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ORIGINAL ARTICLE

Seroprevalence of specific immunoglobulin G antibodies against aspergillus fumigatus among chronic persistent asthma

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ABSTRACT

Background: Aspergillus fumigatus (AF) is responsible for 90% of human infections. The lung is the predominate site of infection. It is able to colonize in respiratory tract of asymptomatic population and changed clinical features from noninvasive to invasive according to immuncomponent state of individuals. The aim of the present study was to determine the frequency of AF immunoglobulin (IgG) antibodies among chronic persistent asthmatic patients in Tehran.
Materials and methods: Chronic asthmatic patients, aged 15-60 years, were sequentially enrolled from out-patient respiratory clinics. The specific AF IgG antibodies, white blood cells count, peripheral eosinophil count, and immunoglobulin E antibodies were also measured.
Results: Totally, 497 chronic stable asthmatic patients were studied with the mean age of 45 years. Aspergillus IgG antibodies were detected in 285 subjects (57.3%). The mean (±standard deviation) serum IgE level was 257.22± 338.07IU/mL (ranged from 3.9 to 4333 IU/mL). Chest X -ray abnormalities were noted in 25 patients (<0.01%).
Conclusion: AF IgG antibodies were observed in more than half of the chronic stable asthmatic patients. Therefore, significant colonization of aspergillus fumigatus occurred in asthmatic patients without prominent clinical symptoms.

Keywords: *Aspergillus fumigatus, Asthma, Seroprevalence*.
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INTRODUCTION

The genus mold Aspergillus *(A)* is ubiquitous of the airborne saprophytic fungi, occur worldwide, and is the fourth leading cause of hypersensitivity respiratory disorders (1). The aspergillosis occurs predominantly in the lung while the severity of clinical conditions probably depends on the quantity and virulence of the inhaled mold and the status of the host defense. Aspergillus fumigatus (AF) is one of a few pathogens for human from over 200 species of Aspergillus and is responsible for over 90% of human infections (2). It is able to induce various pulmonary disorders such as allergic aspergillosis, colonizing aspergillosis and other invasive diseases (3). Environmental surveys indicate that all humans inhale at least several hundred AF conidia per day (4), but disease is rare. It readily transmits infection to the patients with various forms of immunodeficiency, receiving supraphysiologic adrenal glucocorticoides and affects individuals with intact immune system as well (5,6). The Aspergillus can induce and give rise to sensitization in asthmatic patients as an allergen

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(7,8), however, the rate of colonizing aspergillosis as saprophyte in chronic persistent asthmatic patients in urban of Tehran is unknown.

The aim of the present study was to ascertain the frequency of seroprevalence of specific AF IgG antibodies among chronic persistent asthmatic patients in Tehran and to determine status of frequency of AF in a selected allergic asthmatic population.

PATIENTS and METHODS

This cross-sectional study was conducted in Loghman-Hakim hospital affiliated to Shahid Beheshti Medical University. The hospital serves both as a general hospital and tertiary referral center for asthma and respiratory disorders, and especially covered patients from south of Tehran. The study was designed to identify serologically the frequency of colonization of AF in chronic stable asthmatic patients and allergic asthma subgroup. The sample population was sequentially enrolled at subsequent visit to the outpatient chest clinics. The number of outpatient visits for respiratory diseases are estimated to be over 3500 per year. The severity of asthma was categorized based on forced expiratory volume in the first second (FEV1), and the diurnal variability in Peak Expiratory Flow Rate (PEFR) (mild persistent FEV1=>80%, moderate FEV1=60-80%, severe FEV1<60%) (9). Therefore, their categorizations were as follow: mild 28%, moderate 34% and severe 38%.

The following baseline inclusion criteria were applied: age 15 to 60 years, peak expiratory flow>15%, and diurnal variation of peak expiratory flow rate >20% (10,11). The exclusion criteria were tuberculosis, bronchiectasis, interstitial lung fibrosis, use of immunosuppressive drugs, cancer, leukemia, and chronic obstructive pulmonary disease (COPD). Then, all subjects were arranged for chest X-ray and pulmonary function testing. Totally, 497 subjects fulfilled the desired criteria from 2003 to 2004.

Total immunoglobulin E antibodies (Padtan Elm, Iran), AF IgG antibodies (IBL, Hamburg, Germany) and complete blood cell counts were performed according to the manufacturers' recommendations. Specific IgG antibodies against AF were determined by enzyme-linked immunosorbent assay (ELISA) method. The cut-off point value of the specific IgG was 12U/ml in our laboratory with (mean±20 percentage). The cut-off point of allergy levels for the total IgE ELISA was >200IU/ml and eosinophilia was defined >5% (12,13).

All patients were requested to complete an informed consent. Data were analyzed by SPSS for Windows (version 13, SPSS Inc., USA) and student t-test, one-way ANOVA, and Tukey, and chi-square tests were used, when appropriate. For all tests, significance was defined as $p<0.05$.

RESULTS

The study population included 282 (56.7%) females and 215 (43.3%) males with a mean age (± standard deviation) of 34.1±12.5 years.

The mean level of AF IgG antibodies was 27.8±39.7U/ml. Totally, 285 (57.3%) of patients were positive for AF IgG antibodies. The total serum IgE level ranged between 3.9 and 4333IU/mL with a mean of 257.2±338.1IU/ml. The mean white blood cell count (WBC) was 7410.9±2159.2/mm^3, however, the mean peripheral eosinophilia percentage was 3.2±2.6 (a range, 0-21%). Totally, 22% of subjects showed eosinophilia. The total duration of illness was 5.9±1.9 years (a range, 3-11 years).

Abnormalities in chest radiographs were noted in 25 patients (<0.01%). Transient pulmonary infiltrates were present in 7 patients. However, chest abnormal subgroup did not meet defined criteria of allergic brochopulmonary aspergillosis (eosinophilia; 2.1±0.9 percent; a range, 1-4% and mean IgE antibody 72.9±6.7IU/ml, a range, 2-176IU/ml). The correlation between total IgE and

specific AF IgG antibodies was weakly positive, however, it did not reach statistically significant level (r=0.03, p=0.49).

Of 497 subjects, 201 (98 males and 103 females) and 296 (117 males and 176 females) were assigned in allergic and non-allergic subgroups, respectively. AF IgG antibodies were more commonly found in allergic patients when compared with non-allergic subjects (60.7% vs. 55.1%, NS). The mean total IgE level was significantly higher in allergic subgroup than non-allergic patients (p<0.001), meanwhile, significant differences were observed between groups based on WBC count (p<0.03) and eosinophilia (p<0.001). Table 1 summarizes characterization of variables in both subgroups.

One–way ANOVA revealed non-significant differences between subgroups of asthma severity according to AF IgG antibodies (p=0.9).

Table 1. *Characterization of variables in allergic and non-allergic subgroups of chronic stable asthmatic patients*

	Allergic subgroup	Non-allergic subgroup	P
Number of patients	201	296	
Immunoglobulin E (IU/ml)	532.8±388.5	70.1±54.3	0.001
AF IgG antibody level (U/ml)	28.6±41.4	27.2±38.6	NS
Eosinophilia (%)	3.7±2.9	2.9±2.2	0.001
White blood cell (/mm^3)	8358.2±9226.5	7154.6±2159.2	0.03
Seroprevalence of AF	122 (60.7%)	163 (55.1%)	NS
Duration of asthma (year)	5.9±2.1	5.8±1.9	NS

AF: Aspergillus fumigatus

DISCUSSION

Results revealed a highly significant positive AF IgG antibodies level among among chronic persistent asthmatic subjects (57.3%). This is in accordance with a number of prior studies, however, different levels of Aspergillus in the airborne of geographic areas tightly contribute to susceptible conditions of growing fungi spore such as rural, urban and industrial environments (14). AF can be colonized as saprophytic in respiratory tract of human and presents in a variety of respiratory disorders such as asymptomatic (colonizing respiratory tract), allergic, and invasive aspergillosis. Tehran as the capital of Iran, has a quite high concentration of particulates in ambient air, diesel exhaust particulates and industrial pollutants (15). Exposure to components of air pollution has been strongly associated with adverse effects on respiratory health. Susceptible subjects show enhanced airway responses to inhaled allergens (16). This condition predisposes subjects to bronchial hyperresponsivness and may lead to bronchial asthma (17,18). People who live in urban areas tend to be affected more by allergic respiratory diseases (19). The saprophytic colonization of Aspergillus species are also facilitated in these environments and occur among asthmatic population (20).

The noticeable frequency of AF may be also coinciding with the prevalence of bronchial asthma in populations. It is reported in a wide range of 2-30% of adults in general population (21). Moreover, the changes of environmental factors and lifestyle have been implicated to increase the prevalence of asthma and allergy in developed countries (22).

On the other hand, the average duration of asthma, eosinophilia, and IgE antibody level were significantly higher among selected asthmatic population. Prior investigators have indicated that aspergillosis occurs more commonly in asthmatic patients who have moderate to severe airway obstruction, significantly longer duration of illness, higher mean total leucocyte count, absolute peripheral eosinophilia, elevated serum IgE level and oral steroid intake (13,23).

The present study confirms that the seroprevalence of AF is higher in allergic asthmatic

patients. The prevalence of respiratory allergy to fungi spores is estimated 20-30% of atopic individuals (24). At least two thirds of asthmatic patients are atopic with skin reactivity to common allergens (25).

In conclusion, a quite high seroprevalence of AF was noted among chronic persistent asthmatic subjects in Tehran. This could be in part explained by colonization of AF in respiratory tract of asthmatic patients. The frequency distribution of AF antibodies was considerable high in both subgroups of allergic and non-allergic asthmatic subjects.

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