Association of Serum Immunoglobulin E Levels with the Severity of Asthma in North Indian Populations

Priyanka Gaur¹, Gaurav Singh², Sandeep Bhattacharya¹*, Surya Kant³, Pooja Gaur³

¹Department of Physiology, King George’s Medical University, U.P., Lucknow, India.
²Department of Biotechnology, Kunwar Satya Vira College of Engineering and Management, Bijnor, India.
³Department of Respiratory Medicine, King George’s Medical University, U.P., Lucknow, India.

Corresponding author: *Dr. Sandeep Bhattacharya, Department of Physiology, King George’s Medical University, U.P., Lucknow, India.

Abstract

Background: Bronchial asthma is a major public health problem worldwide. The prevalence of allergic respiratory disorders in particular asthma is increasing. Elevated total serum immunoglobulin E is considered as an objective marker of allergy and has been associated with a number of respiratory disorders including asthma. Immunoglobulin E and associated cellular responses are responsible for allergic airway diseases. A hypersensitivity reaction initiated by immunologic mechanisms, mediated by IgE antibodies occurs in allergic asthma. To estimate and compare serum IgE levels in mild, moderate, and severe asthmatics and in normal subjects and to find the association between serum IgE levels and severity of asthma.

Material and methods: This study enrolled 233 asthmatic subjects and 58 Healthy controls. The serum IgE levels were investigated in asthma patients and controls subjects. Serum IgE levels were also compared with the severity of asthma. The severities of asthma were determined by pulmonary function tests.

Results: This study shows that there is a significant difference between control and mild asthma patients (p<0.01), between control and moderate group of asthmatic subjects also significant difference found (p<0.001) and between severe asthmatic and control also significant difference found (p<0.001).

Discussion: The IgE level is increasing with the severity of disease. The present study suggests that the serum IgE level may reflect the severity of bronchial asthma assessed by pulmonary function tests and clinical history.

Keywords: Asthma, Immunoglobulin E, Allergy, hypersensitivity
before and after inhaling bronchodilators. Asthma is defined as a chronic disease of the lung and asthma attacks may be immediate, delayed or dual in onset. A strong association between exposure of allergens and development of asthmatic symptoms has been noted. The single most important risk factor for development of asthma is ats, a tendency to produce excessive amounts of IgE antibodies in the exposure of allergens. IgE is produced by B-Lymphocytes. Allergic asthma is a complex chronic inflammatory disease of the airways and its etiology is multifactorial. Bronchial asthma is a type I hypersensitivity where a combination of allergens with IgE antibodies produces the airway inflammation and asthma symptoms. IgE is a trace protein normally accounts for less than 0.001% of total serum immunoglobulin. The concentration of IgE in serum is age dependent and normally remains at levels less than 10 IU/ml in most of the infants during the first year of life. Serum IgE levels are also associated with the degree of airflow obstruction. Allergic diseases, including asthma are characterized by an increase in serum Immunoglobulin E (IgE) levels. A hypersensitivity reaction initiated by immunologic mechanisms mediated by IgE antibodies occurs in allergic asthma. IgE plays a central role in the initiation and propagation of the inflammatory cascade and thus the allergic response. IgE has been considered the most important biological target in the treatment of allergy and asthma with many investigators trying to interfere with its production or its function in the immune system. This is supported by the success of the anti-IgE monoclonal antibody (mAb) in the treatment of allergy and asthma. This study was designed to estimate and compare the serum IgE levels in mild, moderate, severe asthmatics and in normal subjects.

Materials and methods
Patients and samples
This study enrolled 233 asthmatic subjects and 58 Healthy controls from the department of respiratory medicine. The study was ethically approved by the ethics committee of the institution and all the patients gave their consent. All the asthmatic patient included in this study. The subjects having other diseases such as COPD, lung cancer, Diabetes, Interstitial lung diseases were excluded from the study. This study also included healthy controls. All the subjects of asthmatic group and the control group are between 15-60 years. Patient name, age, sex, and duration of symptoms were noted. A detailed history regarding the duration of asthma symptoms, frequency, and severity of exacerbations each patient was taken. All the subjects were given a respiratory questionnaire consisting demographic. The questionnaire included questions on respiratory symptoms, smoking habits, and previous medical history. Age and sex matched 30 healthy volunteers were taken as a control group in this study. Pulmonary function tests were done in all patients. Pulmonary function tests were done before and 10 minutes after giving nebulised Salbutamol, 400 mg. The pulmonary function test was done using computerized Spirometry. Severity of asthma was categorized as mild, moderate and severe based on GINA (Global Initiative for Asthma) guidelines.

Collection of blood samples and serum separation
5 ml Blood sample was collected by vein puncture, allowed to clot and separate the serum by centrifugation at room temperature sample were stored at -80°C till the processing.
Detection of Serum IgE level
The serum IgE level of asthmatic and controls were determined by the Elisa kit methods.

Statistical analysis
All values were expressed as mean ± SEM. Statistical analyses were done by one-way analysis of variance (ANOVA). P values of less than 0.05 indicated a statistical significance.

Results
The result of this study shows that there is a significant difference found between the serum IgE level of asthmatic patients and control. This study shows that between the control and asthmatic groups of mild, moderate and severe group there is a significant difference found between control and mild asthmatics subjects (p<0.01), between control and moderate group of asthmatic subjects (p<0.001) and between severe asthmatic and control (p<0.001). When compared mild asthmatic subjects to moderate and severe asthmatic groups there is also significant difference found (p<0.001) and between moderate and severe asthma groups a significant difference is found (p<0.001).

Discussion
Asthma is of two types - extrinsic and intrinsic types. Atopic asthma is a subtype of extrinsic asthma, in which patients who have a hyper-responsive airway, the scene for the reaction is set in large part by initial sensitization to inhaled antigens and chemical antigens. 8,9 [6,7] These stimulate induction of TH2 type T cells, which release IL-4 and IL-5 cytokines. These cytokines promote IgE production by B cells, growth of mast cells (IL-4) and growth and activation of the eosinophil. Subsequent IgE mediated reaction to inhaled allergens elicits acute and late phase reaction. 10

Table: 1 Demographic Character of Asthmatic Subjects and Controls and Serum IgE Level According to Asthma Severity of Subjects.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Asthmatic Subjects</th>
<th>Control (N=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe (N=110)</td>
<td>Moderate (N=49)</td>
</tr>
<tr>
<td>Age (Mean±SEM)</td>
<td>31.22 ± 1.305</td>
<td>34.41 ± 2.123</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 76(69%)</td>
<td>39(76%)</td>
</tr>
<tr>
<td></td>
<td>Female 34(31%)</td>
<td>12(24%)</td>
</tr>
<tr>
<td>IgE (Mean±SEM)</td>
<td>1929±55.38</td>
<td>667.8 ±14.23</td>
</tr>
</tbody>
</table>

***P< 0.001 when compared with control to severe asthmatic subjects,
***P< 0.001 when compared with control to moderate subjects.
**P< 0.01 when compared with control to mild asthmatic subjects
***P< 0.001 when compared with mild to moderate and severe asthmatic subjects
***P< 0.001 when compared with severe to moderate subjects

41
Increased serum IgE levels in asthma may due to increases in IgE-dependent processes and cellular components of the immune system. The secretion of IgE by lymphocytes defines the allergic state of an individual. The cellular events associated with IgE-dependent processes are very much important in asthma. Higher IgE levels indicate some types of inherent susceptibility or presence of a disease process involving airway inflammation. When comparing the severity of asthma with serum IgE levels in bronchial asthma the present data indicated that the more severity of the asthma greater is the elevation in serum IgE. The most important risk factor for the development of extrinsic asthma is atopy. An atopic individual responds to antigenic stimuli to which normal people will not respond. The basic pathology in bronchial asthma is airway hyper-responsiveness. The airway hyper-responsiveness is an excessive response of the airway epithelium to antigenic stimuli. The airway response in asthma is mediated by lymphocytes. Antigenic exposure to T-lymphocytes leads to their differentiation into active T-cells, which secrete a series of biologically active proteins called cytokines. B-lymphocytes and plasma cells in airways, gastrointestinal tract, and regional lymph nodes produce IgE. Patients with clinical symptoms and higher serum IgE levels are likely to be suffering from allergic diseases.

The molecular mechanisms underlying immune system activation for allergen-induced asthma include stimulation of Cd4+ Th2 immune response and the subsequent production of IgE antibody. Re-exposure to allergen results in the recruitment of mast cells (via high affinity IgE Fce receptors), eosinophils, and other leukocytes. In particular, mast cells that release the vasoactive amines, histamine, and other ligands from large Serum IgE levels reflect the severity of asthma granules produce a local systemic hypersensitivity reaction. The ensuing inflammation amplifies an individual's hypersensitivity reaction by the recruitment of other cells and perpetuates the clinical symptoms (wheezing, shortness of breath, and chest tightness). In atopic individuals IgE receptors send strong signals when cross-linked, resulting in secretion of high levels of IL4 from mast cells, which results in an overproduction of IgE antibodies. Mast cells and basophils are the primary initiating cells of IgE mediated allergic reaction. IgE is responsible for the release of various inflammatory mediators in asthma, such as histamine, prostaglandins, and leukotriens. These inflammatory mediators increase airway narrowing due to excessive mucus production, airway smooth muscle spasm, and edema of the airway mucosa. Serum levels of other immunoglobulins. Such as IgG and IgA levels increase along with IgE whereas serum IgM levels decreases in bronchial asthma.

References
5) Rage E, Jacquemin B, Nadif R, Oryszczyn MP, Siroux V, Aguilera I, et al. Total serum IgE levels are associated


