ORIGINAL ARTICLE

The role of molds in the relation between indoor environment and atopy in asthma patients

Emel Ceylan[1], Sibel Doruk[2], Sebahat Genc[3], Ayşe Aydan Ozkutuk[4], Fisun Karadag, Gul Ergor[5], Bahriye Oya Itil[6], Arif Hikmet Cımrın[6]

Departments of Pulmonary Medicine, [1]Adnan Menderes University, Aydın, [2]Gaziosmanpasa University, Tokat, [3]Mustafa Kemal University, Hatay, [4]Departments of Microbiology and Clinical Microbiology, [5]PublicHealth, [6]Pulmonary Medicine, Dokuz Eylül University, Izmir, Turkey

Background: The effect of mold fungi to allergic sensitization is not well-known. We aimed to evaluate the role of molds in the relation between indoor environment and atopy in asthmatics. **Materials and Methods:** The air samples obtained from 66 stable asthmatics and 35 control subject's houses were sprayed into Sabouraud dextrose agar. Allergy skin testing were performed in both groups. The temperature and humidity of each house were measured. **Results:** The incidence of atopy was similar in cases (59.1%) and controls (51.4%). The average amount of mold was 35.9 CFU/m^3 and 34.3 CFU/m^3, respectively. The number of household residents was positively correlated with the amount of molds. There was no difference in the amount of mold with respect to dosage of inhaler corticosteroids as well as symptom levels in asthmatics. The most frequently encountered allergens were *Dermatophagoides farinae*/*Dermatophagoides pteronyssinus*, grass/weeds and molds. Spending childhood in a village was more common among atopics. **Conclusion:** Living environment during the childhood might affect atopy and asthma. Based on the identification of molds as the second most frequent allergen after mites in our study population, assessment of mold sensitization as well as in forming patients about ways to avoid them seem likely to contribute to the effective management of uncontrolled asthma.

Key words: Air pollution, asthma, indoor environment, mold

How to cite this article: Ceylan E, Doruk S, Genc S, Ozkutuk AA, Karadag F, Ergor G, Itil BO, Cımrın AH. The role of molds in the relation between indoor environment and atopy in asthma patients. J Res Med Sci 2013;18:1067-73.

INTRODUCTION

Early life exposure to the environmental factors and aeroallergens has a strong impact on the development of allergic airway diseases. Consisting of house dust mites, pet danders, and mold fungi, indoor allergens play a crucial role in the exacerbation of pre-existing allergic diseases like asthma as well as allergic sensitization.[1-3] Ulrik *et al*. determined an increase in the prevalence of asthma with sensitivity to house dusts while asymptomatic bronchial hypersensitivity was suggested to be a major risk factor for the development of asthma.[4]

The individual or familial atopy has been considered as the most significant risk factor in the development of bronchial asthma.[5] The presence of atopy does not necessarily signal the clinically apparent disease, and neither an isolated exposure to allergens alone lead to bronchial inflammation. Various environmental factors, viral infections, smoking, environmental air pollution have been indicated to facilitate the penetration of allergens into the airways.[6] Mites, cat danders, and cockroach antigens are the most important indoor antigens in susceptible individuals.[7] Though, sensitivity to mold antigens has been indicated to be a risk factor for developing allergic diseases and asthma, currently it is not yet clear whether the allergic sensitization is a risk factor for the development of asthma.[8] Albeit the exact mechanisms by which household molds produce asthma are not known, IgE-mediated hypersensitivity reactions to mold fungi antigens as well as the effects of released mycotoxins have been suggested among the responsible factors.[9]

In asthmatics, allergic reactions to house dust mites and mold fungi, occurring more frequently in a humid environment, are quite common. A humid, dark,and poorly aerated indoor environment encourages the growth of mold fungi. Although the correlation between indoor humidity and fungal growth has been definitely established[10] it is not clear whether there is a direct relation between the household conditions and the level of indoor fungi. Fungal growth might be influenced by many factors such as ambient temperature, humidity, modes of indoor warming, availability of air-conditioning facilities, the presence of pets or leaks in the plumbing system. The presence of these factors was

Address for correspondence: Dr. Sibel Doruk, Department of Pulmonary Medicine, Gaziosmanpasa University, Tokat 60100, Turkey.
E-mail: sibeldoruk@yahoo.com
Received: 08-08-2012;; **Revised:** 01-01-2013; **Accepted:** 29-04-2013

consistently reported to have adverse effects on asthmatic symptoms in various studies.[1-13]

Based on spending most of the daily time at home or work place by several people, exposure to indoor pollutants, particularly house dust is quite common. In our country, atopy against mold fungi and its influential factors have not been comprehensively evaluated. Therefore, this study is aimed at evaluating household conditions for asthmatics in relation to the effects of household molds on the incidence of atopic manifestations.

MATERIALS AND METHODS

Study population

Being selected from our previous study concerning the growth of mold fungi in the indoor air,[13] a total of 66 asthma patients (mean age = 52.8 years, male/female = 11/55) were included in the present study to compose the case group. Physician-diagnosed asthma was based upon symptoms and the results of the reversibility test in each patient, according to Global Initiative for Asthma consensus report.[6] Control group was composed of 35 adults (mean age = 45.9 years, male/female: 9/26) who gave consent for allergy skin testing and selected from close neighborhood of the cases with similar socio-economic status and gender distribution. To be <18 years of age, presence of pregnancy and concomitant diseases including Chronic Obstructive Pulmonary Disease, heart failure or acute asthma attack and to be under treatment with tricyclic antidepressants or systemic corticosteroids were the exclusion criteria of the study.

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study, which was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki"and approved by the Institutional ethics committee.

Questionnaire and pulmonary function tests

An interviewer-administered questionnaire survey including items on the demographic characteristics of participants, the house hold conditions (the age of the building, optimum daylight conditions, healthy indoor climate, dampness in the home, heating system, any plumbing repair), the number of people living in the same residence, drying clothes indoor, house hold pets, potted plants in the house, and the type of flooring was applied through the face-to-face interview method.

Severity and duration of asthma, respiratory symptoms within the past 12 months, allergic symptoms, family history, home and workplace environment, use of health-care services and medications were also recorded. Respiratory function was evaluated using a rolling seal spirometer (SensorMedics, YorbaLinda, CA) according to American Thoracic Society criteria.[14]

Collection and mycological analysis of indoor air samples

During home visits performed at the second half of the winter season, 150 ml of air samples were aspirated (Air Ideal®, BioMereux/France) from the center of living rooms between the hours of 09:00 am and 13:00 pm before opening the windows and prior to house ventilation. Air samples taken 1.5 m above the ground were sprayed directly on sabouraud dextrose agar and then incubated at 25°C for 7-10 days. Number of colonies demonstrating the growth of the mold fungi was calculated and expressed as CFU/m^3. Relative humidity (%) with TFA hygrometer (Dostmann GmbH, Germany), which hanged on the wall 2 m above the floor for 10 min and ambient temperature of the same room were measured.

Allergy skin testing

The presence of allergy was determined using skin tests against aeroallergens most frequently reported in our country. Allergy test set included 14 different allergens (*Dermatophagoides pteronyssinus, Dermatophagoides farinae*, *Aspergillus fumigatus*, *Penicillium notatum*, *Alternaria alternata*, *Cladosporium*, Mold mixII [*Mucor*, Neurosp., Pullularia, *Rhizopus*], cat and dog danders, a mixture of herbs [*dactylis*, *festuca*, *lolium*, *phleum*, *poa*], weeds [artemis, chenapo, pariet, *plantago*], and plants [*betula*, *fraxinus*, *olea*, *quercusilex*, *robinia*], cockroach antigens [*Blatella germanica*] and rabbit fur [ALK-Abello; Albio]). As a positive control, histamine solution in distilled water (10 mg/mL), and as a negative control glycerol buffered serum saline were used. Skin test was performed on the volar surface of the forearm using prick lancets. Skin reaction of each allergen were evaluated and compared with the reactions of positive and negative controls after 15 min of the testing. The induration of ≥3mm in diameter was considered as a positive reaction.

Statistical analysis

Statistical analysis was performed using the commercially available computer software (SPSS version 10.0, SPSS Inc. Chicago, IL, USA). While, Chi-Square test was used to compare the categorical variables, Student's *t* test was used for comparisons of numerical values. The correlation of indoor characteristics to the amount of mold growth, the clinical features and medications was performed via Spearman's correlation analysis. Mann Whitney U test was performed for comparisons of the groups with abnormal distribution. One-way ANOVA test was used for comparisons of means for more than two independent groups. Results are reported as the mean ± standard deviation and percent (%) where appropriate. $p < 0.05$ was considered statistically significant.

RESULTS

Demographic characteristics in the groups are summarized in Table 1. Control subjects were determined to be significantly younger than patients ($p < 0.001$). The number of females was greater in each group, but the ratio of female to male was not different in each group. Mean duration of follow-up by a pulmonary specialist was 12.2 years in asthma patients.

Various characteristics of study groups and their home environment are shown in Tables 2 and 3. Allergy testing demonstrated similar ratios for sensitivity to at least one antigen in the case (59.1%) and the control (51.4%) groups. The mean amount of mold in indoor air samples was detected as 35.9 CFU/m^{3}among asthma cases and 34.3 CFU/m^3 in controls.

Albeit not significant likely due to scarcity of participants, past history of a non-asthmatic allergic disease was positive in 43.8% of asthmatics and 25.7% of controls. Case and control groups were similar in terms of the presence of allergic disease and symptoms in the first-degree relatives [Table 2].

There was no difference between asthma and control groups with respect to exposure of second hand smoke at home. However, the prior history of pet ownership was significantly higher in the cases compared to controls (p = 0.046) [Table 2].

A positive correlation was determined between the number of house hold residents and the amount of indoor mold [r = 0,288, $p < 0.004$; Figure 1]. A positive but weak correlation was observed between the frequency of symptoms and the use of inhaler steroid therapy (r = 0.227, p = 0.024). There was no significant difference in mold amount with respect to different doses of inhaler steroids used(low/moderate/high), and past history of acute asthma attack within the last year (p = 0.160 and p = 0.967 respectively). There was no significant difference in mold amount with respect to frequency of asthma symptoms (p = 0.457) [Table 4]. No correlation was determined between the frequency of asthmatic symptoms, use of short acting beta-2-agonists, daily dosage of inhaler corticosteroids, asthma attacks within the previous year,and the presence of atopy.

A total of 57 cases had positive allergy test of the allergens applied. The most frequently encountered allergens were *D. farinae* (54.4%), *D. pteronyssinus* (45.6%), grasses and weeds (45.1%), and mold fungi (26.3%) [Figure 2]. *Alternaria* (n = 6), *Cladosporium* (n = 4), and *Penicillium* (n = 2) were the mostly detected mold fungi.

There was no influence of asthma severity on the incidence of atopy [Figure 3].

The specific features of the indoor environment in patients with or without atopy are given in Table 5. Spending childhood in a village (51.3%) was more common while living in an apartment was less common (68.4%) among atopic compared to the cases without atopy (29.6%; p = 0.001 and 90.9%; p = 0.007, respectively).

Table 1: General characteristics of study groups

	Asthma group (n = 66)	Control group (n = 35)	P value
Age/year (Mean±SD)	52.8±10.3	45.9±12.3	P<0.001
[a]Gender			
Male (%)	11 (16.7)	9 (25.7)	P>0,277
Female (%)	55 (83.3)	26 (74.3)	

[a]Data were shown as number (percent)

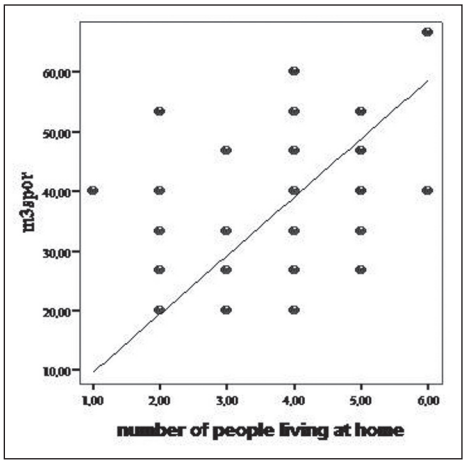

Figure 1: The relationship between the number of people living at home and the amount of mold at home

Table 2: Various characteristics of asthma group and controls according to their home environment

	Asthma group (n = 66)	Control group (n = 35)	P value
Room temperature (°C)	20.9±3.6	20.5±2.8	0.530
Humidity (%)	45.0±12.4	49.6±8.7	0.055
The amount of mold colony (CFU/m^3)	35.9	34.3	0.370
The age of the residential building (year)	18.1±9.3	16.2±9.1	0.029
The number of people living at home (year)	3.3±1.2	3.3±1.1	0.930
The presence of visible mold at home (n [%])	32 (48.5)	13 (37.2)	0.378

Allergy to mold fungi was identified only in nine cases. There was higher amount of indoor mold in patients with mold allergy compared to patients not allergic to molds (p = 0.047). There was need for high doses of inhaled corticosteroids in patients with mold allergy (555.4 and 911.1 µg as equivalent to beclomethasone dipropionate, respectively; p = 0.025) compared to the rest of asthmatic patients.

DISCUSSION

In this study, the presence of atopy in asthmatics and household conditions were investigated and no difference was found in the frequency and severity of the symptoms, the frequency of admission to hospital because of asthma attacks within the previous year, the dosage of the inhaler corticosteroid, and the amount of the spores of indoor molds. Asthmatics with a higher concentration of mold spores in indoor air were found more allergic to mold fungi and required relatively higher dosages of inhaler corticosteroids. Atopy was found more frequently in patients who lived in rural areas in their childhood.

Mold fungi together with house dust mites are important indoor allergens leading to sensitization. In various countries, different mold fungi have been mainly identified in the indoor environment. The most frequently identified fungi in countries such as Germany, Sweden, Denmark, Holland, and UK were reported as *Penicillium* spp. and *Cladosporium* spp.[4,8,15,16] In general, *Aspergillus* and

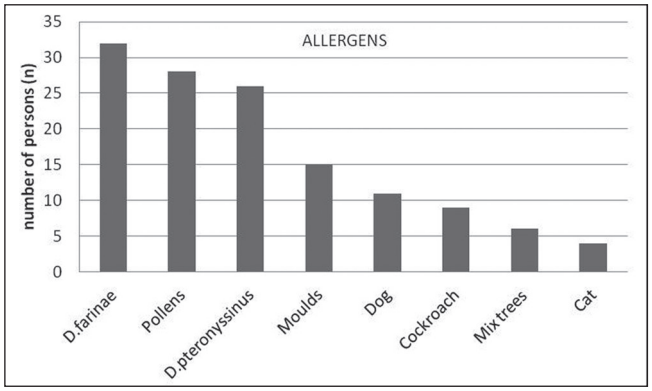

Figure 2: The allergens mostly detected in the cases with positive skin tests

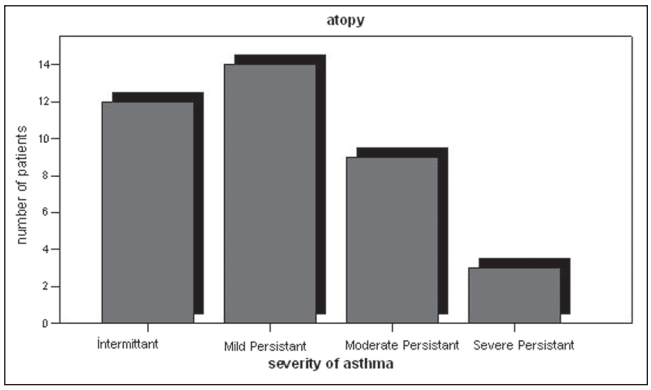

Figure 3: The frequency of atopy according to asthma severity

Table 3: Various characteristics of study groups

	Asthma group (n = 66) n (%)	Control group (n = 35) n (%)	P value
Smoking at home	23 (34.8)	17 (50.0)	0.143
Atopy	39 (59.1)	18 (51.4)	0.460
Allergic rhinitis	35 (53.0)	16 (45.7)	0.480
Allergic dermatitis	32 (49.2)	16 (45.7)	0.730
Family history of allergy	39 (60.0)	19 (54.3)	0.580
History of having pet (previous/now)	44 (67.7)	16 (47.1)	0.046
Living in rural areas in childhood	42 (63.6)	24 (68.6)	0.620

Table 4: The relationship between the amount of mold in the resident air and the frequency of symptoms of the asthma patients

The frequency of asthma symptoms*	The amount of molds (CFU/m³)[a]
Asymptomatic cases or cases with symptoms less than 1 time/week (n=33)	34.5±9.5
Cases with asthma symptoms 2-3 times/week (n=17)	37.3±8.8
Cases with asthma symptoms 4-5 times/week or frequently symptomatic cases (n=15)	37.8±8.9

[a]Data were shown as mean±standard deviation. One-way ANOVA test showed no difference between the groups (P = 0.433)

Table 5: Various characteristics of cases according to skin test

The characteristics of the cases	Skin test		P value
	Positive (n = 57)	Negative (n = 44)	
Age/year (mean±SD)	50.1±11.5	50.9±11.5	0.710
The amount of mold colony/CFU/m³ (mean±SD)	34.8±8.9	36.1±9.9	0.502
The age of the residential building/year (mean±SD)	18.1±9.5	16.6±8.9	0.430
A family history of allergy	36 (63.2)	22 (51.2)	0.229
History of having pet (previous/now)[a]	38 (67.9)	22 (51.2)	0.092
Living in rural areas in childhood[a]	31 (54.4)	10 (22.7)	0.001
Apartment life	39 (68.4)	40 (90.9)	0.007

[a]Data were shown as number (percent)

Penicillium are considered to be the most important indoor molds, whereas *Alternaria* has been reported as the most important outdoor mold. In our previously published study, in which the study group of the present study was also included, we reported *Aspergillus* and *Penicillium* to be the most frequently encountered household molds.[17] The presence of mold fungi in the indoor environment depends on the degree of humidity and temperature, which are the vital factors for house dust mites as well. Therefore,the presence of visible mold at the surface of the house suggests that indoor conditions might be also appropriate for the growth of house dust mites. In addition, concomitant presence of higher concentrations of mites and mold fungi in the indoor environment indicate the preference of similar environmental conditions for the growth. As noted in the literature, the greater the number of persons usually resident in a household, the larger amount of mites. Hence, our finding of positive correlation between the number of household residents and the amount of indoor mold is compatible with the above-mentioned findings.

Yazicioglu *et al*. reported higher amount of fungi in the indoor environment of asthmatic children than non-atopic controls.[15] In asthmatic patients sensitive to fungal allergens, more severe clinical course of the disease was reported while even these allergens *perse* were reported to be responsible for higher mortality rates in asthmatics.[16] Since, the most important source of indoor fungi is the outdoor air, the features of the outdoor should also be considered in assessment of the internal environment. Although, similar amount of mold was detected in our asthmatic cases with respect to past history of acute asthma attack within the past year or the presence of severe symptoms, relatively higher amount of mold growth in nine individuals with detected allergy to mold suggests an important role of indoor conditions in the development of atopy against molds. In addition, requirement for higher doses of inhaled corticosteroids in patients sensitive to mold suggests that control of mold is important in the management of asthma.

Sensitization to molds is a risk factor for allergic diseases.[17,18] In patients with respiratory tract allergies, prevalence of allergic sensitization to mold has been reported to a range from 2% to 30% in various studies.[17] This wide range of prevalence may be related to geographic characteristics, the climate of the regions studied and the diversities in the living conditions of the patients as well as the differences in the diagnostic tests used for the evaluation of atopy. Pediatric exposure to spores of mold was demonstratively associated with allergic sensitization and atopy.[17,19] In a past study by Jaakkola *et al*. sensitization to house dusts was reported to be the most frequent risk factor for the development of adult onset asthma.[20]

Sensitization to mold was reported to a range from 5% to 18.5% in asthmatics with frequent development against to *Aspergillus*, *Alternaria*, *Penicillium*, and *Cladosporium*.[3,21,22] Evaluation of patients with symptoms related to respiratory and allergic diseases in a past study revealed the sensitization of mold to be 9%.[23] Our finding indicating incidence of sensitization to molds in 17% of asthmatic cases and 8.9% of controls suggest that asymptomatic sensitization to mold might occur even in cases without asthma.

Assessing the exposure to house dust allergens is crucial for the evaluation of the risk factors effective for sensitization. This may play a role in controlling the environmental factors, which affect the severity of asthma.[24] In a study by Ulrik *et al*., house dust sensitization was reported to be associated with an increase in asthma prevalence within the 12 months and asymptomatic bronchial hyperreactivity was suggested to be a major risk factor for the development of asthma.[4] In addition, increase in both the ratio of the skin test positivity (from 26% at baseline to 44% at the end of the 1st year) and sensitivity to house dust antigens (from 14% at baseline to 26% at the end of the1st year) was reported in the same study.[4] In a study, from Aegean region of Turkey, *D. pteronyssinus* type 1 or *D. farinae* type 1 was identified in 53.8% of dust with the pre-dominance of *D. pteronyssinus* type 1 (71.4%). Sensitization to *D. farinae* or *D. pteronyssinus* was determined in 84.0% of the allergic cases and it was emphasized that the indoor humidity and residing at the seaside may be a predictor of more frequent sensitization to house dust.[25] Accordingly, sensitivity to *D. farinae* was the most frequently identified finding in allergy skin testing in our study population composed of the case and control subjects from similar climatic and environmental conditions.

The symptoms related to atopy were detected in 57.6% of asthmatic children in a study from Istanbul, Turkey. Skin prick test revealed atopy in 60.3% of cases. Sensitization was detected mostly against house dust, grasses and weeds.[5] Similar ratios for atopy were evident in our asthmatic patients composed of mainly mild asthmatics. In Erzurum, grasses and weeds and tree pollens were reported as the most frequent allergens (70.3%) in asthma patients. The sensitivity to house dust mites (32.1%) and mold (5%) were also reported. In Tokat, asthmatics were determined to be mostly allergic to *D. pteronyssinus* and *D. farinea* (58.1%) and pollens (49.5%).[22] In Antalya, house dusts were reported as the most common allergen with the ratio of 20.9%.[26] It seems reasonable to expect the increase in sensitivity to house dust mites parallel to increase in weather temperature and humidity toward Western and Southern regions also for sensitivity to mold.

The rates of atopy in different levels of asthma severity were reported as 85% in mild intermittent asthma, 57% in mild persistent and moderate asthma, and 10% in severe asthma in a past study from Turkey.[27] However, similar ratios for atopy were evident with respect to asthma severity in our asthmatic patients composed mainly of patients with mild asthma. Regional difference in the prevalences of asthma, allergic rhinitis, and atopy were reported in Turkey, including respective prevalence's of 9.4, 27.7, and 31.1% in Southern regions while 7.46%, 8.1%, and 15.7% in central regions.[26,28] The positivity for at least one allergen was determined in 20.3% of asthma patients.[28]

In a past study by Celik *et al*. prevalence of asthma, allergic rhinitis and atopy was reported as 6%, 16% and 25% in a large population representative of our country.[2] Our finding related to similarly high frequency of atopy in both control and case groups may be secondary to differences in criteria used in the interpretation of the skin test results and certain regional differences. In addition, given the fact that high incidence of familial history of allergic diseases and high rates of atopy in our control subjects might be explained by the likelihood of higher tendency among subjects with personal and familial history of symptoms suggesting allergic diseases to be voluntary for skin allergy testing.

Assessment of particular familial and environmental factors in subjects with allergic airway disease in relation to the presence of atopy in a cross-sectional study by Celik *et al*. revealed that place of birth, sibship size,and atopic status of the mother were significantly associated with the development of allergic airway disease after adjustment for confounding factors. According to their data, birth rate in villages and sibship size were lower in the atopic group compared to non-atopic group. Based on higher rate of birth in urban regions among atopic patients particularly in patients with isolated allergic rhinitis and higher rate of living in an apartment during the childhood among atopics than non-atopic controls in that study, rural life-style was indicated to be protective against development of atopy in Turkey. Hence, certain factors with a direct or indirect relation to urban life-style during the early childhood were suggested to have an impact on the frequency allergic respiratory diseases.[2] Albeit contradictory to report by Celik *et al*., our finding concerning higher rates for spending childhood in a rural area among atopic than non-atopic patients seems to suggest the possible impact of the life-style as well as the location of residence on the development of atopy and allergy.

The relationship between the indoor conditions, atopy, and symptoms of asthma is noteworthy in adults. Identification of indoor allergens and training of patients about protection against these allergens is crucial, especially in patients with perennial symptoms. Avoiding the allergen with known sensitivity seems to enable more successful asthma control. Hence, allergy to mites and molds should be evaluated especially in the "difficult to control" asthma.

One of the major limitations of the present study was that the assessments were limited to indoor air and only for molds. Further studies are needed to evaluate other allergens in the indoor environment and to investigate the factors affecting the sensitization and the development of asthma. Another limitation of the study is related to the selection of the control group and the controls were selected by previous study of the authors based on their consent to allergy testing. This may lead to incidence of allergic diseases other than asthma and percentage of sensitization in the control group to be as high as in the study group, since people suffering from allergy may be more willing to be examined.

In conclusion, our findings revealed no impact of life-style, habits, and indoor airborne fungal growth on the development of asthma, but the likelihood of living environment during childhood to affect existing allergic disease and asthma. Detecting higher concentration of molds in the houses of patients who have the skin test positivity to molds might suggest the importance of these allergens in asthma control.

REFERENCES

1. Sherrill D, Stein R, Kurzius-Spencer M, Martinez F. On early sensitization to allergens and development of respiratory symptoms. Clin Exp Allergy 1999;29:905-11.
2. Çelik G, Sin B, Keskin S, Ediger D, Bavbek S, Mungan D, *et al*. Risk factors determining allergic airway diseases in Turkish subjects. J Asthma 2002;39:383-90.
3. Burr ML, Mullins J, Merrett TG, Stott NC. Indoor moulds and asthma. J R Soc Health 1988;108:99-101.
4. Ulrik CS, Backer V, Hesse B, Dirksen A. Risk factors for development of asthma in children and adolescents: Findings from a longitudinal population study. Respir Med 1996;90:623-30.
5. Cengizlier MR, Misirlioglu ED. Evaluation of risk factors in patients diagnosed with bronchial asthma. Allergol Immunopathol (Madr) 2006;34:4-9.
6. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. NHLBI/WHO Workshop Report. National Institute of Health. National Heart, Lung and Blood Institute. Revised 2006. Available from: http://www.ginasthma.com.
7. Lau S, Falkenhorst G, Weber A, Werthmann I, Lind P, Buettner-Goetz P, *et al*. High mite-allergen exposure increases the risk of sensitization in atopic children and young adults. J Allergy Clin Immunol 1989;84:718-25.
8. Lau S, Illi S, Sommerfeld C, Niggemann B, Bergmann R, von Mutius E, *et al*. Early exposure to house-dust mite and cat allergens and development of childhood asthma: A cohort study. Multicentre Allergy Study Group. Lancet 2000;356:1392-7.
9. Zock JP, Jarvis D, Luczynska C, Sunyer J, Burney P, European Community Respiratory Health Survey. Housing characteristics,

reported mold exposure, and asthma in the European Community Respiratory Health Survey. J Allergy Clin Immunol 2002;110:285-92.
10. Burge HA. Airborne allergenic fungi classification, nomenclature, and distribution. Immunol Allergy Clin North Am 1989;9:307-19.
11. Ren P, Jankun TM, Belanger K, Bracken MB, Leaderer BP. The relation between fungal propagules in indoor air and home characteristics. Allergy 2001;56:419-24.
12. Phipatanakul W. Environmental indoor allergens. Pediatr Ann 2003;32:40-8.
13. Ceylan E, Ozkutuk A, Ergor G, Yucesoy M, Itil O, Caymaz S, *et al*. Fungi and indoor conditions in asthma patients. J Asthma 2006;43:789-94.
14. Standardization of Spirometry, 1994 Update. American Thoracic Society. Am J Respir Crit Care Med 1995;152:1107-36.
15. Yazicioglu M, Asan A, Ones U, Vatansever U, Sen B, Ture M, *et al*. Indoor airborne fungal spores and home characteristics in asthmatic children from Edirne region of Turkey. Allergol Immunopathol (Madr) 2004;32:197-203.
16. Zureik M,Neukirch C, Leynaert B, Liard R, Bousquet J, Neukirch F, *et al*. Sensitisation to airborne moulds and severity of asthma: Cross-sectional study from European Community respiratory health survey. BMJ 2002;325:411-4.
17. Jacob B, Ritz B, Gehring U, Koch A, Bischof W, Wichmann HE, *et al*. Indoor exposure to molds and allergic sensitization. Environ Health Perspect 2002;110:647-53.
18. Katz Y, Verleger H, Barr J, Rachmiel M, Kiviti S, Kuttin ES. Indoor survey of moulds and prevalence of mould atopy in Israel. Clin Exp Allergy 1999;29:186-92.
19. Garrett MH, Rayment PR, Hooper MA, Abramson MJ, Hooper BM. Indoor airborne fungal spores, house dampness and associations with environmental factors and respiratory health in children. Clin Exp Allergy 1998;28:459-67.
20. Jaakkola MS, Ieromnimon A, Jaakkola JJ. Are atopy and specific IgE to mites and molds important for adult asthma? J Allergy Clin Immunol 2006;117:642-8.
21. Mirici A, Girgiç M, Tutar Ü, Kaynar H, Saglam L, Görgüner M, *et al*. The frequency of atopy in asthmatic patients in Erzurum. Archives of Lung 2001;2:64-8.
22. Yilmaz A, Inonü H, Öcal SG, Çelikel S, Doruk S, Etikan I, *et al*. Skin prick test sensitivity and its association with pulmonary function tests in asthmatic patients in Tokat region. Asthma Allergy Immunol 2009;7:44-51.
23. Tezcan D, Uzuner N, Şule Turgut C, Karaman O, Köse S. Retrospective evaluation of epidermal skin prick tests in patients living in Aegean region. Allergol Immunopathol (Madr) 2003;31:226-30.
24. National Asthma Education and Prevention Program, Expert Panel Report 2. Guidelines for the diagnosis and management of asthma. Vol. 97. Bethesda, MD: National Institutes of Health, National Heart Lung and Blood Institue NIH Publication No.; 1997.p. 40-51.
25. Gülbahar O, Mete N, Kokuludağ A, Sin A, Sebik F. House dust mite allergens in Turkish homes. Allergy 2004;59:231.
26. Dinmezel S, Öğüş C, Erengin H, Çilli A, Özbudak O, Özdemir T. The prevalence of asthma, allergic rhinitis, and atopy in Antalya, Turkey. Allergy Asthma Proc 2005;26:403-9.
27. Bavbek S, Çelik G, Ediger D, Mungan D, Sin B, Demirel YS, *et al*. Severity and associated risk factors in adult asthma patients in Turkey. Ann Allergy Asthma Immunol 2000;85:134-9.
28. Unlü M, Orman A, Dogan N. The prevalence of asthma among secondary school students in Afyon, Turkey. Asian Pac J Allergy Immunol 2002;20:1-6.

Source of Support: Nil, **Conflict of Interest:** There is no conflict of interest for authors.