# ASSOCIATION BETWEEN SKIN PRICK TEST AND SERUM SPECIFIC IMMUNOGLOBULIN E OF HOUSE DUST MITE ALLERGENS IN ALLERGIC RHINITIS PATIENTS

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**Abstract.** Skin prick test (SPT) and serum specific immunoglobulin E (sIgE) are well-established methods for detecting IgE-mediated allergen sensitization. The primary aim of this study was to investigate the association between the results of SPT and sIgE of house dust mite (HDM) allergens in Thai patients with clinical allergic rhinitis (AR). The secondary aim was to evaluate association between severity of AR and both the size of SPT mean wheal diameter (MWD) and sIgE. This cross sectional study was conducted in patients aged 6-25 years diagnosed with clinical AR during September 2012 to October 2013. SPT and sIgE (ImmunoCap) of *Dermatophagoides pteronyssinus* (*Dp*) and *Dermatophagoides farinae* (*Df*) were performed. Fifty-eight AR patients with a mean age of 13.5 (range: 6-25) years were included. One-third of cases (37.9%) had comorbid asthma. Forty-four patients (75%) had positive SPT and sIgE to *Dp*, and 43 patients (74%) had positive SPT and sIgE to *Df*. All cases with positive SPT and sIgE to *Dp* had positive SPT and sIgE to *Df*. Significant correlation was observed between mean wheal diameter (MWD) of SPT and sIgE levels for both *Dp* and *Df* ($r$=0.95, $p$<0.001 and $r$=0.97, $p$<0.001, respectively). Significant correlation was also found between disease severity and MWD and between disease severity and sIgE levels for both *Dp* ($p$<0.001) and *Df* ($p$<0.001).Significant correlations were observed between MWD of SPT and sIgE levels, between disease severity and MWD, and between disease severity and sIgE levels for both *Dp* and *Df*.

**Keywords:** house dust mite, skin prick test, specific immunoglobulin E, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*

## INTRODUCTION

Allergic rhinitis (AR) is a global health problem that affects millions of people around the world. AR is one of the most common chronic non-communicable diseases. The prevalence of AR was reported to range from 20% to 40% among different populations (Bousquet *et al,* 2008). The diagnosis of AR is based on clinical manifestations and confirmation by skin prick test (SPT) or serum specific immunoglobulin E (sIgE) to aeroallergens (Bousquet *et al,* 2008). House dust mite (HDM) is the most common aeroallergen in patients with allergic rhinitis. SPT is easy to perform and safe when performed by a specialist, but patients are required to discontinue antihistamine 1 week before SPT and there

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must be no skin lesion at the test area. sIgE is also a safe test, but it is more expensive and it takes longer to get the test result than SPT. In contrast to SPT, sIgE can be performed in patients that have skin lesion and in patients that are currently taking antihistamines. A previous study among 158 AR patients found the accuracy, sensitivity, and specificity of the ImmunoCAP specific IgE system (Phadia AB, Uppsala, Sweden) to be 0.810, 0.819, and 0.872, respectively; whereas, the accuracy, sensitivity, and specificity of SPT were 0.780, 0.741, and 0.862, respectively (Jiang *et al,* 2010). The accuracy between the two test systems was not significantly different ($p$>0.05). The ImmunoCAP system was reported to have a higher sensitivity, while SPT was found to have a higher specificity (Jiang *et al,* 2010). The association between skin prick test (SPT) and specific immunoglobulin E (sIgE) of HDM has not yet been reported in Thai patients with AR.

The primary objective of this study was to investigate the association between the results of SPT and sIgE of HDM allergens in Thai patients with clinical AR. The secondary objective was to evaluate association between severity of AR and both the size of SPT mean wheal diameter (MWD) and sIgE.

## MATERIALS AND METHODS

### Study design and study subjects

This cross sectional study was conducted among patients aged 6-25 years that were diagnosed with allergic rhinitis (AR) by clinical signs and symptoms during the September 2012 to October 2013 study period. The study protocol was approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Patients were categorized into 1 of the following 3 age groups: 6-12 years, 13-19 years, or 20-25 years. AR was diagnosed when patients had symptoms of rhinorrhea, sneezing, itchy nose and/or eyes, or nasal congestion together with clinical signs, such as allergic shiner, adenoid face, or swollen and pale inferior nasal turbinate. Severity of AR was classified as mild intermittent, mild persistent, moderate to severe intermittent, or moderate to severe persistent, according to Allergic Rhinitis and its Impact on Asthma (ARIA) guideline (Bousquet *et al,* 2008). Patients with other systemic diseases, severe skin diseases, severe and uncontrolled allergic diseases or who were pregnant were excluded. The demographic and clinical characteristics of patients were recorded and analyzed. SPT to *Dermatophagoides pteronyssinus* (*Dp*) and *Dermatophagoides farinae* (*Df*) was performed on each patient's back after antihistamine and local and systemic corticosteroid (more than 20 mg) were stopped for at least 7 days. Isotonic saline and 10 mg/ml histamine dihydrochloride were used as negative and positive controls, respectively. MWD (defined as the longest diameter plus the perpendicular diameter and then divided by 2) of >3 mm larger than the negative control at 15 minutes after the prick was interpreted as a positive SPT. sIgE of *Dp* and *Df* was also performed during the same SPT test session. sIgE was measured by ImmunoCap (UniCAP 100; Phadia AB, Uppsala, Sweden). The result of sIgE was interpreted as positive when the level was >0.35 kUA/l. sIgE values were interpreted, as follows: <0.35 KUA/l = negative; 0.35 to 0.7 KUA/l = very low IgE level; 0.7 to 3.5 KUA/l = low IgE level; 3.5 to 17.5 KUA/l = high IgE level; and, 17.5 to >100 KUA/l = very high IgE level.

### Statistical analysis

Data were analyzed using SPSS Statistics version 18 (IBM, Armonk, NY). Rank correlation between MWD and level of sIgE was calculated using Spearman's rank correlation coefficient. Linear correlation between MWD and level of sIgE was calculated using linear regression analysis. Data are presented as number and percentage (%) or mean ± standard error (SE). A $p$-value <0.05 was considered to be statistically significant.

## RESULTS

Fifty-eight AR patients with a mean age of 13.5 (range: 6-25) years were included, and 32 (55%) of them were male. The most heavily populated age group was 6-12 years (58%). AR severity among patients is shown in Table 1. More than 60% of cases were categorized as having moderate to severe intermittent or persistent AR. Half of cases had allergic conjunctivitis and 37.9% of patients had asthma as a comorbidity.

Forty-four patients (75%) had positive SPT and sIgE to *Dp*, and 43 patients (74%) had positive SPT and sIgE to *Df.* All patients with positive SPT to *Df* had positive SPT to *Dp*, while 97.7% (43/44) of cases with positive SPT to *Dp* had positive SPT to *Df*. All cases with positive SPT to *Dp* had positive sIgE to *Dp*, and all cases with positive SPT to *Df* had positive sIgE to *Df*. A substantially high significant positive correlation was observed between MWD of SPT and sIgE levels for both *Dp* and *Df* (Spearman's rank correlation coefficient ($r$) = 0.95, $p$<0.001 and

Table 1
Demographic and clinical characteristics of allergic rhinitis (AR) patients ($N$ =58)

| Characteristic | *n* (%) |
|---|---|
| Male | 32 (55.2) |
| Age (years) | |
| 6-12 | 34 (58.6) |
| 13-18 | 8 (13.8) |
| 19-25 | 16 (27.6) |
| Comorbid allergic diseases | |
| Allergic conjunctivitis | 29 (50.0) |
| Allergic asthma | 22 (37.9) |
| Atopic dermatitis | 11 (19.0) |
| Family history of atopy | |
| In first-degree relatives | 39 (67.2) |
| In second-degree relatives | 9 (15.5) |
| History of smoking in family | 23 (39.7) |
| Pets in area around the house | 21 (36.2) |
| Controller for allergic rhinitis | |
| Oral antihistamine | 43 (74.1) |
| Intranasal corticosteroids | 25 (43.1) |
| Sleep disturbance | 35 (60.3) |
| Severity of allergic rhinitis | |
| Mild intermittent | 11 (19.0) |
| Mild persistent | 12 (20.7) |
| Moderate to severe intermittent | 17 (29.3) |
| Moderate to severe persistent | 18 (31.0) |

0.97, $p<0.001$, respectively) (Fig 1).

The MWD of SPT and the levels of sIgE for both *Dp* and *Df* also had significantly positive correlation with the severity of AR (Table 2). Patients with moderate to severe persistent AR had the highest MWD of SPT and the highest level of sIgE of *Dp* and *Df*, followed by patients with moderate to severe intermittent. Patients with mild intermittent and mild persistent AR had significantly lower MWD of SPT and level of sIgE of *Dp* and *Df* than moderate to severe persistent and moderate to severe intermittent AR. Mean sIgE levels for both *Dp* and *Df* of patients with mild intermittent and mild persistent AR were in the low to very low ranges, while the levels of patients with moderate to severe intermittent and moderate to severe persistent AR were in the

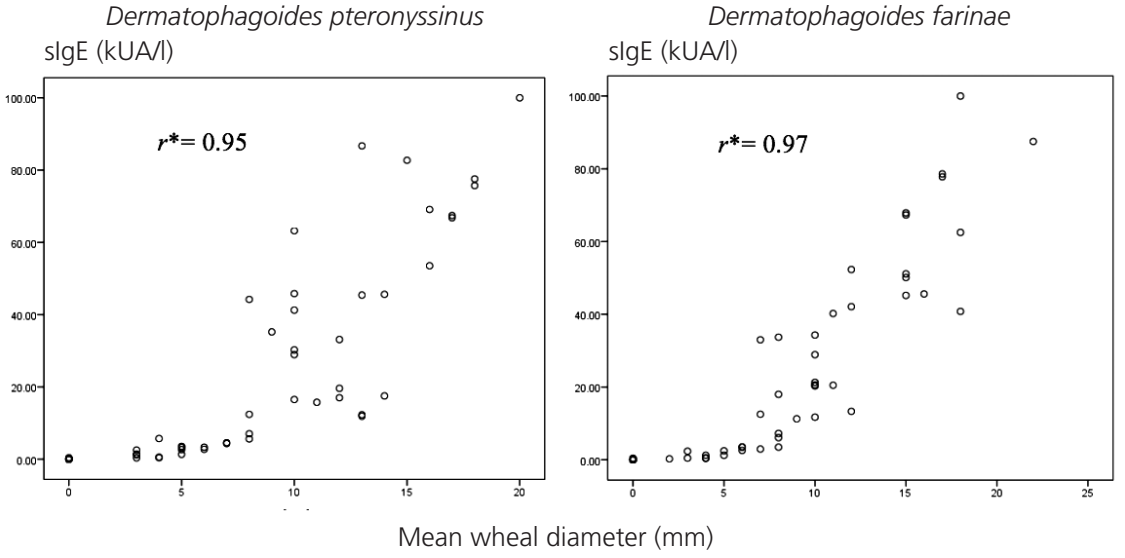


Fig 1– Correlation between mean wheal diameter of skin prick test and level of serum specific IgE of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*. *r**, Spearman's rank correlation coefficient.

Table 2
Mean wheal diameter of skin prick test (SPT) and mean levels of serum specific IgE (sIgE) of *Dermatophagoides pteronyssinus* (*Dp*) and *Dermatophagoides farinae* (*Df*) for different severities of allergic rhinitis.

| Severity (*n*) | Mean±standard error (SE) | | | |
|---|---|---|---|---|
| | SPT *Dp* (mm) | sIgE *Dp* (kUA/l) | SPT *Df* (mm) | sIgE *Df* (kUA/l) |
| Mild intermittent (11) | 2.73±1.09 | 3.91±2.61 | 3.00±1.43 | 5.56±4.50 |
| Mild persistent (12) | 3.58±0.73 | 1.98±0.50 | 3.92±1.10 | 3.35±1.82 |
| Moderate to severe intermittent (17) | 8.71±1.36 | 18.64±5.23 | 8.12±1.20 | 19.21±4.98 |
| Moderate to severe persistent (18) | 11.89±1.28 | 49.05±7.05 | 12.17±1.42 | 44.41±7.08 |
| *p*-value | <0.001 | <0.001 | <0.001 | <0.001 |

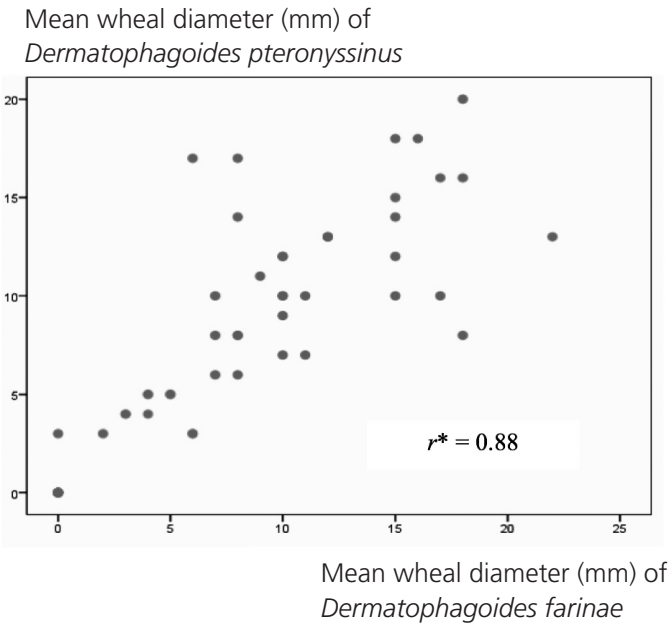


Fig 2– Correlation between mean wheal diameter of skin prick test of *Dermatophagoides pteronyssinus* and mean wheal diameter of skin prick test of *Dermatophagoides farinae*. *r**, Spearman's rank correlation coefficient.

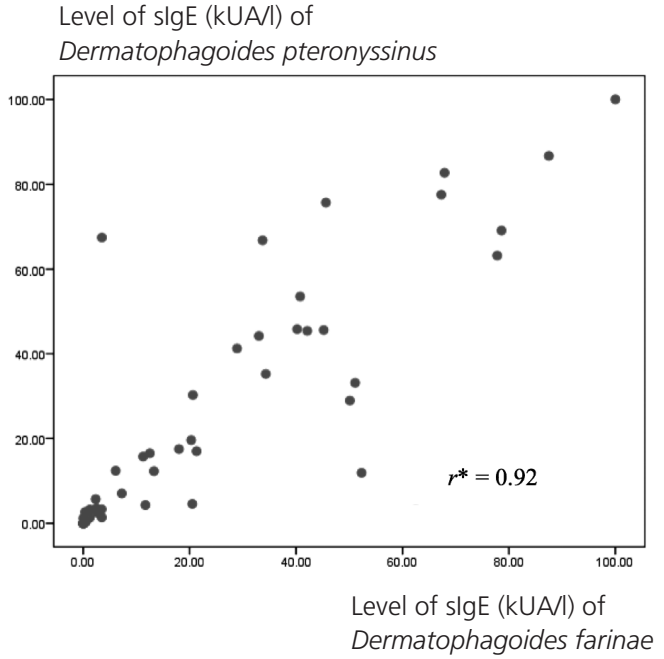


Fig 3– Correlation between level of serum specific IgE (sIgE) of *Dermatophagoides pteronyssinus* and level of sIgE of *Dermatophagoides farinae*. *r**, Spearman's rank correlation coefficient.

high to very high ranges. Significant correlation was also found between disease severity and MWD, and between disease severity and sIgE levels for both *Dp* ($p<0.001$) and *Df* ($p<0.001$). There were no significant differences between MWD and sIgE of *Dp* and *Df* among the 3 different age groups.

A significant positive correlation was found between MWD of SPT of *Dp* and MWD of SPT of *Df* ($r=0.88$) (Fig 2), and between levels of sIgE of *Dp* and levels of sIgE of *Df* ($r=0.92$) (Fig 3). When compared with sIgE, which is regarded as being a gold standard test, SPT for both *Dp* and *Df* showed 100% for both positive predictive value and negative predictive value.

## DISCUSSION

This study among 58 AR patients aged 6-25 years showed male predominance (55%) and the 6-12 year age group being the most heavily populated age group (58%). Male predominance was also found in several other previous studies (Meng *et al,* 2010; Hardjojo *et al,* 2011; Miranda *et al,* 2011). Our study found that more than half of cases (58%) had allergic conjunctivitis as a comorbidity. This was consistent with a previous study that found that 42% of 316 children with rhinitis had concomitant allergic conjunctivitis (Gradman and Wolthers, 2006).

Forty-four patients (75%) in this study had positive SPT and sIgE to *Dp*, and 43 patients (74%) had positive SPT and sIgE to *Df*. A previous study reported that positive SPT to aeroallergen was found in 75% of Thai children with AR (Vichyanond *et al,* 2010). A study from China in 412 patients with asthma and/or rhinitis found a prevalence of positive SPT for *Dp* and *Df* of 80.3% and 83.7%, respectively, and a prevalence of positive sIgE to *Dp* and *Df* of 61.1% and 60.2%, respectively (Zhang *et al,* 2012). The difference in percentage of positive sIgE between our study and the immediately aforementioned Chinese study may be due to the use of different IgE measurement methods. That study used ADVIA Centaur® immunoassay system (Bayer Healthcare LLC, Tarrytown, NY) and we used ImmunoCap (UniCAP 100; Phadia AB, Uppsala, Sweden). A more recent study in AR children in China from the same primary investigator also showed lower sensitization rates, as follows: 55.0% and 54.1% positive sIgE to *Dp* and *Df*, and 68.8% and 79.8% positive SPT for *Dp* and *Df*, respectively (Zhang *et al,* 2013).

A previous study conducted by our research team found a prevalence of positive SPT reaction to *Dp* and *Df* in non-atopic Thai volunteers aged 18-60 years of 35.29% (Visitsunthorn *et al,* 2010). In contrast, a previous study by Hardjojo *et al* (2011) found that 30% of AR patients had negative SPT or sIgE. A high proportion of negative SPT results may be due to inaccurate diagnosis, poor antigen quality, and/or incorrect test technique. Variability in SPT results can occur as a result of several factors, including the biological responsiveness of the subject's skin; the skill and experience of the clinician performing the test; the standardization of the skin-testing technique (needle and application method) used to perform the puncture; the reagents [stability, vehicle (*eg*, 50% glycerol), allergen concentration, and purity]; and, the method used to delimit, measure, and report skin reactions (Nelson *et al,* 1998). SPT can also change from negative to positive test when patients grow older. A previous study in Thai children found that 41% of children that had been previously diagnosed as non-AR by negative SPT developed sensitization to aeroallergens (positive SPT) by the 3-year follow-up (Veskitkul *et al,* 2013). The most common aeroallergens to which children became sensitized were *Dp* and *Df* (59.7% and 54.2% of cases with positive SPT, respectively).

This study found that all patients with positive SPT to *Df* had positive SPT to *Dp*, and 97.7% of patients with positive SPT to *Dp* had positive SPT to *Df*. Therefore, among the AR patients in

this study, SPT to *Dp* alone was sufficient for the evaluation of house dust mite sensitization. In this study, all cases with positive result of SPT to *Dp* had positive result of sIgE to *Dp*, and all cases with positive result of SPT to *Df* had positive result of sIgE to *Df*. The results of this study show that in AR patients aged 6-25 years, positive SPT to *Dp* or *Df*, or sIgE (as measured by immunoCAP system) of *Dp* or *Df* could be enough to diagnose HDM allergy.

However, the results reported from the present study and the results of some other studies vary considerably. One previous study reported a significant difference between allergen-specific SPT results and sIgE test results for common aeroallergens, which prompted them to suggest that both SPT and sIgE testing should be performed when diagnosing allergic sensitization in young children (range: 18-48 months) at high risk for asthma (de Vos *et al,* 2013). In a comparison between that study and our study, the age and diagnosis of patients was <4 years *vs* >6 years and asthma *vs* allergic rhinitis, respectively. The methods between that study and the present study for the measurement of sIgE were also different. The previous study used the Immulite® system, while our study used the immunoCAP system. The de Vos *et al* (2013) study showed fair agreement between SPT and sIgE test for HDM (kappa=0.35). Another study showed a significant difference between SPT and sIgE levels for house dust mites (*Dp*, $r$=0.568; *Df*, $r$=0.506; $p$<0.01) and a significant difference in positive rates between sIgE and SPT for *Dp* ($Chi^2$=11.605, $p$<0.01), but not for *Df* ($Chi^2$=0, $p$>0.05) (Wei *et al,* 2013). Another study reported a good correlation between sIgE and SPT, but that SPT had higher sensitivity; however, they concluded that SPT was not a suitable substitute for sIgE and vice versa (Zhang *et al,* 2013). Factors that may explain differences in results among studies include the age group(s) being studied within each study population, a lack of allergen standardization, and the methods used to measure SPT and sIgE.

Our study showed that MWD of SPT and levels of sIgE for both *Dp* and *Df* were also significantly positively correlated with severity of AR. However, the findings of one previous study do not support our findings (Wei *et al,* 2013). That study found no correlation between positive degree of SPT/sIgE and severity of clinical symptoms in AR. However, a study by Li *et al* (2011) found that moderate to severe asthma was associated with increasing MWD and sIgE in response to *Dp* and *Df* ($p$<0.001). That same study also reported that a significantly higher percentage of patients with moderate to severe intermittent rhinitis were sensitized to outdoor allergens, while the percentage of patients sensitized to indoor allergens (*Dp* and *Df*) was increased with increasing severity of asthma.

A study in 82 patients with HDM-related symptoms and positive SPT results showed that an increasing sIgE level was correlated with larger SPT size in both *Dp* and *Df* (Zhang *et al,* 2011). In that study, the positive correlation between SPT and sIgE reaction to HDM varied according to the age of AR patients. Moreover, the correlation coefficient revealed an increase in the sensitization value with aging, and the 31- to 40-year age group demonstrated the highest value for both *Dp* and *Df* (Zhang *et al,* 2011). Another previous study reported that the highest odds ratio (OR) associated with family physician decision to perform sIgE in AR was for symptom severity (OR = 12.11; 95% CI: 7.1-20.7) (Szeinbach *et al,* 2008).

A notable weakness of this study is the age range of the AR study population (6-25 years so the study results could be applied in only AR patients aged 6-25 years. The strength of this study is that it was conducted at a university-based national tertiary referral center that has experienced personal to perform SPT and to measure sIgE. Moreover, our laboratory received accreditation (ISO 15189:2012 and 15190:2003) from the Bureau of Laboratory Quality Standards

of the Thailand Ministry of Public Health to use the immunoCAP system.

Using an experienced technician with good technique, a very high correlation between MWD of SPT and sIgE levels of *Dp* and *Df* in AR patients aged 6-25 was found. Based on our findings, the use of either SPT or sIgE of *Dp* or *Df* is sufficient for evaluating HDM sensitization in this patient population. Moreover, larger MWD or higher levels of sIgE of HDM might predict AR severity.

In conclusion in our investigation of *Dp* and *Df* sensitization in AR patients aged 6-25 years, we found that SPT using standardized antigen extracts and performed with good technique was comparable to sIgE measurement using the immunoCAP system. SPT is simple, accurate, safe and inexpensive – so it can be used as a screening method to evaluate allergen sensitivity. However, when a patient has extensive skin lesion, cannot stop antihistamine therapy, and/or when the value/level of sensitization is required, sIgE should be the preferred method.

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## CONFLICTS OF INTEREST

The authors hereby declare no personal or professional conflicts of interest regarding any aspect of this study.

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