Original Article

The Age and Residence Impact on IgE Serum Level in Patients with Allergic Asthma

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Abstract

Background: Immunoglobulin E (IgE) has a role in mediating allergic reactions and their powerful effector functions, but numerous factors influence its value. **Objective:** To find any difference in total and specific IgE serum levels at the different age groups and residences. **Materials and Methods:** Eighty-seven asthmatic children, including 57 males and 30 females with asthma aged between 1 and 16 years old, 32.2% living in rural and 67.8% living in urban, were collected at Kerbala Teaching Hospital for Children. All asthmatic children in this study were subjected to measuring total IgE level using AccuBind IgE ELISA kit, Human *Chlamydia pneumoniae* IgG using Cpn IgG ELISA kit, and Human *C. pneumoniae* IgE using Cpn IgE ELISA kit. **Results:** There was a significant positive linear correlation between age and total IgE level and a significant negative correlation between age and *C. pneumoniae* IgE in asthmatic children (0.255, $P = 0.017$, -0.233, $P = 0.03$, respectively). Further, there was a significant positive linear correlation between total IgE and *C. pneumoniae* IgE under age controlling (0.225, $P = 0.019$). In urban residents, the asthmatic children more than eleven years old had a low *C. pneumonia* IgE serum level (5.845 ± 1.821 ng/L) compared with asthmatic children who lived in rural areas (8.206 ± 2.793 ng/L). Depending on age groups, there was a significant difference ($P = 0.047$) in *C. pneumonia* IgE serum levels in asthmatic children who lived in urban areas. **Conclusion:** *C. pneumonia*-specific IgE decreased in early adulthood urban asthmatic children.

Keywords: Allergic asthma, *Chlamydia pneumoniae*, IgE, ELISA test

Introduction

Allergic asthma is the most common asthma phenotype. It is an airway inflammatory disease characterized by recurrent wheezing episodes and bronchoconstriction. Usually, it is caused by sensitization to environmental allergens. Chronic inflammation may finally lead to structural damage, followed by airway remodeling.[1,2] It is well-established that allergen-specific T helper 2 (Th2) cells and their cytokines, such as interleukin-4 (IL-4), IL-5, and IL-13, are thought to play central roles in developing allergic asthma and driving disease pathology in patients.[3,4]

Further, there is evidence that CD4+ lymphocytes with a Th2-cytokine pattern play a pivotal role in the pathogenesis of asthma. These cells orchestrate the recruitment and activation of the primary effector cells of the allergic response (mast cells and eosinophils) through the release of cytokines (IL-4, IL-5, and IL-13).[5,6] In allergic disease, there is a polarization of T-lymphocyte responses and enhanced secretion of cytokines involved in regulating immunoglobulin E (IgE), mast cells, basophils, and eosinophils, ultimately leading to inflammation and disease.[7,8] However, the IgE antibody is necessary to initiate the allergic cascade.[9] IgE plays a central role in the initiation and propagation of the inflammatory cascade and, thus, the allergic response.[10]

The incidence of allergic asthma is highest in early childhood and steadily decreases with advancing age.[11] The average age of onset of allergic asthma is younger

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than that of nonallergic asthma.[1] There is recognition that innate and adaptive immune functions, including IgE production, progressively decline over time, such as growing up and aging.[12,13] Aging is accompanied by a progressive decline in almost all immune system functions. Thus, allergy prevalence tends to decline with age.[14,15] Nevertheless, other studies detected that total IgE increased with age, but allergen-specific IgE levels significantly decreased with age but with differences between allergens.[13,14]

Otherwise, the previous study supports a hypothesis that farm living is inversely associated with allergy.[16] Allergy and sensitization rates are significantly higher in urban than in their rural counterparts.[17,18] Urbanization is associated with the risk of developing allergic conditions.[19]

This study aims to detect if there is any correlation between age and concentration of total and specific IgE. Also, to find any difference in total and specific IgE at the different residences of the same age groups.

Materials and Methods

Study design and subjects

A cross-sectional study was carried out at Karbala Teaching Hospital for Children; the study was conducted from January to May 2022, including 87 asthmatic children (57 males and 30 females), and the mean age of patients was 7.833 ± 3.652 years old (ranging from 1 to 16 years old) [Table 1]. All children in this study were diagnosed as asthmatic patients by a clinician. A questionnaire was framed for collecting the information and clinical data from patients or their parents. All patients underwent a total serum IgE test and excluded asthmatic patients with a total IgE concentration of less than 100 IU/mL from the study.

Ethical approval

The Ethical Committee approved the study protocol in the Babylon medical college (1354, 2022) and the relevant ethical committee in the health directorate (20719, 2022). Verbal approval was obtained from patients and/or their parents before sampling.

Table 1: Demographic and clinical characteristics of asthmatic children

Demographic and clinical characteristics		
Age mean ± SD		7.833 ± 3.652 (years)
Age groups no. (%)	Less than 6	30 (34.5%)
	From 6 to 11	41 (47.1%)
	More than 11	16 (18.4%)
Sex no. (%)	Male	57 (65.52%)
	Female	30 (34.48%)
Geographic areas no. (%)	Urban	59 (67.8%)
	Rural	28 (32.2%)
Total IgE (IU/mL) mean ± SD		398.889 ± 227.156
Chlamydia pneumoniae IgG (ng/L)		24.899 ± 16.654
C. pneumoniae IgE (ng/L)		8.037 ± 4.646

SD: Standard deviation, No.: Number

Patient consent form

The participants who revealed readiness to participate in this study were supplied with written informed consent and verbal information regarding the aim of the study.

Sample collection and processing

Sera were collected from each participant; sera were used to determine the total serum IgE level by Combiwash Max-Planck-Ring 21 automated immunoassay analyzer (Human, Germany) using AccuBind total IgE ELISA kit, USA (LOT NO. 25K1D1). IgG antibody plasma levels against the *Chlamydia pneumoniae* (Human *C. pneumoniae* IgG, Cpn IgG ELISA kit, LOT NO. 20220426, SUNLONG, China) and IgE antibody plasma levels against the *C. pneumoniae* (Human *C. pneumoniae* IgE, Cpn IgE ELISA kit, LOT NO. 20220426, SUNLONG, China) were measured to all subjects using commercial quantitative ELISA kits in an automated instrument (Combiwash Max-Planck-Ring 21).

Statistical analyses

All the statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) version 21 (GraphPad Software, San Diego, California). Quantitative data were expressed as mean ± standard deviation (SD) using the Mann–Whitney *U* test. Kruskal–Wallis test is a nonparametric test used to compare the mean when the *P*-value of Levene's test was less than 0.05. Spearman's test measured the correlation between age and total IgE, *C. pneumoniae* IgG, and *C. pneumoniae* IgE. Partial correlation measured the correlation between total IgE and *C. pneumoniae* IgE by excluding the age effect. Pearson Correlation measured the correlation between total IgE and *C. pneumoniae* IgE. *P*-value <0.05 was considered to indicate statistical significance and is highly significant if *P*-value <0.001.

Results

The characteristics of the subjects

In the present study, the mean age of asthmatic children was 7.833 ± 3.652, and the percentage of age groups (less than 6 years, from 6 to 11 years, and more than 11 years) were 34.5%, 47.1%, and 18.4%, respectively. Approximately 65.52% of asthmatic children were male, and 34.48% were female. Most asthmatic children in this study lived in the urban area than the rural (67.8% in urban and 32.2% in rural). Total serum IgE was 398.889 ± 227.156 IU/mL, while the *C. pneumoniae* IgG level was 24.899 ± 16.654 and *C. pneumoniae* IgE level was 8.037 ± 4.646, as shown in Table 1.

Correlation between the immunological parameters and age of asthmatic children

Table 2 shows a correlation between age and immunological parameters (total serum IgE, *C. pneumoniae* IgG, and *C. pneumoniae* IgE). The results found a positive linear correlation between age and total IgE while a negative linear correlation between age and *C. pneumoniae* IgE. On the other hand, there was no correlation between age and *C. pneumoniae* IgG.

Correlation between total IgE and *C. pneumoniae* IgE in asthmatic patients

The result showed a significant positive linear correlation between total IgE level and human *C. pneumoniae* IgE ($P = 0.019$) under age control [Table 3]. Notably, the study detected a highly significant positive linear correlation between total IgE level and human *C. pneumoniae* IgE only at less than 6 years of age groups ($P = 0.000$). While there was no significant correlation in other age groups, as shown in Table 4 and Figure 1.

Comparison between immunological parameters of asthmatic children depending on age groups and geographic areas

Table 5 shows no significant difference in immunological parameters (total IgE, *C. pneumoniae* IgG, and *C. pneumoniae* IgE) between urban and rural areas of asthmatic children aged from one to eleven years old. Paradoxically, there was a significant difference in *C. pneumoniae* IgE levels between urban and rural asthmatic children aged more than eleven years (*P*-0.036). In urban residents, the asthmatic children more than eleven years old had a low *C. pneumoniae* IgE level (5.845 ± 1.821 ng/L) compared with asthmatic children who lived in rural areas (8.206 ± 2.793 ng/L).

Depending on age groups, there was a significant difference ($P = 0.047$) in *C. pneumoniae* IgE levels in asthmatic children who lived in urban areas. The *C. pneumoniae* IgE level in urban asthmatic children decreased with increased age. On the other hand, there was no significant difference in *C. pneumoniae* IgE level in rural asthmatic children depending on age groups ($P = 0.228$), as shown in Figure 2.

Discussion

IgE plays a crucial role in allergic immune responses.[20] It contributes significantly to developing bronchial hyperresponsiveness in asthma.[7,21] Children with asthma are more likely to have elevated IgE levels than adults.[22–24] Previous studies showed that total and specific IgE values depend on age. However, the results of this study demonstrate that the concentration of serum total and specific IgE is not only dependent on age but also residence.

In this study, we detected that total IgE levels increase with age increase in asthmatic children younger than sixteen. In contrast, *C. pneumoniae*-specific IgE decreases with age increase. This result agrees with a previous study that mentioned total IgE increased with age, but allergen-specific IgE levels significantly decreased when age increased.[14,25] Indeed, we cannot say that *C. pneumoniae*-specific IgE decreases with age since this IgE is not affected by age in asthmatic patients who live in rural [Figure 2]. The low specific IgE value is detected only in urban asthmatic children over eleven [Table 5]. Thus, we cannot make a possible explanation based on age since many factors can interfere with and affect the outcome,

Table 2: Correlation between age and parameter in asthmatic patients

Age	Parameter	Spearman's rho	*P*-value
	Total IgE (IU/mL)	0.255	0.017*
	Chlamydia pneumonia IgG (ng/L)	0.012	0.910
	C. pneumoniae IgE (ng/L)	-0.233	0.030*

*Correlation is significant at the 0.05 level (two-tailed)

Table 3: Correlation between Total IgE and *Chlamydia pneumoniae* IgE in asthmatic patients under age control

	Parameter	Partial correlation	*P*-value
Chlamydia pneumoniae IgE (ng/L)	Total IgE (IU/mL)	0.225	0.019*

*Correlation is significant at the 0.05 level (one-tailed)

Table 4: Correlation between Total IgE and *Chlamydia pneumoniae* IgE in asthmatic patients without age control

	Parameter	Age groups	Pearson correlation	*P*-value
Chlamydia pneumoniae IgE (ng/L)	Total IgE (IU/mL)	Less than 6	0.580	0.000**
		6–11	-0.001	0.497
		More than 11	-0.388	0.069

**Correlation is significant at the 0.01 level (one-tailed)

as shown in the present study, the effect of residents on specific IgE levels.

The other possible explanation is that reducing exposure to the allergen is associated with improved sensitization.[26] Paradoxically, this study showed no decrease in Chlamydial infection since *C. pneumoniae* IgG has not changed, and there is no significant difference in this immunoglobulin value between age groups in rural and urban asthmatic children.

The third explanation is that each allergen exhibits a particular trend with age. House dust mites, for example, induced the earliest IgE response, while the response to Alternaria was characteristic of adolescents and young adults. In the same way, Pollens and grasses induced early IgE production, which declined after 30 years.[14] Indeed, we cannot accept this hypothesis since early adolescent rural asthmatic children had the same *C. pneumoniae*-specific IgE level as other age groups of asthmatic children.

The fourth explanation could be that early adolescent asthmatic children in urban areas have been exposed more heavily or widely to different allergens, which is not occurring in the case of younger age categories or rural asthmatic children. A significantly higher percentage of allergic rural rather than urban children

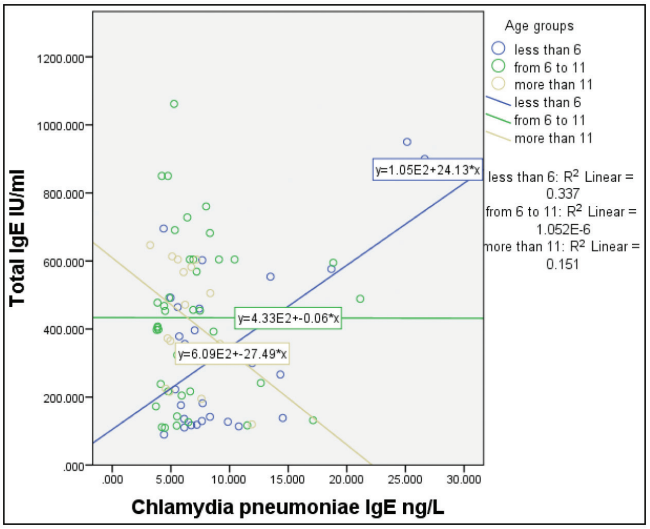

Figure 1: Scatterplot to total serum IgE according to *Chlamydia pneumoniae* IgE

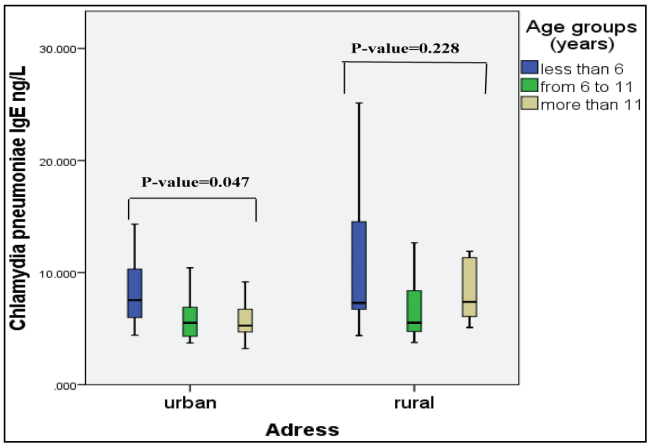

Figure 2: Comparison between *Chlamydia pneumoniae* IgE levels in asthmatic children depending on age groups and geographic areas

Table 5: Comparison between immunological parameters of asthmatic children depending on age groups and geographic areas

Age groups		Geographic areas	Total IgE	*Chlamydia pneumoniae* IgG	*C. pneumoniae* IgE
Less than 6	Urban	Mean	304.261	25.814	9.228
		N	21	21	21
		Std. deviation	206.828	17.138	5.008
	Rural	Mean	419.235	26.053	10.783
		N	9	9	9
		Std. deviation	285.486	16.419	7.099
P-value			0.141	0.464	0.447
From 6 to 11	Urban	Mean	425.828	27.162	7.599
		N	28	28	28
		Std. deviation	220.726	22.185	4.755
	Rural	Mean	448.261	20.018	6.765
		N	13	13	13
		Std. deviation	275.429	8.791	2.886
P-value			0.418	0.191	0.439
More than 11	Urban	Mean	434.413	20.745	5.845
		N	10	10	10
		Std. deviation	152.345	7.962	1.821
	Rural	Mean	407.673	26.894	8.206
		N	6	6	6
		Std. deviation	218.408	8.4222	2.793
P-value			0.356	0.09	0.036*

*Significant difference at *P*-value 0.05

was monosensitized or sensitized to two to four allergens. In contrast, an almost four-fold higher rate of allergic urban children was sensitized to five or more allergens.[27,28] Clearly, a positive relationship exists between cumulative exposure to an allergen and the risk of allergic sensitization.[29,30] Depending on this, it may be a decrease in *C. pneumoniae*-specific IgE resulting from increased sensitization to other antigens or selected other allergens, or it is probably due to pollen exposure. The clinical sensitivity to pollen is higher among subjects living along roads with heavy traffic.[31,32] Indeed, we cannot know the mechanism that redirected allergic responses toward one allergen over another or whether exposure to many allergens will reduce specific IgE to one allergen over another. All we know is that previous observations suggest the operation of environment-specific regulatory mechanisms affects the risk of sensitization and the magnitude of specific IgE production.[33,34] Further, different interactions of potential allergens with airway epithelial cells and other cells located within and below the epithelium will affect the outcome of antigen exposure.[35] On the other hand, asthma is a common disease with a complex risk architecture, including both genetic and environmental factors; thus, many polymorphisms may effect on immunological parameters.[21,36]

The present study detected a positive linear correlation between total and *C. pneumoniae*-specific IgE under age control. This result agrees with previous research that suggests increased specific IgE can lead to increased total IgE.[37]

Conclusion

IgE has a role in mediating allergic reactions and their powerful effector functions, but numerous factors influence its value. In the present study, we detected that *C. pneumoniae*-specific IgE decreased in early adulthood urban asthmatic children. The possible explanation is that exposure to the poly allergen may redirect the immune response from one allergen to another. However, until now, this is just a hypothesis because this mechanism remains not understood, and we cannot determine if exposure to many allergens will reduce specific IgE to one allergen over another. All we know is the effect of environment-specific regulatory mechanisms on the magnitude of particular IgE production.

Limitation of study

The present study has some limitations that must be pointed out. First, the study included children attending the asthma clinic at Karbala Teaching Hospital for Children without considering other provinces in other parts of Iraq. Second, the total IgE level was measured in all patients with different types of treatment, which may have contributed to the inconsistent understanding of the level of IgE without treatment. Third, we measured only total IgE and *C. pneumoniae*-specific IgE, so recommended to measure specific IgE against poly allergen to detect the change in specific IgE levels.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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