Hanchate	A	A	A	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	P	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A
37	Sheela prasad	P	P	A	A	A	A	P	P	A	P	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	P	P	P	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	P	A	A	A	A	A
38	Devaki ningappa rogi	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A
39	Kalpana Kanchyani	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	P	P	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
40	Kamalabai hiremath	P	P	P	A	P	P	P	P	P	P	P	P	P	P	A	A	A	A	P	A	A	A	P	P	A	P	P	P	P	P	A	A	A	A	P	A	P	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
41	Dastagir kaladgi	P	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	P	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	P	A	A	A	A	P	P	A	A	A	P	A	A	A	A
42	Prashant kumar rai	P	A	A	A	A	P	P	P	P	P	P	A	P	A	A	A	A	A	A	A	A	A	P	P	P	A	P	A	A	A	A	A	A	A	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
43	Ajit kumar	P	P	P	A	A	A	P	A	P	P	A	A	P	P	A	A	A	A	A	A	A	P	A	A	A	A	P	P	A	A	A	P	P	A	A	P	P	A	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	P
44	Shankargouda patil	P	P	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	P	A	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A