Total Serum IgE Level in Relation to Some Risk Factors of Childhood Asthma

Haidar A. N. Abood*, Mohammad R. I. Ghazal**, Zuhair M. Al-Musawi***

* Department of Pharmacology, College of Medicine-Kerbala University, ** Department of Pharmacology, College of Medicine-Baghdad University, *** Department of Pediatrics, College of Medicine-Kerbala University

Key words: Childhood asthma, Total serum IgE, Risk factors.

E-mail: haidar_abood@hotmail.com

(Received: July2013, Accepted: Dec2013)

Abstract:

Measurement of total serum IgE (TSIgE) levels in asthmatic children can be used for supporting the diagnosis of allergic asthma, predicting asthma severity and monitoring response to therapy. Elevated TSIgE level is important risk factor for persistent childhood asthma. The present study aims to determine the extent of elevation in TSIgE levels among asthmatic children and its association with some risk factors of childhood asthma. This cross sectional study was conducted in Kerbala Teaching Hospital for Children on 154 asthmatic children. An interview was conducted with patients (including their parents) through a questionnaire prepared for this purpose to report patient's information and clinical data. All patients were screened for the presence of elevated TSIgE by a qualitative method followed by quantitative measurement of TSIgE concentration. Absolute eosinophils count was also determined. Seventy five (48.7%) patients showed positive IgE screening test and 79 (51.3%) patients showed negative IgE screening test. 61.4% of asthmatic children in the age group 5-10 years and 55.5% of patients in the age group >10 years were IgE (+ve), while only 33.3% of patients in the age group <5 years were IgE (+ve)**.** The mean TSIgE level was 874.97±1323.85 IU/ml for IgE (+ve) patients (56% had levels <500, 21.3% between 500-1000, and 22.7% >1000 IU/ml) and 38.19±19.23 IU/ml for IgE (-ve) patients. The ages of patients in the IgE (+ve) group were significantly higher (P<0.01) than those for patients in the IgE (-ve) group. No significant differences (P>0.05) were observed between patients in both groups regarding absolute eosinophils count, patient's weight, gender, positive personal history of atopic dermatitis and/or allergic rhinitis, positive family history of asthma and exposure to smoking . In conclusion, there is high association between age and TSIgE levels in asthmatic children, with elevated levels mostly seen in older children. No association present between elevation in TSIgE and other risk factors for childhood asthma like; male gender, positive family history of asthma, exposure to tobacco smoke and peripheral blood eosinophilia.

مستوى المصل الكلي للغلوبيولين المناعي نوع E وعلاقته ببعض عوامل خطورة الإصابة بالربو عند الأطفال

- حيدر عبد الأمير نجم عبود / فرع الفارماكولوجي - كلية الطب – جامعة كربلاء
- محمد رشاد إبراهيم غزال / فرع الفارماكولوجي - كلية الطب – جامعة بغداد
- زهير مهدي الموسوي / فرع الأطفال - كلية الطب – جامعة كربلاء

مفتاح البحث: ربو الأطفال، مستوى المصل الكلي للغلوبيولين المناعي نوع E، عوامل الخطورة.

الخلاصة:

إن قياس مستوى المصل الكلي للغلوبيولين المناعي نوع E (IgE) في الأطفال المصابين بالربو يستخدم في دعم تشخيص الربو التحسسي بالإضافة لتحديد شدة المرض ورصد الاستجابة للعلاج. يعتبر ارتفاع مستوى المصل الكلي للغلوبيولين المناعي نوع E أحد عوامل الخطورة المهمة للإصابة بالربو عند الأطفال. .إن الهدف من هذه الدراسة هو تحديد مدى الارتفاع في مستويات المصل الكلي للغلوبيولين المناعي نوع E بين الأطفال المصابين بالربو وارتباطه مع بعض عوامل خطورة الإصابة بالربو عند الأطفال. أجريت هذه دراسة في مستشفى كربلاء التعليمي للأطفال على 154 طفل مصاب بالربو. بعد مقابلة المرضى وملئ الاستمارات الخاصة بالدراسة, تم إجراء الفحص النوعي على أمصال المرضى لتحديد وجود مستويات مرتفعة من الغلوبيولين المناعي نوع E تلاها قياس كمي لتركيز الغلوبيولين المناعي نوع E في المصل و كذلك تم حساب العدد المطلق لكريات الدم البيضاء الحمضية لجميع المرضى. أظهرت الدراسة أن 48.7٪ من المرضى لديهم مستويات مرتفعة من الغلوبيولين المناعي نوع E (IgE+ve) بينما 51.3٪ كانت لديهم مستويات طبيعية (IgE-ve). كانت المستويات مرتفعة في 61.4٪ من المرضى في الفئة العمرية (5-10 سنوات), 55.5٪ من المرضى في الفئة العمرية (أكثر من 10 سنوات) و 33.3٪ من المرضى في الفئة العمرية (أقل من 5 سنوات). إن متوسط مستوى المصل الكلي للغلوبيولين المناعي نوع E هو 874.97 ± 1323.85 وحدة دولية لكل ملليلتر في المجموعة مرتفعة المستوى (56٪ لديهم مستويات أقل من 500، 21.3٪ بين 500-1000، و 22.7٪ أكثر من 1000 وحدة دولية / مل) و38.19 ± 19.23 وحدة دولية لكل ملليلتر في المجموعة طبيعية المستوى. كانت أعمار المرضى في المجموعة مرتفعة المستوى (IgE+ve) أعلى إحصائيا من أعمار المرضى في المجموعة طبيعية المستوى (IgE-ve). لم تلاحظ أي فروقات ذات دلالة إحصائية بين المرضى في كلا المجموعتين فيما يتعلق بالعدد المطلق لكريات الدم البيضاء الحمضية، الوزن، الجنس، التهاب الجلد التأتبي أو التهاب الأنف التحسسي، إصابة أحد أفراد العائلة بالربو و التعرض للتدخين. من ذلك نستنتج ارتباط ارتفاع مستوى المصل الكلي للغلوبيولين المناعي نوع E بالعمر لدى الأطفال المصابين بالربو حيث تكون المستويات مرتفعة في الغالب في الأطفال الأكبر سنا. وعدم وجود علاقة بين ارتفاع مستوى المصل الكلي للغلوبيولين المناعي نوع E مع عوامل الخطورة الأخرى للإصابة بالربو عند الأطفال مثل جنس الذكور، التاريخ العائلي الإيجابي للربو،التعرض لدخان التبغ وارتفاع نسبة كريات الدم البيضاء الحمضية في الدم.

Introduction:

Childhood asthma is a common disease and continues to be the leading serious chronic illness among children in different countries [1-3]. In Iraq, the prevalence of childhood asthma is 16.4% in primary school children [4] and 15.8% in children aged less than 5 years [5]. There are two main types of childhood asthma; *Transient wheeze* that occurs in early childhood and *Persistent wheeze* which usually occurs in older children and persists into later childhood [6]. Persistent childhood asthma is subdivided into two phenotypes; *Atopic* phenotype (allergic or atopic asthma) and *non-atopic* phenotype (non-allergic or non-atopic asthma) [7]. The diagnosis of allergic asthma requires the presence of sensitization to an inhalant allergen documented by positive allergen-specific IgE test or skin prick test [8].

Risk factors associated with the development of persistent childhood asthma include, allergy (atopic dermatitis, allergic rhinitis, elevated total serum immunoglobulin E (IgE) levels, and inhalant allergen sensitization), parental asthma, male gender, late age at

presentation, lower respiratory tract infections, peripheral blood eosinophilia and environmental tobacco smoke (ETS) exposure [1]. Among other risk factors, allergy is the most important single factor and allergic asthmatic children often continue to have the disease in adulthood [6].

The concentration of IgE in serum is age dependent. It remains normally at levels less than 10 IU/ml in most infants and gradually increases throughout childhood reaching a peak level (about 75 IU/ml) at 8-12 years of age [9]. Elevated total serum IgE (TSIgE) levels are seen in patients with atopic diseases and some invasive parasitic diseases [10]. Atopy is the genetic predisposition to develop IgE antibodies in response to allergens [11]. TSIgE level can be used to differentiate between atopic (allergic) and non-atopic (non-allergic) asthma prior to allergen-specific IgE determination. Also it is helpful in predicting severity and monitoring response to therapy [12].

Objectives: This study aims to determine the extent of elevation in TSIgE levels among asthmatic children and its association with some predisposing factors for childhood asthma.

Patients and Methods:

This cross sectional, hospital based study was conducted in Kerbala Teaching Hospital for Children in the period from June 2011 to June 2012 on asthmatic children visited the outpatient clinic of the hospital. Patients with at least 3 attacks of reversible bronchoconstriction in the past 12 months [13] without history of invasive parasitic disease (documented by normal general stool exam) were included in the study. An interview was conducted for all patient (including their parents) through a questionnaire planned for this purpose to report patient's information and clinical data.

After blood collection, whole blood was used for WBC count and blood film preparation while serum was used for qualitative and quantitative IgE determination. IgE Serum RapiCard InstaTest (Cortez, USA, LOT No. 1102081) was used as a screening (qualitative) test for elevated TSIgE. The test detected IgE levels above 80 IU/ml (cutoff value). Measurement of TSIgE concentration was done by TOSOH AIA-360 automated immunoassay analyzer (TOSOH, Japan) using ST AIA-PACK IgE II kit (LOT No. AX17759 and B617765). Total WBC count was measured using Sysmex KX-21N automated haematology analyzer (Sysmex, Japan). The percentage of eosinophils was determined by direct examination of blood films under the microscope, then absolute eosinophils count (AEC) was calculated by multiplying WBC count by the percentage of eosinophils. Collected data were analyzed using SPSS version 20. P values <0.05 were considered as statistically significant.

Results:

The study included 154 asthmatic children aged from 1-13 years. Seventy five (48.7%) patients showed elevated TSIgE levels (positive IgE screening test) and 79 (51.3%) patients showed normal TSIgE levels (negative IgE screening test). Table -1- showed that 61.4% of asthmatic children in the age group 5-10 years and 55.5% of patients in the age group >10 years had elevated TSIgE, while only 33.3% of patients in the age group <5 years had elevated TSIgE (figure -1-).

The TSIgE levels ranged from 97.2 to 6662.0 IU/ml for IgE (+ve) asthmatic children (mean ± SD = 874.97±1323.85 IU/ml) and from 3.1 to 76.5 IU/ml for IgE (-ve) patients (mean ± SD = 38.19±19.23 IU/ml). There was significant elevation (P<0.05) in TSIgE levels for IgE (+ve) patients compared to IgE (-ve) patients. Regarding asthmatic children with elevated TSIgE levels, in 42 (56%) patients the IgE levels were less than 500 IU/ml, in 16

(21.3%) patients the levels were between 500-1000 IU/ml, and in 17 (22.7%) patients the IgE levels were more than 1000 IU/ml (table -2-).

Comparing major risk factors of childhood asthma between IgE (+ve) and IgE (–ve) asthmatic children, table -3- showed highly significant difference ($P<0.01$) in patients ages between IgE (+ve) and IgE (–ve) asthmatic children. The ages of patients in IgE (+ve) group were 32% higher than those in IgE (–ve) group. The mean weight of children in the IgE (+ve) group (23.61±11.04 kg) was slightly higher than mean weight of children in the IgE (-ve) group (20.28±9.95 kg) with non-significant difference ($P>0.05$). The absolute eosinophils count was higher in the IgE (+ve) group compared to IgE (-ve) group (280.48±269.45 cell/µl versus 207.56±181.97 cell/µl respectively) but the difference was not statistically significant ($P>0.05$). Male gender was predominant in both groups (65.3% of IgE (+ve) and 53.2% of IgE (-ve) patients) with no significant difference ($P>0.05$) between the two proportions. Most patients in both groups have positive family history of asthma (82.7% of patients in IgE (+ve) and 84.8% of patients in IgE (-ve) groups) with non-significant difference ($P>0.05$). No significant difference ($P>0.05$) was found between IgE (+ve) and IgE (-ve) asthmatic children regarding personal history of other atopic diseases (atopic dermatitis and allergic rhinitis). The exposure to smoking at home (environmental tobacco smoke) was slightly higher in IgE (+ve) group (40.0% of patients) compared to IgE (-ve) group (30.4% of patients) but the difference was not statistically significant ($P>0.05$).

Discussion:

The present study showed that 48.7% of asthmatic children (regardless of their age) had elevated TSIgE. This is in line with previous reports showed that allergic asthma accounts for 40-50% of childhood asthma [7].

When the age of patients is considered, these data are greatly affected. It has been shown that the prevalence of atopy in children is increased with age, being 5% at 2 years, 20% at 4 year, and 60% of population at school age [14,15]. In asthmatic children atopy was reported in 40% of preschool patients and 90% of school patients [16]. The results of this study are in consistence with these reports and showed that elevation in TSIgE was present in 33.3% of patients aged less than 5 years, 61.4% of patients aged 5-10 years and 55.5% of patients aged more than 10 years (table -1-)

In previous studies, TSIgE level was found to be closely related to asthma severity. Levels higher than 1000 IU/ml were associated with severe persistent asthma [17,18]. In this study 22.7% of patients in the IgE (+ve) group had levels higher than 1000 IU/ml and the higher range level for this group exceeded 6500 IU/ml.

Regarding the comparison of major risk factors for childhood asthma between IgE (+ve) and IgE (–ve) asthmatic children (table -3-), the present study showed that patients in IgE (+ve) group had significantly higher ages than those in IgE (–ve) group. This is agreed with previously discussed reports on the relationship between atopy and age of asthmatic children [16].

Despite increasing evidences suggesting strong association between asthma and obesity particularly in adolescents [19], no significant association was found between increased BMI and total serum IgE in asthmatic children by Yao *et al* [15]. The same finding was observed in this study regarding the relation of body weight to TSIgE level. The slightly higher mean body weight for IgE (+ve) patients is probably because they are older in age.

In the present study, it was observed that mean absolute eosinophils count (AEC) for patients in IgE (+ve) group was 26% higher than that for patients in IgE (–ve) group, but this difference was not statistically significant ($P = 0.078$). These findings did not correlate with the general presumption that allergic asthma is associated with peripheral eosinophilia [10]. This non-significant result is explained probably by limited sample size due to high standard deviation of mean and borderline *P* value.

Childhood asthma was reported to be more prevalent in boys than in girls in different parts of the world [2,3] including Iraq [4,5]. The same findings were observed in this study and male gender was predominant in both IgE (+ve) and IgE (-ve) asthmatic children. The present study also observed non-significant association between TSIgE and gender. This result agrees with Yao *et al* study [15].

Parental asthma is important risk factor for persistent childhood asthma [1]. Studies in Iraq reported high association between occurrence of childhood asthma and positive family history of asthma [20,21]. In the present study, most asthmatic children (82.7% of IgE (+ve) and 84.8% of IgE (-ve) patients) had positive family history of asthma, these results agrees with both Aljanabi *et al* [20] and Alsamarai *et al* [21] studies. No significant association was found by this study between positive family history of asthma and TSIgE. This is in line with previous Iraqi study done in Tikrit Teaching Hospital [22].

It is well recognized that the majority of patients with atopic dermatitis or allergic rhinitis have elevated levels of TSIgE [23]. However there are limited data about the prevalence of both conditions in asthmatic children with elevated TSIgE levels. In the present study, there was no significant difference between IgE (+ve) and IgE (-ve) asthmatic children regarding personal history of atopic dermatitis and/or allergic rhinitis. These findings depend on history only, further studies considering physical examination and specific investigations may be needed to confirm these results.

In the present study, the exposure to tobacco smoke (the presence of at least one smoker in the house, smoking at least 20 cigarettes per day) was found slightly higher among patients with elevated TSIgE (40% of patients) compared to patients with normal TSIgE (30% of patients). Although this difference was not statistically significant, but it may play a role in increasing the prevalence of IgE (+ve) patients in older age groups, since previous reports showed that passive smoking significantly increased TSIgE levels among adolescents [24].

Conclusions:

In childhood asthma, there is high association between age and TSIgE levels, with elevated levels mostly seen in older children. No association present between elevation in TSIgE and other risk factors for persistent childhood asthma like; male gender, positive family history of asthma, exposure to tobacco smoke and peripheral blood eosinophilia.

Recommendations:

Based on this study, it is recommended to estimate total serum IgE levels for all asthmatic children, since the presence of most risk factors can not predict elevation in serum levels. Many patients included in this study showed high TSIgE levels and may benefit from anti-IgE therapy, so further studies are needed to evaluate the response of these patients to the monoclonal antibody, omalizumab.

References:

1- Herzog R and Cunningham-Rundles S. *Mt Sinai J Med* 78(5): 645 (2011).
2- Lai CK, Beasley R, Crane J, et al. *Thorax* 64(6): 476 (2009).
3- Guill MF. *Pediatrics in Review* 25(9): 299 (2004).
4- Al-Thamiri D, Al-Kubaisy W and Ali SH. *East Mediterr Health J* 11(1-2): 79 (2005).
5- Salem MB, Al-Sadoon IO and Hassan MK. *East Mediterr Health J* 8(4-5): 503 (2002).
6- Gelfand EW. *Proc Am Thorac Soc* 6: 278 (2009).
7- Fan YC. *World J Pediatr* 2(2): 85 (2006).

8- Helms PJ and Henderson J. Respiratory disorders. In: McIntosh N, Helms PJ, Smyth RL, *et al*., (eds.). Forfar and Arneil's textbook of pediatrics. 7th ed., Churchill Livingstone-Elsevier: 657 (2008).
9- Nguyen-Thi XH, Chabane MH and Lafay M. *Allerg Immunol* 18(7): 11 (1986).
10- Stone KD, Prussin C and Metcalfe DD. *J Allergy Clin Immunol* 125(2): 73 (2010).
11- Gold MS and Kemp AS. *Med J Australia* 182: 298 (2005).
12- Owen CE. *Pharmacol Ther* 113: 121 (2007).
13- Wonderen KE, Mark LB, Mohrs J, et al. *Eur Respir J* 36: 48 (2010).
14- Arshad SH, Tariq SM, Matthews S, et al. *Pediatrics* 108(2): e33 (2001).
15- Yao TC, Ou LS, Yeh KW, et al. *J Asthma* 48(5): 503 (2011).
16- Pearce N, Pekkanen J and Beasley R. *Thorax* 54: 268 (1999).
17- Anupama N, Vishnu Sharma M, Nagaraja HS, et al. *Thai Journal of physiological sciences* 18(3): 35 (2005).
18- Sandeep T, Roopakala MS, Silvia CR, et al. *Lung India* 27(3): 138 (2010).
19- Fiueroa J, Chinn S and Rona R. *Thorax* 56: 133 (2001).
20- Aljanabi MK, Alhammash SJ, Waill N, et al. *The Iraqi postgraduate medical journal* 9(1): 6 (2010).
21- Alsamarai AM, Salih MA, Al-Obaidy AH, et al. *J Rural Trop Public Health* 8: 45 (2009).
22- Saeed MS and Mahmood YA. *Iraqi postgraduate medical journal* 5(3): 279 (2006).
23- Herr M, Just J, Nikasinovic L, et al. *J Allergy Clin Immunol* 130(2): 389 (2012).
24- Mlinaric A, Popovic Grle S, Nadalin S, et al. *Eur Rev Med Pharmacol Sc* 15(8): 973 (2011).

Table 1: The distribution of asthmatic children according to total serum IgE screening in different age groups

Age group	Patients with elevated TSIgE (IgE +ve) No. (%)	Patients with normal TSIgE (IgE -ve) No. (%)	Total
< 5 years	22 (33.3%)	44 (66.7%)	66 (100%)
5-10 years	43 (61.4%)	27 (38.6%)	70 (100%)
> 10 years	10 (55.5%)	8 (44.5%)	18 (100%)
Total	75 (48.7%)	79 (51.3%)	154 (100%)

Table 2: The distribution of patients according to total serum IgE levels in asthmatic children with positive IgE screening test.

TSIgE level	Number of patients	Percentage of patients
< 500 IU/ml	42	56%
500-1000 IU/ml	16	21.3%
>1000 IU/ml	17	22.7%
Total	75	100%

Table 3: Comparison of major risk factors for childhood asthma between IgE (+ve) and IgE (–ve) asthmatic children.

Risk factors	IgE (+ve) patients (N = 75)	IgE (-ve) patients (N = 79)	*P* value
Data presented by mean ± SD			
Age (years)	6.53±3.18	4.95±3.06	0.002 *
Weight (kg)	23.61±11.04	20.28±9.95	0.194 º
Absolute eosinophils count (cell/µl)	280.48±269.45	207.56±181.97	0.078 º
Data presented by percentage			
Male patients	65.3%	53.2%	0.125 º
Positive family history of asthma	82.7%	84.8%	0.718 º
Positive personal history of atopic dermatitis and/or allergic rhinitis	12.0%	16.5%	0.115 º
Exposure to tobacco smoke	40.0%	30.4%	0.211 º

* = Highly significant difference (P<0.01).
º = Non significant difference (P>0.05)

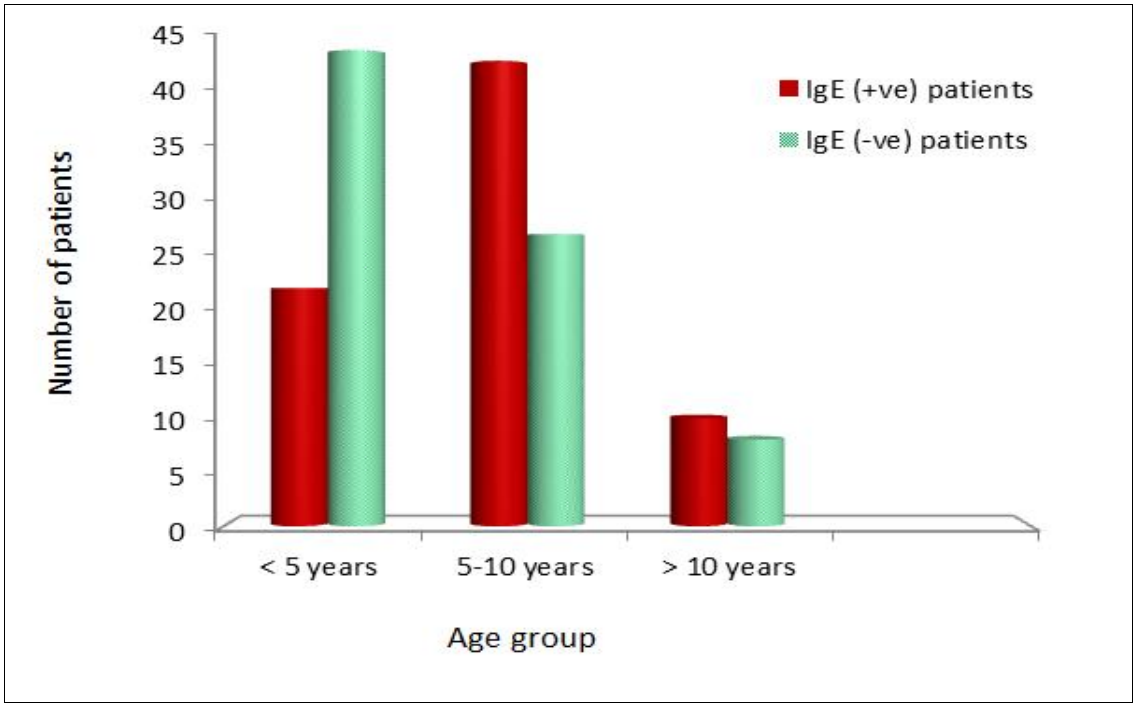

Figure 1: The distribution of IgE (+ve) and IgE (-ve) asthmatic children in different age groups