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Research Article

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Hypersensitive allergic reactions are caused by Pollen abundantly found in air during the spring and autumn seasons

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ABSTRACT

Local climate changes can impact on a number of factors, including air pollution, that have been shown to influence both the development and attacks of allergic respiratory diseases, and thus, they represent an important consideration for the allergist. Atmospheric pollution caused by the pollen abundantly found in air are responsible for a number of hypersensitive allergic reactions like bronchial asthma, conjunctivitis, rhinitis, dermatitis etc. among the people living around the world. The basic concept of aero-palynology revolves round the monitoring of prevalence of the pollen in the atmosphere in relation to meteorology. Keeping in mind this concept a detailed study was conducted in the highly affected areas of Kashmir valley to know the allergic disorders caused by the airborne pollen. Hence the present study was taken to monitor the pollen grains daily in the atmosphere of North Kashmir which is witnessing an increase in allergy related disorders. These aeroallergens are present in the atmosphere mostly during spring and autumn seasons. Air monitoring of the area was carried out continuously for all the four seasons in the study sites and the data compiled revealed that there are many pollen types in the atmosphere of the area out of which some are already known to cause allergy. Keeping in view the prevalence of unknown allergic pollen, an apprehension was concealed that there may be some allergic disorders among the population of the area and this assumption was confirmed from the data collected from government hospitals working in the area where number of patients attended have been diagnosed with various hypersensitive reactions. The blood samples were collected from the patients in order to evaluate the concentration of total IgE and specific IgE levels in such patients. Two bio allergens were tested against specific IgE by sandwitch ELISA in selected patients aged between 14 – 52 years including both sexes. All the samples showed presence of high levels of IgE and specific IgE against these two bioallergens showed moderate to high specific IgE levels. The detailed information on indigenous pollen will surely be very useful in diagnosis and management of allergic patients and may immensely help the physicians of the area in treating the patients suffering with various hypersensitive allergic disorders.

Keywords: *Hypersensitivity, Rhinitis, Allergens, Respiratory , Asthma, Climate, Pollen, IgE.*

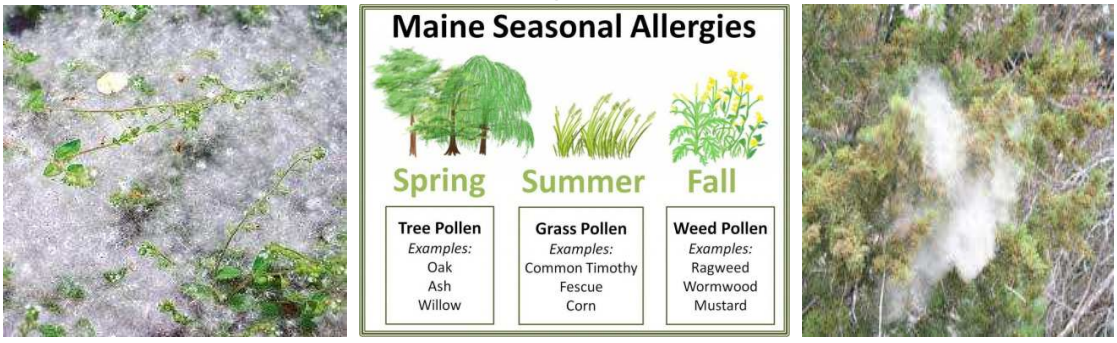
INTRODUCTION

Allergic diseases are amongst the most common chronic disorders worldwide. Today, more than 300 million of the population is known to suffer from one or other allergic ailments affecting the socio-economic quality of life [1]. Major causative agents implicated are pollen grains, fungal spores, dust mites, insect debris, animal epithelia, etc [2]. Several aerobiological studies have been conducted in different parts of the world to ascertain aerial concentration and seasonality of pollen grains and fungi. Especially from clinical point of view, it is important to know the details about the pollen season and pollen load in the atmosphere. The flowering time of higher plants are events that come periodically in each season, but the time of blooming may differ from year to year, in different geographic locations. Based on differences

recorded in several years of observations in airborne pollen, pollen calendars are drawn as an aid to allergy diagnosis and management [3-6]. The bioparticulates implicated to cause allergic symptoms are pollen grains, fungal spores, insect debris, house dust mites, animal dander, chemicals, foods, etc. Among all these agents, pollen grains and fungal spores are the most predominant allergens in the air. However, for the effective diagnosis and therapeutic management of these ailments, a detailed information on the daily, seasonal and annual variations of various Pollen grains as aeroallergen are well studied from across the world and are important cause of pollinosis. Respiratory system is the direct target organ of airborne pollen taken in by inhalation. This results in immediate hypersensitivity disorders, in genetically predisposed individuals and late hypersensitivity in others causing clinical manifestations of allergic rhinitis, allergic alveolitis, asthma, atopic dermatitis, etc. [7-14] The transport of pollen grains by wind or by the insects, from floral anther to recipient stigma is the critical reproductive event among higher plants. The dispersion of replicate units in massive abundance assures the success of wind pollination as well as its human health effects including asthma, rhinitis, atopic dermatitis, etc. Pollen prevalence (grains per cubic meter) at any point reflects (plant) source strength and location as well as the dynamics of the intervening environment conditions such as climatic factors, pollution and degree of exposure. The presence of pollen, profile of species, concentration, etc depends on various climatic factors such as temperature, humidity, wind direction, sunshine, substrate precipitation and other seasonal factors. Because of change in the climatic conditions, the study of variations in the diurnal and seasonal prevalence becomes very important [15].

The Kashmir considered paradise on earth for its natural and scenic beauty seems to be bearing the brunt of the cotton-type pollen produced by Russian poplars introduced in Kashmir in 1980s under the Social Forestry Scheme aided by World Bank [16]. The hypersensitive reactions caused by these pollen has turned into a major health concern in Kashmir which has about 15-20 million of these trees with experts having little to offer to the masses except some precautionary measures. Since mid-April whole of Kashmir has been caught in this trouble with children and elderly persons being the worst affected. The pollen from these trees floating in the air is the female fertilizing agent, which trigger seasonal allergic rhinitis known as pollen allergy. Most of these trees are female which produce this cotton type of pollen. Male versions of these trees also produce pollen which is invisible to the human eye but is more harmful to health as compared to the female pollen. People are seen using surgical masks to avoid the pollen entering their body through nose or mouth. One-fourth of Kashmir population is battling this allergy [17-18]. Keeping the graveness and severity in mind the local administration has imposed a blanket ban on plantation of Russian poplar trees in the summer capital of Jammu and Kashmir keeping in view the large scale complaints of allergy being caused by its pollen.

Fig. 1



Pollen Menace in Kashmir valley

Allergic response to an allergen

Allergy refers to immediate (type I) hypersensitivity to environmental antigens. It is characterized by wheal and flare reactions to skin testing with common environmental antigens, usually with appropriate clinical history. Atopy is demonstration of allergy and familial aggregation of this trait. The early phase of

an allergic response is predominately mediated by Th2 cytokines, such as interleukin (IL)-4 and IL-6; however, a cascade of pro-inflammatory agents including Th1 immunoactive molecules (e.g., cytokines and chemokines) are also released [19] .

Advances in basic immunology research have enhanced our understanding of the cellular and molecular basis of the allergic response. A prominent characteristic of the allergic response is a persistently elevated level of IgE antibodies against specific antigens (allergens) to which the affected individual is regularly exposed by inhalation, ingestion, or contact with the skin [20]. Allergic sensitization involves processing of the antigen by an antigen-presenting cell (APC) and presentation, in association with a class II major histocompatibility complex (MHC) protein, to a T-cell receptor. While dendritic cells (and macrophages) predominantly act as APCs in primary immunization, B cells may also participate in secondary immune responses to allergens. Activation of T cells requires the signal from this trimolecular interaction and an additional costimulatory signal resulting from the binding of B-7 (CD80/86) on an APC to CD28 or CTLA4 on a T cell (21). When stimulated by antigens, helper T (T_H) cells produce specific cytokines that have been designated as either T_H 1 cytokines (interleukin [IL]-2, interferon [IFN]-gamma, and tumor necrosis factor [TNF]-beta) or T_H 2 cytokines (IL-4, IL-5, IL-9, IL-10, and IL-13). The state of T-cell activation depends on several factors [21, 22]. The first of these factors is the strength of the interaction between the antigen and the T cell. The site of the antigen recognized by the T cell is termed the *epitope*. The affinity of a T cell for a specific epitope depends on the concentration of the antigen, the type of APC [23] and the cytokine milieu of the T cell during antigen interaction. Thus, IFN-gamma and IL-12 promote a T_H 1-like response, whereas IL-4 promotes a T_H 2-like response [24]. Additionally, host immune system genes may bias the overall immune responsiveness of an individual to favor a T_H 1- or T_H 2-like phenotype. A T_H 2-like cytokine profile is associated with the induction of IgE antibody (Ab) production in vitro and in vivo [25]. Specifically, IL-4 favors the development of T_H 2-like cells from uncommitted T cells, and both IL-4 and IL-13 play a role in IgE antibody production. Manifestation of an allergic reaction depends on the specific IgE levels and the amount of exposure at the time of the reaction. Although an allergic condition is a risk factor for asthma, 20% to 30% of asthmatics do not show positive skin tests to allergens. In general terms, asthma is an inflammatory disease in which not only lymphocytes but mast cells, basophils, eosinophils, and epithelial cells play a role. Studies to date suggest that T_H 2-like cytokines, such as IL-4 and IL-5, also play an important role in nonatopic asthma [26-27].

Fig. 2

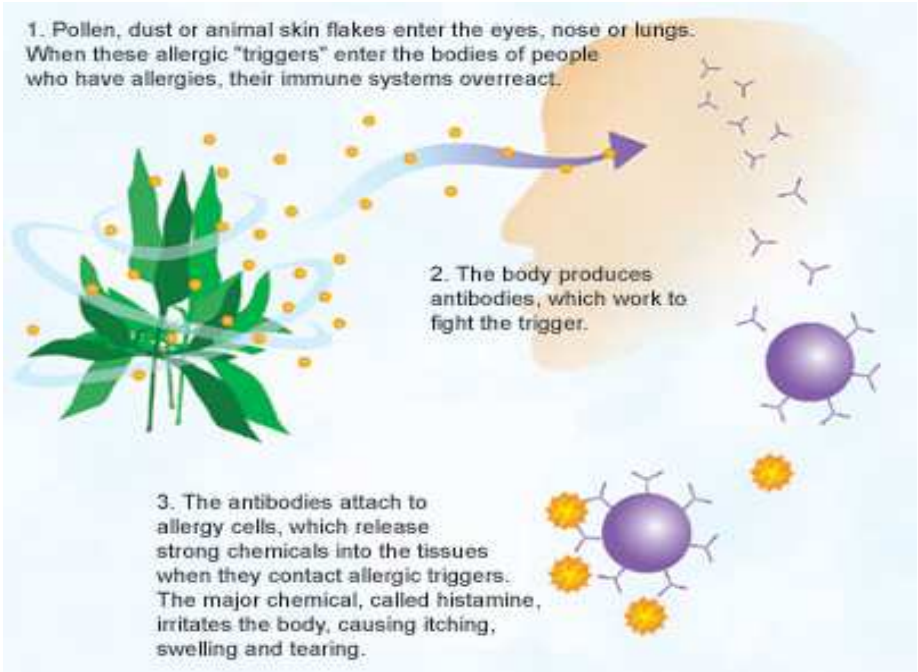
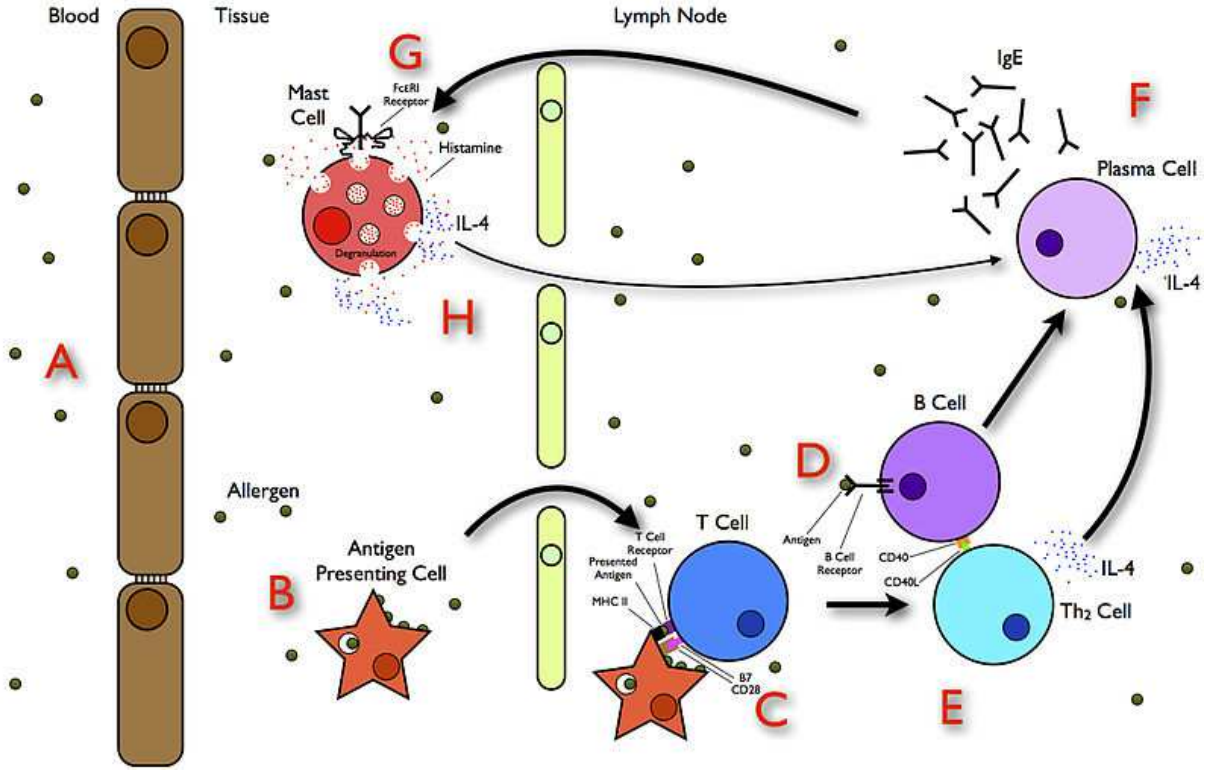


Diagram showing how allergies caused due to allergens like pollen make us sneeze and wheez.

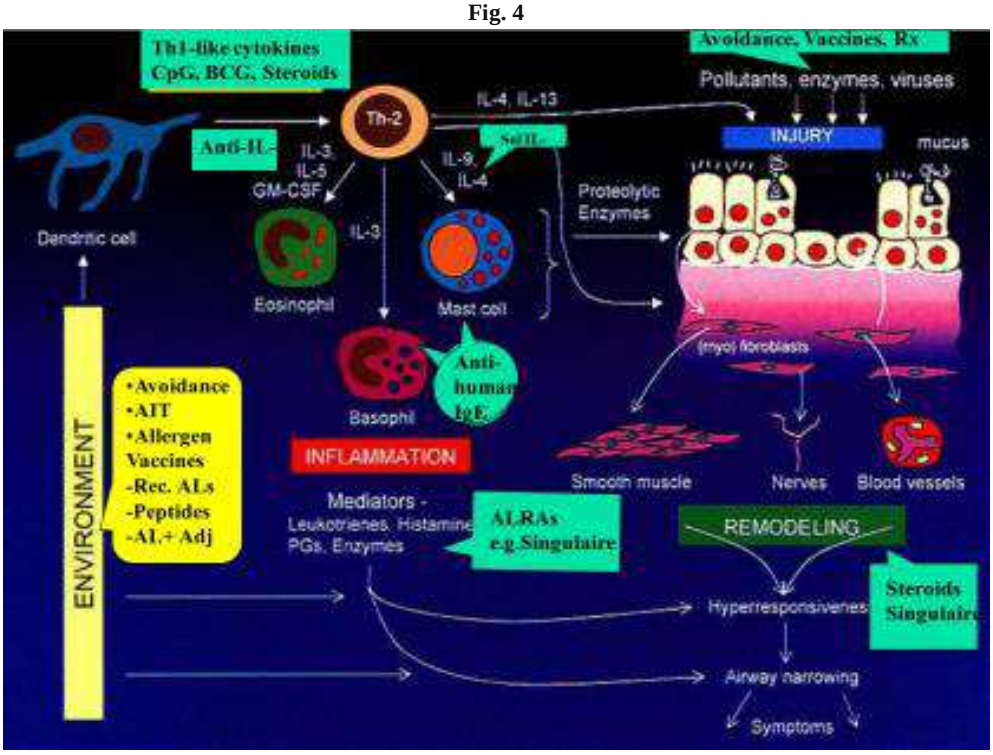
Fig. 3: Simplified diagram showing key events that leads to allergy initiation



A. the allergen enters the body.**B.** an Antigen-presenting cell takes up the allergen molecule and presents its epitopes, through the MHC II receptor, onto its surface. The activated antigen presenting cell then migrates to the nearest lymph node **C.** where its activates T cells that recognize the allergen. They then give the decision for the T cell to differentiate to Th2 cell.**D.** at the same time, B cells recognize the allergen and through the activated Th2 cell **E.** the B cell would be activated. **F.**and differentiate into plasma cells, at which point they would actively synthesize antibodies of the IgEisotype. **G.** the IgE antibody, that now recognizes epitopes of the allergen molecule, circulates around the body through the lymphatic andcardiovascular systems and finally binds to its FcεRI receptor on mast and basophil cells. **H.** when the allergen re-enters the body at a later time it binds to the IgE, which is on the cell surface, resulting in an aggregation of the receptor causing the cells to release pre-formed mediators. One of these mediators is histamine which causes the 5 symptoms of allergic inflammation: heat, pain, swelling, redness and itchiness. Another mediator is IL-4, which affects more B cells to differentiate into plasma cells and produce more IgE and thus the vicious cycle continues.

The pathophysiology of allergy response has been explained by conceptualization sometimes called the Th1-Th2 paradigm of CD4 T helper cells. Antigen presenting cells display dipeptide antigens, either allergen or infectious, in their cell surfaces for recognition by native T cells. Native T cells differentiate into Th1 or Th2 cells depending on the nature of antigen, Th1 cells secrete IFN-γ, while Th2 cells secrete IL-4, IL-5 and IL-13, Th2 cells promote allergic inflammation through the production of cytokines including IL-4, IL-5 and IL-13, IL-4 and IL-13 include B lymphocyte to differentiate into IgE producing plasma cells. IL-5 play role in eosinophilopoiesis and resistance to apoptosis. A Th1 response results in activation of macrophages and natural killer cells by elaboration TNF-α and IL-2 cytokines plays a role in complement binding and opsonization. Th1 and Th2 cells have been observed to synergistically promote inflammation and airways hyper-responsiveness. It is found allergic disorders viz; Allergic rhinitis, allergic asthma and urticaria are associated with IL-4, IL-5, IgE production, and INF-γ production is associated with airway hyper-reactivity and skin test reactivity [28].

Fig. 4



Mechanism underlying allergic diseases: allergens induce an immunological response via APC-T cell interactions leading to the production of specific cytokines which in turn help B cells to produce IgE antibodies. Each of these steps can be targetd for therapeutic intervention. (Adapted from Steve Holgate JACI 2006)

Impact of Climate change on pollen allergy:

A body of evidence suggests that major changes involving the atmosphere and the climate, including global warming induced by human activity, have an impact on the biosphere and human environment [29]. Studies on the effects of climate changes on respiratory allergy are still lacking, and current knowledge is provided by epidemiological and experimental studies on the relationship between asthma and environmental factors, for example, meteorological variables, airborne allergens, and air pollution.

Table showing the possible potential effects on the prevalence of allergic disease due to climate change

Climate change event	Potential Environmental Impact	Effect on allergic disorder prevalance
Increase in temperature	Migration of stinging and biting insects into new environments and increase in the population of existing insect species Change to crop patterns, with the potential to introduce new allergenic pollen into the atmosphere and new food proteins to local diet Earlier and longer pollination seasons Increase in humidity associated with higher temperatures which inturn will lead to higher numbers of coackroaches, house dust mites, and molds hence increasing allergen load	Sensitization to new stinging and biting insect species and to foods, with potential increase incase of IgE mediated anaphylaxis New pollen and mould sensitization leading toincreased prevalence and attacks of allergic rhinoconjuncivitis and asthma; longer pollen Season leading to increased duration of symptoms
Increase in precipitation and drought, leading to lower crop yields, damaged crops, food shortage and lack of work	Population migration	Development of sensitization to new allergens, leading to development of allergic respiratory and skin conditions
Increase in thunderstorms in spring and summer months	Thunderstorms cause pollen grains to rupture, increasing the levels of respirable allergens and also lead to an increase in ozone level	Increased hospital admissions due to asthma
Source: Site of World Allergy Report 2008		

Climate changes affect allergenic plants and pollen distribution worldwide [30-34]. There is also considerable evidence that subjects affected by asthma are at an increased risk of developing obstructive airway attacks with exposure to gaseous and particulate components of air pollution.11 Climate change coupled with air pollutant exposures may have potentially serious adverse consequences for human health in urban and polluted regions

Pollen allergy is frequently used to study the interrelationship between air pollution and allergic respiratory diseases (rhinitis and asthma). Epidemiologic studies have demonstrated that urbanization, high levels of vehicle emissions, and westernized lifestyle are correlated with an increase in the frequency of pollen-induced respiratory allergy in people who live in urban areas compared with those who live in rural areas. [32]

Studies on plant responses to elevated CO_2 concentrations indicate that plants exhibit enhanced photosynthesis and reproductive effects and produce more pollen [31-34].An earlier start and peak of the pollen season is more pronounced in species that start flowering early in the year. Moreover, plants flower earlier in urban areas than in the corresponding rural areas with earlier pollination of approximately 2 to 4 days. Meteorological factors (temperature, wind speed, humidity, thunderstorms, etc) along with their climatic regimens (warm or cold anomalies and dry or wet periods, etc) can affect both biological and chemical components of this interaction. In addition, by inducing airway inflammation, air pollution overcomes the mucosal barrier, leading to the priming of allergen-induced responses.

Climatic factors (temperature, wind speed, humidity, thunderstorms, etc) can affect both components (biological and chemical) of this interaction [34] . By attaching to the surface of pollen grains and of plant-derived particles of paucimicronic size, pollutants could modify not only the morphology of these antigen-carrying agents but also their allergenic potential. In addition, by inducing airway inflammation, which increases airway permeability, pollutants overcome the mucosal barrier and could be responsible for “priming” the allergen-induced responses of pollinosis in allergic and atopic individuals. However, the relationship between air pollution, pollen exposure, and respiratory allergy is based on an individual's response to air pollution, which depends on the source and components of the pollution, as well as on climatic agents [35-40].

MATERIALS AND METHODS

For day to day monitoring vertical cylinder rod were used being 95% efficient. These vertical cylinder rods were installed at three different sites for study site like Iqbal Market (Site-A), Bohipora (Site-B) and Kulangam (Site-C). The samplers were installed on the roof of buildings at a height of 10 meters above the ground level. The trapping surface is 18 x 18 mm vaseline coated cellophane wound glass rod clubbed vertically under a protective shield. After 24 hours the exposed traps were thoroughly scanned under the compound microscope and pollen grains were identified by comparing the standard source slides prepared directly from the source plants. A detailed study of allergic aspects was carried out in collaboration with department of immunology SKIMS Soura, Sriangar.

Percentage for trapped pollen grains was calculated using formulae:

$$\%\text{age for pollen grains} = \frac{\text{No. of particular grains}}{\text{Total No. of trapped pollen grains}} \times 100$$

While making calculations a correlation factor was used to obtain uniformity.

$$\text{Corrected month count} = \frac{\text{The No. of days in a month}}{\text{Actual No. of days x Actual count}} \times 100$$

RESULTS

The air borne pollen found and monitored in this study has been grouped into three categories like trees, herbs and shrubs. The identified pollen type belongs to 22 families (Angiosperms and Gymnosperms). Air of research study sites were monitored from May 2011 to April 2012 revealed a total of 30 pollen types. The monthly incidence of each pollen type is present in tubular form. From the tables data it is clear that the pollen incidence at three different sites vary significantly. Pollen concentration remains high at site-B than that of site-A and site-C because of the presence of high no. of all types of pollen producing plants and the area is more prone to winds. However all the trapped pollen grains shows marked seasonal variation? As shown in table- A (spring season) table –B (summer season) table –C (autumn season) and table –D (winter season). The pollen concentration remains highest from March-September because during spring season all the flowing plants of valley are in full bloom due to which the high concentration of pollen is in the air. During winter season concentration of pollen remains very low as plants do not flower during winter (minimum temperature 0.9ºC – 4.8ºC, max. 5.7ºC – 15.8ºC). The pollen concentration also showed decrease during autumn while highest pollen counts found during April – May and lowest in January-February at all sites.

Table-1:- Pollen types found in the atmosphere of North Kashmir in spring season (April-June)

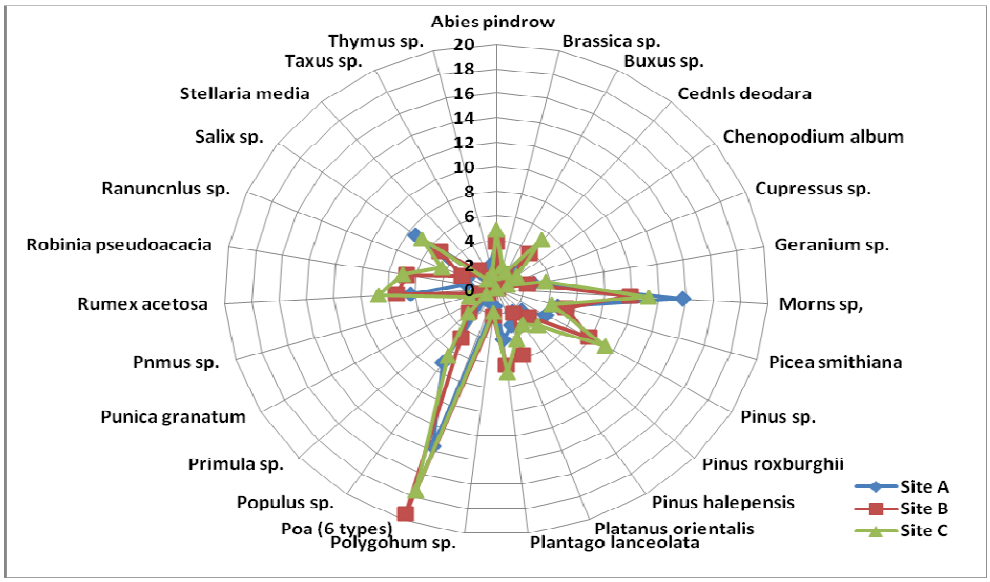


Table-2:- Pollen types found in atmosphere of North Kashmir– Summer season (July – September)

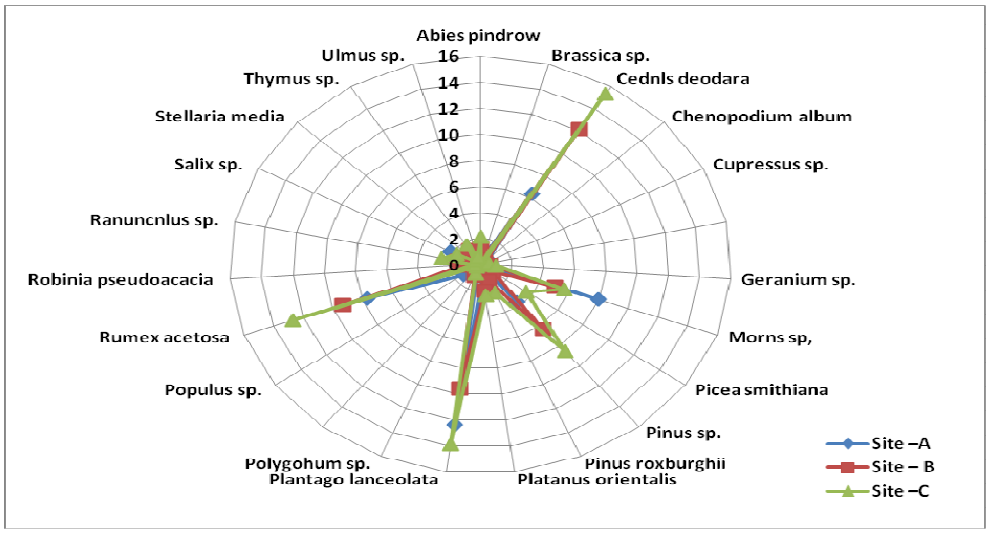


Table-3: Pollen types found in atmosphere of North Kashmir- Autumn season (Oct.–Dec.)

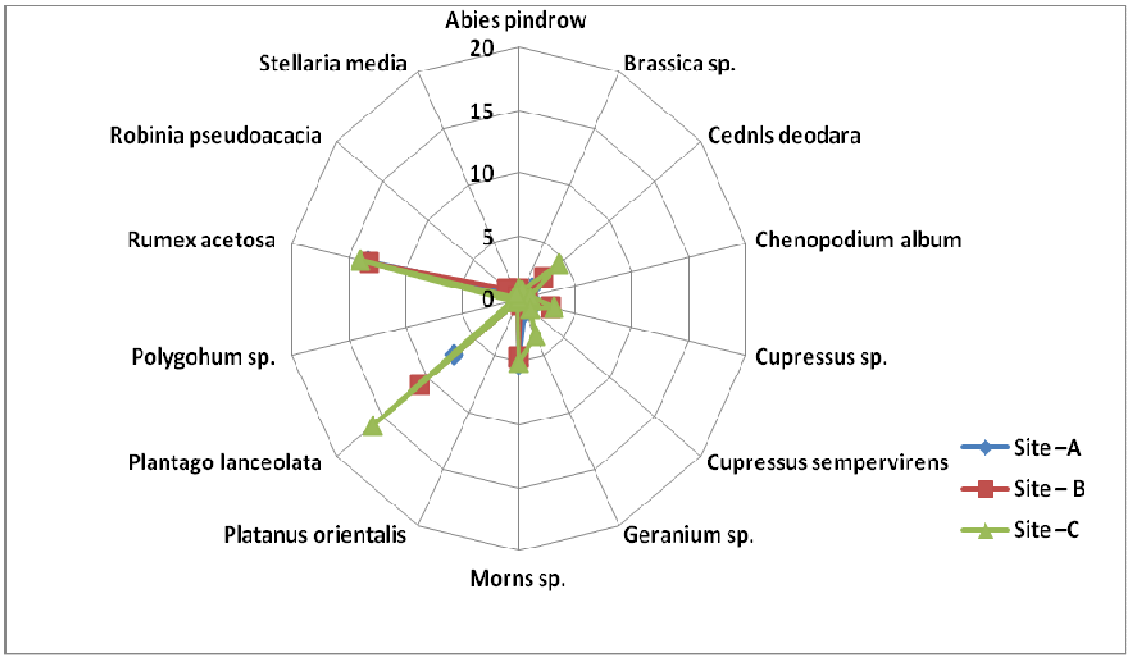
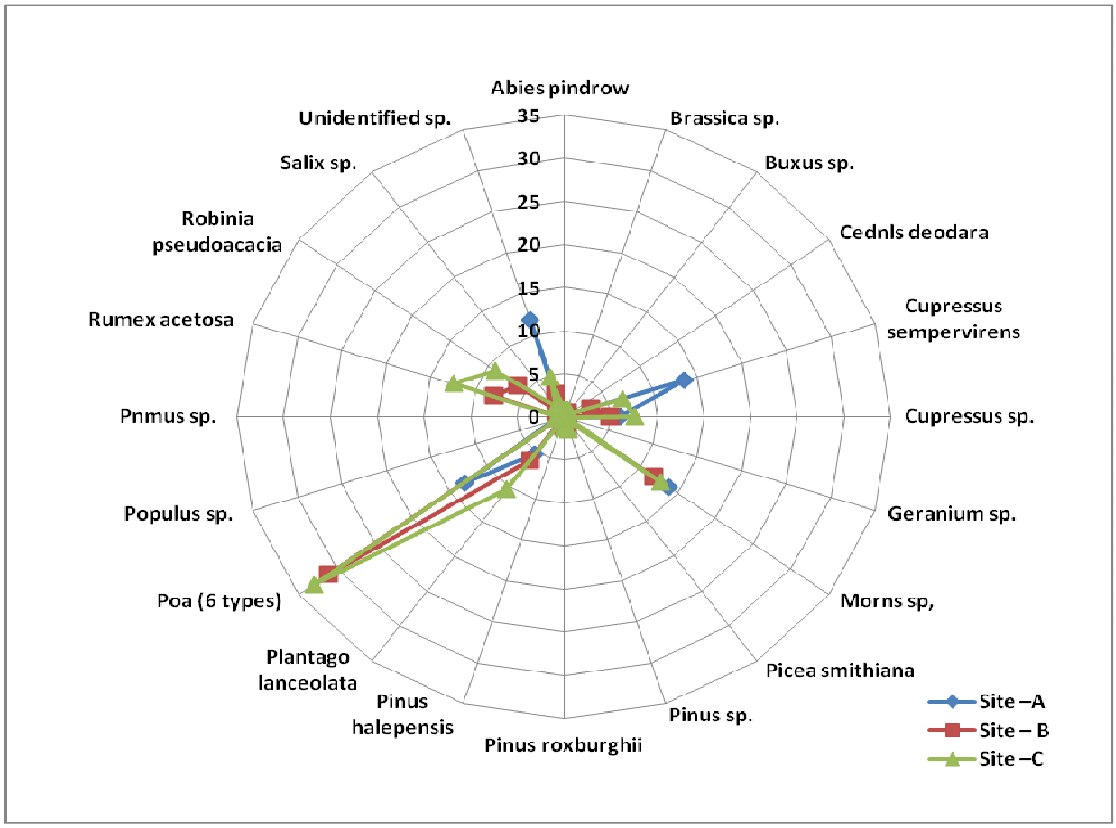
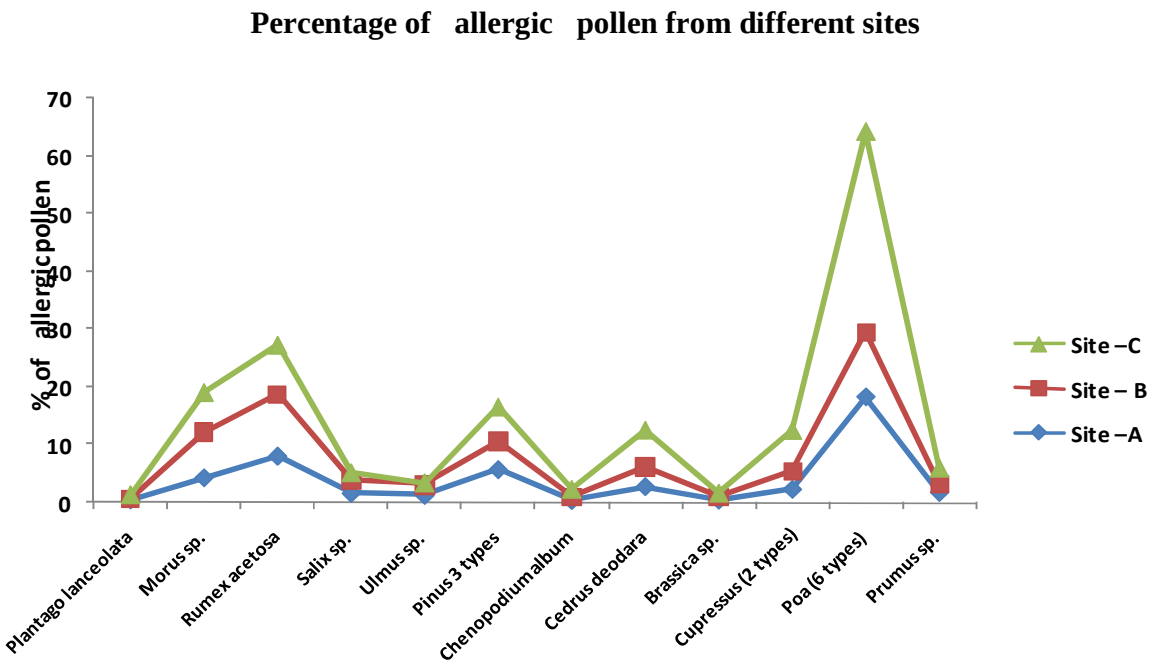


Table 4-Pollen types found in atmosphere of North Kashmir-Winter season (Jan.–March)



Percentage of allergic pollen from these different sites:

Out of 32 pollen types 23 types are already known to be allergic and cause various allergic disorders among the human population of the world. The main allergic disorders caused by these allergic pollen types are allergic rhinitis allergic dermatitis, bronchial asthma, conjunctivitis. Allergic pollen types reported from the atmosphere of Kupwara are presented in table.



Response in allergic individuals

Many scientific discoveries proved that human allergic diseases resulted from the formation of anti bodies belonging to a immunoglubin isotype termed IgE. Patients suffering from various types of allergies like allergic rhinitis conjunctivitis, dermatitis and brochial asthma were selected for the study. Each Patient was clinically evaluated and careful history of allergic conditions were recorded blood samples from suspected patients were collected after proper investigation from each patient by Venipuncture and serum was separated and divided into two aliquots and were stored at -20◦c until further processed.

Total IgE Response

Each Serum was subjected to total IgE measurement using commercially available total IgE kit [IUB Magiwell USA] based on sandwich ELISA technique and following the manufactures protocol. Each assay included ten control subjects (apparently healthy and non allergic). The absorbance of the final step was read 450 nm using a software driver ELISA reader and concentration of total IgE in each sample was recorded. All the samples showed presence of high levels total IgE equivalent to 650-1200 1µ/ml.

Specific IgE response

Two bio allergens namely *Poa pretance and cynodon dactylon* were tested against specific IgE in 138 Patients. Out of which 121 serum samples showed presence of IgE levels against different grass and tree pollen at varying concentrations ranging from 1.1 to 75.0 1µ/ml. out of all the grass and tree pollen most of samples were reactive for mixed antigens especially for *cynodon dactylon* (25 patients) and *poa pretance* (63 patients) 14 male and 11 female patients showed positive reactions for *cynodon dactylon* and 42 male and 21 female patients showed positive reactions for *poa pretance*. 33 serum samples didn't show any specific reactions to pollen specific antigens used in study. These samples probably had specific IgE levels against other pollens diluted but not used in the current study.

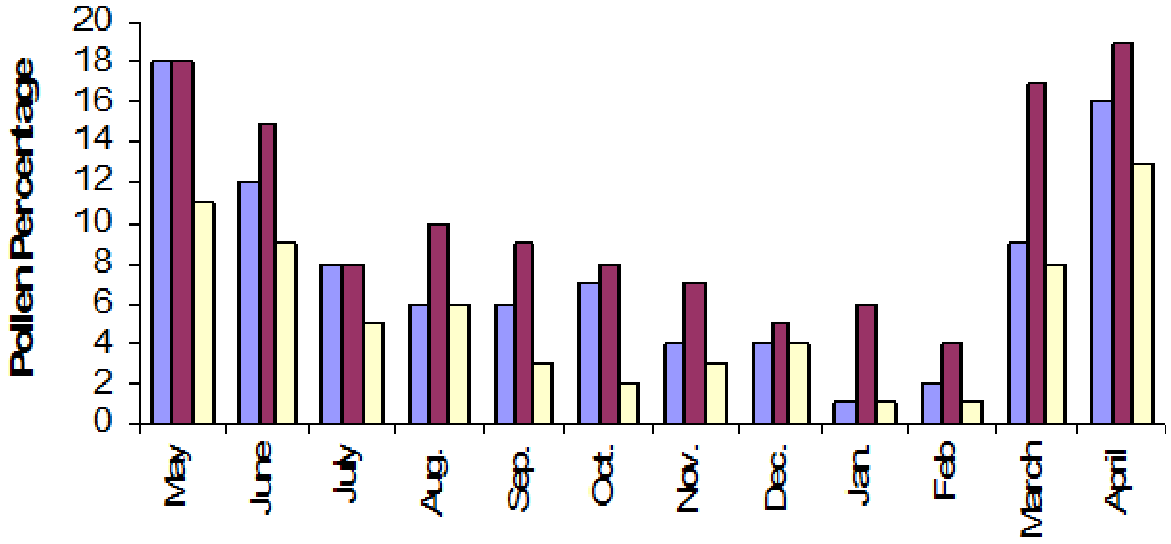


Figure showing the total monthly count of air borne pollen in atmosphere in site A (Yellow bars) site B (Blue bars) and site C (Red bars)

DISCUSSION

The distribution and prevalance of air borne pollen varies with flowering period, weather condition and vegetation type. Plantaginaceae, Pinaceae, Moraceae, polygonaceae, papilonaceae Cupressaceae, Plantanceae etc. and poaceae were found to be the most abundant because many of these taxa are widespread in the surrounding areas.

In the present study the lowest pollen count was registered in winter because rain washes out suspended pollen and low temperature may probably decrease pollen count. The studies on air borne pollen attains unique importance in recent years because it provides first hand information to the physicians and medical practioners for identifying various allergic disorders among the people living in that area.

During the research study an effort has been made for the first time to check total IgE and specific IgE levels in the serum of allergic individuals who complains various allergic symptoms diagnosed by the local physicians.

The pollen concentrations remain highest from March-September During spring season al the flowing plants of valley of Kashmir are in full bloom due to which the high concentration of pollen is in the air. During winter season concentration of pollen remains very low as plants do not flower during winter (minimum temperature 0.8ºC – 4.6ºC, max. 5.9ºC – 15.5ºC). The pollen concentration also shown decrease during autumn while highest pollen counts was found during April – May and lowest in January-February at all.

CONCLUSION

It has been assessed after compiling the data that pollen counts appears to be fluctuated which may be due to weather parameters and flowing period. The survey revealed 30 pollen types, which belongs to families Brassicacia, Buxaceae, Caryophyliaceae, Cupressaceae, Chenopodiaceae, Geraniaceae, Lamiaceae, Moraceae, Pinaceae, Plantanaceae, Primulaceae, Plantaginacea, Polygonaceae, Papilonaceae, Punicaceae, Poaceae, Ranunculaceae, Rosaceae, Salicaceae, Taxaceae and Ulmaceae. 32 identified pollen types includes 21 known allergic pollen types. The detailed information on indigenous pollen will surely be very useful in diagnosis and management of allergic patients and may immensely help the physicians of the area in treating the patients suffering with various hypersensitive allergic disorders.

Recommendations: The remedial action depends on the actual problem and conditions prevailing in different occupational sites, however following preventive measures in general are recommended.

1. All the allergenically significant trees need to be deleted from the list of recommended tree plantation in gazette of India.
2. Ornamentals, insect/bird pollinated and medicinally important trees or others which can help in controlling pollution, should be encouraged in various tree plantation and afforestation programs.
3. The existing allergenically significant trees need to be replaced with non-allergenic trees in a phased manner.
4. On medical ground, citizens should have the right to cut or demand removal of allergy causing trees in close vicinity. However, these should be replaced with some non-allergenic trees.
5. A genuine beginning needs to be made by sensitizing tree lovers/horticulturist/foresters/botanist and other associated with tree plantation so that the share of allergenically significant plants could be minimized in the near future. The earlier it is done the better.

Allergy has been known for more than a century now, but the subject has suffered due to lack of knowledge about basic mechanisms involved in allergic diseases and poor diagnostic procedures. The rapid development in the field of immunology and clinical diagnosis in the pool of knowledge, is of, direct significance to allergy practitioners. The detailed information on indigenous pollen and fungal allergens will be very useful in diagnosis and management of allergic patients.

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