Original Article

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Internal Medicine Section

Aeroallergen Sensitivity Pattern in Poorly Controlled Asthmatics and its Relation to Asthma Control in a Tertiary Care Setting of Central Kerala, India

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ABSTRACT

Introduction: Nasobronchial allergy is an exceedingly common problem in clinical practice. Estimates reveal that the prevalence of nasobronchial allergy is increasing worldwide, including in India. Sensitivity to individual aeroallergens varies depending on geography, genetic and environmental factors.

Aim: To identify the sensitivity pattern to common aeroallergens in poorly controlled asthma patients and to correlate asthma severity with sensitivity to specific aeroallergens.

Materials and Methods: A prospective cross-sectional study was conducted on out-patients attending the Department of Pulmonary Medicine with a diagnosis of asthma as per GINA guidelines. Patients above seven years with features of asthma were included in the study. The Asthma severity was assessed using the Asthma Control Test (ACT) questionnaire and lung function studies. SPT was performed as per clinical indication. The skin allergy sensitivity patterns were compared in groups as per their disease severity and level of control using Chi-square and Spearman rank correlation.

Results: Patients with features of inadequately controlled asthma (ACT score less than 20 and FEV1 less than 80% predicted) showed a higher occurrence of positive reaction in the SPT to multiple aero and food allergens as compared with those having good ACT score and FEV1 >80%.

Conclusion: Allergen sensitivity is very common in asthma. House dust mite, fungal allergens and grass pollens were the common allergen sensitisation identified in subjects with poorly controlled asthma. A correlation was seen between inadequately controlled asthma and sensitisation to multiple aeroallergens. So, vigorous allergen screening and allergen immunotherapy must be included in the management protocol of asthma.

Keywords: Allergen sensitivity, Atopy, Immunotherapy, Skin prick test

INTRODUCTION

Allergy is an exaggerated response of the human body to potentially harmless agent. The term is often used synonymous with hypersensitivity. Allergy can be atopic or non-atopic. Atopy refers to an inherited tendency to produce Immunoglobulin E (IgE) antibodies in response to small amounts of common environmental protein. It can occur as an asymptomatic sensitisation or as an atopic disorder. Allergy can affect almost every organ of body with varying severity, respiratory tract being one of the commonest sites. The natural history of atopic diseases is referred as atopic march, which denotes occurrence of atopic dermatitis along with food allergy in early childhood, sequentially progressing to asthma and allergic rhinitis in later childhood or adult life [1].

The prevalence of allergic disorders is on rise worldwide including developing countries like India due to life style changes, urbanisation and alteration in the indoor and outdoor environment. Estimates reveal that more than 30% of world population is suffering from one or the other allergic disease. In India more than 20% population bears the ill effect of some form of IgE mediated allergic disorder [2]. Among the allergic individuals, sensitivity to individual allergens (especially aeroallergens) vary widely [3]. Identification of culprit allergens is of benefit to the practising clinician in multiple ways. Positive SPT firmly establishes the allergic nature of the clinical syndrome. Sensitivity to certain agents is linked with severe disease. Allergen avoidance is a cornerstone of treatment in allergic states wherever feasible. Allergen immunotherapy is an established modality in the management of allergic disorders. Therefore identification of sensitivity to specific allergen constitutes an important step in the management of such patients.

Skin tests are the best means to diagnose allergic response in vivo. Reactivity depends on an intact immune system, the presence of IgE sensitised mass cells that release mediators when exposed to antigen and an intact skin that can respond with the development of inflammatory response (with erythema and induration). Skin testing is preferred over blood tests, as it is more sensitive and specific, simpler to use and less expensive [4]. The position papers on skin tests by the European Academy of Allergy and Clinical Immunology (EAACI) and the US Joint Council of Allergy, Asthma and Immunology {American Academy of Allergy, Asthma and Immunology (AAAAI), ACAAI} state that properly performed prick test is convenient for good clinical correlation and is economical [5]. On similar lines, the World Allergy Organisation (WAO) has recommended SPT as the best screening method for detecting S.IgE antibodies [6]. They are highly reproducible when carried out by trained individuals. SPTs are minimally invasive, have high specificity, and have a lower rate of systemic effects as compared to the intradermal tests. SPT may be considered as the gold standard diagnostic method to detect allergen sensitisation. Therefore, the present study was conducted with an aim to identify the sensitivity pattern to common aeroallergens in poorly controlled asthma patients and to correlate asthma severity with sensitivity to specific aeroallergens.

MATERIALS AND METHODS

The present study was of cross-sectional nature conducted in out-patients attending the Department of Pulmonary Medicine with a diagnosis of asthma as per GINA guidelines. The study was approved by institution ethics committee, NO: RAJH 18006. Patients above seven years with features of asthma were included in the study.

The Asthma severity was assessed using the ACT questionnaire [Annexure 1] and lung function studies. Any patient with an ACT score less than 20 and FEV1 value less than 80 were defined as poorly controlled asthma [7-9]. All the patients were residents of central part of Kerala. The study was conducted from January 2018-May 2018. Any patient less than seven years of age, patients with inability to perform an acceptable pulmonary function test, and subjects with active upper limb dermatitis or truncal dermatitis precluding a SPT were excluded from the study. Informed consent was obtained from all the subjects.

After detailed clinical examination, complete blood count, S. IgE levels, chest radiograph and pulmonary function test were performed. From this group, all subjects with a diagnosis of asthma as per study definition, in whom SPT was done were included in the study. SPT was done using 38 allergens in aero and food allergen panels. The antigens were obtained from Merck AllergoPharma, Germany which included two types of dust mite, five varieties of grass and pollen each, fungal antigens, dander.

Skin Prick Test Procedure

After thorough cleaning both upper limbs the test sites were marked and numbered from 1 to 38. About 0.1 mL of each allergens were dropped to the concerned sites using dropper. Then using a skin prick lancet the allergens were pricked through the skin. The area was kept undisturbed for 20 to 30 minutes. The results were read after this period. First to see the histamine and normal saline induration which were used as positive and negative controls. Then the induration corresponding to each allergen is measured and recorded. Any induration more than 3 mm was taken as significant.

STATISTICAL ANALYSIS

All the statistical analysis were done with SPSS software version 25. A Chi-square test was used to compare the data. A Spearman's rank correlation was run to determine the relationship between FEV1 and ACT values. A p-value of less than 0.05 was considered as significant.

RESULTS

A total of 187 patients meeting the inclusion criteria were included in the study. A total of 7106 SPT were done in them. Average age of the study group was 29 years. The [Table/Fig-1] shows number of patients in each age group. Almost equal number of males and females were enrolled into the study (93 male patients and 94 female patients). Average IgE level in the study population was 1099. Most of the patients showed positive reactions to multiple allergens. Allergens that had a high occurrence of sensitisation in the study subjects include house dust mite (72%), *Aspergillus fumigatus* (45%), mugwort (37% etc.,). [Table/Fig-2,3] summarises the prevalence of allergen sensitivity in the study group. Most of the patients showed erythema and induration, but formation of pseudopodia and indurations more than 15 mm were observed in 6 patients. Patients with features of inadequately controlled asthma (ACT score less than 20 and FEV1 less than 80 % predicted) showed a higher occurrence of positive reaction in the SPT as compared with those having good ACT score and FEV1 >80%. When we compared the allergen sensitivity among patients with FEV1 <80 and FEV1 >80, we found that all patients (100%, N=107) with low FEV1 having sensitivity to one or another aeroallergen as compared to 33.75% (N=27) in good FEV1 group. The allergen sensitivity among patients with good and poor ACT score also showed a significant difference. It was noticed that all 116 patients with low ACT score showed an allergen sensitivity as compared to 25.3 % (N=18) patient with good ACT score. A Chi square test was used to compare the data. All these differences were statistically significant with a p-value of less than 0.0001. A Spearman's rank correlation was run to determine the relationship between 187 patient's FEV 1 and ACT values. There was a weak, positive correlation between FEV 1 and ACT values, which was statistically not significant (r=0.065, p=0.375).

The test was extremely safe in all subjects and no serious adverse events were reported. None of the patients tested reported any adverse reaction except local itching. No systemic allergic features or anaphylactic reactions occurred and no subjects required any injectable medications in the 12 hour post-test period.

Age (years)	Frequency	Percentage
<20	72	38.50
20-40	60	32.09
>40	55	29.41

[Table/Fig-1]: Age distribution.

Sl. No.	Name of allergen	No of patients with FEV1 <80% (N=107)	No of patients with FEV1 >80% (N=80)	Total number of patients having positive reaction	Percentage
1	*Dermatophagoides farinae*	107 (100%)	27	134	71.6%
2	*Dermatophagoides pteronyssinus*	97	12	109	58%
3	*Aspergillus fumigatus*	64	21	85	45%
4	Mugwort	57	13	70	37%
5	Ragweed	47	13	60	32%
6	*Cladosporium herbarum*	45	14	59	31%
7	Cow epithelium	43	11	54	28.9%
8	Burmuda grass	40	6	46	24%
9	Thimothy grass	40	7	47	25.1%
10	Lambs quarter	34	8	42	22.4%
11	Shrimp	34	9	43	22.9%
12	Corn	33	4	37	19.7%
13	*Alternaria tenius*	32	6	38	20.2%
14	Kentucky grass	29	5	34	18.1%
15	*Rhizopus cineria*	27	2	29	15.5%
16	Cat dander	25	6	31	16.5%
17	Egg	24	4	28	14.9%
18	Milk	17	0	17	9%
19	Peanut	16	0	16	8%

[Table/Fig-2]: Frequency of allergen sensitization among study group in terms of FEV1.
Chi-square value (χ^2)=104.241, p=0.0001

Sl. No.	Name of allergen	No of patients with ACT <20 (N=116)	No of patients with ACT >20 (N=71)	Total number of patients having positive reaction	Percentage
1	*Dermatophagoides farinae*	116 (100%)	18	134	71.6%
2	*Dermatophagoides pteronyssinus*	97	0	97	51.8%
3	*Aspergillus fumigatus*	69	0	69	36.8%
4	Ragweed	47	0	47	25.1%
5	Mugwort	45	0	45	24%
6	Thimothy grass	42	0	42	22.4%
7	Shrimp	34	0	34	18.2%
8	Burmuda grass	30	0	30	16%
9	*Cladosporium herbarum*	30	0	30	16%
10	Lambs quarter	29	0	29	15.5%
11	*Rhizopus cineria*	29	0	29	15%
12	Cat dander	25	0	25	13.3%
13	Egg	24	0	24	12.8%
14	Milk	19	0	19	10.1%
15	*Alternaria tenius*	19	0	19	10.1%
16	Kentucky grass	14	0	14	7%
17	Cow epithelium	10	0	10	5%
18	Corn	10	0	10	5%
19	Peanut	10	0	10	5%

[Table/Fig-3]: Frequency of allergen sensitization among study group in terms of ACT score.
Chi-square test was used and p-value is 0.0001; A Spearman's rank correlation was run to determine the relationship between 187 patient's FEV 1 and ACT values. There was a weak, positive correlation between FEV 1 and ACT values, which was statistically not significant (rs=0.065, p = 0.375)

DISCUSSION

Atopy refers to an inherited tendency to mount IgE antibodies mediated allergic response to small amounts of common environmental protein. Common sites of manifestation of allergic disorders include upper and lower respiratory tract, skin, eyes etc., among other. Skin prick test offers the most convenient method of identifying the culprit antigen. All patients who were subjected to SPT in the present study had reaction to at least one aeroallergen tested. This is in agreement with previously published studies. Giridhar BH et al., reported 87.5%1 and Rao P et al., described 80% sensitivity to at least one antigen [10,11].

A previous study conducted in Lucknow [12] in patients with nasobronchial allergy revealed that the common offending allergens were insects (21.2%), followed by dusts (12.0%), pollens (7.8%), animal dander (3.1%), and fungi (1.3%). Another study conducted in the same geographic territory (Central Kerala) had similar results [13]. Housefly, rice grain dust and insect allergen were the common aeroallergen observed. Prawn was the most common food allergen identified. Regional variation do exists with regard to the allergens as well as pattern of clinical presentation.

Previous research has found that cockroach exposure and sensitivity are more prevalent in the inner-cities of the Northeast United States, and its effect on asthma morbidity can be greater than other household allergens, such as dust mite or pet dander [14,15]. Haselkorn T et al., recognized predictors of severe exacerbations in children and found that patients with 3 to 4 allergic triggers (from pollen, dust, pets and mould) were at 2 fold greater risk of future asthma exacerbation in comparison to those with no allergic triggers [16].

Our study revealed significant number of patients with inadequately controlled asthma have sensitization to grass pollens like mugwort (*Artemisia vulgaris*) and ragweed (*Ambrosia*). But previous many studies have shown that pollen such as Artemisia vulgaris and *Ambrosia artemisifoliais* are commonly associated with upper airway allergies. These two plants got a larger sized allergen compared with other aeroallergens including house dust mites. Due to its size and aerodynamic properties, they are mainly deposited in the upper airway and induces local inflammatory or pathological changes [17,18]. An inadequately controlled upper airway allergy could be led to a lower airway changes would be a possible explanation. The enzymatic activity of *Dermatophagoides pteronyssinus* mites seems to be important in the pathogenicity of lower airway and systemic inflammations [19].

We identified in addition to HDM and grass pollens fungal group of allergens also poses an important role in causing allergy and it affects the therapy also. Fungal agents according to their spore sizes cause either upper airway or lower airway allergy or sometimes both [20]. The major fungal agents detected in our study were *Aspergillus, Cladosporum, Alternaria and Rhizopus.*

Almost all patients were having one or another form of allergen sensitivity. As per GINA guidelines for asthma control allergen immune therapy against house dust mite has been recommended along with pharmacotherapy. Apart from conventional management strategies a small subset of these patients may benefit from immunotherapy to fungal agents and grass pollens too, apart from house dust mite. So efforts must be taken to identify allergen sensitivity in those patients with inadequately controlled asthma actively and an individualised allergen desensitisation protocol must be considered in each patient along with pharmacotherapy. Proper weed and environmental control and inclusion of these agents too in the immuno therapy should be practised routinely.

LIMITATION

Considering the importance of aeroallergens in the pathogenesis of asthma, the present study used a limited number of aeroallergen panel than previously conducted similar studies. The allergen panel did not have insect allergens which might have implications in the geographic location of the study. The study did not encounter even a single case of systemic allergic reaction. This probably due to the fact that the allergens used in current study has substantially more purified allergens. Further, SPT results were not correlated with specific IgE allergens by RAST.

CONCLUSION

House dust mite, fungal allergens and grass pollens were the common allergen sensitisation identified in subjects with poorly controlled asthma in the present study. A correlation was seen

between inadequately controlled asthma and sensitisation to multiple aeroallergens. So vigorous allergen screening, weed control and allergen immunotherapy must be included in the management protocol of asthma.

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ANNEXURE 1

ACT Questionnaire used.

1. **In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?**
   1) All of the time 2) Most of the time 3) Some of the time 4) A little of the time 5) none of the time
2. **During the past 4 weeks, how often have you had shortness of breath?**
   1) More than once a day 2) Once a day 3) 3 to 6 times a week 4) Once or twice a week 5) Not at all
3. **During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, and shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?**
   1) 4 or more nights a week 2) 2 to 3 nights a week 3) Once a week 4) Once or twice 5) Not at all
4. **During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?**
   1) 3 or more times per day 2) 1 to 2 times per day 3) 2 or 3 times per week 4) Once a week or less 5) Not at all
5. **How would you rate your asthma control during the past 4 weeks?**
   1) Not controlled at all 2) Poorly controlled 3) Somewhat controlled 4) Well controlled 5) Completely controlled