

# Predictive Accuracy of Total IgE in Detection of Inhalant Allergens Sensitization

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**Abstract:** *Background:* The role of total IgE (TIGE) in detecting inhalant allergens (IA) sensitization in asthmatics is controversial and frequently underestimated. *Objective:* To test the relationship between TIGE and IA sensitization in asthmatics. *Methods:* One year duration cross-sectional study commencing from January in 2014. 118 asthmatics with mean age of 30±15 years collected from King Abdulaziz University Hospital (KAUH). TIGE and skin prick test (SPT) was done. Data were statistically analyzed by statistical package for the social sciences program (SPSS). Two by two tables was done to correlate TIGE and IAs sensitization. Sensitivity, specificity, positive predictive values (+PV) and negative predictive values (-PV) were calculated. *Results:* SPSS two by two tables was used to correlate TIGE with IA sensitization by sensitivity, specificity and predictive values. TIGE versus mites showed high sensitivity: Dermatophagoides pteronyssinus (DP) 80.3, Dermatophagoides farina (DF) 83.7 and low (specificity, +PV and -PV). TIGE versus mold showed high -PV to (Aspergillus 82.1, Cladosporium 78.5) and low (sensitivity, specificity and +PV). TIGE versus German cockroach showed high sensitivity 90 and high -PV 92.8, however both specificity and +PV were low. All the values were statistically significant with P values below 0.05. *Conclusion:* Raised TIGE in asthmatics is of value in predicting dust mites and cockroach sensitization and exclusion of mold sensitization. High TIGE in asthmatics almost certainly mean the presence of mite sensitization. Conversely, normal TIGE in asthmatics can exclude mold sensitization. TIGE have both roles with German cockroach (highly sensitive, high -PV).

**Keywords:** Allergy, Total IgE, Inhalant Allergen, Sensitization, Atopy, Skin Prick Test

## 1. Introduction

Humoral immunity start from T helper lymphocytes number two (Th2). Th2 cells are activated by cytokines secreted from CD4. Th2 lymphocytes are the main cells responsible about B lymphocyte induction to produce immunoglobulins (Igs) in response to a specific triggering agent. Igs are mainly IgG, IgM, IgE and IgD. [1]

IgE is responsible about allergic type I hypersensitivity reaction. It lands over mast cells after the first exposure to allergen in a process called sensitization. With re-exposure to the same allergen mast cells explode and produce a lot of inflammatory mediators which could induce allergic cascade. The allergical symptoms related these organs can appear in

the eyes, nose, sinuses, lung and skin. [2]

Immunoglobulin E (IgE) is of two types: specific IgE (sIgE) against a specific allergen and TIGE which is the sum of all sIgEs against all allergens. sIgE can be tested in two ways: *in vivo* skin prick test (SPT) or *in vitro* radioallergosorbent blood test (RAST). High TIGE give a general clue about the presence of allergy, however positive sIgE is more useful than TIGE because it determines the causative allergen. [3]

Asthma can be divided into allergic asthma (AA) and non-allergic asthma (NAA). AA is the type which is triggered by a specific allergen while NAA isn't. Thus, the detection of sIgEs or high TIGE in asthmatics is suggestive for AA. After diagnosing the causative allergens which trigger AA, it's a

crucial step to educate the patients about ways of its avoidance as a step in AA management. [4]

In asthmatics, it's an evidence practice to test the sIgEs of the IAs to discover the causative allergen. However, measuring TIGE routinely in asthmatics to expect IA sensitization is still a debatable subject. Several international asthma guidelines either ignore the role of TIGE in IA diagnosis in asthmatics or state that it's a useless diagnostic tool. Nevertheless, other studies indicate that TIGE is of diagnostic help in asthmatics if other biomarkers are positive. [5]

Up to our knowledge, after searching for evidence it's an assumed suggestion that the link between TIGE and IAs in asthmatics was not done before.

## 2. Methodology

One year period cross-sectional study started from January in 2014. 118 asthmatics both adults and children were selected from King Abdulaziz University Hospital (KAUH) in Jeddah. Local research ethics committee at KAUH approved study protocol. *In vitro* TIGE and *in vivo* SPT was done. Data were loaded and statistically analyzed by SPSS program. Two by two tables was done to discover the connection between TIGE and IAs sensitization. Sensitivity, specificity, +PV and -PV was calculated. P values less than 0.05 was accepted as a statistically significant.

*In vivo* SPT was done for the following IAs: mold like aspergillus, fusarium, penicillium, candida, cladosporium and alternaria alternata. Mites like: DP and DF. German cockroach. Pollens like: mesquite, amaranthus retro, mimosa, oleaceae, timothy, bermuda, rye, mugwort, plantain, salsola kali, chenopodium album and date palm.

*In vivo* SPT results were checked on the forearm after 15 minutes of pricks. Patients were asked to quit oral antihistamines and steroids several days before the test. Positive control is histamine hydrochloride while phenolated glycerol-saline is the negative control. Positive sensitization to allergens is diagnosed if the wheal is  $\geq 3$  mm diameter.

## 3. Results

Results of plotting TIGE versus IAs gives an important results as follow: for mite it shows high sensitivity, low (specificity and predictive values). For mold it displays a high -PV, low (sensitivity, specificity and +PV). For German cockroach it illustrates both high sensitivity and -PV, specificity and +PV were low.

*Dermatophagoides Pteronyssinus* (DP) sensitivity was 80.3, while specificity value is 39.1, +PV was 59.4 and -PV is 64.2. *Dermatophagoides farina* (DF) sensitivity level is 83.7, while specificity is 38.9, +PV is 52.1 and -PV is 75. The readings were considered as significant because P value was 0.029 and 0.012 for DP and DF respectively (table 1).

Nevertheless, TIGE show a high -PV to mold as follow: Aspergillus 82.1, Cladosporium 78.5. Sensitivity, specificity and +PV of TIGE to mold are low. All the values are

considered as significant with P values as 0.020, 0.007 for Aspergillus and Cladosporium correspondingly (table 1).

However, TIGE value in detecting German cockroach sensitization display a double pictures as a high (sensitivity and -PV). Sensitivity of TIGE to German cockroach is 90, while the -PV is 92.8. Both specificity and +PV were low. Values are statistically significant because P value is 0.029 (table 1).

## 4. Discussion

TIGE is of worth in approving mite and in excluding mold sensitization in asthmatics, however with German cockroach TIGE have both roles at the same time. Elevated TIGE in asthmatics is of high sensitivity for mites, thus if asthma case is associated with high TIGE this could indicate the presence of sensitization to mites and it's a logical rationale to test for sIgEs against mites (table 2).

In contrast, normal TIGE is of high -PV to mold, therefore if TIGE is normal it's a logical approach to exclude mold sensitization if sIgE test against mold is negative. TIGE with German cockroach have both roles (high sensitivity and high -PV) which means the high possibility of the presence of sensitization to it with high TIGE plus its exclusion with normal TIGE (table 2).

Routine TIGE *in vitro* test in each asthmatic is still a controversial issue. National and international asthma guidelines which don't mention TIGE test in asthmatics are: Canadian, [6] New Zealand, [7] British Thoracic Society (BTS) [8] and Saudi Initiative for Asthma (SINA) guidelines. [9] Additionally, other guidelines which have illustrated that TIGE is useless in asthmatics are: Global Initiative of Asthma guideline (GINA) [10] which demonstrate that TIGE has no value as a diagnostic test for atopy. World Allergy Organization Guideline (WAO) [11] demonstrate that TIGE is not recommended for screening in asthmatics.

However, other guidelines which have stated that TIGE is of some help in asthmatics are: National Asthma Education and Prevention Program guideline (NAEPP) [12] which display that higher caregiver stress was significantly associated with high TIGE and atopic immune profile. Moreover, the American Academy of Allergy, Asthma & Immunology (AAAAI) [13] guideline indicate that sum of TIGE plus sIgE positive tests may represent an efficient diagnostic tool in asthmatics.

However, there are a plenty of other evidences which could indicate that TIGE and asthma are related. Peter J study clarify that TIGE is higher in asthmatics with positive sIgE (at least 1 allergen), [14] while Hema Satwani found that raised TIGE can be considered as a predictor of allergy in asthmatic children. [15] Moreover, Cissy B conclude that TIGE is higher in asthmatic child under five years with eosinophilia. [16] Even asthmatic elderly patients have higher TIGE than non-asthmatics. [17]

Duane L correlate TIGE in asthmatic child with early sensitization and wheeze. This study established that TIGE is higher in early sensitized children and in persistent wheezer

children. However, TIGE is highest in children who have both of the two factors (early sensitization and wheeze). [18]

Furthermore, TIGE is related to airway hyperactivity (AWH). M.R. Sears study elucidate that TIGE is high in asymptomatic children with AWH. Moreover, this study express that TIGE is higher in asthmatic children when compared to the non-asthmatic ones. [19] Additionally, another study display that there is a strong association between high TIGE and bronchial hyperactivity (BHR) in offspring of asthmatic parents. [20]

Likewise, TIGE is related to asthma control and severity. Maneechotesuwan *et al* study confirmed that higher TIGE is significantly correlated with uncontrolled Asthma, [21] while Koshak E study approve that the higher TIGE the greater asthma severity will be. [22] TENOR Study emphasize that a higher TIGE is associated with more severe or difficult to treat asthma. [23]

Raised TIGE level have several uses in asthmatics. High TIGE can be used as a marker for atopy if associated with positive SPT, [24] high blood eosinophil count and mast cells in nasal smear. [25] Additionally, TIGE can be used to detect the response to specific immunotherapy (SIT) in asthmatics because SIT may decrease TIGE in 36% of cases. [26] Furthermore, sIgE/TIGE ratio can be used as a predictor of

clinical response to SIT and when to stop it. [27] Lastly, high TIGE can be used to measure the dose of omalizumab given to allergic asthma. [28]

TIGE can be used to differentiate between allergic and non-allergic asthma in conjunction with other biomarkers. Koshak E study reveal that phadiatop and TIGE can be utilized as a complementary tool in the identification of AA. [29] Tollerud DJ study determine that TIGE is considered as one of the phenotypic markers of atopy in asthmatic's if associated with positive SPT or high eosinophilia. [30]

### 5. Conclusion

Elevated TIGE in asthmatics almost certainly mean the presence of mite sensitization because TIGE is highly sensitive to mites. Conversely, normal TIGE in asthmatics could exclude mold sensitization because TIGE have high – PV to mold. TIGE have both roles with German cockroach (highly sensitive and high –PV). In asthmatics, in spite TIGE is controversial; it has a possible role as a cheap crude screening device for optimal diagnosis of IAs sensitization.

### Addendum

Table 1. Correlation of high TIGE to inhalants sensitization.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	P value
Dermatophagoides Pteronyssinus	80.3	39.1	59.4	64.2	0.029
Dermatophagoides Farina	83.7	38.9	52.1	75	0.012
Cockroach G	90	33.7	26	92.8	0.029
Aspergillus	28.9	25.5	2.8	82.1	0.020
Cladosporium	25	24.7	2.8	78.5	0.007

Table 2. The meanings of normal and high TIGE.

Inhalant Allergens	High TIGE	Normal TIGE		
	Could Indicate Sensitization	Don't Indicate Sensitization	Almost Exclude Sensitization	Don't Exclude Sensitization
Dermatophagoides Pteronyssinus	√			√
Dermatophagoides Farina	√			√
Cockroach G	√			√
Aspergillus		√	√	
Cladosporium		√	√	

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