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# Association of house dust mite-specific IgE with asthma control, medications and household pets

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**Background:** Evidence is conflicting regarding the effectiveness of creating a low-allergen environment or reducing allergen exposure to control asthma exacerbations.

**Objective:** This study determined the association of house dust mite (HDM)-specific IgE levels with asthma symptom control, selected medications, family history of allergic disease, and exposure to second-hand smoke and household pets.

**Methods:** Serum samples from 102 doctor-diagnosed allergic asthma patients and 100 non-atopic controls were subjected to enzyme-linked immunosorbent assay using the HDM species *Dermatophagoides pteronyssinus* (Dp), *Dermatophagoides farinae* (Df), and *Blomia tropicalis* (Bt) allergens. Point-biserial correlation coefficient, Pearson R correlation, and logistic regression analyses were used to determine association of HDM-specific IgE levels with the abovementioned variables.

**Results:** Of the 102 cases, 38.24%, 47.06%, and 33.33% were sensitized to Bt, Df, and Dp, respectively. Sensitized patients showed greater probability [Bt (OR = 1.21), Df (OR = 1.14), and Dp (OR = 1.35)] to manifest symptoms than those who were not. Obtained *p*-values [Bt ($p = 0.73$), Df ($p = 0.83$), and Dp ($p = 0.59$)], however, proved that HDM-specific IgE levels had no significant contribution in predicting or explaining occurrence of asthma symptoms. Bt- and Df-specific IgEs showed moderately weak but significant relationship with bambuterol HCl and expectorant, respectively. Patients currently on said medications registered higher HDM-specific IgE levels than those who were not. No significant correlation between IgE levels and family history of allergic disease or with exposure to second-hand smoke was seen. Dp-specific IgE levels of patients exposed to household pets were significantly lower compared to those without exposure.

**Conclusion:** This study proves that sensitization to Bt, Df, and Dp allergens is not significantly associated with asthma symptoms and control. Although cases were shown to be sensitized to HDMs, their current medications were at least effective in controlling their asthma symptoms.

**Key words:** *Dermatophagoides pteronyssinus; Dermatophagoides farinae*; *Blomia tropicalis*; Asthma control; Medications; Household pets

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## INTRODUCTION

Asthma is a chronic inflammation and constriction of the respiratory passages caused by interactions among genetic, environmental, and social factors [1]. Its clinical manifestations are so heterogenous that diagnosis can be subjective and qualitative. To ate, no validated quantitative criteria for asthma diagnosis has been established and standardized. Patients are customarily evaluated based on airflow obstruction over short periods of time, airway or bronchial hyper-responsiveness (AHR or BHR), and cellular pathology of the airway [2]. Lung function tests are neither easily nor routinely used especially in children [3]. Skin prick tests help identify the triggers of the asthma symptoms but cannot be regularly done particularly in patients with unstable asthma and are at risk of anaphylaxis [4]. Thus, the diagnostic value of blood allergen-specific IgEs, being distinct and specific to the allergen that triggered their production [5], is often considered in the screening, treatment and management of asthma [2]. IgE, which is produced upon sensitization to at least one allergen, has been proven a strong risk factor for developing asthma [6].

House dust mite (HDM)-specific IgEs are the most consistently associated with asthma development [7]. *Dermatophagoides pteronyssinus* (Dp), *Dermatophagoides farinae* (Df), and *Blomia tropicalis* (Bt) HDMs are among the most implicated asthma triggers [8-10]. Thus, this study aimed to determine the association of HDM-specific IgE levels with asthma symptom control, selected medications, family history of allergic disease, and exposure to second-hand smoke and household pets. Past studies have investigated the effects of steroids [11-16], $\beta_2$-agonists [17-18], leukotriene receptor antagonists [16-19], and omalizumab [20-21] on total and specific IgE. In addition to the above medications, expectorant and antibiotic use was also correlated with HDM-specific IgE levels.

## MATERIALS AND METHODS

Asthma and control subjects were university students, 16-21 years old, without any history of helminth infection, and of Filipino descent. A total of 102 doctor-diagnosed allergic asthma patients were recruited, and 100 non-atopic individuals without any personal or family history of allergy and with specific serum IgE levels <50 IU/mL served as controls. History of helminth infection was an exclusion criterion to prevent cross-reaction between the HDMs and parasites [22]. All case and control subjects, after giving their written informed consent, completed standardized questionnaires based from the International Study of Asthma and Allergy in Childhood and by the International Primary Care Airways Group regarding age at onset, duration, and frequency of the asthma symptoms, medication(s) received, family history of allergic disease, and exposure to cigarette smoke or household pets. The design, sampling, experimental protocols, questionnaires and other pertinent documents had been presented before and approved by the ethics committee of the University of Santo Tomas, Manila, Philippines.

Enzyme-linked immunosorbent assay (ELISA) was performed on plasma samples of asthma and control subjects following standard protocols. All procedures were done at room temperature unless otherwise indicated. Briefly, 50 µg/mL of previously prepared HDM aqueous extracts [10] diluted with 0.1 M $NaHCO_3$ (pH 8.3) were coated onto ELISA plates and incubated overnight at 4°C. Plates were blocked with 1% BSA (Sigma, USA) in Phosphate Buffered Saline containing 0.05% Tween 20 (PBS-T) for 1 h. Diluted (5×) plasma was dispensed onto the wells and incubated overnight at 4°C. Biotinylated anti-human IgE (Pharmingen, USA) diluted 1,000× in blocking buffer (1% BSA in PBS-T) was added and let stood for 1h prior to addition of 2,000× dilution of Extravidin-alkaline phosphatase conjugate (Sigma, USA). Absorbance (405 nm) was read after 1h colorimetric reaction with p-Nitrophenyl phosphate (Sigma, USA). Human IgE (Pharmingen, USA) was used as a standard per plate in the calculation of IgE concentration. The mean + 1Standard Deviation (SD) of the HDM-specific IgE levels (IU/mL) of the control samples served as cut-off values in determining positive reactions among the asthma samples. All asthma samples that registered values ≥cut-off values were considered sensitized by the aforementioned HDM allergens.

For data analysis, SPSS 16 point-biserial correlation coefficient was used to determine association of HDM-specific IgE levels with selected medications, family history of allergic disease, and exposure to second-hand smoke and household pets. Pearson R correlation was used to analyze relationship between HDM-specific IgEs. Logistic regression analysis was done to investigate relationship of asthma symptom control (dependent binary variable) with independent or explanatory variables such as HDM-specific IgE levels, use of asthma medications, family history of allergic disease, and exposure to second-hand smoke and household pets.


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## RESULTS

### ELISA profile

A total of 202 samples (102 asthma cases and 100 non-atopic controls) were analyzed by ELISA for HDM-specific IgE. The mean + 1SD of the HDM-specific IgE levels (IU/mL) of the control samples served as cut-off values. All asthma samples with IgE levels ≥cut-off values (Bt = 25.54 IU/mL, Df = 29.21 IU/mL, and Dp = 27.34 IU/mL) were considered sensitized by the aforementioned HDM allergens. Highest Bt-, Df- and Dp-specific IgE values obtained were 1,328.17 IU/mL, 8,041.62 IU/mL, and 3,509.69 IU/mL, respectively. Of the asthma samples, 38.24% was sensitized to Bt, 47.06% to Df, and 33.33% to Dp. Only 19.61% was sensitized to all three HDM species. While 11.76% was sensitized to both Bt and Df but not Dp; 8.82% to both Df and Dp but not Bt; none showed sensitization to a combination of Bt and Dp. Furthermore, only 6.86% among the asthma samples became sensitized to Bt alone; 4.90% to Dp alone; and 6.86% to Df alone. Pearson R correlations analysis (Table 1) proved Bt-specific IgE levels to have moderate and significant correlation with Df; Dp to have high and significant correlation with Df; and Bt to have no significant correlation with Dp.

**Table 1.** Pearson R correlations of IgE among different dust mite species (n = 102)

| | | Bt | Df | Dp |
|---|---|---|---|---|
| Bt | Pearson correlation | 1 | 0.561 | 0.159 |
| | Sig. (2-tailed) | | 8.34E-10 | 0.111 |
| Df | Pearson correlation | 0.561 | 1 | 0.811 |
| | Sig. (2-tailed) | 8.34E-10 | | 5.68E-25 |
| Dp | Pearson correlation | 0.159 | 0.811 | 1 |
| | Sig. (2-tailed) | 0.111 | 5.68E-25 | |

Dp: *Dermatophagoides pteronyssinus*, Df: *Dermatophagoides farinae*, Bt: *Blomia tropicalis*.

### HDM-specific IgE correlated with asthma medications and symptom control

Asthma symptoms of the 102 cases were categorized into well-controlled (symptoms manifested ≤2 days per week without any interference with normal activity) and totally-controlled (no asthma symptoms for the past 12 months). Of the 68 who had totally-controlled asthma symptoms, only 24, 29, and 21 were sensitized to Bt, Df, and Dp, respectively. Only 15, 19, and 14 of the cases with well-controlled asthma symptoms were sensitized to Bt, Df, and Dp, respectively (Table 2).

In a logistic regression analysis of the data, asthma symptom control served as dependent binary variable (Y = 1 if asthma symptoms were well-controlled and Y = 0 if totally controlled); and Bt, Df, and Dp-specific IgE levels, medications used, family history of allergic disease, and exposure to second-hand smoke and pets were the independent variables. While holding all the other independent variables constant, Bt, Df, and Dp-specific IgE levels were equal to 1 if subject was sensitized to that particular HDM and 0 if otherwise. Table 3 shows that patients sensitized to Bt (OR = 1.21), Df (OR = 1.14), and Dp (OR = 1.35) proved greater probability to manifest symptoms than those not sensitized. However, since Bt ($p$ = 0.73), Df ($p$ = 0.83), and Dp ($p$ = 0.59) -specific IgE $p$-values were >0.05, sensitization to specific HDMs is

**Table 2.** Participant characteristics

| Characteristic | Control subjects n = 100 | Asthma cases n = 102 | |
|---|---|---|---|
| | | Totally-controlled* n = 68 | Well-controlled† n = 34 |
| Age (mean) | 18.41 | 18.10 | 18.24 |
| Gender | | | |
| male | 39/100 = 39% | 20/68 = 29.41% | 7/34 = 20.59% |
| female | 61/100 = 61% | 48/68 = 70.59% | 27/34 = 79.41% |
| Number of cases sensitized to | | | |
| Bt | | 24/68 = 35.29% | 15/34 = 44.12% |
| Df | | 29/68 = 42.65% | 19/34 = 55.88% |
| Dp | | 21/68 = 30.88% | 14/34 = 41.18% |

Bt: *Blomia tropicalis*, Df: *Dermatophagoides farinae*, Dp: *Dermatophagoides pteronyssinus*. *No asthma symptoms for the past 12 months. †Symptoms manifested ≤ 2 days per week without any interference with normal activity.

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**Table 3.** Relationship of house dust mite-specific IgE with asthma control (Asthma control as dependent variable; Bt, Df, Dp IgE levels, medications, family history of allergic disease, and exposure to second-hand smoke and pets as independent variables)

| Asthma control | OR | SE | z | *p*-value | 95% CI |
|---|---|---|---|---|---|
| Bt IgE | 1.21 | 0.68 | 0.35 | 0.73 | 0.41-3.62 |
| Df IgE | 1.14 | 0.71 | 0.21 | 0.83 | 0.34-3.86 |
| Dp IgE | 1.35 | 0.75 | 0.54 | 0.59 | 0.45-4.02 |

Bt: *Blomia tropicalis*, Df: *Dermatophagoides farinae*, Dp: *Dermatophagoides pteronyssinus*. Odds ratios (OR) were computed using logistic regression. Dependent variable was whether the asthma symptoms were well-controlled (symptoms manifested ≤2 days per week without any interference with normal activity; Y = 1) or totally-controlled (no asthma symptoms for the past 12 months; Y = 0). The independent variables were Bt, Df, Dp IgE levels, medications, family history of allergic disease, and exposure to second-hand smoke and pets. Bt, Df and Dp IgE levels as binary variables were equal to 1 if patient was sensitized and 0 if otherwise. n = 102.

said to have no significant contribution in predicting or explaining occurrence of asthma symptoms.

The data was re-run, omitting in the model the independent variables like family history of allergic disease and exposure to second-hand smoke and pets. Obtained OR values [Bt (OR = 1.22), Df (OR = 1.20), and Dp (OR = 1.33)] in Table 4 were very close to Table 3. Computed *p*-values of Bt ($p = 0.71$), Df ($p = 0.76$), and Dp ($p = 0.60$) levels were >0.05. Thus, the omitted variables proved no significant contribution in the manifestation of asthma symptoms.

In a point-biserial correlation coefficient analysis of the data, HDM-specific IgE levels and asthma medications served as continuous and dichotomous variables, respectively. The binary variable was equal to 1 if the subject used that particular medication and 0 if not. Corrected level of significance was 0.003125 or 0.3125%. Thus, any *p*-value <0.3125% level of significance indicated significant correlation between the two variables. Table 5 shows moderately weak but significant relationship between bambuterol HCl use (r = 0.31; $p = 0.000$) and Bt-specific IgE level. Df-specific IgE levels demonstrated weak but significant relationship with expectorant (r = 0.25; $p = 0.001$) use. The rest of the medications did not prove any significant relationship with the HDM-specific IgE levels.

### Association of HDM-specific IgE levels with family history of allergic disease, exposure to second-hand smoke and household pets

Point-biserial correlation coefficient analysis was also used here. Binary variable 1 was assigned to cases with family history of allergic disease and exposure to second-hand smoke and household pets while 0 for those without. Bt (r = −0.07; $p = 0.487$), Df (r = 0.033; $p = 0.744$), and Dp (r = 0.094; p = 0.351) -specific IgE levels were not significantly associated with history of allergic disease in the family. Neither was there significant relationship between second-hand smoke and serum Bt (r = 0.154; $p = 0.124$), Df (r = 0.157; $p = 0.116$), or Dp (r = 0.157; $p = 0.116$) -specific IgE. A significant but weak relationship of Dp-specific IgE (r = −0.181; $p = 0.068$) with exposure to household pets was shown. Since correlation coefficient was a negative value (Table 6), Dp-specific IgE of subjects previously exposed to pets were expected to be considerably lower. Bt (r = 0.103; $p = 0.302$) and Df (r = −0.111; $p = 0.265$) -specific IgE levels were not significantly associated with household pet exposure. Dog, cat, hamster, rat, rabbit, guinea pig, bird, fish, and turtle were among the pets the subjects were exposed to.

**Table 4.** Relationship of house dust mite-specific IgE with asthma control (Asthma control as dependent variable; Bt, Df, Dp IgE levels and medications as independent variables)

| Asthma control | OR | SE | z | *p*-value | 95% CI |
|---|---|---|---|---|---|
| Bt IgE | 1.22 | 0.66 | 0.38 | 0.71 | 0.43-3.51 |
| Df IgE | 1.20 | 0.73 | 0.31 | 0.76 | 0.37-3.97 |
| Dp IgE | 1.33 | 0.71 | 0.52 | 0.60 | 0.46-3.80 |

Bt: *Blomia tropicalis*, Df: *Dermatophagoides farinae*, Dp: *Dermatophagoides pteronyssinus*. Odds ratios (OR) were computed using logistic regression. Dependent variable was whether the asthma symptoms were well-controlled (symptoms manifested ≤2 days per week without any interference with normal activity; Y = 1) or totally-controlled (no asthma symptoms for the past 12 months; Y = 0). The independent variables were Bt, Df, Dp IgE levels and medications. Bt, Df and Dp IgE levels as binary variables were equal to 1 if patient was sensitized and 0 if otherwise. n = 102.

## DISCUSSION

ELISA demonstrated multiple HDM-specific IgE reactivity of the subjects in this study. Although IgEs are said to be distinct and specific to the allergen that triggered their production [10], Dp- and Df-specific IgEs have been found to be highly cross-reactive [9]. This study, however, does not recognize whether the multiple-reactivity seen in some of the subjects is due to cross-reactions or actual presence of HDM-specific IgEs in their sera.

At present, there is conflicting evidence about whether measures to create a low-allergen environment in patient's home


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**Table 5.** Correlation coefficient and *p*-values between house dust mite-specific IgE and medications (n = 102)

| Medications used | Bt | | Df | | Dp | |
|---|---|---|---|---|---|---|
| | CC | *p*-value | CC | *p*-value | CC | *p*-value |
| Salbutamol/ Albuterol | 0.04 | 0.041 | 0.10 | 0.019 | 0.06 | 0.04 |
| Salmeterol | 0.05 | 0.039 | –0.05 | 0.039 | –0.03 | 0.05 |
| Terbutaline sulfate | –0.05 | 0.039 | –0.05 | 0.041 | –0.01 | 0.06 |
| Procaterol HCl | –0.03 | 0.049 | –0.02 | 0.051 | –0.02 | 0.05 |
| Bambuterol HCl | 0.31 | 0.000 | 0.00 | 0.062 | –0.02 | 0.05 |
| Budesonide + formoterol | 0.15 | 0.008 | –0.02 | 0.052 | –0.02 | 0.05 |
| Corticosteroids | 0.22 | 0.002 | 0.12 | 0.014 | 0.08 | 0.03 |
| Albuterol + ipratropium | –0.03 | 0.049 | –0.02 | 0.051 | –0.02 | 0.05 |
| Antihistamine | –0.05 | 0.039 | –0.04 | 0.045 | –0.01 | 0.06 |
| Aminophylline | –0.02 | 0.051 | –0.02 | 0.051 | –0.02 | 0.05 |
| Montelukast | –0.04 | 0.045 | –0.03 | 0.048 | 0.00 | 0.06 |
| Mucolytic | –0.05 | 0.038 | –0.05 | 0.039 | –0.05 | 0.04 |
| Nasal decongestant | –0.03 | 0.049 | –0.02 | 0.053 | –0.02 | 0.05 |
| Expectorant | 0.14 | 0.009 | 0.25 | 0.001 | 0.02 | 0.05 |
| Antibiotics | –0.06 | 0.035 | –0.05 | 0.037 | –0.05 | 0.04 |
| Allergy sensitization | –0.03 | 0.049 | –0.02 | 0.051 | –0.02 | 0.05 |

Bt: *Blomia tropicalis*, Df: *Dermatophagoides farinae*, Dp: *Dermatophagoides pteronyssinus*, CC: correlation coefficient. Corrected level of significance = 0.003125 or 0.3125%. General rule in interpreting the correlation coefficient: 0-0.25, weak relationship; 0.26-0.5, moderately weak relationship; 0.51-0.75, moderately strong relationship; 0.76-1, strong relationship.

**Table 6.** Correlation coefficient and *p*-values between house dust mite-specific IgE and family history of allergic disease, exposure to SHS, and household pets (n = 102)

| Factor | Bt | | Df | | Dp | |
|---|---|---|---|---|---|---|
| | CC | *p*-value | CC | *p*-value | CC | *p*-value |
| Family history of allergic disease | –0.070 | 0.487 | 0.033 | 0.744 | 0.094 | 0.351 |
| Exposure to SHS | 0.154 | 0.124 | 0.157 | 0.116 | 0.157 | 0.116 |
| Exposure to household pets | 0.103 | 0.302 | –0.111 | 0.265 | –0.181 | 0.068 |

SHS: second hand smoke, Bt: *Blomia tropicalis*, Df: *Dermatophagoides farinae*, Dp: *Dermatophagoides pteronyssinus*, CC: correlation coefficient. General rule in interpreting the correlation coefficient: 0-0.25, weak relationship; 0.26-0.5, moderately weak relationship; 0.51-0.75, moderately strong relationship; 0.76-1, strong relationship.

or reduced exposure to indoor allergens are effective at reducing asthma symptoms. While aeroallergens are often implicated in asthma development, this study showed that HDM-specific IgE levels were not associated with prevalence of asthma symptoms. It was also mentioned previously that HDM did not significantly influence asthma severity [23]. Furthermore, HDM-sensitized children with moderate to severe asthma did not demonstrate differences in respiratory symptoms or lung function after a year of using mite-occlusive mattress cover [24]. Meanwhile, the National Asthma Education and Prevention Program recommends identifying allergens to which an individual is sensitized and employing strategies of allergen avoidance or reduced exposure [25]. Considering that asthma results from the complex interplay between genetic susceptibility and ubiquitous environmental factors, avoiding the latter completely may not only seem impossible but impractical and very limiting to the patient. It is more important, therefore, to resolve the HDM level that could result to either sensitization or tolerance since sensitization to HDMs among asthmatic adolescents has been demonstrated to be not significantly different from non-asthmatics [26].

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Although previous studies have demonstrated that resistance or susceptibility to a certain drug is genetically-linked [27, 28], the interactions between and among HDM-specific IgE levels, asthma medications, and genetic make-up are not altogether known. Bt and Df-specific IgE levels showed moderately weak but significant associations with bambuterol HCl and expectorant use, respectively. Subjects currently on said medications during blood sample collection registered higher HDM-specific IgE levels compared to those who were not. This finding, however, is not conclusive and may only be due to chance. Increased inflammation and mucus production could have required increased amount of medication. Thus, a more controlled study using a bigger population size must be done to substantiate this. Factors that influence effectiveness of asthma medications, such as route of administration, dose, and period of treatment, in association with HDM-specific IgE production and genetic factors must also be considered.

Family history of allergic disease, which is considered strong risk factor in allergic rhinitis or asthma development [29], and second-hand smoke were not associated with HDM-specific IgE levels. While cigarette smoking is currently considered an important predictor of asthma severity and poor asthma control [30], our results agree with that previously done on a selected Japanese population in which second-hand smoke showed no association with HDM sensitization [31]. Moreover, subjects previously exposed to household pets registered lower Df-specific IgE levels. Reduced asthma incidence in schoolchildren exposed to pets during their first year of life may be attributed to the IgG and IgG4 produced against the pets, without risk of sensitization and asthma development [32, 33]. Yet, this seems to confer only a protective but not a preventive effect [29].

In conclusion, this study proves that sensitization to Bt, Df, and Dp allergens is not significantly associated with asthma symptoms and control. Although cases were shown to be sensitized to HDMs, their current medications were at least effective in controlling their asthma symptoms. It is further recommended that future studies also focus on genetic factors associated with HDM sensitization and response to therapy.

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