

## **Total IgE and Absolute Eosinophils Count as a Predictor of Allergic Diseases in Children**

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### **Abstract**

**Objective:** To study the role of both serum total IgE levels and the absolute eosinophils count, total IgE alone, absolute eosinophils count alone as a marker of allergy in children, and to see their association with the host factors (age and sex)

**Methods:** A retrospective study was conducted at King Abdul Aziz University Hospital – Jeddah (KAUH), during the year 2008. Three hundred children below the age of fifteen years meeting the inclusion criteria were enrolled for the study. Serum total IgE levels and absolute eosinophils count were done in all patients. Data was collected and tabulated. Chi-square was applied to test the association of the variables using SPSS and p-value of <0.05 was taken as statistically significant.

**Results:** Out of 300 patients, 27(9%) had raised both serum total IgE and absolute eosinophils count, 146(48.67%) had raised serum total IgE alone, 40(13.3%) had raised absolute eosinophils count alone. Both IgE plus absolute eosinophilic count, total IgE alone and absolute eosinophilic count alone are not significantly related to the child sex with (P-values 0.759, 0.742, 0.699) respectively, however all are related significantly to the child age (P-values <0.004, <0.001, <0.012) respectively. All are not related significantly to systemic allergies except the significant relation between the absolute eosinophils count with atopic dermatitis (P-value <0.031)

**Conclusion:** Serum total IgE level and absolute eosinophils count, total IgE alone and absolute eosinophils count alone are not a good predictor of allergy in children except that the absolute eosinophils count can be considered as a strong predictor of atopic dermatitis in children. It's clear now, that as the child age increase the positivity of all the tests increase also.

### **Introduction**

There is growing evidence that the prevalence of allergic diseases such as asthma, hay fever and eczema is increasing worldwide (Beasley 2000. Downs 2001). Although there is greater awareness of allergy, it is not easy to assess the true prevalence because many people do not consult health professionals for their symptoms and some will self-medicate using over the counter medications (Walker *et al*, 2005).

It's well known that allergic diseases can be associated with each others. Rhinitis has a strong association with asthma and atopic dermatitis in preschool children (Peroni *et al*, 2003). Individuals with concomitant allergic rhinitis and asthma complain of a higher rate of asthma attacks and more emergency room visits than others without concomitant allergic rhinitis (Bouquet *et al*, 2005).

Al Frayh *et al* (2001) indicated that there was a significant increase in the prevalence of bronchial asthma and, to a lesser extent, in the prevalence of allergic rhinitis in the Kingdom of Saudi Arabia. Prevalence of other childhood allergic diseases isn't clear because of the paucity of studies in this field.

Although the diagnostic value of specific IgE levels against definite allergic disease is well accepted, there are conflicting results about the predictive values of total serum IgE and absolute eosinophils levels in childhood allergies (Sapigni *et al*, 1998).

The aim of this study is to estimate the predictive value of using both total serum IgE plus absolute eosinophils levels in children against various allergic disorders, to see how useful a tool they are to indicate allergy.

## Patients and methods

A retrospective study was conducted for three hundred sample size children below the age of fifteen years who presented to KAUH with the diagnosis of allergic diseases were included in the study. We looked at children who present to KAUH during the year 2008. Age and sex of each child was noted.

Registered allergic diseases were allergic rhinoconjunctivitis, asthma, atopic dermatitis, urticaria and angioedema, contact dermatitis, food allergy, drug allergy and anaphylaxis. Each allergic disorder was registered alone.

Diagnostic workup involved the total IgE and CBC with differential to look for the absolute eosinophils count were done in each child, and the results were

compared with the standard ranges for age and sex (Glader, 2004). Serum total IgE levels were estimated by immunoassay (Vidal *et al*, 2005), while absolute eosinophils count was done using coulter machine. Any total IgE or absolute eosinophils count values above the normal range were considered as abnormal.

Specific allergens in these children were not studied as the aim was to determine the utility of total Serum IgE levels and the absolute eosinophils count, as a predictor of allergy in children.

Correlation coefficient was used to test the relation between total IgE and absolute eosinophils count while the descriptive analysis was used to clarify the relation between both total IgE plus eosinophils count with the clinical allergic presentations.

Results were compiled, tabulated and analyzed using Pearson's chi-square test for association between serum total IgE levels, absolute eosinophils count and clinical presentation of allergic diseases. Differences were considered to be significant at  $p < 0.05$ . All calculations were done through SPSS (Statistical Package for Social Sciences).

## Results

For the raised levels of both IgE plus absolute eosinophilic count, the percentage of the positive results increase with the child age with a significant relation ( $p < 0.004$ ), while there is no significant relation with the child sex ( $p = 0.759$ ), no significant association with all systemic allergies,  $p$ -values as (asthma 0.827, Allergic rhinitis 0.583, Allergic conjunctivitis 0.327, Atopic dermatitis 0.186, Food allergy 0.888).

**Table 1: Association of host factors with serum total IgE levels and Absolute Eosinophilic count.**

Host factors	n=259	Serum total IgE levels and absolute eosinophilic count raised (n=27)	P-value
Age			
1-5	115	6(5.2%)	<0.004*
6-10	62	5(8.1%)	
11-15	82	16(19.5%)	
Sex			
Male	156	17(10.9%)	0.759
Female	103	10(9.7%)	

*P-value <0.05 were taken as statistically significant*

**Table 2: Association of Systemic allergies with serum total IgE levels and Absolute Eosinophilic count (AEC).**

Systemic allergy	(n=259)	High IgE & AEC(n=27)	P-value
Bronchial asthma			
Yes	91	10(11%)	0.827
No	168	17(10.1%)	
Allergic rhinitis			
Yes	69	6(8.7%)	0.583
No	190	21(11.1%)	
Allergic conjunctivitis			
Yes	8	0	0.327
No	251	27(10.8%)	
Atopic dermatitis			
Yes	60	9(15%)	0.186
No	199	18(9%)	
Food allergy			
Yes	21	2(9.5%)	0.888
No	238	25(10.5%)	

*P-value <0.05 were taken as statistically significant.*

For the raised levels of IgE alone, the percentage of the positive results increase with the child age with a significant relation ( $p < 0.001$ ), while there is no significant relation with the child sex ( $p = 0.742$ ), no significant association with all systemic allergies, p-values as (asthma 0.677, Allergic rhinitis 0.347, Allergic conjunctivitis 0.228, Atopic dermatitis 0.689, Food allergy 0.689).

**Table 3: Association of host factors with serum total IgE levels.**

Host Factors	(n=270)	Serum Total IgE levels raised(n=146)	P-value
Age			
1-5	120	50(41.7%)	<0.001*
6-10	68	40(58.8%)	
11-15	82	56(68.3%)	
Sex			
Male	164	90(54.9%)	0.742
Female	106	56(52.8%)	

*P-value <0.05 were taken as statistically significant.*

**Table 4: Association of Systemic allergies with serum total IgE levels.**

Systemic allergies Patients (n=270)	Total number of IgE levels (n=146)	Raised serum	P-value
Bronchial asthma			
Yes	95	53(55.8%)	0.677
No	175	93(53.1%)	
Allergic rhinitis			
Yes	71	35(49.3%)	0.347
No	199	111(55.8%)	
Allergic conjunctivitis			
Yes	8	6(75%)	0.228
No	262	140(53.4%)	
Atopic dermatitis			
Yes	64	36(56.2%)	0.689
No	206	110(53.4%)	
Food allergy			
Yes	22	11(50%)	0.689
No	248	135(54.4%)	

*P-value <0.05 were taken as statistically significant.*

For the raised levels of absolute eosinophilic count alone, the percentage of the positive results increase with the child age with a significant relation ( $p < 0.012$ ), while there is no significant relation with the child sex ( $p = 0.699$ ), a significant relation with atopic dermatitis ( $p < 0.031$ ) but no significant association with the other systemic allergies, p-values as (asthma 0.449, Allergic rhinitis 0.219, Allergic conjunctivitis 0.221, Food allergy 0.409).

**Table 5: Association of host factors with Absolute Eosinophilic count.**

Host Factors	(n=288)	High Absolute Eosinophilic count (n=40)	P-value
Age			
1-5	131	11(8.4%)	<0.012*
6-10	68	9(13.2%)	
11-15	89	20(22.5%)	
Sex			
Male	172	25(14.5%)	0.699
Female	116	15(12.9%)	

*P-value <0.05 were taken as statistically significant.*

**Table 6: Association of Systemic allergies with serum Absolute Eosinophilic count.**

Systemic allergies Patients (n=288)	Total no of eosinophilic count (n=146)	High Absolute	P-value
Bronchial asthma			
Yes	100	12(12%)	0.499
No	188	28(14.9%)	
Allergic rhinitis			
Yes	73	7(9.6%)	0.219
No	215	33(15.3%)	
Allergic conjunctivitis			
Yes	9	0(0%)	0.221
No	279	40(14.3%)	
Atopic dermatitis			
Yes	69	15(21.7%)	<0.031*
No	219	25(11.7%)	
Food allergy			
Yes	26	5(19.2%)	0.409
No	262	35(13.4%)	

*P-value <0.05 were taken as statistically significant.*

### Discussion:

As the child grow up the percentage of the positive results increase for both IgE plus absolute eosinophilic count, total IgE alone and absolute eosinophilic count alone, while all are not related to the child sex nor to the systemic allergies except of the significant relation between atopic dermatitis and the absolute eosinophilic count.

The link between the environment and IgE level is well established. Infants at 9 month

respond to environmental stimuli like the exposure to the local aeroallergens by the production of high levels of IgE antibodies and the persistent wheezing (Sherrill *et al*, 1999). Serum total IgE level is influenced by early weaning, early bottle feeding, exposure to passive smoking, pollens, cold, and pets; and is associated with blood eosinophilia (Satwani *et al*, 2009).

Dietary and environmental measures may influence the IgE response in atopy-prone children, thus confirming the role of environmental factors in the modulation of

the phenotypic expression of atopy (Bruno *et al*, 1995). IgE and atopy are closely related. It has been found that the IgE level in Indian allergic patients is significantly related to atopy (Sharma *et al*, 2006).

Geographical location can affect total IgE levels. It has been found that the geometric mean of total serum IgE levels of Costa Rican children with either asthma or allergic rhinitis are higher than those of children with asthma or allergic rhinitis in most industrialized countries, the relationship among markers of allergy, asthma, rhinitis, and eczema in Costa Rica is similar to that found in countries with a Western lifestyle and different from that found in rural areas of Asia and Africa (Celedón *et al*, 2002). High levels of IgE found in Ethiopian children on arrival to Israel declined to Israeli control levels after several years of living in the new environment. Ethiopian children born in Israel had normal levels of IgE, suggesting that environment is the main factor affecting IgE levels in this population. Israeli born Ethiopian children with asthma had significantly increased serum IgE levels compared to asthmatics of Israeli origin (Iancovici *et al*, 2005).

Although the diagnostic value of specific IgE levels against definite allergens is well accepted, there are conflicting results about predictive value of total serum IgE Levels (Sapigni *et al*, 1998).

There are many studies which support the role of total IgE in the diagnosis of allergy in children. Serum total IgE level is a good predictor of allergy in children especially in asthmatics (Satwani *et al*, 2009). The highest IgE level was noted in children with combined allergic diseases (Lo *et al*, 1997).

But there are other studies which don't support the predictive value of total IgE in allergy diagnosis which shows a wide overlap of IgE levels in patients and healthy subjects, its diagnostic significance in Indian population seems to be limited (Sharma *et al*, 2006). The measurement of serum total IgE is not helpful for the

diagnosis of allergic respiratory diseases because it has a quite good sensibility, a poor specificity and a poor negative predictive value. The test was more sensible and less specific in children (Fajraoui *et al*, 2008).

It's a logic approach to increase the predictive value of diagnosing allergies in children by doing both the total serum IgE levels plus the peripheral eosinophils counts in all cases presenting with suspected symptoms of allergies (Chowdary *et al*, 2003). Serum total IgE level is usually associated with blood eosinophilia (Satwani *et al*, 2009). IgE values and eosinophilia are markedly increased in these children under 5 years of age in Bandung, Indonesia, and the highest values are found in the 7% with asthma (Kartasamita *et al*, 1994). In spite of that there are other studies about severe childhood asthma show that it may be related to a high level of total IgE but not to blood eosinophils counts (Siroux *et al*, 2003).

Skin testing was found to be the most effective measure of atopy in asthmatics more than the other tests (Khadadah *et al*, 2000). Total IgE is highly influenced by allergen skin prick test reactivity (Backer *et al*, 1992). Skin testing and total serum IgE measurement may be considered complementary to one another in diagnosing allergic respiratory disorders (Gharagozlou *et al*, 2005).

In a recent study which is considered as the first one to compare results of allergy tests according to age. This study concludes that for patients over 50 years of age the ImmunoCAP was found to be the preferred method for detecting allergy to house-dust mites and for patients less than 30 years old skin prick test is the recommended first choice (Jung *et al*, 2010).

In asthma, serum total IgE level is a strong predictor of allergy in children (Satwani *et al*, 2009). Serum IgE level may be used to differentiate between asthmatic and non-asthmatic individuals in conjunction with other biomarkers (Al Obaidi *et al*, 2008).

IgE antibodies in blood may be beneficial not only to diagnose allergic diseases in young children but especially to serve as a marker of severity of asthma (Wickman *et al*, 2003). In patients with severe or difficult-to-treat asthma a higher total IgE levels were observed in children and associated with asthma severity among younger patients (Borish *et al*, 2005).

In asthmatic children increasing atopy is associated with increasing asthma severity. However, the relationships between asthma severity and skin prick tests, and asthma severity and total serum IgE values, appear subtly different (Carroll *et al*, 2006).

Total serum IgE, specific IgE, airway caliber, and asthma symptoms are the main independent factors influencing the occurrence of bronchial hyper-responsiveness in a young adult (Rusznak and Davies, 1998). Airway hyper-responsiveness appears to be closely linked to an allergic diathesis, as reflected by the serum total IgE level (Sears *et al*, 1991).

Eosinophilia role in asthma diagnosis is contradictory. Studies which support its role in asthma show that the blood eosinophils after exercise correlate significantly with the maximal percent fall in FEV(1) after exercise (Lee *et al*, 2006), eosinophils can't be a marker for asthma in children (Oryszczyn *et al*, 2006). While other studies don't support its role in the persistence and severity of asthma (Siroux *et al*, 2003).

In allergic rhinitis total IgE levels are contradictory; however the skin prick test, specific IgE levels and eosinophils count are highly predictive (Droste *et al*, 1996). There is a close relationship between the skin prick test, specific IgE positivity and the reported symptoms of nasal allergy in a general population. Skin testing and specific IgE measurement may be considered complementary to one another in diagnosing allergic rhinitis (Droste *et al*, 1996).<sup>32</sup> But in spite of skin test and specific serum IgE are correlated, they are

not consistent with the results of the total serum IgE (Bañuelos *et al*, 2003).

But as a contradiction to the total IgE predictive value, another study shows that the serum total IgE levels increase in patients with allergic rhinitis (Pinar *et al*, 2005). The levels of total IgE correlate significantly with the recovery of symptoms of rhinitis in children (Choi *et al*, 2005).

Eosinophils count is highly predictive in rhinitis. The levels of total eosinophils count correlate significantly with the recovery of nasal eosinophils in children with symptoms of rhinitis (Choi *et al*, 2005).<sup>35</sup> Nasal eosinophils count which is an organ-specific allergic inflammatory marker correlate well with the severity of rhinitis in children (Chen *et al*, 2006).

The data suggests that levels of total or specific IgE do not correlate with severity of chronic sinusitis in children. Nonetheless, the severity of chronic sinusitis and asthma correlate well with each other irrespective of total and specific IgE (Lin *et al*, 2001).

In atopic dermatitis (AD) the major predictive value is for the eosinophils count levels. Absolute eosinophils count correlates significantly with various objective clinical scores and chemokine markers (AD), and is a useful indicator for predicting moderate to severe (AD) in children (Hon *et al*, 2007). Peripheral blood eosinophilia could serve as a diagnostic parameter in differentiating allergic AD from non-allergic dermatitis (Jenerowicz *et al*, 2007).

In conclusion, both IgE plus absolute eosinophilic count, total IgE alone and absolute eosinophilic count alone are not significantly related to the child sex nor the systemic allergies, however all are significantly related to the child age, atopic dermatitis is related significantly to the absolute eosinophilic count.

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## الغلوبولين المناعي هـ وعدد الحمضات المطلق كمؤشر لتوقع أمراض الحساسية في الأطفال

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**الهدف:** دراسة دور كلٍّ من: الغلوبولين المناعي هـ في مصل الدم مع عدد الحمضات المطلق، الغلوبولين المناعي هـ وحده، و عدد الحمضات المطلق وحدها كعلامة للحساسية لدى الأطفال، والنظر إلى ارتباطهم مع عوامل المضيف (العمر والجنس).

**الطريقة:** أجريت الدراسة بأثر رجعي في مستشفى جامعة الملك عبدالعزيز بجدة خلال العام 2008 ميلادي. التحق بالدراسة ثلاثمائة طفل دون سن الخامسة عشر استوفوا معايير الإدراج للدراسة. تمّ قياس الغلوبولين المناعي هـ في مصل الدم وعدد الحمضات المطلق لجميع المرضى. تمّ جمع البيانات وتبويبها. تمّ تطبيق مربع كاي الإحصائي لاختبار ارتباط المتغيرات باستخدام برنامج إحصائي، واعتبار القيمة الاحتمالية أصغر من 0.05 ذات دالة إحصائية.

**النتائج:** من أصل 300 مريض، 27 (9%) لديهم ارتفاع في كلٍّ من الغلوبولين المناعي هـ في مصل الدم وعدد الحمضات المطلق ، 146 مريض (48.67%) لديهم ارتفاع في الغلوبولين المناعي هـ في مصل الدم وحده، 40 مريض (13.3%) لديهم ارتفاع في عدد الحمضات المطلق وحده. ارتفاع كلٍّ من الغلوبولين المناعي هـ وعدد الحمضات المطلق ، ارتفاع الغلوبولين المناعي هـ وحده أو ارتفاع عدد الحمضات المطلق وحده، جميعها لا ترتبط بشكل كبير بجنس الطفل (القيمة الاحتمالية 0.759، 0.742، 0.699) على التوالي. ومع ذلك فإنّ جميعها ترتبط إلى حد كبير بعمر الطفل (القيمة الاحتمالية أصغر من 0.012، 0.001، 0.004) على التوالي. لا يرتبط الجميع إلى حد كبير بالحساسية الجهازية باستثناء وجود علاقة ذات دالة إحصائية بين عدد الحمضات المطلق وحدوث التهاب الجلد التأتبي (القيمة الاحتمالية أصغر من 0.031).

**الاستنتاج:** إنّ كلٍّ من الغلوبولين المناعي هـ في مصل الدم و عدد الحمضات المطلق، الغلوبولين المناعي هـ وحده، و عدد الحمضات المطلق وحدها، جميعها ليست مؤشراً جيداً للحساسية في الأطفال باستثناء أنّ عدد الحمضات المطلق يعتبر مؤشراً قوياً على التهاب الجلد التأتبي في الأطفال. من الواضح أنّه كلما زاد سنّ الطفل تزيد إيجابية جميع الاختبارات أيضاً