Variability of Total Serum IgE in Allergic Patients and Healthy Subjects According to Age

Haitham B. Fathi
Department of Medicine, Ninevah College of Medicine, University of Mosul

ABSTRACT

Background: Atopy is an immunogenetic status in which an increase in production of IgE occurs in response to common environmental allergen. Almost 20% of people worldwide are considered atopic individuals and their prevalence is increasing and nowadays it is described as epidemic.

Aim: To explore the variability of total serum IgE according to age and sex in allergic and healthy non-allergic subjects.

Patients and Methods: A cross-sectional study was conducted at Allergy Clinic, in Al-Jamhoori Teaching Hospital in Mosul City on 751 individuals (561 patients with various atopic disorders and 190 apparently healthy non-allergic subjects) with age range from 11 to 59 years. Total serum IgE was estimated by ELISA.

Results: The mean total serum IgE in allergic patients was 259.9±8.0 IU/ml while in healthy non-allergic subjects, it was 137.3±10.6 IU/ml, a difference of highly significant value (p=0.0001). Total serum IgE level was within normal range (<150 IU/ml) in around 20-30% of allergic patients while more than one third of healthy subjects had a pathological value (≥150 IU/ml). Negative correlation was observed between total serum IgE level of asthmatic patients and age (p=0.0001). No significant differences were observed between total serum IgE levels at various age groups in the rest of allergic patients and healthy non-allergic subjects. The concentration of total serum IgE persisted at high level in patients with allergic rhinitis and increased in dermatitis and urticaria cases till the age of 59 years. No significant difference was observed in total serum IgE between study groups according to sex.

Conclusions: A high total serum IgE is of an important value in the diagnosis of allergic diseases. Determination of local normal reference value is needed. Non-IgE-dependent mechanism plays more important role in cases of asthma in advancing age. A high level total serum IgE in healthy subjects and low in allergic patients is possible and needs further studies to assess their best discriminative threshold in health and disease.

Key Words: total IgE, asthma, rhinitis, urticaria

INTRODUCTION

Atopy is an immunogenetic status in which an increase in production of IgE occurs in response to common environmental allergen. Almost 20% of people worldwide are considered atopic individuals and their prevalence is increasing and nowadays described as epidemic. Since IgE was identified in the late 1960, a number of variables had been shown to affect serum levels of total IgE, which makes the definition of what is "normal" complex. In Western developed countries where parasitic infestation is rare, raised total IgE is considered as a marker of allergic diseases. Furthermore, other factors have been demonstrated to affect total serum IgE level including age, gender, tobacco smoke, and occupational exposure.
There is a growing body of evidence describing changes in the function of immune system upon aging, a phenomenon referred to as ‘immunosenescence’ (6). The literatures on immuno-senescence has focused mainly on T cell impairment (7), however, B cells function is also profoundly affected (8). This is supported by observation of epidemiological studies of decrease of both incidence of onset and severity of atopic diseases in aging (9). This observation might explain in part by age-related changes in immunoglobulin. The effects of age on total serum IgE levels are not clear and controversial with studies showing decline, no change or increase (10). Similar inconsistent conclusions can be pooled from literatures interested in IgE gender differences (11).

However, few studies investigate the relationship total serum IgE according to age and gender have been conducted. This knowledge gap prompts us to conduct this study aiming to explore these variation among different allergic patients and to compare it with that found in healthy non-allergic individuals.

PATIENTS AND METHODS

The sample of patients of this cross-sectional study had been recruited from attendance of the Allergy Clinic at Al-Jamhouri Teaching Hospital in Mosul/Iraq from October 2010 to December 2011. All eligible patients who fulfill the inclusion criteria (history and clinical examination of one of the allergic diseases, age from 11-59 years, and currently not using immune suppressive medications) were asked to participate in the current investigation.

One hundred ninety apparently healthy individuals were randomly selected from the attendance of the outpatient clinic. The selection criteria were based on absence of personal or family history of allergic diseases, normal eosinophil count, no history of worm infestation. Their age ranged between 10 to 60 years.

Five ml of blood was taken from each participants for determination of total serum IgE using the DRG® IgE (EIA-1788) (DRG International Inc, USA) by ELISA. According to the instruction of the manufacturer, blood was centrifuged and serum was stored till testing. Total serum IgE levels <150 IU/ml was considered normal or borderline range, amount of ≥150 IU/ml was considered pathological according to manufacturer.

Comparison of total serum IgE among different allergic subgroups and age groups were conducted by ANOVA test. In a case of significant difference, post hoc Waller Duncan test was used to identify the non-homogenous subgroup/s. Comparison of difference in total serum IgE between gender was performed by the use of independent two sampled Student t test. Pearson simple linear regression was used to study age-associated changes in total serum IgE. A p-value =<0.05 was considered significant. All statistical analyses were conducted by the use of statistical software SPSS ver 11 (Chicago Inc. ILL).

RESULTS

Study sample consisted of 751 individuals. Their age ranged from 11 to 59 years with mean and standard deviation of 32.42 and 12.50 years respectively. There were 387 (51.5%) males and 364 (48.5%) females. The sample consisted of 202 (26.9%) with allergic rhinitis, 176 (23.4%) with bronchial asthma, 98 (13.0%) with dermatitis, 85(11.3%) with urticaria, and 190 (25.3%) were apparently healthy non-allergic subjects. The mean age ± SD of studied sample were as follows: allergic rhinitis (32.4±12.2) years, bronchial asthma (32.6±13.2) years, dermatitis (32.6±11.3) years, urticaria (31.9±12.5) years and healthy non-allergic subjects (31.1±11.6) years. The difference in the mean age was not significant. The studied subjects was divided into groups according to age groups according to their allergic status which is shown in Figure 1.
The mean±SEM of the total serum IgE in allergic patients was 259.9±8.0 IU/ml with 95% confidence interval of (244.2-275.6) IU/ml. While in healthy non-atopic subjects it was 137.3±10.6 IU/ml (95% CI, 116.4-158.3) a difference of highly significant (p=0.0001). The mean±SEM of the total serum IgE in the subgroups of allergy with 95% confidence interval were as follows: allergic rhinitis 262.9±13.5 IU/ml (95%CI, 236.2-289.7), asthma 266.1±15.4 IU/ml (95%CI, 235.7-296.6), dermatitis 255.7±18.7 IU/ml (95%CI, 218.5-292.9), urticaria 244.6±16.6 (95% CI, 211.5-277.8). The difference in mean total serum IgE among allergic subgroups was not significant. Figure 2 shows the values of 5 points box plot distribution of total serum IgE of the studied sample. The figure reveals the followings: a low median total serum IgE in healthy non-allergic subjects, wide range among asthmatic patients, a none significant differences among allergic subgroups while highly significant difference of allergic patients particularly asthmatic patients in comparison to healthy non-atopic subjects.
The total serum IgE is divided into either normal/borderline (<150 IU/ml) or pathological value (≥150 IU/ml) the distribution among the subgroup is shown in Table 1. The tables shows that around 20-30% of allergic patients has normal or borderline range of total serum IgE and at the same time more than one third of healthy subjects (37.4%) has a pathological range of total serum IgE.

Table (1): Distribution of normal and pathological range in subgroups of the studied sample

<table>
<thead>
<tr>
<th>Types of allergy</th>
<th>Total IgE range</th>
<th>Normal/borderline (&lt;150 IU/ml)</th>
<th>Pathological (&gt;150IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>44 (21.8)</td>
<td>158 (78.2)</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>55 (29.0)</td>
<td>125 (71.0)</td>
<td></td>
</tr>
<tr>
<td>Dermatitis</td>
<td>31 (31.6)</td>
<td>67 (68.4)</td>
<td></td>
</tr>
<tr>
<td>Urticaria</td>
<td>22 (25.9)</td>
<td>63 (74.1)</td>
<td></td>
</tr>
<tr>
<td>Healthy non-allergic</td>
<td>119 (62.6)</td>
<td>71 (37.4)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>267 (35.6)</td>
<td>484 (64.4)</td>
<td></td>
</tr>
</tbody>
</table>

The changes in total serum IgE according to age groups in healthy subjects and allergic patients are shown in Figure 3. The mean total serum IgE gradually increase to reach its peak at age of 30-39 years in both healthy males and females and drop sharply after that in females; while it keeps raising in males. A peak in mean total serum IgE was observed at age 20-29 years. After that, different trend was observed in different allergic status. Sharp continuous declination in asthmatics till it reach the normal or border line range at age of 50-59 years. Gradual rise in allergic rhinitis to reach a peak at age of 40-49 years and drop slightly after that. Continuous rising levels in dermatitis and urticaria and at the age of 50-59 years their levels are twice that of normal range.

Figure (3): Changes in mean total serum IgE in healthy subjects (a) and allergic patients (b) according to age groups
Figure 4 reveals the correlation of total serum IgE with age. The results showed: a non significant correlation in allergic rhinitis ($r=0.08$, $p=0.2$); inverse linear highly significant correlation in asthmatics ($r=-0.3$, $p=0.0001$); a positive just significant correlation in dermatitis and urticaria ($r=0.2$, $p=0.04$).

**Figure (4): The correlation of Total serum IgE (IU) with age in allergic rhinitis(a), asthma(b), dermatitis (c) and urticaria (d)**

Table 2 reveals the mean±SEM total serum IgE of different sample subgroups according to age and gender. A significantly high total IgE was observed in asthmatic patients in the age 20-29 years and very low level in age 50-59 years. A non significant differences in the level of total IgE were observed in different age groups and gender in the rest of allergic status and healthy group. Despite of this, one can notice general trend of higher total serum IgE in males, and those from age group 20 to 40 years.
Table (2): Mean±SEM of total serum IgE (IU/ml) in the subgroups of the studied sample according to age group and sex

<table>
<thead>
<tr>
<th>Variables</th>
<th>Rhinitis N=202</th>
<th>Asthma N=176</th>
<th>Dermatitis N=98</th>
<th>Urticaria N=85</th>
<th>Healthy N=190</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age groups (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11-19</td>
<td>257.5±27.5</td>
<td>306.0±33.5</td>
<td>194.7±36.4</td>
<td>169.5±19.2</td>
<td>100.2±14.7</td>
</tr>
<tr>
<td>20-29</td>
<td>222.5±22.0</td>
<td>354.4±34.7</td>
<td>262.0±30.2</td>
<td>279.6±37.1</td>
<td>140.9±18.3</td>
</tr>
<tr>
<td>30-39</td>
<td>254.7±21.9</td>
<td>246.8±30.0</td>
<td>218.0±30.7</td>
<td>222.6±17.6</td>
<td>173.5±33.1</td>
</tr>
<tr>
<td>40-49</td>
<td>326.7±38.3</td>
<td>227.3±32.1</td>
<td>305.5±66.0</td>
<td>285.2±55.8</td>
<td>139.9±20.6</td>
</tr>
<tr>
<td>50-59</td>
<td>269.8±60.2</td>
<td>127.7±17.1</td>
<td>357.6±61.1</td>
<td>323.8±64.4</td>
<td>149.6±39.2</td>
</tr>
<tr>
<td>p-value</td>
<td>0.1</td>
<td>0.0001</td>
<td>0.1</td>
<td>0.03</td>
<td>0.2</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>271.9±18.9</td>
<td>287.5±22.8</td>
<td>262.1±25.0</td>
<td>249.4±26.4</td>
<td>134.0±13.2</td>
</tr>
<tr>
<td>Females</td>
<td>251.6±19.2</td>
<td>242.7±20.3</td>
<td>249.3±28.1</td>
<td>240.4±21.2</td>
<td>140.6±16.5</td>
</tr>
<tr>
<td>p-value</td>
<td>0.4</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.1</td>
</tr>
</tbody>
</table>

DISCUSSION

To the best of our knowledge, this is the largest study of its kind conducted in Iraq. Two limitations of this study that may threaten generalization of results: first, uncertainty of diagnosis due to unavailability of gold standard diagnostic procedure for allergic diseases, second, it is a hospital-based convenient sample rather than community-based random sample study (12).

The current study provides additional support to the key role played by IgE in mediating, maintaining, and severity of the allergic response in allergic patients manifested by the elevated levels of IgE compared with non-allergic people.

The value of total IgE in the current study in both healthy and allergic patients were higher than that reported internationally and in the neighboring countries (4,5,13). Many factors cumbersome the comparison of reported IgE figures in the literatures particularly "reference range" of healthy subjects. These factors include: utilization of different kits and procedures which have different quality and accuracy in detecting total amount of IgE (14); different units of measurement (IU/ml, KU/L, etc); different summarizing estimate of the central tendency like arithmetic mean, geometric mean, median, etc (15); overlap between atopic and non atopic individuals (16); Lastly, sampling differences are due to the broad diverse factors that may affect total IgE levels like gender, race, smoking status, environmental factors, pollution, parasitic and microbial flora in different region of the world (11).

Epidemiological study conclusions of decline in the incidence and severity of atopy in geriatric people stimulate many researchers to study age-related changes in level of total IgE (17). Unfortunately, they yield controversial conclusions lie between decline, incline, or no changes. Furthermore, inconsistent findings are extended to individual allergic disease (18).

The current study reveals that total IgE levels in asthmatics are age-related, but the peak levels occurred during childhood, usually between the ages of 8 and 12 years, and typically decreasing thereafter (19,20), while in current study it occurs at age 20-29 years. This peak difference may be due to limiting the included age in this study to patients 11 years and older. The mean total IgE level of the asthmatics in current study was 266.1±15.4 IU/ml (95%CI, 235.7-296.6) while in TENOR study of
asthma was 106.6 IU/ml (95% confidence interval, 101.5–112.0 IU/ml) (21). The difference may be attributed to use of geometric mean "the 'n'th root product of 'n' numbers" in Chipps et al study which usually yield lower value compared to arithmetic mean "average" used in the current investigation. In conclusion the age-related down-regulation of total IgE levels suggest that non IgE-dependent mechanism play a role in cases of asthma in advancing age (22).

The current study shows minor reduction in total IgE at the age of 50-59 years. This finding is to some extent in agreement with Delorenzo et al. (23) who follow 180 Italian patients with allergic rhinitis for 15 years since 1995. They conclude that rhinitis symptoms tend to become milder and the all allergic parameters both in vivo and in vitro usually decrease in the long run; however, the changes in rhinitis symptoms appear to be related to changes in the nasal eosinophils, independently of skin prick test and serum IgE. The decline reported in the current investigation was far less than that reported by Madiaty. This probably due to age structure difference in the two studies. The current study excludes those older than 60 year while Madiaty et al study age range to 75 years (19).

The results revealed that no changes in level of total IgE were observed in cutaneous allergic diseases (i.e. dermatitis and urticaria). The finding was consistent with finding of 0ther researchers (16,19,24).

In conclusion high total serum IgE is an important value in the diagnosis of allergic diseases but we need to refine the "normal level" locally by a large scale study rather than depending on international range. Non IgE-dependent mechanism play more important role in cases of asthma in advancing age. A high level total serum IgE in healthy subjects and low in allergic patients is possible and in need of further researches to assess its role in health and disease.

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