A study on the levels of IgE as a biomarker in the management of bronchial asthma patients

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Abstract

Background: IgE is a major contributing factor for the development of bronchial hyper responsiveness in asthmatics. Serum IgE levels also shows association with degree of airflow obstruction. Therefore, a study was undertaken to estimate the serum IgE level in bronchial asthma patients, and to correlate the severity of airway obstruction with serum IgE level in bronchial asthma patients. A total of 75 cases in the age group of 21-60 years, of Tertiary care Hospital, Madagadipet, Puducherry-India was included in the study. Spirometry with reversibility testing was done in all cases. Serum IgE level was estimated using Quantia IgE, which is a turbid metric immunoassay. Patients with bronchial asthma had elevated serum IgE, which increased with increase in the severity of airflow obstruction and it was found to be statistically significant ($p < 0.05$). It was concluded that Serum IgE level increases as the severity of airflow obstruction increases. It helps to classify the Bronchial asthma patients based on IgE and to guide anti IgE therapy for the patients with difficult to treat allergic asthma and to assess its response.

Keywords: Allergic asthma-; Serum IgE; Severity of obstruction; Spirometry-IgE therapy

Introduction

Asthma is increasing in prevalence, due to urbanisation, air pollution and environmental tobacco smoke[1]. Asthma impact is manifested in patients, their families, and the community as a whole in terms of lost work and school days, poor quality of life, frequent emergency department visits, hospitalizations, and death cases[2]. Global prevalence of asthma ranges from 1% to 18% of the population in different countries. As of 2010, 300 million people were affected by asthma worldwide. In 2009, asthma caused 250,000 deaths globally[3]. According to the Global Initiative for Asthma (GINA), Asthma is defined as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are usually associated with widespread, but variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment[3]. In India about 2-8% of the population is estimated to suffer from bronchial asthma[4]. There are two types of asthma - extrinsic and intrinsic types based on the presence of allergy[5].

Allergic asthma patients have a hyper-responsive airway due to sensitization to inhaled antigens and chemical antigens[6,7]. These stimulate the induction of T_{H2} type T cells, which release cytokines like IL- 4 and IL- 5. The released cytokines in turn promote IgE production by B cells, growth of mast cells (IL- 4) and growth and activation of eosinophils. Subsequent IgE mediator reaction to inhaled allergens elicits acute and late phase reaction[8].

Spirometry is the gold standard for diagnosis of bronchial asthma. Forced expiratory volume in one second (FEV1) from spirometry is a reliable for diagnosing airflow obstruction. A reduced FEV1 may be found with many other lung diseases, but a reduced ratio of FEV1 to forced vital capacity (FVC) indicates airflow limitation.

IgE has also been shown to be a major contributing factor for the development of bronchial hyper responsiveness in asthmatics[9]. Serum levels of allergen-specific and total IgE are strongly associated with the clinical grade of sensitization and disease severity in allergic patients[10]. Atopy is a tendency to produce an excessive amount of IgE antibodies when exposed to allergens. Bronchial asthma is a type 1 hypersensitivity reaction where combination of allergens with IgE antibodies produces the airway inflammation and asthmatic symptoms. Serum IgE levels also shows association with degree of airflow obstruction[11]. Therefore, the present study was designed to study the serum IgE levels in Bronchial asthma patients, and to correlate the severity of airway obstruction with serum IgE level in Bronchial asthma patients.

Material and Methods

This cross sectional study was carried out in Tertiary Care Hospital, Madagadipet, Puducherry for period of two years. The sample size was 75 (Based on previous study with standard deviation -44, Confidence interval - 95% and Relative error-10%)[12].

Patients attending the Pulmonary Medicine OPD with symptoms of episodic onset of cough, breathlessness, chest tightness and wheezing were subjected to spirometry and those patients who had

spirometric values showing reversibility of more than and/or equal to 12% in forced expiratory volume in 1s (FEV1), or at least 200mL from baseline after inhalation of salbutamol (4×100 mcg) given by metered dose inhaler using a spacer device was included in the present study.

Patients who were <18 years old were excluded from the study. Smokers and patients with acute severe asthma, sputum positive pulmonary tuberculosis, COPD and asthmatics using bronchodilators were also excluded from the study

Approval from the institutional ethical committee and fully informed written consent from the patient were obtained before starting the study. Patients in the age group of 18 to 60 years are included in the study. Patient's Name, Age, Sex is noted, and detailed history is taken in each patients regarding the duration of the asthma symptoms, frequency and severity of the exacerbation, smoking history and previous medical history.

Other investigations: Chest X-Ray, Complete blood count, ESR, Electrocardiography, Sputum for AFB and Gram's stains were done for study subjects. A detailed explanation of the purpose of the study, procedure adopted and the safety measures undertaken while doing spirometry were clearly given to patients participating in our study.

Spirometry: Spirometry including reversibility testing was performed according to ATS recommendation using spirometer (RMS Medspiror with transducer model no. AOON_2003). All tests were carried out at the fixed time of the day (10.00 – 14.00 hours) to minimize diurnal variation. The usual instructions were given to patients prior to pulmonary function tests as per WHO guidelines.

The standardized methods of performing spirometry as mentioned in the ATS guidelines by the ATS/ERS task force for standardization on lung function testing was adopted for the present study.

Reversibility Testing: For reversibility testing, a dose of inhaled beta-agonist (400 micrograms of salbutamol) was administered after the initial test and spirometry was repeated 20 minutes later. Absence of improvement of 12% or more and 200 ml or more in post bronchodilator FEV1 was taken as absence of reversibility. Post bronchodilator FEV1 was recorded in all bronchial asthma patients to assess the severity of airflow obstruction.

Estimation of Serum IgE: Serum IgE was estimated in patients who were diagnosed as bronchial asthma.Estimation of serum IgE was done using Quantia IgE which is a turbidimetric immunoassay for estimation of immunoglobulin IgE in human serum.

Statistical analysis*: C*hi square was used to test the hypothesis, association of levels of serum IgE with severity of airway obstruction on bronchial asthma patients, Pearson bivariate correlation coefficient was used to quantify the extent of correlation between spirometric parameters with serum IgE level among bronchial asthma patients. For all statistical analysis p <0.05 was considered as statistically significant.

Results

Most of the study subjects among 75 were in the age group of 41-50 years and 39 were females and 36 were males. Distribution of severity of obstruction that 22 patients showed severe obstruction followed by18 patients with moderately severe obstruction. Very severe obstruction was noted only among 14 patients. Regarding gender wise distribution, the number of female subjects (52%) were more than males (48%). The dominant age group among the study subjects was 41-50 (34.7%) followed by 21-30 (26.7%). The distribution of severity of air way obstruction is given in Table 1. It is well noted that majority of the cases were having moderately severe (24%) and severe (29.33%) airway obstruction. From the Table 2, it is noted that dyspnoea (58.67%) is the most common symptom among cases followed by cough (49.33%) and wheeze (36%). The distribution of cases based on IgE levels indicated that the IgE levels ranged 101-500 IU/ml (Table 3). Many of the cases (45.33%) had exhibited the level of IGE as 401-500 UL/ml followed by 301-400 UL/ml (26.67%) and 201-300UL/ml (17.33%) respectively. Elevated IGE level was noted among 41-50 age group of the study subjects and it was found that distribution of IgE based on age was found to statistically insignificant (X^2=72.41, DF=63, p< 0.05)(Table 4). It was found that serum IgE was higher in males than females which is found to be statistically significant(X^2=36.12, DF=21, p<0.05) (Table 5). It was found that serum IgE increased as the severity of airway obstruction increased and it was found to be statistically significant (X^2=23.56, df=12, p<0.05). Cases with very severe obstructions were found to have higher levels of IgE than the other conditions of obstructions (Table 6).

Mean levels of IgE was found more pronounced in age groups 31-40 and 51-60 respectively (Table.7).When considering sex of the cases, the levels of IgE was higher in males (380Ul/ml) than females (369UL/ml).

Table 1: Distribution of severity of airway obstruction among the cases

Severity of Obstruction	FEV1	No. of Cases n = 75	Percentage
Mild	>70	12	16
Moderate	60 - 69	9	12
Mod. Severe	50 - 59	18	24
Severe	36 - 49	22	29.33
Very severe	<35	14	18.67

Table 2: Distribution of symptoms among the cases

Symptom	No. of Cases n= 75	Percentage
Dyspnoea	44	58.67
Cough	37	49.33
Wheeze	27	36

Table 3: Distribution of cases based on IgE levels

IgE (IU/ml)	No. of Cases	Percentage
101-200	8	10.67%
201-300	13	17.33%
301-400	20	26.67%
401-500	34	45.33%

Table 4: Age wise distribution of IgE in cases

Age (in years)	IgE(IU /ml)			
	101 - 200	201 – 300	301 - 400	401 - 500
21 -30	2	3	8	7
31 -40	1	3	3	7
41 - 50	5	3	7	11
51 - 60	0	4	2	9
	8	13	20	34

Association of serum IgE with age among the cases

	Value	df	Asymp.sig
Pearson chi square	72.41	63	0.195
Likelihood ratio	77.15	63	0.108
No. of valid cases	75		

Table 5: Gender wise distribution of IgE in cases

Gender	IgE (IU/ml)				Mean IgE
	101-200	201 - 300	301-400	401 - 500	
Male	4	6	8	18	380.13
Female	4	7	12	16	369.97

Association of serum IgE with gender among the cases

	Value	df	Asymp.sig
Pearson chi square	36.12	21	0.021
Likelihood ratio	46.36	21	0.001
No. of valid cases	75		

Table 6: Distribution of serum IgE levels based on the severity of obstruction among the cases

FEV1	IgE (IU/ml)			
	101-200	201-300	301-400	401-500
Mild	4	1	3	4
Moderate	0	3	5	1
Moderately Severe	1	3	8	6
Severe	1	5	4	12
Very Severe	0	2	3	9

Association of serum IgE level with severity of airway obstruction among the cases

	Value	df	Asymp.sig
Pearson chi-square	23.56	12	0.023
Likelihood ratio	21.607	12	0.42
No. of valid cases	75		

Table 7: Mean distribution of IgE (IU/ml) according to age

Age (in years)	No. of cases	Mean IgE(IU/ml)
21- 30	20	363
31 -40	14	384
41-50	26	369.42
51 - 60	15	388.66
	75	374.3+/- 11.4

Discussion

The higher prevalence of bronchial asthma in female patients corroborates with the earlier findings and this may be due to increased thoracic size in adult females after puberty when compared to males[13-16]. In our study, the most common symptom was dyspnea as seen in 58.7% patients followed by cough among 49.3% and wheeze in 36% patients. This might be due to severe air way obstruction in many of our study subjects. In a study conducted on the prevalence of asthma in urban and rural children in Tamil Nadu, usual symptoms such as breathlessness (17.9%), wheezing (17.7%) and nocturnal dry cough (20.7%) were reported but without dyspnea[17].

In our study, male patients had higher IgE levels compared to female patients and the same had been reported in an earlier study conducted among the age group of 6 or older[18]. The same trend was noticed in a study carried out on correlation with age, sex, smoking and atopic status[19]. Similarly, an unselected Danish population also showed higher mean level of IgE in males than in females[20]. Another study conducted on the prevalence of serum IgE level among drug users and non-drug users, it was found that the males had elevated level of IgE when compared to women[21]. A study on the association of age, gender and smoking with total IgE and specific IgE, it was found that among non-smokers geometric mean total IgE was higher in men than women but unrelated to age[22]. A study on the epidemiology of immunoglobulin E levels in a defined population revealed that age-adjusted geometric mean IgE levels in 621 older subjects were higher in men (26.3 kU/L) than in women (19.1 kU/L)[23]. The most probable reason for the higher prevalence of IgE levels in men is cigarette smoking[23].

In our study, the mean serum IgE value of bronchial asthma patients was 374.3 IU/ml that is higher than the general population as noted by previous studies. One of

the studies had reported that serum total IgE level was significantly higher (P<0.001) in asthmatic adults compared to that of healthy subjects[24]. An earlier study conducted in India, had recorded that the mean IgE levels ranged from 151.95 IU/ml in normal subjects to 1045.32 IU/ml in severe asthmatics[25]. The mean total IgE level of the population was found to be 106.6 IU/ml whereas higher mean total IgE level was observed patients with severe asthma have a higher mean IgE level (280.2 IU/ml) [18]. A study on the relationship between obesity and Immunoglobulin E in bronchial asthma subjects, serum IgE level in control subjects was 139+/- 37.5 whereas in asthma patient it was 163.8+/- 17.59. This indicates that IgE level is elevated in obese bronchial asthma patients[26]. Similarly, elevation of mean IgE level has been reported in adult atopic patients [14]. Higher mean level of IgE has been found in asthma patients with rhinitis[27]. It has been reported that *Lozenzo et al.*, serum levels of total IgE and soluble CD23 in bronchial asthma patients, he observed that serum IgE in bronchial asthma patients was 190+/-45.8IU/ml compared to healthy subjects (87+/-19.4 IU/ml)[28]. Thus the earlier studies cited above show that serum IgE is higher in bronchial asthma patients that are similar to our study.

It was found that that serum IgE value increased with the increase severity of airway obstruction and it was to be statistically significant (p<0.05) as observed in a study conducted within the age group of 18-60 years[25]. This suggests that treatment of bronchial asthma patients warrants necessary correlation between IgE levels and severity of obstruction. Patients with severe asthma have a higher mean IgE level (280.2 IU/ml) than patients with moderate (145.8 IU/ml) or mild (137.8 IU/ml) asthma hence IgE levels increased as asthma severity increased[15,18]. The same trend is reflected in both older and younger bronchial asthma patients[20]. The severity of bronchial asthma in obese patients is indicated by the increase in the levels of IgE[26]. It was noted that serum IgE is elevated in bronchial asthma patients and a significant correlation was found between total IgE and lung function which is measured as bronchial responsiveness to inhaled methacholine[25]. A study on asthmatic children in Australia revealed that higher IgE levels in patients with more severe persistent asthma compared with those with mild, episodic asthma [29]. The reports of all the studies cited in the foregoing paragraph corroborate with our finding that serum IgE levels increased as the severity of asthma increased.

Conclusion

Our study concludes that the serum IgE level in bronchial asthma patients is elevated and it increases with the increase in the severity of airway obstruction which paves the way for better understanding about the nature of disease and disease progression. This also helps us to guide the anti IgE therapy for the patients with difficult to treat allergic asthma and to assess its response. However serum IgE level is also elevated in various atopic disorders which compounds its utility largely.

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