

# Allergy to *Dermatophagoides pteronyssinus* (Der p1) and *Dermatophagoides farina* (Der f1) in Patients with Atopic Asthma

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**Abstract:** Background: House dust mites (HDMs) are important sources of indoor allergens. The prevalence of sensitization to HDM in atopic patients is around 70% to 90% worldwide. Objective: Our aim was to measure the specific IgE to components of Der p1 and Der f1 in asthmatic patients at Qena Governorate, Egypt. Methods: We performed a prospective evaluation of 48 HDM sensitized asthmatic patients with positive skin prick test to *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farina* (Der f). Patients underwent Immuno CAP for specific IgE to Der p 1, Der f 1. Results: Skin prick test were done to 132 patients asthma with attending to Qena University Hospital to *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farina* (Der f) and other allergenic components, also skin prick test were done to 38 healthy people as a control group. Skin prick test were positive in 48 patients (36.36%) (P value is < 0.015). Forty-eight asthmatic patients had detectable serum specific IgE to Der p 1 and Der f 1 by ImmunoCAP assay. There was a significant positive correlation between skin prick test and specific IgE to Der p1 and Der f1 (P value is 0.000). According to sex there was a highly correlation among sensitivity to Der p1 and Der f1 in both males and females (P value is 0.000), also there were a highly significant relation among sensitivity to Der p1 and Der f1 (P value is 0.000) and residence (rural or urban) of the studied patients. Conclusion: Sensitization to HDM especially *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farinae* (Der f) is similar to previous studies. Determination of Der p 1 and Der f1 specific IgE helps in obtaining additional information in regards to atopic asthma and other allergic diseases.

**Keywords:** Egypt, Patient, Asthma, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, Immuno CAP.

## 1. Introduction

House dust mites (HDM) are major source of inhalant allergens responsible for allergic asthma *Spijksma and Dieges, (2004)*. There are many species of dust mites infested in and around the houses worldwide *Dermatophagoides pteronyssinus* (Dp) and *Dermatophagoides farina* (Df) are of the most common house dust mites (HDMs) *Arlian and Platts-Mills (2001)*.

Extensive studies have been done to understand the biological, chemical and structural properties of such mite allergens and most characterized allergens are from *Dermatophagoides farina* (Df) and *Dermatophagoides pteronyssinus* (Dp) that are coexisting in most geographical regions *(Yasue et al., 1998 and Platts-Mills et al., 1992)*. Secretions, feces and body degradation products of HDM can cause human allergic diseases *(Arlian and Platts-Mills, 2001 and Fernandez-Caldas, 2002)*.

Type I allergic diseases, including allergic asthma, allergic rhinitis and atopic dermatitis are increasingly prevalent, and becoming one of global health problems, which

affected as high as 10% to 30% of the world population *(Ferreira et al., 2002)*. Asthma is a chronic airway inflammatory disease, characterized by lung leukocyte and eosinophilic infiltration accompanied by mucus hypersecretion and airway hyperresponsiveness *(Li and Hua (2014) and kim et al., 2010)*, and closely associated with activated T cells in the lung. Development of asthma depends on an interaction between genetic factors and environmental allergens, especially house dust mites (HDM) *(Sporik et al., 1990 and Lau et al., 2000)*. Allergic exposure leads to sensitization, and sensitization to HDM is an important risk factor for the development of asthma in childhood *Wahn et al., (1997)*. The prevalence of sensitization to HDM in atopic patients is around 70% to 90% worldwide *Montealegre et al., (2004)*

## 2. Aim of the Work

Aim of the prospective study to assess the role of House Dust Mites (HDM), *Dermatophagoides pteronyssinus* (Der p1) and *Dermatophagoides farina* (Der f1) in asthmatic patients at Qena Governorate by skin prick test and also to measure by Immuno CAP assay specific IgE to

Der p 1 and Der f 1 in the studied asthmatic patients and control group.

### 3. Material and Methods

132 patients (65 males and 67 females), 21 children (5-15 years) and the rest were adults and according to residence 68 were from rural areas and 64 from urban areas, those patients attending to Chest Disease Department outpatient clinic, Pediatric outpatient clinic and inpatients of this departments complaining from chronic or recurrent cough with wheezy chest and diagnosed as bronchial asthma. The diagnosis of asthma was based on the criteria of the 2002 Global Initiative for Asthma (GINA) guidelines (*National Institutes of Health, National Heart, Lung, and Blood Institute, 2002*). All patients enrolled for analysis of percentage of sensitization to indoor allergens had positive results to the methacholine bronchial provocation test. Also 38 healthy people recruited in the study as a control group. Skin prick test were done to all enrolled patients and control group in the study, the antigens used for skin prick test were *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*, *Aspergillus fumigatus*, *Penicillium notatum*, *Candida albicans*, Grass pollen, hay dust, duck and pigeon feather, bird excreta, cat and dog hair, and cockroach extract. Histamine phosphate (5mg/ml, as a positive control) and negative control solution were also used (the antigens and positive and negative controls were supplied by the Allergopharma Joachim Ganzer KG company). The test was considered positive if the mean diameter of the wheal at 15 minutes was > 3 mm than the negative control. 48 asthmatic patients were with positive skin prick test to House Dust Mites (HDM), *Dermatophagoides pteronyssinus* (Derp1) and *Dermatophagoides farinae* (Der f1) were enrolled in the study and blood samples for IgE assay of ImmunoCAP (Pharmacia CAP System; Pharmacia Diagnostics AB, Uppsala, Sweden) *Paganelli et al., (1998)*. The studied patient's and control divided to four groups according to age as following 5-15 years 7 cases, 15-30 years 30 cases, 30-45 years 24 cases and 45-60 years.

Blood samples were taken by venipuncture using anticoagulant-free tubes to obtain serum for antibody determinations Specific IgE levels against *Dermatophagoides pteronyssinus* (Der p1) and *Dermatophagoides farinae* (Der f1).

Specific serum Ig E Der p1 crude extract, Der f1 crude extract, Der p 1 and Der f1 were measured with the ImmunoCAP immunofluorimetric assay, components and reagents (Thermo Fisher Scientific, Immuno Diagnostics, Uppsala, Sweden). Measures of total IgE levels were expressed in international units per unit volume (IU/mL, 1 IU equals 2.4 ng). Specific IgE levels were expressed in arbitrary units per unit volume (IU/mL). The measuring range of total IgE was between 2 and 5,000 IU/mL and that of specific IgE to Der p extract and molecular components were between 0 and 100 IU/mL. In case a measure was too high for the measuring range, we assumed IgE to be 100 IU/mL. The Immuno CAP 250 machine underwent monthly quality controls (Euro EQAS

for Total IgE, Euro EQAS for Specific IgE, Phadia Quality Club for specific IgE).

The Pharmacia CAP system defines seven quantitative classes by the following criteria:

- Class 0, below 0.35 kUA/l.
- Class 1, 0.35 to 0.7 kUA/l.
- Class 2, 0.7 to 3.5 kUA/l.
- Class 3, 3.5 to 17.5 kUA/l.
- Class 4, 17.5 to 50 kUA/l.
- Class 5, 50 to 100 kUA/l.
- Class 6, above 100 kUA/l.

A value of 0.35kUA/l or above is identified as a positive result and considered positive sensitization to allergen *Pastorello et al., (1995)* and *Official abstracts of papers of the XIII International Congress of Allergology and Clinical Immunology (ICACI) (1988)*.

The Immuno CAP results were analyzed to investigate the percentage of sensitization to HDM (positive results of specific IgE assay for both Der p1 and Der f1). Demographic characteristics including age, gender and residence were evaluated for associations with the percentage of allergic sensitization. The studied 48 asthmatic patients and 16 from 34 with negative skin prick test to HDM were randomly recruited in the study as a control group, divided into 4 age groups as following: 5-15 years (7 patients), 15-30 years (25 patients and 5 controls), 30-45 years (14 patients and 10 controls) and 45- 60 years (2 patients and 1 control). The residential variables were classified as urban (30 patients and controls) and rural (34 patients and controls).

Stool samples from all patients and control group were macroscopically examined. Then, the samples were microscopically examined as the stained direct smear and by sedimentation and Kato-Katz techniques to exclude helminthic infection (*Katz et al., 1972*).

### 4. Statistical Analysis

Data are expressed as the mean  $\pm$  SD, and were analyzed using SPSS 16.0 software (SPSS, Inc., Chicago, IL, USA). The chi-square test or Fisher's exact test were used to examine the percentage difference of sensitization to individual allergens within different age groups, gender and residential variables. The chi-square test was used to compare the percentage difference of sensitization to HDM among age groups, gender and residence. P value is <0.05 was considered to indicate a statistically significant result.

The study was approved by the Ethical Committee of South Valley University Qena Faculty of medicine. Signed informed consent was obtained from patients or their parents.

### 5. Results

The study period, 132 asthmatic patients adults and children who visited the Out Patients Clinics (Chest Disease Department and pediatric Department) of Qena University Hospital and /or admitted to this department.

All the studied patients diagnosed as asthma according to (GINA) guidelines, skin prick test were done to them and it was positive to HDM in 48 patients (36.36%). Within the 48 patients sensitized to HDM, 13 were found to be with low positive skin prick test, 14 were found to be with moderate positive skin prick test and 21 were found to be with high positive skin prick test, while in control group (38), it was 2 were found to be with low positive skin prick test and 2 were found to be with moderate positive skin prick test with significant relation between skin prick test in asthmatic patients in comparison control group (P value is 0.015). Specific IgE levels for *Dermatophagoides pteronyssinus* (Der p1) and *Dermatophagoides farinae* (Der f1) were analyzed to all studied patient's and controls who were divided into four groups according to age as following 5-15 years 7cases, 15-30 years 30 cases, 30-45years 24 cases and 45-60 years and specific IgE to Der

**The following tables showing results of the present study:**

p1 and Der f1 by Immuno CAP assay were detected in 91.66% and in control group it was 25% and there were a high significant relation of (P value is 0.000). According to sex there was a highly significant relation among sensitivity to Der p1 and Der f1 in both males and females (P value is 0.000). According to age groups there were a high significant correlation in age group 2 (P value is 0.000) and low significant correlation (P value is 0.029) while there were no significant relation among age groups 1 and 4 (P value is 0.156) and (P value is 0.199) respectively. In accordance to residence sensitivity to Der p1 and Der f1 was highly significant correlation (P value is 0.000) in both rural and urban residence of the studied patients but sensitivity to Der p1 and Der f1 were more severe in rural patients.

**Table 1:** Skin prick test results of the studied cases and control groups

		Skin prick test				Total	P value
		-Ve	High	Moderate	Low		
Case		84	21	14	13	132	.015
Control		34	0	2	2	38	
Total		118	21	16	15	170	

**Table 2:** Skin prick test and specific IgE in asthmatic and control groups

Case-control			Skin Test				Total	P value
			-Ve	Low	Moderate	High		
Case	Test Results	Class 0	0	4	0	0	4	.000
		Class 1	0	8	4	0	12	
		Class 2	0	4	6	0	10	
		Class 3	0	0	6	0	6	
		Class 4	0	0	5	1	6	
		Class 5	0	0	2	3	5	
		Class 6	0	0	0	5	5	
Total			0	9	23	9	9	
Control	Test Results	Class 0	12	0	0	0	12	
		Class 1	1	0	0	0	1	
		Class 2	3	0	0	0	3	
		Class 3	0	0	0	0	0	
		Class 4	0	0	0	0	0	
		Class 5	0	0	0	0	0	
		Class 6	0	0	0	0	0	
Total			16	0	0	0	16	

**Table 3:** Skin prick test IgE and its relation to gender of asthmatic patients and control group

Sex			Skin Test					P value
			-Ve	Low	Moderate	High	Total	
Female	Test Results	Class 0	5	2	0	0	7	.000
		Class 1	0	4	2	0	6	
		Class 2	0	4	3	0	7	
		Class 3	0	0	4	0	4	
		Class 4	0	0	1	0	1	
		Class 5	0	0	1	0	1	
		Class 6	0	0	0	1	1	
Total			5	10	11	1	1	

Male	Test Results	Class 0	7	2	0	0	9	
		Class 1	1	4	2	0	7	
		Class 2	3	0	2	0	5	.000
		Class 3	0	0	2	0	2	
		Class 4	0	0	5	1	6	
		Class 5	0	0	1	3	4	
		Class 6	0	0	0	4	4	
		Total		11	6	12	8	8

**Table 4:** Skin prick test, IgE and its relation to age groups of asthmatic patients and control group

Age groups			Skin Test				Total	P value
			-Ve	Low	Moderate	High		
Group1	Test Results	Class 0	0	0	0	0	0	
		Class 1	0	2	0	0	2	
		Class 2	0	1	1	0	2	.156
		Class 3	0	0	0	0	0	
		Class 4	0	0	0	0	0	
		Class 5	0	0	0	1	1	
		Class 6	0	0	0	2	2	
Total			0	3	1	3	6	
Group 2	Test Results	Class 0	4	1	0	0	5	
		Class 1	0	4	3	0	7	
		Class 2	1	2	2	0	5	
		Class 3	0	0	4	0	4	.000
		Class 4	0	0	4	0	4	
		Class 5	0	0	1	2	3	
		Class 6	0	0	0	2	2	
Total			5	7	14	4	30	
Group3	Test Results	Class 0	8	2	0	0	10	.029
		Class 1	0	2	1	0	3	
		Class 2	2	1	2	0	5	
		Class 3	0	0	2	0	2	
		Class 4	0	0	2	1	3	
		Class 5	0	0	1	0	1	
Total			10	5	8	1	23	
Group 4	Test Results	Class 0	0	1	0	0	1	
		Class 1	1	0	0	0	1	.199
		Class 2	0	0	0	0	0	
		Class 3	0	0	0	0	0	
		Class 4	0	0	0	0	0	
		Class 5	0	0	0	0	0	
		Class 6	0	0	0	1	1	
Total			1	1	0	1	3	

**Table 5:** Skin prick test and IgE and its relation to residence of studied cases

Residence			Skin Test				Total	P value
			-Ve	Low	Moderate	High		
Rural	Test Results	Class 0	4	3	0	0	7	
		Class 1	0	3	2	0	5	
		Class 2	0	3	2	0	5	
		Class 3	0	0	4	0	4	.000
		Class 4	0	0	6	1	7	
		Class 5	0	0	0	1	1	
		Class 6	0	0	0	5	5	
Total			4	9	14	7		
Urban	Test Results	Class 0	8	1	0	0	9	
		Class 1	1	5	2	0	8	
		Class 2	3	1	3	0	7	
		Class 3	0	0	2	0	2	.000
		Class 5	0	0	2	0	4	
		Class 6	0	0	0	0	0	
Total			12	7	9	0	30	

## 6. Discussion

House dust mites (HDMs) are important sources of indoor allergens *Spieksma and Dieges (2004)*. Sensitization to HDM in the general population is 9-16% *Squillace et al., (1997)*. HDM are major allergen sources for almost 50% of allergic patients *De Blay et al., (1994)*.

In the present study, we aimed to define the prevalence of sensitization to Der p1, Der f1 among patients with atopic asthma in Qena Governorate.

In the present study 132 asthmatic patients children and adults who was diagnosed as asthma according to (GINA) guidelines, skin prick test were done to them and it was positive to HDM (*Dermatophagoides pteronyssinus* (Der p1) and *Dermatophagoides farinae* (Der f1) in 48 patients (36.36%), while skin prick test in control group was 15.78% with a significant difference (P value is 0.015) (table 1) and this agree with a study by *Helal et al., (1999)* they found sensitivity to HDM by skin prick test was 32.4%, also *Mohamed et al., (2000)* in a study on asthmatic patients at Assuit Governorate sensitivity to HDM by skin prick test was 35% and *Gutarowska et al., (2005)* found that 38.8% of allergic patients had positive skin prick test to HDM. *Lee et al., (2008)* stated that the sensitivity to *Dermatophagoides pteronyssinus* (Der p1) 26.6% and to *Dermatophagoides farinae* (Der f1) 22.7% which more or less agree with the results obtained in the present study, also *Castro- Almarales et al., (2006)* in a study done on Cubans asthmatic patients stated that sensitivity to (*Dermatophagoides pteronyssinus* (Der p1) and *Dermatophagoides farinae* (Der f1) was 31.9%.

On the hand *Kamal et al., (2008)* in a study done at Sohag Governorate found that sensitivity to *Dermatophagoides pteronyssinus* (Der p1) was 52%, *El- Shinawy et al., (1989)* conducted that 80% of asthmatic patients were sensitive to *Dermatophagoides pteronyssinus* (Der p1) which was higher than the results obtained in the present work.

Der p 1 and Der f 1 are cysteine proteases with multiple effects on mite-host interaction. These proteases facilitate allergen delivery to the sub-mucosa and its antigen-presenting cells, leukocyte recruitment and activation, including mast cell and eosinophil degranulation, bronchial smooth muscle contraction and proliferation (*Gregory and Lloyd (2011), Jacquet (2011), Lambrecht and Hammad (2009) and Miglino et al., (2011)*).

In the present study, we measure specific IgE for *Dermatophagoides pteronyssinus* (Derp1) and *Dermatophagoides farinae* (Der f1) to asthmatic patients and healthy control group, so blood samples for IgE assay of Immuno CAP asthmatic patients, and we found that there was a significant relation between serum specific IgE to Der p1 and Der f1 in patients in comparison to control group where specific IgE to Der p1 and Der f1 detected in 91.66% in asthmatic patients while it was 25% in control group (P value is 0.000), also there was a significant correlation between skin prick test and the levels of IgE to Derp1 and Derf1 where its level was high with moderate and higher with strong positive skin prick test and its level was low or negative with low skin prick test (P value is 0.000), finding and control group this agree with *Hala et al., (2007)* they reported that the level of serum IgE concentration increase in allergic patients in comparison to healthy population also *Haung et al., (2006)*.

In the present study there were no difference in sensitivity to HDM (Der p1 and Der f1) to both male and female asthmatic patients and it was highly significant (P value is 0.000) and this may be attributed to somewhat to the

limited number of the studied patients. *Tang et al., (1995)* who revealed that male gender had a higher frequency of sensitization to HDM, also *Liccardi et al., (1998)* stated that there was a higher percentage of sensitization to HDM among the male gender.

In the present study sensitivity to Der p1 and Der f1 in relation to age groups there were a high significant correlation in age group 2 (P value is 0.000) and low significant correlation (P value is 0.029) while there were no significant relation among age groups 1 and 4 (P value is 0.156) and (P value is 0.199) respectively. In a study on Taiwanese atopic children they stated that sensitization to Der p1 and Der f1 was 90.2% and 88.2% respectively. Also according to a study involving French children in 2012, prevalence of Der p 1 sensitization was 95% *Bronnert et al., (2012)*. In another study involving Austrian children and adults, prevalence of Der p 1 sensitization was 91% *Pittner et al., (2004)*. Another study conducted in Singapore, which has a tropical climate, reported Der p1 sensitization prevalence of 64% of the studied population *Kidon et al., (2011)*. While in a study done by *Hwan et al., (2015)* the prevalence of sensitization in Korean children to Der p was 98.8%, Der f was 100%, Der p 1 was 82.5%, and there were a marked difference in the present work in comparison to the results obtained by the previous studies and this may be due to all the previous studies done on children only while our study done on the all age groups, so we recommend to select to study only children in another studies.

In according to residence of the studied patients and control group sensitivity to Der p1 and Der f1 was highly significant correlation (P value is 0.000) in both rural and urban residence of the studied patients but sensitivity to Der p1 and Der f1 were more severe in rural patients.

In the present study, Der p 1 and Der f1 sensitization rates were more or less equal to previous studies but the strongpoint of our study lies in the fact that Immuno CAP was used to determine specific IgE while Previous studies usually used allergen dot immune-blot arrays that are known to be prone to nonspecific IgE binding as well as nonspecific inhibition of IgE binding by the presence of large quantities of antigen specific IgG in patients sera *Fonseca et al., (2009)* and *Bronnert et al., (2012)*.

## 7. Conclusion

Sensitization to HDM and its components in Egyptian asthmatic patients is similar to previous studies from temperate climate and all over the world. The determination of Der p 1 and Der f1 IgE helps in obtaining additional information about role of HDM in atopic asthma and other allergic disease which may help in treatment and control of asthma.

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