ASSOCIATION OF IGE LEVELS AND SERUM INTERLEUKINE-6 IN ADULT MALES WITH ASTHMA

*Mohammadi Mahnaz1, Asadi Fatemeh1 and Reza Naseri Rad2
1Department of Biology, Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
2Department of Physical Education and Sport Science, Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
*Author for Correspondence

ABSTRACT
The aim of this study was to assess the association between measures of serum interleukin-6 (IL-6) and immunoglobin E (IgE) in 24 adult’s men (35 to 45 years, weight, 94 ± 11 kg) with mild to moderate asthma. For this purpose, fasting blood venous were collected of all participant in order to measuring serum IL-6 and IgE. Spirometry was performed in accordance with American Thoracic Society standards. Pearson's correlations were performed to identify possible relationship among the assessed variables. Data were considered significant at P< 0.05. Data of Pearson analysis showed significant positive correlation between serum IgE and IL-6 in studied asthma subjects. Based on these data, we can say asthma is an inflammation disease and serum inflammatory cytokines is associated with allergic indicators in asthma patients.

Keywords: Inflammation, Asthma, Allergic

INTRODUCTION
During recent years, the recognition of asthma as an inflammatory disease provided the context for implementation of numerous studies to determine the effect or the relationship between inflammatory mediators or symptoms such as cytokine secreted from adipose tissue and other body tissues with outbreak of allergic, respiratory or asthmatic diseases (Venge et al., 1994; O’Byrne et al., 1994; Eizadi et al., 2014). Asthma is a chronic pulmonary disease, which is the cause of a great number of annual deaths around the world. Ten percent of Iranian peoples have asthma according to statistics reported from Asthma and Allergy Clinic (Figueroa-Munoz et al., 2001).
Based on scientific evidence, it seems that impaired inflammatory or anti-inflammatory cytokine affect the prevalence or changes in the severity of respiratory diseases such as asthma. Increased levels of IL-6 as an inflammatory cytokine is reported frequently in allergic conditions (Deetz et al., 1997). Evidence obtained from clinical studies suggests that IL-6 levels as an inflammatory cytokine increase significantly in asthmatic patients compared to healthy subjects (Brodie et al., 1992). Significant increase in this type of cytokine is frequently reported in these patients, especially during asthma attacks (Yokoyama et al., 1995). Inflammatory symptoms in respiratory pathways due to consumption of antigens are the same as the time the IL-6 levels increase (Yokoyama et al., 1997). The importance of above-mentioned function in pathophysiology of asthma is investigated repeatedly by investigators (Matsuda et al., 2006). For example, it is reported that these inflammatory cytokines causes IgE synthesis, which is considered as allergic symptoms due to increased activity of IL-4. It also inhibits the growth of fibroblasts and bronchial epithelial cells (Deetz et al., 1997). Immunoglobin E (IgE) is also a suitable predictor in recognition of allergic diseases and asthma (Matsuda et al., 2006). Accordingly, increase in plasma concentrations of IgE are associated with increased asthma severity (Rotsides et al., 2009). This evidence supports the direct relationship between IL-6 and IgE. Although IL-6 is often introduced as an inflammatory cytokine among inflammatory mediators, several studies showed anti-inflammatory properties of this cytokine (Neveu et al., 2009). Several studies noted that IL-6 is often introduced as an inflammatory cytokine among inflammatory mediators, several studies showed anti-inflammatory properties of this cytokine (Neveu et al., 2009). According to conflicting findings on inflammatory role of IL-6 in asthma, it is not easy to derive a general conclusion about the relationship between IL-6 and IgE. Hence, present study mainly aimed to determine relationship between IL-6 and IgE in asthmatic patients.
MATERIALS AND METHODS
Subjects were twenty four adult males aged 38 - 7 year and BMI of 31 - 3 kg/m² with mild to moderate intensity of chronic asthma. This study was aimed to determine serum IL-6 with IgE in mentioned studied. Asthma diagnosis and its severity were determined by FEV1/FVC. After the nature of the study was explained in detail, informed consent was obtained from all participants. Inclusion criteria to study were asthma history of At least for 3 years ago. Participants were non-athletes, non-smokers and non-alcoholics. The exclusion criteria were infections, renal diseases, hepatic disorders, diabetes and cardiovascular disease and other chronic diseases.

Anthropometry and Spirometry Test
The weight and height of the participants were measured by the same person. Body weight was measured in duplicate in the morning following a 12-h fast. Height of the barefoot subjects was measured to the nearest 0.1 cm. Abdominal circumferenece and hip circumferences were measured in the most condensed part using a non-elastic cloth meter. Body Mass Index (BMI) was calculated as weight (kg) divided by squared height (m). Subjects were asked to refrain from tea, coffee, chocolates and caffeinated soft-drinks on the day of recording Spirometry (Minispire, Italia). Subjects were instructed to take maximum inspiration and blow into the pre-vent pneumotach as rapidly, forcefully and completely as possible for a minimum of 6 seconds, followed by full and rapid inspiration to complete the flow volume loop. The best of the three trials was considered for data analysis. Spirometry test used to assess FEV1, FVC, FEV1/FVC% and other respiratory function parameters.

Laboratory Assays
Fasting blood samples were collected from brachial vein in sitting position at the hormone laboratory from all the subjects who came after a 12-h overnight fast. All participants refrained from any severe physical activity 48 h before measurements. Blood samples were dispensed into EDTA-coated tubes and centrifuged for 10 minutes in order to separate serum. Serum used to measuring IL-6 and IgE. ELISA method (Enzyme-linked Immunosorbent Assay for quantitative detection of human IL-6, Biovendor-Laboratorial kit made by Biovendor Company, Czech) used for determine Serum IL-6. The Intra-assay coefficient of variation and sensitivity of the method were 5.87% and 1.0 IU/mL, respectively for IgE (Monobind Inc, CA 92630, USA).

Data Analysis
Statistical analysis was performed with the SPSS software version 16.0 using a Pearson correlation method to determine the relationship between serums IL-6 with IgE in studied asthma patients. The results were considered statistically significant for p<0.05.

RESULTS
As above mentioned, our study aim was to determine relationship between serum IgE and IL-6 in asthma patients. Body weight and anthropometrical parameters during experimental protocol are shown in Table 1. Data were expressed as individual values or the mean ± SD. Table 2 presents the spirometry parameters and serum circulating, fasting concentrations of IL-6 and IgE in studied patients. A significant positive correlation was found between serum IL-6 and IgE in studied asthma patients (p = 0.020, r = 0.47, Figure 1).

Table 1: Mean and standard deviation of anthropometric characteristics of studied subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age (years)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Abdominal C (cm)</th>
<th>HlipC (%)</th>
<th>AHO (Abdomin88/Hip)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>38 (7)</td>
<td>173 (2.1)</td>
<td>94 (11)</td>
<td>105 (10)</td>
<td>0.99 (0.04)</td>
<td>31.3 (3.5)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: AC: Abdominal Circumference, HC: Hip circumference, AHO: abdominal to Hip ratio, BMI, body mass index

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Table 2: Mean and SD of spirometry and clinical characteristics of studied patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced vital capacity (%)</td>
<td>88.5</td>
<td>8.8</td>
</tr>
<tr>
<td>Forced expiratory volume in 1 s (%)</td>
<td>76.6</td>
<td>9</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>68.9</td>
<td>3</td>
</tr>
<tr>
<td>Peak expiratory flow (%)</td>
<td>78.8</td>
<td>14.7</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>59.5</td>
<td>14.6</td>
</tr>
<tr>
<td>Expiratory vital capacity (%)</td>
<td>53.3</td>
<td>15.4</td>
</tr>
<tr>
<td>IgE (IU / ml)</td>
<td>342</td>
<td>105</td>
</tr>
<tr>
<td>IL-6 (pg / ml)</td>
<td>4.9</td>
<td>3.6</td>
</tr>
</tbody>
</table>

Figure 1: Relation between serum IL-6 and IgE. Data showed a significant positive correlation between these variables in studied asthma patients

DISCUSSION
Recognition of asthma as an inflammatory disease led to implementation of several studies in the field of determining certain symptoms of inflammation such as inflammatory cytokine like IL-6 in inflammation of respiratory pathways. The findings obtained the present study showed a direct relationship between serum levels of IL-6 and IgE in men with asthma. In other words, this finding showed that increased serum levels of IL-6 as an inflammatory cytokine is associated with increase in serum levels of IgE as a predictor of allergic diseases or asthma in patients with mild to moderate asthma. Although increased levels of IgE cannot be attributed to increased systemic levels of IL-6 in these patients with certainty, it may be concluded that increased levels of IL-6 leads to increased inflammation in respiratory pathways in asthmatic patients.
However, several studies showed that IL-6 levels solely increase in response to inflammatory conditions. Nevertheless, IL-6 does not have a central role in inflammatory processes (Neveu et al., 2009). However, researchers showed that the presence of IL-6 in pulmonary cells is not the result of inflammatory
responses. In this context, IL-6 was introduced as a non-specific inflammatory marker with less inflammatory role, despite extensive studies on the importance of other inflammatory markers in diseases associated with the immune system. On the other hand, several academic sources reported increased IL-6 secretion from alveolar macrophages in asthmatic patients (astro-Rodríguez et al., 2007). Several other studies revealed that serum levels and expression of IL-6 increase in bronchial epithelial cells (Yudkin et al., 1999). Secretion of IL-6 from mast cells and eosinophils also increases in patients with asthma (Bradding et al., 1994; Hamid et al., 1992).

It should be noted that IL-6 as an inflammatory cytokine activates T cells and natural killer cells, which are considered as characteristic of asthma. IL-6 is a cofactor or effective stimulator of IgE secretion from ß-cells due to increased effect of IL-4. This shows inflammatory role of this mediator in T2 cells responses and presence of asthma (Deetz et al., 1997). IL-4 levels in children with asthma are significantly higher than their healthy peers, particularly those with family history of this disease (Settin et al., 2008). This information revealed that disruption in IL-6 levels is associated with pathophysiologic changes in respiratory pathways. Therefore, increased IL-6 levels leads to increased resistance or narrowing of respiratory tract. Increased mucus production induced by IL-6 from pulmonary epithelium during inflammation of respiratory pathways in inflammatory diseases such as asthma can physically block the respiratory pathways, which is associated with increased resistance of respiratory pathways. This ultimately leads to pulmonary dysfunction (Rogers et al., 2004; Agrawal et al., 2007).

In another study, increased levels of both IL-4 and IgE were reported in asthmatic patients compared to healthy subjects (Settin et al., 2008). Increased accumulation of eosinophils in the lungs in response to IL-6 levels was observed earlier (Wang et al., 2000; Qiu et al., 2004). Furthermore, inhibition of IL-6 function by neutralizing or inhibiting IL-6 receptor in asthmatic mice reduced accumulation of eosinophils in lungs (Doganci et al., 2005). In a general summary, the findings obtained from this study showed the close and significant relationship between IL-6 as an inflammatory cytokine with IgE as an allergic factor in asthmatic patients.

REFERENCES
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