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A cross-sectional study of skin prick test to *Aspergillus fumigatus* antigen in asthmatic patients seen at a tertiary healthcare center

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Abstract:

INTRODUCTION: Asthma is a significant public health problem. The severity of asthma varies from patient to patient and the reasons for this are not fully understood. Atopy is known to play an important part in the pathogenesis of asthma. Sensitization to aeroallergens like house dust mite, animal dander from pets and environmental fungi are evaluated in asthmatics. Severe asthma seems to be associated to environmental fungi with sensitization especially to *Aspergillus* species.

AIMS AND OBJECTIVE: The study aimed at determining the prevalence of Cutaneous Sensitization to *Aspergillus* species by Skin Prick Test (SPT) in moderate- severe asthmatics.

MATERIAL AND METHODS: This study was done on 205 clinically diagnosed asthmatic patients, between September 2012 and August 2013. SPT and spirometry was done in all subjects along with a detailed history.

RESULTS: The prevalence rate of *Aspergillus* sensitized patients is 59.5%. Observations of this study also suggest that the severity of asthma is more in *Aspergillus* sensitized patients when compared to non-sensitized patients and the duration of asthma was more in Non sensitized. There was no significant association between AEC, total IgE levels and *Aspergillus* species culture positivity in *Aspergillus* sensitized patients. *Aspergillus terreus* was the predominant fungal isolate from both SPT positive and negative patient. There was no significant correlation of fungal culture with SPT.

CONCLUSIONS: High levels of *Aspergillus* sensitization is seen in south Indian subjects and is associated with greater severity and shorter duration of asthma.

Keywords:

Aspergillus, *Aspergillus fumigatus*, asthma, skin prick test

Introduction

Asthma is a significant health problem affecting about 2% of the adult population in India.^[1,2] Sensitization could happen to allergens like pollen grains, dust mites, animal dander, and molds; among which severe asthma seems to be strongly associated with atopy, especially to mold

allergens like *Aspergillus fumigatus*.^[3,4] *Aspergillus* is one of the most common molds and it represents about 0.1%–22% of the total air spores sampled. Only few among the 250-odd species of *Aspergillus* are pathogenic which cause various forms of disease in humans.^[3]

Allergic bronchopulmonary aspergillosis (ABPA) is a spectrum of disease characterized by chronic asthma,

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recurrent pulmonary infiltrates and bronchiectasis. It is an immunologic pulmonary disorder, and the initial step in the pathogenesis is the *Aspergillus* hypersensitivity (AH). AH is detected by cutaneous hypersensitivity to *Aspergillus* antigens by skin prick test (SPT). Lung fibrosis and bronchiectasis are the debilitating end stage manifestations with very poor clinical outcome. Hence, ABPA has to be diagnosed early for better outcomes.^[5]

The association between *A. fumigatus* and ABPA has been now well established. This makes it imperative to know the frequency of sensitization to *Aspergillus* antigens in all asthmatic patients. The SPT can help in detecting the debilitating illness at its early stages and reduce the morbidity.^[3] Many patients with ABPA may be minimally symptomatic or asymptomatic; therefore, a high index of suspicion should be maintained while managing any patient with bronchial asthma whatever the severity or the level of control. This underscores the need for routine screening of all patients with asthma with an *Aspergillus* skin test.^[3]

In Indian population, the prevalence of *Aspergillus* cutaneous Type 1 sensitization is not known. A few studies from North India report its prevalence in asthmatic patients to vary between 28% and 50%.^[4] A study of 564 asthmatic patients from India reported *Aspergillus* sensitization in 223 (39.5%) and documented ABPA in 126 (22.3%) of these patients.^[6] Despite such a high prevalence of Type 1 *Aspergillus* cutaneous hypersensitivity reported from hospital-based studies from North India there are no such reports from South India till date. It is, therefore, still under-recognized and underdiagnosed in our country. Hence, the present study was undertaken to screen asthmatic patients for *Aspergillus* sensitization by cutaneous hypersensitivity testing to identify those at risk for developing ABPA and establish a baseline data on *Aspergillus* sensitization in asthmatic patients seen at a tertiary care center in south India.

Materials and Methods

This was a cross-sectional study conducted on 256 patients attending Chest Medicine Out-Patient Department of St John's Medical College (SJMC) with a clinical diagnosis of asthma. The study period was between September 2012 and August 2013. The study was approved by the Ethics committee of SJMC.

Patients

Adult patients with a clinical diagnosis of asthma were included in the study. The following were the exclusion criteria: (i) Patients in acute exacerbation; (ii) chronic obstructive pulmonary disease, congestive cardiac failure, pulmonary tuberculosis, alpha-1 antitrypsin

deficiency; (iii) Pregnant patients; (iv) Patients who could not be kept off antihistamines and leukotriene antagonists for 1 week.

Clinical categorization of patients

A detailed clinical history was taken after a clinical diagnosis as mild, moderate, or severe asthmatics was made by the pulmonologist. Demographic details of age, sex, address (rural/urban), occupation, duration and age of the onset of asthma, history suggestive of allergic rhinitis, eczema, a family history of asthma (defined as positive if at least one first-degree relative, such as a parent, sibling, or child had asthma) and a history of symptoms such as cough, expectoration, wheeze, dyspnea, chest tightness, and sputum plug expectoration were obtained. Medication history if any was recorded.

After obtaining a written informed consent, the patients were advised to undergo a series of investigations which included: spirometry, total and differential leukocyte Count (total count, differential count), absolute eosinophil count (AEC), SPT, radiological investigations such as Chest X-ray and or computed tomography-scan and total immunoglobulin E (IgE).

Spirometry was performed at the pulmonary function test laboratory by a trained personnel and interpreted by the chest physician as mild obstruction (forced expiratory volume 1 [FEV1] or peak expiratory flow [PEF] $\geq 80\%$ predicted), moderate obstruction (FEV1 or PEF 60%–80% predicted), and severe obstruction (FEV1 or PEF $\leq 60\%$ predicted).^[7]

Assessment of the severity of asthma was done according to the 2002 Global Initiative for Asthma recommendations, and the patients were categorized as mild, moderate, and severe asthmatics.^[8]

Skin prick test

SPT was performed on all those asthmatics found to be fit to undergo the test. Emergency kit for resuscitation was kept at the site of performance of the SPT. Patients on antihistamines underwent SPT 1 week after discontinuation of the drugs. The panel of allergens included were: *A. fumigatus*, *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus versicolor*, *Parthenium hysterophorus*, Spider web dust, Cockroach, Mite *Dermatophagoides pteronyssinus*, Mite *Dermatophagoides farinae*, and *Cynodaidactylon*. Histamine dihydrochloride (10 mg/ml or 0.1%) was used as positive control and buffered normal saline as negative control.

Sputum microscopy and culture

Sputum samples from moderate to severe asthmatic patients were collected in a sterile leak-proof container.

The sputum samples were subjected to direct microscopy using 10% potassium hydroxide and culture on Sabouraud dextrose agar containing chloramphenicol and cycloheximide (0.5 mg/L). The culture tubes were incubated both at room temperature (25°C) and 37°C. Cultures yielding mold form of fungi were further identified and speciated based on macroscopic and microscopic colony morphology. Microscopic examination included a lactophenol cotton blue tease mount and slide culture technique.

Statistical analysis

All the statistical analysis of data was performed using SPSS version 18.0 (PASW Statistics for Windows SPSS Inc, Chicago, USA). Data was presented descriptively as mean (standard deviation), median (interquartile range) or number (percentage). The normalcy of distribution was evaluated using the Shapiro–Wilk test. The differences between continuous variables were analyzed using the Mann–Whitney U-test (for median values) or Kruskal–Wallis test if not normally distributed and Independent Student's *t*-test (for means) if normally distributed. The differences between categorical variables were analyzed using the Chi-square test. Values of $P < 0.05$ were considered statistically significant.

Results

During the study, a total of 256 patients were included, of whom SPT was done in only 205 (99 females and 106 males) patients [Figure 1].

The epidemiologic, clinical, and laboratory features of 205 asthmatic patients are summarized in Table 1.

Out of 205 asthmatic patients, 181 (88.3%) patients underwent spirometry, of whom 33 (18%) patients had mild obstruction, 74 (41%) patients had moderate obstruction and 74 (41%) patients had severe obstruction. Twenty-four (12%) patients could not undergo spirometry due to cough or poor effort during the study visit; they had a previously documented spirometry showing obstruction with reversibility in the past 1 year.

All patients with a positive result on SPT for any of the *Aspergillus* allergens were considered SPT positive.

Of the 205 patients, 122 (59.6%) were SPT positive and 83 (40.4%) were SPT negative.

All 122 patients showed immediate hypersensitivity to one or more *Aspergillus* antigens; 66 (32.2%) patients were sensitive to *A. fumigatus*, 51 (25%) to *A. flavus*, 50 (19.5%) to *A. niger*, and 43 (21%) to *A. versicolor*. 114 (93.4%) patients (Group A) out of 122 were positive to at least one of other aeroallergens used

Table 1: Clinical profile of the study group

Variables	Study group n=205
Sex - Females	99 (48%)
Males	106 (52%)
Age in years, mean (SD)	38 (12.75)
Duration of asthma (yrs)	7 (1-15)
Median (IQR)	
Cough	193 (94%)
Wheeze	183 (89%)
Allergic rhinitis	174 (85%)
Eczema	31 (15%)
Conjunctivitis	53 (26%)
Night awakening	105 (51%)
Mucus plugs in sputum	126 (61%)
Family history of asthma	127 (62%)
Day symptoms	
≤2 week ⁻¹	74 (36%)
>2 week ⁻¹ , <1 day ⁻¹	103 (50%)
Daily	28 (14%)
Night-time symptoms	
≤2month ⁻¹	82 (40%)
>2month ⁻¹	103 (50%)
Daily	20 (10%)
Oral steroids	38 (19%)
Inhaled steroids use	98 (48%)

Table 2: Distribution of positivity by SPT to *Aspergillus* and other aeroallergens in the study group

SPT POSITIVE n=122		SPT NEGATIVE n=83	
Group A	Group B	Group C	Group D
114 (93%)	8 (7%)	69 (83%)	14 (17%)

Group A-SPT positive to *Aspergillus* antigen + one or more aeroallergen, Group B-SPT positive to only *Aspergillus* antigen, Group C- positive to at least one of other aeroallergens used but negative to *Aspergillus* antigen. Group D - negative for both *Aspergillus* and other aeroallergens

other than *Aspergillus*. Eight patients (Group B) were reactive solely to a single *Aspergillus* allergen. Out of 83 SPT-negative patients, 69 (83.1%) patients (Group C) were positive to at least one of other aeroallergens used. Fourteen (17%) (Group D) were negative for both *Aspergillus* and other aeroallergens [Table 2].

A number of variables were compared [Table 3] between SPT-positive and SPT-negative patients. *Aspergillus* skin test reactivity was related to two of these variables which were significantly lower in SPT-positive patients as compared to SPT-negative patients: (i) History of the duration of asthma ($P = 0.004$). (ii) FEV₁ in 1 min ($P = 0.04$).

Comparison of skin prick test with the severity of lung function by spirometry

Spirometry was done on the study day in 181 patients. SPT-positive patients had much more severe airway obstruction as compared to SPT-negative patients

Table 3: Clinical correlation between SPT positive and SPT negative patients

	SPT Positive (122)	SPT Negative (83)	p
Age in years, median (IQR)	38.5 (28-48)	35 (28-44)	0.133
Duration of asthma (yrs.)	4(IQR-1, 10)	5(IQR-2,15)	0.004
Cough	117 (95.5%)	76 (91.6%)	0.194
Wheeze	107 (87.7%)	76 (91.6%)	0.38
Allergic rhinitis	69 (83.1%)	105 (86.1%)	0.565
Eczema	10 (12%)	21 (17.2%)	0.311
Conjunctivitis	17 (20.5%)	36 (29.5%)	0.147
Night awakening	43 (51.8%)	62 (50.8%)	0.890
Mucus plugs in sputum	53 (63.9%)	73 (59.8%)	0.562
Family history of asthma	48 (58.5%)	79 (64.8%)	0.369
Day symptoms			0.93
≤2 week ¹	43 (35.2%)	31 (37.3%)	
>2 week ¹ , <1 day-1	60 (49.2%)	43 (51.8%)	
Daily	19 (15.2%)	9 (10.8%)	
Night-time symptoms			0.43
≤2month ¹	47 (38.5%)	35 (42.2%)	
>2month ¹	62 (50.8%)	41 (49.4%)	
Daily	13 (10.7%)	7 (8.4%)	
Oral steroids	14 (16.9%)	24 (19.7%)	0.612
Inhaled steroids	36 (43.4%)	62 (50.8%)	0.295
*Spirometry:			0.015
Mild obstruction	14 (42.4%)	19 (57.6%)	
Moderate obstruction	53 (71.6%)	21 (28.4%)	
Severe obstruction	47 (63.5%)	27 (36.5%)	
Total count Median (IQR)	8200 (7000-9450)	8400 (6800-10125)	0.45
AEC (Mean)	276	248	0.219

*Spirometry on study date available for 181 subjects

[Figure 2]. Significantly more number of patients with moderate (71%) to severe obstruction (63%) on spirometry were SPT positive ($P = 0.01$).

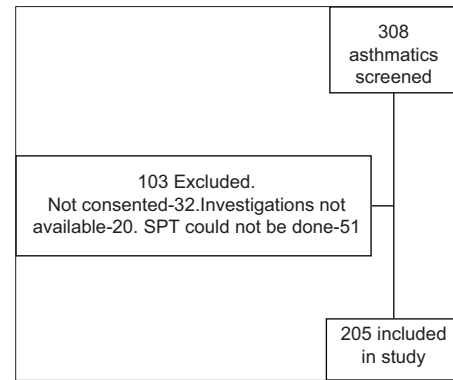
Fungal culture

Sputum samples from 96 moderate-to-severe asthmatic patients were subjected to fungal culture. Forty-two samples yielded mold forms of which *Aspergillus* species accounted for 35 isolates, *Penicillium* species 3, *Cladosporium* species 2 and *Absidia corymbifera* and *Epicoccum* species one each. Other fungal isolates were 9 of *Candida* species. Among *Aspergillus* species, *Aspergillus terreus* (25) was the predominant one followed by *A. flavus* (5), *A. niger* (4), and *A. fumigatus* (1).

Comparison of fungal culture and skin prick test

Both fungal culture and SPT results were available in 85 patients.

Of these 85 patients, 63 (74%) patients were SPT positive for any of one or more of the *Aspergillus* allergens and 22 (26%) patients were SPT negative.

**Figure 1: Study design and patients flow**

Among the 63 SPT-positive patients, 27 (43%) yielded *Aspergillus* species on culture, 5 (8%) yielded molds other than *Aspergillus* species and *Candida* was isolated in 4. Twenty-seven SPT-positive patients yielded no fungal growth on culture.

Among the 22 SPT-negative patients, 8 (36%) patients grew *Aspergillus* species and 1 (5%) patient yielded *Candida*. 13 (59%) of SPT-negative patients were culture negative.

Correlation of *Aspergillus* species with skin prick test

Twenty-seven (43%) SPT-positive patients yielded the following *Aspergillus* species:

A. terreus (19), *A. flavus* (5), *A. niger* (2) and *A. fumigatus* (1). The *Aspergillus* species isolated in 8 (36%) of SPT negative patients were: *A. terreus* (5), *A. flavus* (1) and *A. niger* (2). Five samples yielded *Aspergillus* species correlating with the specific *Aspergillus* allergen positive result on SPT. This included three isolates of *A. flavus* and 1 isolate each of *A. fumigatus* and *A. niger*. In this study, we found that there was no significant correlation between sputum fungal culture among SPT-positive and -negative asthmatic patients.

Discussion

Asthma is a common clinical condition. Although most asthma patients have mild symptoms, a minority of patients suffer from severe symptoms requiring multiple hospital admissions. Severe asthma seems to be strongly associated with atopy especially to mold allergens. Among patients with persistent asthma requiring specialist's referral, 20%–25% has skin test reactivity to *Aspergillus* or other fungi. *A. fumigatus* plays an important role as an allergen in these patients.^[9] The close link between the mold *Aspergillus* and asthma makes it necessary to establish the frequency of *Aspergillus*

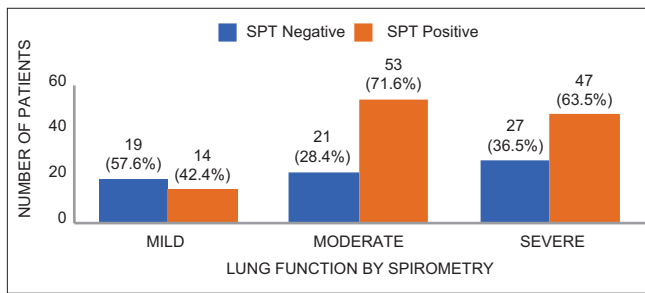


Figure 2: SPT and Lung function by spirometry comparison

sensitization in asthmatic subjects in each geographic region.^[10] In India, population prevalence of *Aspergillus* cutaneous Type 1 sensitization is not known, but few studies from North India report its prevalence in asthmatic patients to vary between 28% and 50%.^[6] The association between *A. fumigatus* and ABPA has been now well established. The SPT can help in detecting the debilitating illness at its early stages and help in modifying management protocols in these patients.^[3]

The literature search revealed no reported data on a screening test such as SPT for *Aspergillus* in asthmatic patients from South India; hence, we undertook this pilot study as the first step to assess the prevalence of *Aspergillus* sensitization in asthmatic patients seen at our hospital.

SPT was chosen instead of the intradermal test, as SPT is already a standardized and established routine diagnostic test for screening asthmatic patients for sensitization to different aeroallergens at our center.

The mean age of our patient population is slightly higher compared to the study by Aggarwal *et al.* from North India which reported a mean age of 34 years in their study group.^[12]

Analyzing the clinical features, the median duration of asthma in the study group was found to be 7 years as compared to 5 years duration reported from the North.^[12] Cough was the predominant symptom in 193 (94%) of the patients. This was much higher than the North Indian studies by Aggarwal *et al.* (82%) and Prasad *et al.* (63.5%).^[11] Wheeze was noted in 183 (89%) and was comparable to the study by Aggarwal *et al.* (84%).^[12] This was probably because our population had more number (82%) of patients with moderate-to-severe airway obstruction.

Majority of the patients 174 (85%) had associated allergic rhinitis. Other allergic manifestations such as eczema and conjunctivitis were seen in 31 (15%) and 53 (26%), respectively. This association of allergic rhinitis among our patient was found to be higher as compared to that by Prasad *et al.* 50.4%. Association of eczema and conjunctivitis was comparable to other studies.^[11]

One hundred and twenty-six (61%) patients had a history of mucus plugs in sputum. This is significantly higher in comparison to a study by Prasad *et al.* who found an association in only 2.9% of his patients. More than half of our patients, i.e., 127 (62%) had a family history of asthma which is almost comparable to findings of the study by Prasad *et al.*^[11] Out of 205 patients our study included a higher number of patients 148 (82%) with moderate-to-severe airway obstruction when compared to the study by Maurya *et al.* with only 43% of moderate-to-severe asthmatic patients.^[9]

Of the 205 patients who underwent SPT, 122 (59.5%) were positive to *Aspergillus* allergens. Of these 122 patients, 59 (48.3%) were reactive to more than one *Aspergillus* allergens. 114 (93.4%) patients out of 122 were also positive to at least one of the other aeroallergens used. Of the 83 (40.4%) SPT-negative patients who did not react to *Aspergillus* allergens 69 (83.1%) patients were atopic based on their reaction to other aeroallergens. Based on SPT, our study group had more atopics when compared to a study conducted by Maurya *et al.*, in which 22 (21%) patients were positive for both common aeroallergens including *Aspergillus* antigens and 75 (71.4%) patients were SPT negative for *Aspergillus* allergens of which 49 (65.3%) were positive for other aeroallergens.^[9]

In our study, 122 of the 205 patients were SPT positive for *Aspergillus* species with a prevalence of 59.5%. A study by Agarwal *et al.* is comparable which showed a prevalence of 52.5% for AH in bronchial asthma patients by intradermal test method using indigenous antigens.^[12]

In our study, there is a higher prevalence rate of AH as the SPT sensitivity depends on the type of population included in the study. In our study, more number of patients (82%) was with moderate-severe airway obstruction. The SPT sensitivity also depends on the nature of the antigen used. In this study commercially, available antigen extracts have been used to perform the test. It was also observed that most of our patients were reactive to more than one type allergens by SPT. Most centers, including ours use crude antigen for the diagnosis of fungal sensitization.

These antigens frequently cross-react and may overdiagnose the prevalence of fungal sensitization in asthma. Furthermore, there is no standard method to assess the accuracy of the diagnosis of fungal sensitization in asthmatics. However, it has been shown in many studies that intradermal tests are more sensitive than SPTs. The meta-analysis by Aggarwal revealed that the prevalence of AH in bronchial asthma was higher in studies with an intradermal test versus studies with a prick test (28.7% vs. 24.8%, $P = 0.002$), but did not vary with the type of antigen used (indigenous or

commercial).^[13] Geographical location has an impact on the local fungal milieu. This can, therefore, affect the sensitization of an individual and have a bearing on SPT results.

Even though SPT was used in our study still there was a higher prevalence rate of AH in our study probably because ours is a tertiary care center most of the study population (82%) were of moderate-to-severe asthma.

The clinical and radiologic picture of ABPA often simulates pulmonary tuberculosis and causes a diagnostic dilemma in areas with high tuberculosis prevalence. These patients often receive anti tuberculous therapy (ATT) while lung damage continues to occur.^[6] During our 1-year study, we had four ABPA patients three of whom had received ATT without any benefits.

Sputum samples from 96 moderate-to-severe asthmatic patients were subjected to fungal culture. Mold forms were isolated from 42 samples of which *Aspergillus* species accounted for 35 isolates, *Penicillium* species 3, *Cladosporium* species 2 and *A. corymbifera* and *Epicoccum* species one each.

The predominant *Aspergillus* isolates in our study was *A. terreus* (71.4%) followed by *A. flavus* (14.2%), *A. niger* (11.4%), *A. fumigatus* (2.8%). In the study reported by Kumar *et al*, *A. fumigatus* was the most commonly isolated *Aspergillus* species (3.4%), followed by *A. niger* (1.5%) and *A. flavus* (0.9%).^[14]

None of the studies in India have so far reported the isolation of *A. terreus*.

Conclusion

The prevalence of SPT to *Aspergillus* allergen in the study population of asthmatic patients was found to be 59.5% which is much higher than that reported by other studies.

SPT positive subjects are likely to have more severe airway obstruction and shorter duration of symptoms. Hence all asthmatics need to be screened to detect this population early. Even in resource poor settings an SPT can be performed to identify asthmatic subjects who need further evaluation.

A. terreus is the predominant species isolated in sputum culture in both SPT positive and SPT negative patients.

Limitations

We did not include specific *A. terreus* allergen in our panel of allergens and hence *A. terreus* culture results could not be correlated with SPT.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Agarwal R, Gupta D. Severe asthma and fungi: Current evidence. *Med Mycol* 2011;49 Suppl 1:S150-7.
2. Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, Jindal SK, *et al*. Prevalence and risk factors for bronchial asthma in Indian adults: A multicentre study. *Indian J Chest Dis Allied Sci* 2006;48:13-22.
3. Agarwal R. Allergic bronchopulmonary aspergillosis. *Chest* 2009;135:805-26.
4. Agarwal R, Noel V, Aggarwal AN, Gupta D, Chakrabarti A. Clinical significance of *Aspergillus* sensitisation in bronchial asthma. *Mycoses* 2011;54:e531-8.
5. Agarwal R, Singh N, Gupta D. Pulmonary hypertension as a presenting manifestation of allergic bronchopulmonary aspergillosis. *Indian J Chest Dis Allied Sci* 2009;51:37-40.
6. Bedi RS. Allergic bronchopulmonary aspergillosis: Indian perspective. *Indian J Chest Dis Allied Sci* 2009;51:73-4.
7. Miller MR, Crapo R, Hankinson J, Brusasco V, Burgos F, Casaburi R, *et al*. General considerations for lung function testing. *Eur Respir J* 2005;26:153-61.
8. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, FitzGerald JM, *et al*. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008;31:143-78.
9. Maurya V, Gugnani HC, Sarma PU, Madan T, Shah A. Sensitization to *Aspergillus* antigens and occurrence of allergic bronchopulmonary aspergillosis in patients with asthma. *Chest* 2005;127:1252-9.
10. Hendrick DJ, Davies RJ, D'Souza MF, Pepys J. An analysis of skin prick test reactions in 656 asthmatic patients. *Thorax* 1975;30:2-8.
11. Prasad R, Garg R, Dixit R. A study on prevalence of allergic bronchopulmonary aspergillosis in patients of bronchial asthma. *Internet J Pulm Med* 2012;9:6-11.
12. Agarwal R, Gupta D, Aggarwal AN, Behera D, Jindal SK. Allergic bronchopulmonary aspergillosis: Lessons from 126 patients attending a chest clinic in North India. *Chest* 2006;130:442-8.
13. Agarwal R, Aggarwal AN, Gupta D, Jindal SK. *Aspergillus* hypersensitivity and allergic bronchopulmonary aspergillosis in patients with bronchial asthma: Systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2009;13:936-44.
14. Kumar A, Sahu RC, Subbannayyar K, Jyothirrata, Rau PV, Shivananda PG. Prevalence of antibodies to aspergilli in bronchial asthmatics. *J Postgrad Med* 1989;35:20-3.

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