

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

Priyanka Gaur¹, Gaurav Singh², Sandeep Bhattacharya^{1*}, 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

Introduction

The prevalence of allergic respiratory disorders in particular asthma is increasing. Bronchial asthma is characterized by lower respiratory tract inflammation leading to bronchial hyper responsiveness (BHR) and

variable, reversible airflow obstruction. Bronchial asthma is characterized by reversible airflow obstruction. Hence, the most important diagnostic investigation in asthma is the demonstration of airway obstruction by pulmonary function test

before and after inhaling bronchodilators ¹ 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 atopy, a tendency to produce excessive amounts of IgE antibodies in the presence of allergens ² 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 ³ 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. ^{4,5} 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. ⁶ 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. ⁷

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 -80⁰C till the processing.

Detection of Serum IgE level

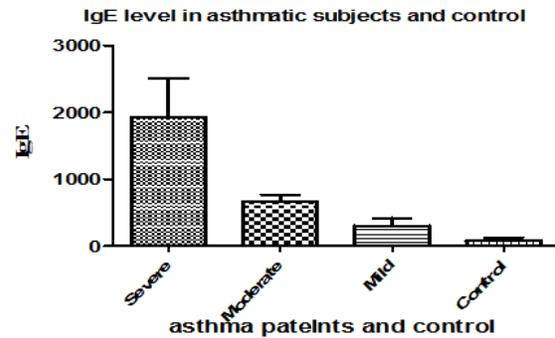
The serum IgE level of asthmatic and controls were determined by the Elisa kit methods.

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.

Parameters	Asthmatic Subjects			Control (N=74)
	Severe (N=110)	Moderate(N=49)	Mild (N=74)	
Age (Mean±SEM)	31.22 ± 1.305	34.41 ± 2.123	30.39 ± 1.567	34.55 ± 1.730
Sex	Male	76(69%)	39(76%)	51(69%)
	Female	34(31%)	12(24%)	23(31%)
IgE (Mean±SEM)	1929±55.38	667.8 ±14.23	306.6±13.33	100.73± 6.645

***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

Increased serum IgE levels in asthma may be 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 asthma¹¹. Higher IgE levels indicate some types of inherent susceptibility or presence of a disease process involving airway inflammation^{12, 13}. 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^{14, 15}. 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 diseases¹⁶.

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 Fcε 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 39 granules produce a local systemic hypersensitivity reaction¹⁷. 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)¹⁸. 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^{19, 20}. Serum levels of other immunoglobulins. Such as IgG and IgA levels increase along with IgE²¹ whereas serum IgM levels decrease in bronchial asthma²².

References

- 1) Juniper EF, Cockcroft DW, and Hargreave FE. Histamine and methacoline inhalation tests: a laboratory tidal breathing protocol. In: Atra Draco AB, ed. Tidal Breathing Methods, 2nd edition. Sweden: LUND, 1994
- 2) Burrows B, Martinez FD, Halonen M, Barbee RA, and Cline MG. Association of asthma with 40 Anupama et al. Serum IgE levels and skin test reactivity to allergens. NEJM 320:270-277, 1989.
- 3) Djukanovic R, Roche WR, Wilson JW, et al. Mucosal inflammation in asthma. Am Rev Respir Dis 142:434-457, 1990.
- 4) Peng Z. Vaccines targeting IgE in asthma and allergy. Hum Vaccine 2009;18:5.
- 5) Rage E, Jacquemin B, Nadif R, Oryszczyn MP, Siroux V, Aguilera I, et al. Total serum IgE levels are associated

- with ambient ozone concentration in asthmatic adults. *Allergy* 2009;64:40-6.
- 6) Buhl R. Anti-IgE antibodies for the treatment of asthma. *Curr Opin Pulm Med* 2005;11:27-34
 - 7) Bethesda. Global strategy for asthma management and prevention. National Institutes of Health. NHBLI Workshop Report 2002;2:3659.
 - 8) Husain AN, Kumar V. The lung. In: Kumar V, Abbas AK, Fausto N, editors. *Robbins and Cotran Pathologic basis of disease*. 7th ed. Philadelphia W B: Saunders; 2007. p. 711-72.
 - 9) Mathias CB, Freyschmidt EJ, Oettgen HC. Immunoglobulin E antibodies enhance pulmonary inflammation induced by inhalation of a chemical hapten. *Clin Exp Allergy* 2009;39:304-6.
 - 10) Kindt TJ, Goldsby RA, Osborne B. *Kuby Immunology*. 6th ed. New York: WH Freeman and Company; 2007. p. 380-5.
 - 11) Villar TMA, Dow L, Coggon D, Lampe FC, and Holgate ST. The influence of increased bronchial responsiveness, atopy, and serum IgE on decline in FEV1. *Am J Respir Crit Care Med* 151:656-662, 1995.
 - 12) Chowdary V S, Vinaykumar E C, Rao J J, Ratna Rao, Ram Babu K, and Rangamani V. A study on serum IgE and eosinophils in respiratory allergy patients. *Indian J Allergy Asthma Immunol* 17:21-24, 2003.
 - 13) Sherril DL, Lebowitz MD, Halonel M, Robert A, Barbee, and Burrows B. Longitudinal evaluation of the association between pulmonary function and total serum IgE. *Am J Respir Crit Care Med* 152:98-102, 1995.
 - 14) Lebowitz MD, Barbee R, and Burrows B. Family concordance of IgE, atopy, and disease. *J Allergy Clin Immunol* 74:259-264, 1984. 21.
 - 15) Peat JK, Toelle BG, Dermand J, van den Berg R, Britton WJ, and Woolcock AJ. Serum IgE levels, atopy, and asthma in young adults: results from a longitudinal cohort study. *Allergy* 51:804-810, 1996
 - 16) Vanichapuntu M, Janwitayanuchit S, Verasertniyom O, Chitrabamrung S, and Vatanasuk M. Serum IgE levels: correlation with skin test reactivity in Thai adults with respiratory allergy. *Asian Pac J Allergy Immunol* 9:147-151, 1991.
 - 17) Janeway CA., Travers P, Walport M., and Shlomchik MJ. *Immunobiology*. New York: Garland Publishing, 2001, p. 683-707, 486-487, 477-478.
 - 18) King TE. A new look at the pathophysiology of asthma. *J National Med Assoc* 91:9S-15S, 1999.
 - 19) Gerrard JW. The biological importance of IgE. *Immunol. Allergy Pract* 25:381-84, 1984.
 - 20) Lebowitz MD, Barbee R, and Burrows B. Family concordance of IgE, atopy, and disease. *J Allergy Clin Immunol* 74:259-264, 1984.
 - 21) Denchev K, Radkov M, and Lipcheva N. Serum immunoglobulin E level in bronchial asthma. *Vutr Boles* 5:88-91, 1976.
 - 22) Zheltvai VV, Kazankevich VP, Chekotilo VM, and Valkovtzi AA. Diagnostic significance of immunoglobulins in infective allergic bronchial asthma. *Zh Mikrobiol Epidemiol Immunol* 11:84- 89, 1981.