

Prevalence of common sensitizing aeroallergens in patients with atopic dermatitis

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ABSTRACT

Background: Atopic dermatitis (AD), a skin disease burden worldwide, is a complex, multifactorial, chronic inflammatory disease. Prevalence of AD is increasing in developing countries and identifying the causative allergens is a major challenge. Aeroallergens are shown to aggravate atopic dermatitis.

Purpose: Explore the prevalence of aeroallergens sensitization in patients with AD and its possible relation with AD severity.

Methods: Cross-sectional study of 132 patients diagnosed to have atopic dermatitis. Atopy was detected by serum specific IgE to a panel of the most encountered aeroallergens.

Results: From the 132 patients, elevated specific IgE was detected in 72.7 % from which 59.1 % were mild and 86.4 % are moderate/severe as well as 15.9 % are mono-sensitized and 54.5 % are poly-sensitized with poly-sensitization being more in severe cases compared to mild cases (68.2 % vs 4.5 %). Regarding specific IgE to different aeroallergens, the most prevalent were *Dermatophagoides pteronyssinus* (50 %), followed by *Dermatophagoides farinae* (34.1 %), Birch pollen (20.5 %), cat epithelium (18.2 %) Ragweed (15.9 %), and Cockroach (9.1 %). However, moderate to severe cases were more sensitized to candida ($p = 0.012$), mix grass pollen ($p = 0.002$), ragweed (0.00), mite ($p = 0.037$) and cat epithelium ($p = 0.007$).

Conclusion: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, Birch pollen, cat epithelium Ragweed and Cockroach are the most frequent sensitizing aeroallergens in atopic dermatitis.

1. Introduction

Atopic dermatitis (AD) is a chronic skin disorder characterized by relapsing and remitting pruritic eczematous lesions with a preference for skin flexures [1]. Pathogenesis of AD is multifactorial including genetic and environmental factors, which vary across different racial groups [2,3] and with different epidemiology [3,4]. Although, the pathogenesis of atopic eczema is still debatable; it is known that aeroallergens can provoke atopic eczema in some patients [5]. Besides, one-third of patients with AD may develop asthma or allergic rhinitis. However, the association between AD and Type I sensitization is less clear when there is no history of inhalant allergy [6,7].

Inside-out and outside-in hypotheses, two theories, have been suggested as explanation of type I hypersensitivity in AD. The inside-out hypothesis proposes that allergen is the trigger which then weakens the skin barrier and permit allergen introduction and presentation [8].

This suggest that inflammation is the cause of an impaired skin barrier, leading to increased penetration of allergens. However, the outside-in hypothesis proposes that presence of a leaky skin barrier allows allergens entrance which then elicits an immune response through allergen uptake by immature DCs in the skin surface. Barrier defects can promote type 2 immunity due to the epidermal production of alarmins (IL-33, TSLP and IL-25). Both theories will predispose to type 2 inflammation. [9].

The clinical picture of AD in adults is not classical as in children and may have different forms as nummular (discoid), prurigo-like, follicular, seborrheic dermatitis [10,11] with erythroderma, but flexural lichenification is uncommon [12]. With the increasing prevalence of AD over the past decades, it affected approximately 15 % to 20 % of children and 1 % to 3 % of adults [4,13]. Few studies have been published.

To the best of our knowledge, no available epidemiological studies thus far on Egyptian population. Therefore, we aimed to investigate the

Abbreviations: AD, Atopic dermatitis; SCORAD, SCORing Atopic Dermatitis; IQR, Inter-quartile range; IgE, Immunoglobulin E; s.IgE, Specific IgE; HDMs, House dust mites.

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prevalence of most common aeroallergen sensitization in Egyptian patients with AD and possible association between degree of sensitization and the severity of dermatitis.

2. Methods

A cross-sectional study conducted on 132 adult patients diagnosed to have atopic dermatitis according to Hanifin and Rajka criteria [14]. They were recruited from Allergy and Immunology clinic of Ain Shams University hospital and Ain Shams Specialized hospital. Participants who full filled ≥ 3 major [pruritus, flexural lichenification or linearity in adults, facial and extensor involvement in infants and children, chronic or chronically relapsing dermatitis or personal or family history of atopy] PLUS ≥ 3 minor criteria [xerosis, ichthyosis, palmar hyperlinearity, or keratosis pilaris, immediate skin test reactivity, elevated serum IgE level, early age of onset, tendency toward cutaneous infections or impaired cell-mediated immunity, tendency toward nonspecific hand/foot dermatitis, nipple eczema, cheilitis, recurrent conjunctivitis, dennie-morgan infraorbital folds, keratoconus, anterior subcapsular cataracts, orbital darkening, facial pallor or erythema, pityriasis alba, anterior neck folds, itch when sweating, intolerance to wool and lipid solvents, perifollicular accentuation, food intolerance, course influenced by environmental/emotional factors, white dermographism or delayed blanch] were enrolled. The study excluded immunocompromised, patients with past history of allergen immunotherapy, or immunosuppressive therapy, urticaria, or allergic airway diseases. The study was reviewed and approved by Faculty of Medicine's Institutional review board, Ain Shams University. An informed consent was obtained from all participants.

Detailed allergy/clinical history (including environmental exposure) and examination were applied for all recruited patients. All information regarding patient's personal history as well as contact with common encountered allergens or having a personal or family history of allergic diseases, age of disease onset, use of systemic corticosteroids or any immunosuppressive drugs were collected.

All patients were assessed by SCORing Atopic Dermatitis (SCORAD) score. It includes the assessment of subjective symptoms (pruritus, sleep loss). The extent of lesions is scored by the rule of nine. The intensity is determined by grading each of the 6 items on a scale from 0 to 3 (erythema, edema/papulation, oozing/crusts, excoriation, lichenification and dryness). The total score is the sum of extent/5 + 7 intensity/2. The score lies between 0 and 83 on which, the severity of AD can be classified into mild (<15), moderate (between 15 and 40) and severe (≥ 40) AD [15].

2.1. Biochemical analysis:

Total Immunoglobulin E (IgE) testing was performed by enzyme-linked immunosorbent assays (IgE Quantitative test kit, Chemux Bioscience, Inc. U.S.A.). A commercially available kit (ImmunoLINE IgE Perennial, IMMUNOLAB GmbH, Kassel, Germany) was used to detect common allergen-specific IgE (s IgE) antibodies in serum by immunoblot technique to a panel of the most encountered inhalation allergens [Cladosporium, Alternaria alternate, Aspergillus niger, Aspergillus fumigatus, Penicillium notatum, Candida albicans, Birch pollen, Mix grasses pollen, Sun flower seed, Ragweed, Mugwort, Mite p (Dermatophagoides pteronyssinus), Mite f (Dermatophagoides farinae), Cat epithelium, Dog epithelium, Horse epithelium, Feather mixture, Cockroach, Bee venom, Wasp venom and Latex]. Sensitization was expressed as: < 0.35 U/ml as negative, $0.35\text{--}2$ U/ml as low titer, $2.1\text{--}17.49$ U/ml as moderate titer and 17.5 U/ml or more as high titer.

2.2. Statistical methodology:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. Quantitative data

were presented as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. Qualitative variables were presented as number and percentages. Comparison between groups with qualitative data was done by using Chi-square test. Comparison between two groups with quantitative data and parametric distribution were done by using Independent t-test while data with non-parametric distribution were done by using Mann-Whitney test. The confidence interval was set to 95 % and the margin of error accepted was set to 5 %. P-value was considered significant at the level of < 0.05 .

3. Results

From the 132 participants enrolled in the current study, 36.4 % were males and 63.6 % were females. Their median age was 28 (17.5 – 41) years, ranging from 2 to 85 years old. Median serum total IgE level was 196 (30 – 851) and ranged from 1.5 to 2500 IU/ml. 50 % have mild and 50 % of the patients have moderate to severe disease course (Table 1). Positive specific IgE to the studied aeroallergens was detected in 72.7 % of our patients. Mono-sensitized patients accounted for 15.9 % of all cases, while poly-sensitized were 54.5 % as shown in Table 2.

As demonstrated in Table 3, Dermatophagoides pteronyssinus was the most frequently sensitizing aeroallergen (50 %), followed by Dermatophagoides farinae (34.1 %), Birch pollen (20.5 %), cat epithelium (18.2 %) Ragweed (15.9 %), and Cockroach (9.1 %). Candida albicans (4.5 %) are the more sensitizing among fungal species. Alternaria alternate, Aspergillus fumigatus, were detected in 9.5 %, 2.3 % respectively. No reported sensitization to Cladosporium, Aspergillus niger nor Penicillium notatum. As regards HDMs, positive s IgE to Dermatophagoides pteronyssinus was observed among 50 % of patients compared to 34.1 % to Dermatophagoides farinae. With respect to animals, dog epithelium followed by cat and horse epithelium were positive in 18.2 %, 6.8 % and 2.3 % of patients respectively. No patients were sensitized to mixed feathers. Birch pollen (20.5 %) are the more sensitizing among pollen. Ragweed, Mix grasses pollen and sunflower seeds were observed in 15.6 %, 6.8 % and 2.3 % respectively.

Table 4 showed highly significant increase in serum total and specific IgE in moderate to severe cases ($p = 0.00$) compared to mild cases. Regarding the number of allergens positivity, poly-sensitization is more in moderate to severe cases compared to mild cases (68.2 % vs 4.5 %) as shown in Fig. 1.

In Fig. 2, we compared frequency of sensitization among mild and moderate to severe cases, moderate to severe cases were more sensitized to candida ($p = 0.012$), mix grass pollen ($p = 0.002$), ragweed (0.00), mite ($p = 0.037$) and cat epithelium ($p = 0.007$).

On comparing serum total Ig E with different disease parameters, only significant increase in moderate to severe dermatitis (59.4 % vs 40.6 %), poly-sensitized (65.6 % vs 18.8 %) patients and with mites, horse epithelium, Alternaria alternata and birch pollen was observed. While on comparing specific IgE, no significant relation was observed with either age or gender. In addition, there was positive correlation between total number of allergen specific IgE and total Ig E ($r = 0.48$, p

Table 1
Demographic characteristics of the studied group:

		Total no. = 132
Gender	Male	48 (36.4 %)
	Female	84 (63.6 %)
Age	Median (IQR)	28 (17.5 – 41)
	Range	2 – 85
Atopic dermatitis	Mild	66 (50.0 %)
	Moderate to severe	66 (50.0 %)
Total IGE	Median (IQR)	196 (30 – 851)
	Range	1.5 – 2500
Specific IGE	Normal	36 (27.3 %)
	Elevated	96 (72.7 %)

Table 2

Results of specific Immunoglobulin E (IgE) positive results to the most encountered allergens.

	Total no. = 132
Negative	39 (29.5 %)
Mono-sensitized	21 (15.9 %)
Poly-sensitized	72 (54.5 %)
2	30 (41.7 %)
3	15 (20.8 %)
4	18 (25.0 %)
5	6 (8.3 %)
6	3 (4.2 %)

= 0.00) was observed as shown in Fig. 3.

4. Discussion:

Identifying environmental allergens is a major challenge in allergy and essential for their prevention [16]. Hence, we aimed to investigate the prevalence of aeroallergen sensitization among patients with atopic dermatitis (AD) and its association with severity. This study was a cross-sectional study conducted on 132 patients diagnosed to have AD. Their ages ranged from 2 to 85 years old with 28 (17.5 – 41) the median age of years. Positive specific IgE to the studied aeroallergens was detected in 72.7 % of our patients. Mono-sensitized patients accounted for 15.9 % of all cases, while poly-sensitized was 54.5 % %. *Dermatophagoides pteronyssinus* was the most frequently sensitizing aeroallergen (50 %), followed by *Dermatophagoides farinae* (34.1 %), Birch pollen (20.5 %), cat epithelium (18.2 %) Regweed (15.9 %), and Cockroach (9.1 %).

In line with ours, house dust mite and cat epithelium proved to be the most common relevant aeroallergens by Ponyai and colleagues. *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* sensitization was high with severe AD. Pollens were observed in patients with recurrent relapse and animal epithelium during flare-up of skin symptoms [17].

These results differ from, studies in Karaj, Isfahan and Zanjan, in which pollen has been reported as the most common allergy, including patients with AD [18–20]. Another study in Khorasan, sensitivity to weed and pollen was the highest [21]. In Ghaderi and Rashavi study, in line with these studies, the sensitivity was more to pollen of trees, weed and cockroach was the highest (35.5 %) [22]. Variation in allergen sensitization can be attributed to different climatic and genetics factors. Most published articles show different allergens sensitivity pattern in different countries and even in different areas of the same country.

The observed increase in warm and especially dry air predispose to more pollen and grasses, as have been detected in Karaj, Tehran, Shiraz but vegetation alone is not a cause of higher sensitivity in AD patients. In Tehran, weeds are the most common allergies [23]. In America and Western Europe, cypress is the most common among trees [24].

In this study, birth pollen (20.5 %) is the more sensitizing among pollens. Regweed, mix grasses pollen and sunflower seeds were observed in 15.6 %, 6.8 % and 2.3 % respectively but it was still common among inhalant allergens. Despite the similarity of the climate, the vegetation of regions if different, the resulting frequency of grass and weeds will be different. In a study in Kuwait, weeds observed as the highest inhalation allergens [25].

Another study in Shiraz, showed that sensitivity to pollens, mites, trees, and passion grass is higher than other allergens. These results are consistent with those reported in warm and dry regions [26,27]. In Pónyai and colleagues 'study [17], as well as a study in Isfahan and Shiraz, the highest inhalation allergen is cypress 35.5 %, followed by weeds and grass 29.1 % and then cockroach 25.8 %. Pollens are found to be the main allergens in Iran and the high correlation of these allergens with atopy suggests their role in the pathogenesis of atopic dermatitis in Iran [28].

The climate in Egypt favors more sensitization of HDMs. In our

sample, 50 % of patients were sensitized to *Dermatophagoides pteronyssinus* and 34.1 % to *Dermatophagoides Farinae*. This is in line with Abd Ella and colleagues who concluded that the prevalence of sensitization to HDMs in atopic patients was 36.36 % [29]. It is well established that HDMs are more prevalent in warm, humid subtropical areas [30]. Also, in the Ghaffari's study, there was an increase in *Dermatophagoides pteronyssinus* in 33 %, *Dermatophagoides farinae* in 32 % of cases [31] but in Ghaderi and Rashavi study, contrary to the previous mentioned studies, there was a small prevalence of Mite (9.7 %), which is different due to different climatic conditions [22].

Fungi are popular aeroallergens, copious both indoors and outdoors and related to increased humidity [32]. In our study, prevalence of fungal sensitization was 4.5 % for *Candida albicans*. *Alternaria alternata*, *Aspergillus fumigatus*, were detected in 9.5 % and 2.3 % respectively. In the Gonabad study, the highest percentage of fungi detected were yeast (31 %), *cladosporium* (30 %), *penicillium* (19.5 %), *aspergillus* (6.3 %), *alternaria* (3.6 %) [33], completely different from the current study. This may be due to the different environmental conditions such as oxygen and moisture, sources are more likely to grow in fungi. In a study in Semnan, the prevalence of allergy to *Aspergillus* was 12.3 %, *Cladosporium* 11 %, *Alternaria* 10.7 %, *Penicillium* 8.3 %. In Ghaderi and Rashavi study, *cladosporium* was 12.9 %, 6.5 % *penicillium*, 3.2 % *alternaria* and 0 % *aspergillus*. But in our study, no reported sensitization to *Cladosporium*, *Aspergillus niger* nor *Penicillium notatum*. However, Awad et al, in a study to explore airborne fungi in urban and rural regions in Egypt, reported that *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium*, and yeasts were the most prevalent indoors and outdoors fungi species in Egypt [34].

Growth of fungi occurs in areas of shadow and moisture, and on rotting leaves. Wind and rain and temperature are effective in the distribution of fungal spores. Therefore, climatic conditions differently cause this difference in the frequency of fungi. In a study in Khorasan, there was no reported sensitivity to *aspergillus* [35].

Animals may induce sensitization by either their dander, epitheliums, salivary protein, perianal or sebaceous glands. Dog epitheliae followed by cat and horse epitheliae were positive in 18.2 %, 6.8 % and 2.3 % of patients respectively in our study. No patients were sensitized to mixed feathers.

We reported highly significant increase in serum total and specific IgE in moderate to severe cases ($p = 0.00$) compared to mild cases. Regarding the number of allergens reactivity, poly-sensitization is more frequent in moderate to severe cases compared to mild cases (68.2 % vs 4.5 %). In line with ours, Schäffer et al. observed that the degree of sensitization is directly associated with the severity of AD and the sIgE response seems to contribute to the severity of the disease. Total and allergen-sIgE antibodies to grass and birch pollen, *Cladosporium herbarum*, *Dermatophagoides pteronyssinus*, and cat epithelium in serum were determined with significant associations between the severity score of AD and concentrations of allergen-sIg after adjustment for other factors [36]. It is likely due to the ability of aeroallergen proteins to penetrate the epidermis and worsen AD severity which may be either through its proteolytic enzyme activity, activation of proteinase-activated receptors-2, or IgE binding, leading to increased inflammation [37].

Also, skin barrier disruption can increase permeability to external allergens thus facilitating Th2 immune response through antigen-presenting cells which predispose to increased IgE production and subsequent hypersensitivity reactions. Hence, IgE has a significant contribution in the pathogenesis of AD and has increased levels in the serum and skin of AD patients with significant association between higher levels of IgE and the severity of AD. However, some patients have normal or even low levels of total serum IgE with positive skin prick test. This points up the importance of specific IgE rather than the total IgE, even if a positive correlation exists between them [38].

When we compared frequency of sensitization among mild and moderate to severe cases, moderate to severe cases were found to be

Table 3

Results of specific Immunoglobulin E (IgE) results to each allergen:

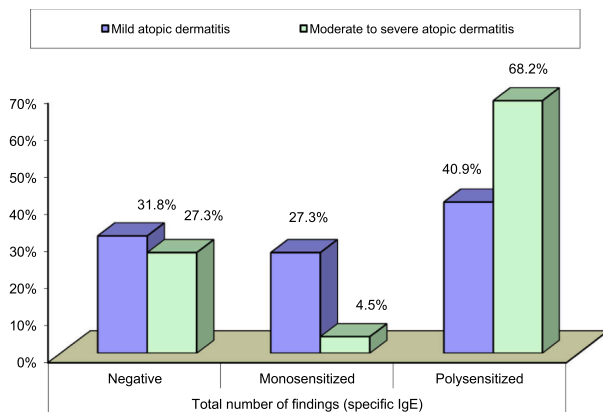
		Total no. = 132
Cladosporium	Negative	132 (100.0 %)
	Positive	0 (0.0 %)
Alternaria alternata	Negative	120 (90.9 %)
	Positive	12 (9.1 %)
	Median (IQR)	11.75 (2.25 – 44.45)
	Range	1 – 68.9
Aspergillus niger	Negative	132 (100.0 %)
	Positive	0 (0.0 %)
Aspergillus fumigatus	Negative	129 (97.7 %)
	Positive	3 (2.3 %)
	Mean $\pm$ SD	0.46 $\pm$ 0.00
	Range	0.46 – 0.46
Penicillium notatum	Negative	132 (100.0 %)
	Positive	0 (0.0 %)
Candida albicans	Negative	126 (95.5 %)
	Positive	6 (4.5 %)
	Mean $\pm$ SD	0.37 $\pm$ 0.01
	Range	0.36 – 0.37
Birch pollen	Negative	105 (79.5 %)
	Positive	27 (20.5 %)
	Median (IQR)	1.5 (0.35 – 2.3)
	Range	0.35 – 9.2
Mix grasses pollen	Negative	123 (93.2 %)
	Positive	9 (6.8 %)
	Median (IQR)	1.6 (0.55 – 3.6)
	Range	0.55 – 3.6
Sun flower seed	Negative	129 (97.7 %)
	Positive	3 (2.3 %)
	Mean $\pm$ SD	10.90 $\pm$ 0.00
	Range	10.9 – 10.9
Regweed	Negative	111 (84.1 %)
	Positive	21 (15.9 %)
	Median (IQR)	3.2 (2.1 – 6.7)
	Range	0.35 – 9.9
		Total no. = 132
Mugwort	Negative	132 (100.0%)
	Positive	0 (0.0%)
Mite p (Dermatophagoides pteronyssinus)	Negative	66 (50.0%)
	Positive	66 (50.0%)
	Median (IQR)	5.9 (1.4 – 8.2)
	Range	0.35 – 35.4
Mite f (Dermatophagoides farinae)	Negative	87 (65.9%)
	Positive	45 (34.1%)
	Median (IQR)	3.7 (1.4 – 6.7)
	Range	0.35 – 35
Cat epithelium	Negative	108 (81.8%)
	Positive	24 (18.2%)
	Median (IQR)	5.85 (3.25 – 12.2)
	Range	0.35 – 100
Dog epithelium	Negative	123 (93.2%)
	Positive	9 (6.8%)
	Median (IQR)	0.9 (0.35 – 30)
	Range	0.35 – 30
Horse epithelium	Negative	129 (97.7%)
	Positive	3 (2.3%)
	Mean $\pm$ SD	0.50 $\pm$ 0.00
	Range	0.5 – 0.5
Feather mixture	Negative	132 (100.0%)
	Positive	0 (0.0%)
Cockroach	Negative	120 (90.9%)
	Positive	12 (9.1%)
	Median (IQR)	0.55 (0.4 – 1.33)
	Range	0.36 – 2
Bee venom	Negative	132 (100.0%)
	Positive	0 (0.0%)
Wasp venom	Negative	129 (97.7%)
	Positive	3 (2.3%)
	Mean $\pm$ SD	0.43 $\pm$ 0.00
	Range	0.43 – 0.43
Latex	Negative	129 (97.7%)
	Positive	3 (2.3%)
	Mean $\pm$ SD	2.70 $\pm$ 0.00
	Range	2.7 – 2.7

Table 4

Relation between SCORAD score and demographic and laboratory investigations.

		Atopic dermatitis		Test value	P-value	Sig.
		Mild	Moderate to severe			
		No. = 66	No. = 66			
Gender	Male	21 (31.8 %)	27 (40.9 %)	1.179*	0.278	NS
	Female	45 (68.2 %)	39 (59.1 %)			
Age	Median (IQR)	34 (21 – 42)	26 (13 – 39)	-1.742 $\neq$	0.082	NS
	Range	10 – 58	2 – 85			
Total Immunoglobulin E (IgE)	Median (IQR)	61.5 (15 – 200)	404.5 (133 – 1142)	-5.326 $\neq$	0.000	HS
	Range	1.5 – 2112	9 – 2500			
Specific Immunoglobulin E (IgE)	Negative	27 (40.9 %)	9 (13.6 %)	12.375*	0.000	HS
	Positive	39 (59.1 %)	57 (86.4 %)			

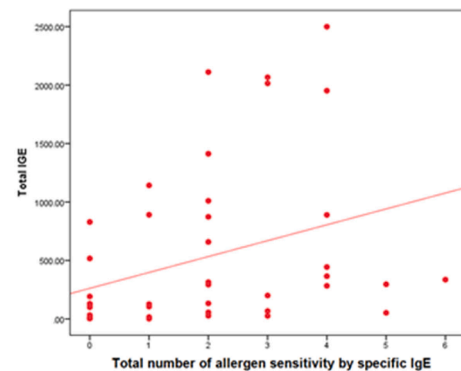
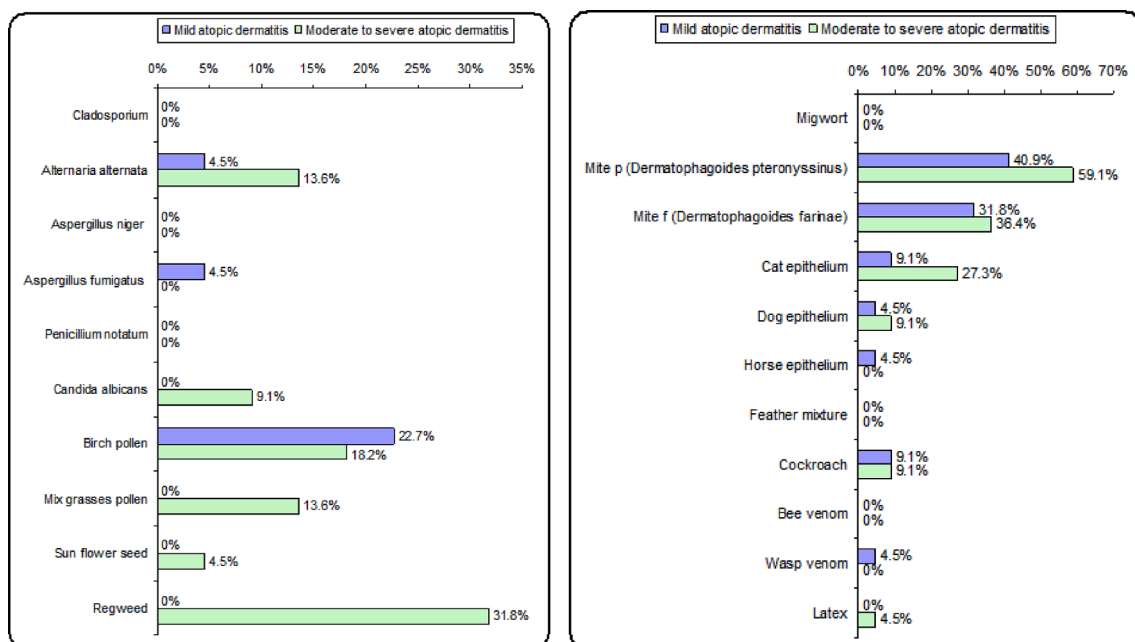
P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant.

*: Chi-square test; $\neq$: Mann-Whitney test.**Fig. 1.** Relation between number of allergen sensitivity by specific IgE and atopic dermatitis severity.

more sensitized to candida ($p = 0.012$), mix grass pollen ($p = 0.002$), ragweed (0.00), mite ($p = 0.037$) and cat epithelium ($p = 0.007$). However, Ponyai and colleagues observed increase of *D. pteronyssinus* and *D. farinae* sensitization particularly in patients with severe skin

symptoms [17].

On comparing serum total E with different disease parameters, only significant increase in moderate to severe dermatitis (59.4 % vs 40.6 %), poly-sensitized (65.6 % vs 18.8 %) patients and with mites, horse epithelium, *Alternaria alternata* and birch pollen was observed. While on comparing specific IgE, no significant relation was observed with

**Fig. 3.** Correlation between serum total Immunoglobulin E (IgE) levels and total number of allergen sensitivity by specific IgE.**Fig. 2.** Relation between specific allergens positive results and severity of atopic dermatitis.

either age or gender similar to Ghaderi and Rashavi study, in which the distribution of inhalation allergens in each gender was the same. In addition, there was positive correlation between total number of allergen specific IgE and total Ig E was detected in the study ($r = 0.48$, $p = 0.00$) [22].

5. Conclusion

Atopic dermatitis exhibits aggravation by aeroallergens with special predilection to *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, Birch pollen, cat epithelium, Ragweed and Cockroach with a significant association between higher levels of specific IgE and the severity of AD. Patients with normal or even lower levels of total serum IgE may show positive skin prick results and high levels of specific IgE. This signifies the importance of specific IgE rather than the total IgE. More prospective studies, however, are required to further assess the benefit of reducing aeroallergen exposure and comparative populations be used in comparable provinces in the same climatic conditions. In addition, specific cytokine profiles and barrier abnormalities characterize different AD groups. This should be considered in future for further therapeutic targeting therapy for patients with AD.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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