

Relevance of skin-prick test and immunoglobulin E estimation in pigeon-exposure asthma patients

Anil K. Mavi, Sonam Spalgais, Kamal Singh, Manoj Kumar, Raj Kumar

Department of Pulmonary Medicine,
Vallabhbhai Patel Chest Institute, University of
Delhi, Delhi, India

Correspondence to Raj Kumar, MD,
Department of Pulmonary Medicine,
Vallabhbhai Patel Chest Institute, University of
Delhi, Delhi 110007, India. Tel: +91 981 014
6835/91011 276 676 67; fax: 011-27666549;
011-27662867;
e-mail: rajkumarvpci@gmail.com

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Background

Pigeon exposure is common in India due to its cultural and religious practice. Hypersensitivity to pigeon allergen is well known as pigeon breeder disease. Limited data also show that pigeon allergen was associated with increased asthma. The aim of this study is to evaluate skin-prick test (SPT) and immunoglobulin E (IgE) levels in pigeon-exposed asthmatics.

Patients and methods

It is a prospective observational study with 200 asthma patients as per Global Initiative for Asthma guidelines. As per the history of exposure to pigeons, patients were divided into two groups: exposed and nonexposed asthmatics. All patients underwent SPT against CAA with pigeon allergen and measurements of serum IgE. The result was compared between two groups.

Results

Out of 200 patients with mean age of 29.83 ± 9.92 years, 108 had pigeon exposure. The SPT against CAA sensitivity was positive in 74% exposed and 63% nonexposed groups. While SPT against pigeon allergen was positive in 17 (15.7%) in exposed patients. The mean total IgE was higher in exposed asthmatics but not significant (538.75 ± 248.5 and 510.2 ± 220.1 IU/ml, $P=0.0078$). The mean specific IgE against pigeon dropping and feather was significantly higher in exposed asthmatics (0.4513 ± 1.01 and 0.1957 ± 0.179 KUA/l, $P=0.003$; 0.3644 ± 0.329 and 0.1176 ± 0.116 KUA/l, $P=0.000$).

Conclusion

The asthmatic patients with exposure to pigeons had higher SPT against pigeon allergen and higher total and specific IgE against pigeon antigens. This may be one of the reasons for higher asthma in urban cities.

Keywords:

asthma, immunoglobulin E, pigeon, skin-prick test

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Introduction

Pigeon fancying or keeping is regarded as a harmless hobby and is being practised worldwide by humans from ancient times. However, there is unawareness with this custom about the associated infections and hypersensitivity disorders. People experience allergies to dogs, cats, bird feather, dander, and bird fecal matter, and also have the potential health risks. The typical allergic symptoms of exposure include breathlessness, chills, dry cough, and chest discomfort, which usually appear within 4–6 h of exposure. Such allergies never grow into anything harmful or cause life-threatening symptoms, so therapy usually consists of medication prescribed by a medical professional [1,2]. The various diseases associated with exposure to pigeons are asthma, rhinitis, allergic alveolitis (bird fanciers disease), and ornithosis [3,4]. Pigeons also cohabit with humans in developing countries such as India, which render antigenic avoidance difficult, and these allergens may exacerbate asthma in specific urban environments where the pigeon harbors. Pigeon droppings have

been proven to be a complex mixture of over 10 different allergenic proteins [5]. Reed and Barbee [6] identified three patients who exhibited chills, nausea, cough, myalgia, and dyspnea while treating pigeons around five decades ago. This was the first evidence of extrinsic allergy triggered by a reaction of hypersensitivity attributable to inhaled pigeon antigens in sensitized lungs [7]. In several similar reports over the years, such early findings have also been verified. Relatively few reports have reported pigeon allergen even in dust and air [8,9].

Hypersensitivity to pigeons by immune complex mediated is well known as pigeon breeder lung. However, pigeon antigens eliciting the immediate type of hypersensitivity are not well known till date. Pigeon exposure-associated asthma is limited to case

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reports and case series. Deo *et al.* [10], in a study of 500 asthmatics, concluded that nearly 17% asthmatic patients showed reactivity to pigeon antigen and this may increase in asthma cases in their city. Investigators later identified potent allergens that came from various parts of the pigeon. Reynaud *et al.* [11] reported that immunoglobulin G (IgG), IgA, IgE, and IgM formation in pigeon-sensitive patients may be triggered by a wide range of proteins in the serum, skin, and neck of pigeons.

IgE is distinguished from other Ig isotypes because of its very low plasma concentrations and short half-life [12]. In 1966, it was identified as transferable serum factor, which mediates immediate hypersensitive reactions, and has a strong correlation with asthma [13]. Burrows *et al.* [14] reported a direct association between serum IgE and asthma rates. Asthma is almost always connected to some form of IgE-related reaction and thus has an allergic origin. Kumar *et al.* [15] in a study suggested the importance of serum IgE calculation in allergic bronchial asthma with a particular reference to food allergy. Our research aims to investigating and evaluating skin-prick test (SPT) and serum IgE levels in asthma patients with exposure to pigeon allergens.

Patients and methods

This is a prospective study conducted at Viswanathan Chest Hospital's Out-Patient Department, Vallabhbhai Patel Chest Institute, Delhi, from January 2016 to January 2018. Asthma cases were diagnosed according to the 2017 Global Initiative for Asthma guideline [16]. We enrolled 200 cases of diagnosed asthma patients. The patients comprised 81 (40.5%) males and 119 (59.5%) females with a mean age of 29.71 ± 10 years. The written consent for participation was taken from all enrolled patients. The study excluded lactating mothers and patients with chronic obstructive pulmonary disease, diabetes, hypertension, and heart disease. The study was approved by the Institutional Ethical Committee, and written consent was taken for inclusion in the study. For skin-prick examination and pulmonary function test, the patients were reassured and also encouraged to give blood for overall serum and precise IgE figures. Serum was obtained for further research and deposited at -80°C . Pigeon exposure is considered positive when an asthma patient has a history of exposure to pigeons at his/her work place or home for a minimum of 1–3 h per day for a minimum of 6 months in the last 2 years.

Skin-prick tests

SPT in all the enrolled patients was performed with a battery of 58 common environmental/aeroallergen allergens, which include pigeon allergens. The allergen extracts (1 : 10 w/v, 50% glycerinated) were procured from All Cure Pharma Pvt Ltd (New Delhi, India). Buffered saline and histamine were also used as, respectively, negative and positive indicators. SPT was performed by applying a drop of antigen on the healthy skin on the volar surfaces of the forearm and pricking it with a 26.5-G sterile needle. The skin-test reactions were graded by calculating the mean diameter as $(D+d)/2$, D =largest diameter and d =orthogonal or perpendicular diameter at the largest width of D after 15–20 min in comparison with the wheel size of positive, that is, buffer saline (10 mg/ml).

A mean wheel diameter of 3 mm or more of negative control indicates a positive result (1+ and above) for a particular allergen. A mean wheel diameter measured 3 mm or greater than negative control (buffered saline), but less than 5 mm was taken as 1+. Similarly, a mean wheel diameter measuring more than or equal to 5 mm and less than 7 mm was taken as 2+, more than or equal to 7, and less than 9 mm as 3+ and so on, respectively. Only 2+, 3+, and 4+ reactions were labeled as significantly positive skin reactions because of the high incidence of 1+ reaction in nonallergic normal people. Before performing SPT, oral drugs, including antihistamines, steroids, and antidepressants, were stopped 1 week before the tests, but inhaled drugs were continued [17,18].

Total immunoglobulin E estimation

For each patient and healthy human, total serum IgE estimate was performed by enzyme-linked immunosorbent assay (ELISA) using Calbiotech ELISA kit (Calbiotech Inc., El Cajon, California, USA), as directed by the manufacturer. In short, in specified wells, coated with streptavidin, the criteria, samples, and the biotinylated antibody reagents such as anti-IgE were applied. Such wells were washed with buffer accompanied by the introduction of conjugates of peroxidase (HRP), then washed off by wash buffer. Subsequently, tetramethylbenzidine substrate was applied to produce color. The reaction to the enzyme has blocked the production of acid. Using a URIT-660 microplate reader (URIT Medical Electronic Co. Ltd, Guangxi, China), the absorbance was then read at 450 nm. The average IgE more than 250 IU/ml was considered positive for males and more than 175 IU/ml for females [19].

Specific immunoglobulin E estimation

ImmunoCAP system (Phadia, Uppsala, Sweden) evaluated the serum of patients showing marked reactions for specific IgE against the respective pigeon antigens. The allergens were permitted to covalently couple to the solid phase and were incubated in the patient sample with the specific IgE. The nonspecific IgE was washed away, and antibodies labeled with enzymes against IgE were introduced to create a complex. Upon incubation, the unbound anti-IgE fraction labeled with the enzyme was cleaned, and a forming agent incubated the bound compound. After the reaction was stopped, the eluate fluorescence was calculated. The higher the fluorescence, the more specific IgE is present in the sample. The specific IgE more than 0.35 kUA/l was considered as positive [20].

Pulmonary function test

Spirometry was conducted on a dry, roll-seal spirometer of the Benchmark design lung function machine (P.K. Morgan, Kent, UK). Full expiratory flow volume curves have been produced as suggested by ATS. In each patient, three appropriate and at least two reproducible curves were produced. The maximum values for forced vital capacity (FVC) and forced expiratory volume 1 (FEV₁) have been picked. Spirometry was performed 15–20 min after inhalation of 200–400 µg of salbutamol. FEV₁/FVC was taken for assessing the pulmonary obstruction, and FEV₁ taken for assessing the severity of asthma was categorized as mild, moderate, moderate–severe, severe, and very severe [21].

Statistical analysis

Independent *t* test was compared with means of both the groups. A two-tailed *P* value of less than 0.05 was considered statistically significant. Examination of the data collected from all topics was evaluated using version 22 of the Statistical System for Social Sciences.

Results

Demographic details

A total of 200 (81 males and 119 females) asthmatics were enrolled for this study. Among the patients, 108 individuals were exposed to pigeons at their living or work place, while 92 were unexposed to pigeons. The mean age of the enrolled patients was 29.71±10.00 years, (11–58 years), and the average body mass index was 25.3±5.51 kg/m². The mean duration of the disease was 5.15±3.90 years. Cough was the most common symptom (89.91%) followed by nasal symptoms (89.71%), breathlessness (64.81%), and wheezing (45.37%). The demographic characteristics are almost similar between exposure and nonexposure groups. The details of the demographic characteristics of patients are shown in Table 1.

Skin-prick test

In pigeon-exposed asthma patients, 74.07% (80/108) were found SPT-sensitive against one of the common aeroallergens and 25.92% (28/108) patients were negative. While in pigeon nonexposed asthmatics, 63.04% (58/92) asthmatics were also sensitized to common aeroallergens and 31.48% (34/92) were nonsensitized. The SPT against pigeon dropping and feather was positive in 17 (15.7%) patients out of 108 pigeon-exposed asthmatics. While no patient was SPT-positive against pigeon allergens in the nonexposure group. Among pigeon antigens SPT-positive, three (two against droppings and one against feather) were categorized as 2+, while 15 (12 against droppings and one against feather) were categorized as 3+ positive. While none of the 17 patients had shown SPT of 1+ and 4+. The number of patients sensitized to pigeon droppings were 13 (76.5%) and pigeon feathers were three (17.6%), while one (5.9%) patient was positive for both pigeon dropping and feather allergens. The details of SPT against pigeon allergens are shown in Table 2.

Table 1 Demographic data of asthmatic patients

Variables	Asthmatics		Total
	Pigeon exposed	Pigeon nonexposed	
Number	108	92	200
Mean age (years)	29.83±9.92	29.57±10.00	29.71±10.00
Male/female	48/60	33/59	81/119
BMI (kg/m ²)	25.8±5.48	24.7±5.51	25.3±5.51
Duration of disease (years)	5.01±3.9	5.32±3.9	5.15±3.90
Symptoms (year)			
Cough	97 (89.91)	86 (93.47)	183 (91.5)
Nasal symptoms	97 (89.71)	79 (85.86)	176 (88)
Breathlessness	70 (64.81)	60 (65.21)	130 (65)
Wheezing	49 (45.37)	43 (46.73)	92 (46)

Data are presented as mean±SD and *n* (%).

Serum total and specific immunoglobulin E in pigeon-exposed and nonexposed asthmatics

The mean total IgE of all asthma patients was 525.6 ± 235.6 IU/ml. The mean IgE among exposed asthmatics was 538.75 ± 248.5 , and in nonexposed asthmatics, it was 510.2 ± 220.1 IU/ml (Fig. 1). The difference in total IgE was not statistically significant ($P=0.078$). The total IgE was positive in 92 (85.1%) in exposure patients with a mean value of 612.7 ± 185.0 IU/ml and in nonexposure patients 86 (93.4%) with a mean value of 537.7 ± 199.9 IU/ml and it is not statistically significant ($P=0.939$).

The overall mean value of specific IgE against pigeon dropping was 0.3337 ± 0.76 KUA/l. The mean of specific IgE against pigeon droppings was 0.4513 ± 1.01 in exposure asthmatics and 0.1957 ± 0.179 KUA/l in nonexposure asthmatics with a statistically significant difference ($P=0.003$) (Fig. 2). The specific IgE against pigeon droppings was positive in 40 (37.03%) among the exposure group with a mean of 0.999 ± 1.52 KUA/l and 12 (13.04%) among the

nonexposure group with a mean of 0.530 ± 0.216 KUA/l. The difference is not statistically significant ($P=0.129$). The mean value of specific IgE against pigeon feather in total 200 asthmatics was 0.2508 ± 0.28 KUA/l. The mean of specific IgE against pigeon feathers was 0.3644 ± 0.329 KUA/l in exposure asthmatics and 0.1176 ± 0.116 KUA/l in nonexposure asthmatics with a statistically significant difference ($P=0.000$) (Fig. 3). The specific IgE against pigeon feathers was positive in 47 (43.51%) with a mean of 0.609 ± 0.34 KUA/l in exposure asthmatics and five (5.43%) with a mean of 0.384 ± 0.030 KUA/l in nonexposure asthmatics with a statistically insignificant difference ($P=0.027$). The details of total and specific IgE against pigeons are shown in Table 3.

Pulmonary function test

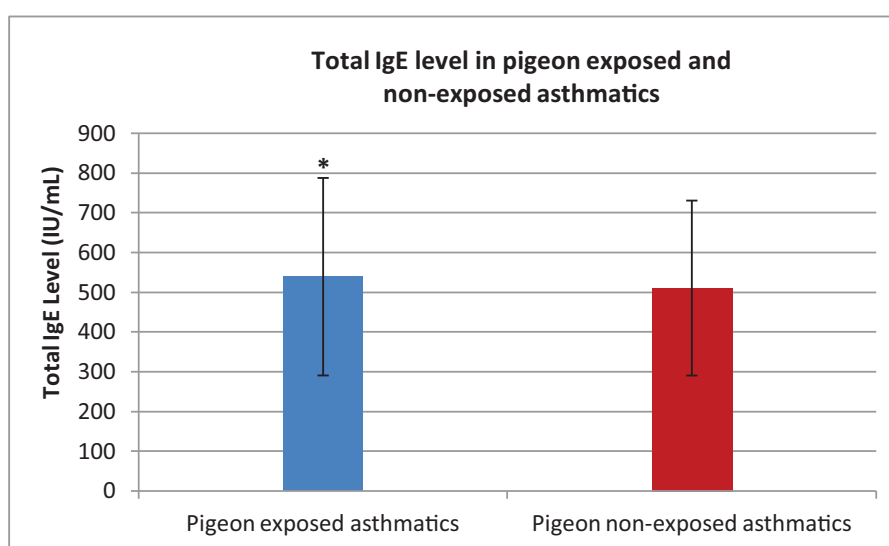
The overall mean of FVC and FEV₁ of all 200 asthma patients on baseline spirometry was 3.32 ± 0.86 l ($91.17 \pm 13.61\%$) and 2.50 ± 0.77 l ($79.33 \pm 18.54\%$). The mean value FVC was 3.36 ± 0.86 l ($89.72 \pm 12.74\%$) in exposure and 3.27 ± 0.87 l ($92.86 \pm 14.52\%$) in nonexposure patients, which is statistically insignificant. The mean value of FEV₁ was 2.55 ± 0.76 l ($79.25 \pm 18.35\%$) in exposure and 2.43 ± 0.77 l ($79.41 \pm 18.86\%$) in nonexposure patients. It is statistically insignificant.

The baseline spirometry showed obstruction in 117 (58.5%) patients. The obstructive defects were found in 59 (54.6%) of exposure group and 58 (63%) of

Table 2 Skin-prick test against pigeon droppings and feathers

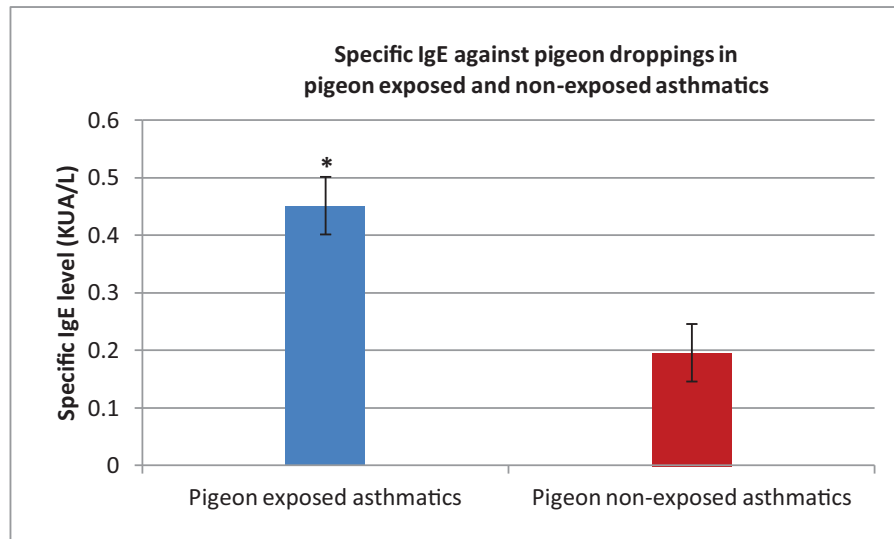
Skin-prick test response	Positive SPT response in patient (N=17) [n (%)]	
	Droppings	Feathers
1+	0	0
2+	2 (11.76)	1 (5.9)
3+	12 (17.58)	3 (17.6)
4+	0	0

SPT, skin-prick test.

Figure 1* $p < 0.078$ pigeon exposed asthmatic patients vs non-exposed asthmatic

Total IgE analysis in exposed and nonexposed asthmatics. IgE, immunoglobulin E.

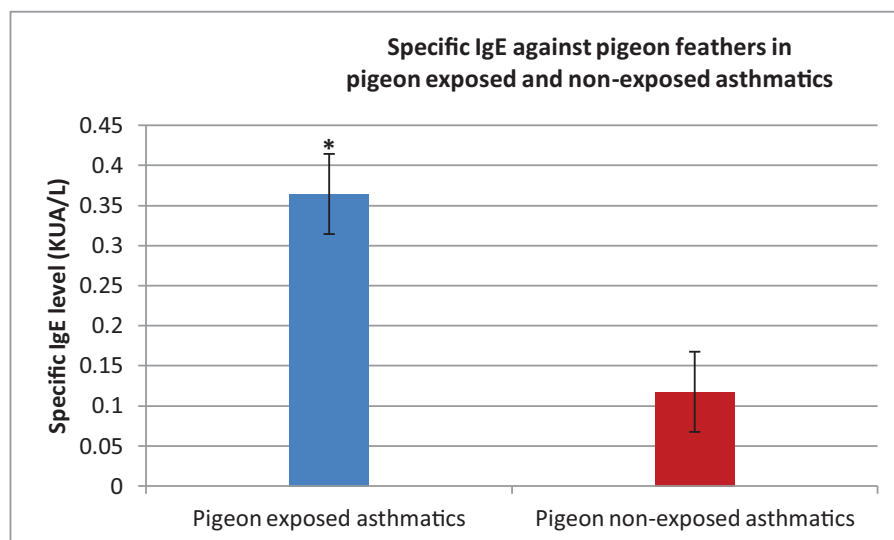
Figure 2



* $p < 0.003$ pigeon exposed asthmatic patients vs non-exposed asthmatic

Specific IgE analysis against droppings in pigeon-exposed and nonexposed asthmatics. IgE, immunoglobulin E.

Figure 3



* $p < 0.00$ pigeon exposed asthmatic patients vs non-exposed asthmatic

Specific IgE analysis against feathers in pigeon-exposed and nonexposed asthmatics. IgE, immunoglobulin E.

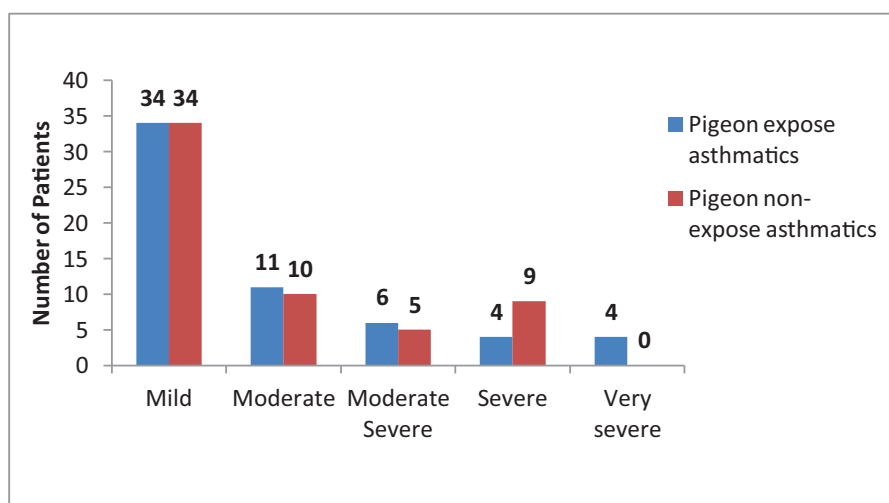
nonexposure patients. It is not statistically significant ($P=0.614$). The severity of obstruction was mild in 57.6% patients, moderate in 18.6%, moderate-severe in 10.1%, and severe and very severe in 6.7% of the exposure group. While the severity of obstruction was mild in 58.6%, moderate in 17.2%, moderately severe in 8.6%, and severe in 15.5% among the nonexposed group. The details of spirometry findings and its severity in exposure and nonexposure groups are shown in Fig. 4 and Table 4.

Discussion

In the present study, hypersensitivity response to two pigeon allergens, that is, pigeon dropping and feather, was qualitatively and quantitatively assessed by SPT and ELISA to measure the variation in possible responses between exposed and nonexposed asthma patients. Evidence for SPT, serum total IgE, and specific IgE was obtained, evaluated, and tested against two pigeon allergens to validate their

Table 3 Serum total and specific immunoglobulin E in pigeon-exposed and nonexposed asthmatics

Variables	Pigeon-exposed (mean±SD) (N=108)	Pigeon nonexposed (mean±SD) (N=92)	P value
Total IgE (IU/ml)	538.75±248.5	510.2±220.1	0.078
Specific IgE (KUA/L) droppings	0.4513±1.01	0.1957±0.179	0.003
Specific IgE (KUA/L) feathers	0.3644±0.329	0.1176±0.116	0.000
Total IgE (+ve)	612.7±185.0	537.7±199.9	0.939
Total IgE (–ve)	113.52±76.91	113.53±74.47	0.482
Specific IgE (+ve) droppings	0.999±1.52	0.530±0.216	0.129
Specific IgE (–ve) droppings	0.129±0.103	0.145±0.104	0.624
Specific IgE (+ve) feathers	0.609±0.34	0.384±0.030	0.027
Specific IgE (–ve) feathers	0.175±0.12	0.103±0.100	0.000

Figure 4

Baseline spirometry in pigeon-exposed and nonexposed groups.

Table 4 Spirometry pattern in expose and nonexpose asthmatics

Parameters	Pigeon expose (N=108)	Pigeon nonexpose (N=92)	P value
Obstruction [n (%)]	59 (59.6)	58 (63)	0.614
FVC (mean±SD)	3.36±0.86	3.27±0.87	0.840
FVC %pred (mean±SD)	89.72±12.74	92.86±14.52	0.084
FEV ₁ (mean±SD)	2.55±0.76	2.43±0.77	0.822
FEV ₁ %pred (mean±SD)	79.25±18.35	79.41±18.86	0.461

FEV₁, forced expiratory volume 1; FVC, forced vital capacity.

function in exposed and nonexposed asthmatics. The SPT sensitization was found in 15.7% of exposure asthmatics and none of the nonexposure patients.

The exposure to pigeon antigens at work/home may be considered as one of the risk factors for sensitization of pigeon allergens in some genetically sensitive asthma patients and exposure to pigeons is a triggering factor. Atopy historically has been seen as a risk factor of having asthma [22]. The sensitization data revealed that a high percentage (74.07%) of patients were atopic to common/environmental allergens indicating their susceptibility to allergic diseases. Of the 200 asthmatic

patients, 108 were exposed to pigeons and 17 (15.7%) of these 108 pigeon-exposed patients were found to be sensitive to either pigeon dropping or feather dropping. Out of pigeon allergen-positive patients, most of the patients 13 (76.4%) were sensitized to dropping. While three (17.6%) patients were sensitized to feathers. It is well established that indoor sensitivity to allergens, like dust mites, cats, pets, and fungi, may increase asthma and other allergic diseases [23]. Previous studies have shown that indoor dwellings increase the incidence of cockroach exposures [24] and mouse allergens [25], which in turn may increase the asthma rates. The incidence of atopy in asthma depends on certain

environmental factors that may at the same time induce atopy in both asthmatic and nonasthmatic people [26,27]. Deo *et al.* [10] in a study show that nearly 17% of asthma patients were sensitized to pigeon allergens. This may increase the asthma in their city. Similarly, we also found that 15.7% asthma patients with exposure to pigeons were sensitive to pigeon allergens. So, an asthmatic patient should avoid the unnecessary exposure to pigeon antigens to better control asthma. Feeding of pigeons is a culture and ritual practice in our country.

The development of a constant inflammatory process of the TH2 type, triggered by inhalation of a particular allergen, is the characteristic feature of allergic (or atopic) asthma, leading to the synthesis of specific IgE in susceptible individuals [28]; hence, the detection of specific IgE in the serum is the key evidence of allergic asthma [13]. The study's findings indicate that the proximity of asthma patients to pigeons induced sensitivity linked to the pigeon antigens. For atopic and pigeon-exposed asthma patients, a higher level of serum total and specific IgE has been observed. In a similar study performed by Kumar *et al.* [15], elevated serum total IgE rates and particular IgE toward food allergens were also identified. Similar to the above studies, we also found that the total and specific IgE against pigeon dropping and feather were higher in pigeon-exposure asthma patient groups compared with nonexposure groups.

Occupational lung disease, that is, pigeon breeder disease, is a well-known 'immune complex mediated' hypersensitivity due to exposure to pigeon antigens at occupation/work place [29,30]. Recent studies from India show that hypersensitivity pneumonitis is one of the common types of interstitial lung disease even without occupational history [31,32]. This high prevalence of nonoccupational HP from India may explain by, as people tend to keep pigeons for their religious purposes, as well as an ancient and valued practice. Bourke *et al.* [33] explain their views in a study of 270 pigeon fanciers for the occurrence of simple chronic bronchitis in relationship to avian exposure and IgG antibody to pigeon sensitization. They found that 26.2% pigeon fanciers had simple chronic bronchitis, while being nonsmokers throughout their life with no other lung diseases. The prevalence of chronic bronchitis increased significantly with sensitization categories. They suggested that host factor is important for the pathogenesis of chronic bronchitis as it was not related to the intensity and duration of exposure. So pigeon exposure leads to the spectrum of

lung disease ranging from simple airway irritation effect to fibrosing interstitial lung diseases with the host response and other environmental factors, it may also increase the symptoms of asthma in sensitive patients.

There is a lack of study on pigeon antigen sensitivity and asthma with exposure to pigeon antigen. The present study and that of Deo *et al.* [10] show that a significant number (>15%) of asthma patients were sensitive to pigeon allergens by SPT. This may increase the asthma cases in urban cities of India. However, there is a need for a larger multicenter study of pigeon allergen sensitivity and asthma with exposure to pigeon antigens at home/work place to identify this allergen for better management, asthma symptom control, and quality of life. We also advised asthma patients to avoid unnecessary exposure of pigeons at home/work place. Our study also demonstrated that the total and specific IgE against pigeon antigens were higher in asthmatic patients, who were exposed to pigeons at home/work place.

Conclusion

Environmental exposure to pigeon antigens is common in India without pigeon-related occupation as keeping of pigeons in home is a cultural and religious practice. This unnecessary exposure to pigeons increases the sensitivity to pigeons, particularly in asthmatic patients with high total and specific IgE along with SPT positivity. This may be one of the reasons for increasing asthma in urban cities of India. We advised to avoid unnecessary exposure to pigeon antigens in asthmatic patients to better disease control.

Author contributions

All of the authors searched for and gathered study records, participated in the writing, and accredited the final model of this paper.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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