

Evaluation of the Total Serum IgE Levels in Asthma

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ABSTRACT

Background: Asthma is a chronic inflammatory disease of the airways, often associated with elevated Immunoglobulin E (IgE) levels. Understanding the correlation between total serum IgE levels and asthma severity could provide valuable insights into disease progression and management. **Objective:** This study aims to evaluate the relationship between total serum IgE levels and asthma severity, categorized as mild, moderate, and severe. **Methods:** Asthma patients were classified into mild, moderate, and severe groups based on clinical symptoms and spirometry value. Total serum IgE levels were measured by ELISA and compared across these groups. Age, gender distribution, and PFT parameters, including FEV₁/FVC ratio, were analysed to determine their association with IgE levels. **Results:** The total serum IgE levels were significantly high in asthmatics than in HC ($P < 0.001$). Total IgE levels in normal, mild, moderate and severe asthmatics were 52.089 IU/mL, 286.59 IU/mL, 540 IU/mL and 636 IU/mL, respectively. Age and gender also influenced IgE levels, with females showing relatively higher IgE concentrations. The receiver operating characteristic curve was constructed to compare the total IgE levels in asthma patients versus HC, and the area under the curve for IgE was 0.587 (95% CI: 0.532–0.643), indicating the test was satisfactory with a statistically significant at $P < 0.005$. **Conclusion:** Elevated total serum IgE levels correlate with asthma severity, suggesting its potential role as a biomarker for disease progression. These findings highlight the importance of IgE assessment in asthma management and pave the way for targeted therapeutic interventions.

Keywords: Asthma, ELISA, Immunoglobulin E, PFT, ROC curve

INTRODUCTION

Asthma is a complex chronic inflammatory disease of the airways, resulting from immunological abnormalities that affect both adults and children. It is characterized by persistent airway constriction, leading to symptoms such as wheezing, airway obstruction, and heightened bronchial responsiveness. Asthma is characterized by an excessive aggregation of IgE antibodies in response to inhaled allergens¹. As per World Health Organization report, 339 million people worldwide suffer from asthma. Approximately 35 million people in India, out of a population of 1.36 billion, are affected from asthma. It impacts people of all ages and is becoming more common in many developing nations². The increased tendency for bronchial smooth muscle contraction seen in asthmatic patients, known as bronchial hyperresponsiveness (BHR), also distinguishes with elevated IgE levels in pedigree analyses³. The diagnosis of allergic disorders can be facilitated by measurements of both total and antigen-specific IgE⁴. Asthma and allergic rhinitis have been linked to higher serum levels of the IgE immunoglobulin antibody, which is essential for the pathogenicity of allergic diseases¹. By releasing several inflammatory mediators, IgE causes bronchoconstriction. In asthmatics, IgE has an important function in the development of bronchial hyperresponsiveness. According to epidemiological research, people with asthma, have greater levels of total IgE than people without asthma⁴.

Since asthma is characterized by elevated IgE levels and eosinophilic airway inflammation, it is widely considered to be a Th2-driven illness⁵. The elevated production of immunoglobulin E, which is essential to the pathophysiology of the condition, is one of the main characteristics of allergic asthma⁶. IgE attaches itself to high-affinity receptors on effector cells, including basophils and mast cells and initiates an inflammatory cascade that contributes to both the acute and chronic symptoms of allergic asthma⁶. IgE contributes significantly to the allergic inflammatory pathway from stimulation to the chronic phase. High-affinity (FcεRI) IgE receptors and low-affinity (FcεRII) IgE receptors are the two categories of IgE receptors. The biological functions of IgE depend on the binding of 2 Cε3 domains to FcεRI and FcεRII, which are present in various target cells. Asthma's underlying immunopathological mechanisms cause persistent airway inflammation, which in turn causes airway remodelling (AR), a process

in which the walls of the airways change structurally. Clinical consequences including more severe obstructions of airflow and airway hyperresponsiveness are linked to remodelling in airway diseases⁷.

In India, where the prevalence of asthma has been rising, understanding the relationship between IgE levels and asthma in the local population is of significant importance. Allergic diseases, including asthma, affect a significant portion of the population, with estimates suggesting that at least 30% of individuals are affected, and nearly 80% of families are impacted⁸.

Assessing the total serum IgE levels in asthma patients may help to identify the underlying causes of the condition and provide more specialized approaches to therapy. Regardless of allergen-specific reactivity or allergic symptoms, a number of studies have found a correlation between the frequency of asthma and total blood IgE levels. Therefore, we aim to study total serum IgE levels in Asthma patients and healthy controls (HC) and also evaluating the association of total serum IgE levels and the severity of the disease.

Materials and methods

Subjects

A total of 400 subjects were recruited, including 200 asthma patients and 200 healthy controls, from Gandhi Hospital and Bhagwan Mahavir Medical Research Centre in Hyderabad, India. All of the asthma patients met the ATS diagnostic criteria, which included Immunoglobulin E (IgE), PFT, and spirometry. FEV1/FVC ratios greater than 0.70 and FEV1 and FVC both above 80% of the expected value are frequently observed in spirometry findings. Additionally, a diffusion capacity above 75% of the predicted value is considered normal. Typically, total IgE levels are <100 IU/mL in healthy individuals. In asthma, IgE levels can vary, ranging from mildly elevated (100–500 IU/mL) to significantly high (>1000 IU/mL) in cases of severe asthma. According to GINA guidelines, IgE reference levels generally fall between 30 and 1500 IU/mL, with documented allergen sensitization being a key criterion. Healthy people without a personal or no family history of asthma were regarded as healthy controls, and patients with a history of autoimmune illnesses or upper respiratory tract conditions were not included in the study.

The study design was approved by the Institute of Genetics and Hospital for Genetic Diseases' ethics committee at Osmania University in Hyderabad, India. Prior to participation, each individual gave written informed consent.

Sample collection

A 5 ml venous blood sample was collected from each study participant, which was then aliquoted in serum clot activator tubes, centrifuged for 10 minutes at 600 rpm, separated serum and kept in cryovials at -20°C until further analysed.

Total serum IgE by ELISA

Principle

During the assay, the interaction of an exogenously supplied biotinylated monoclonal anti-IgE antibody with streptavidin coated on the microplate well results in immobilization at the well's surface. When a serum containing the native antigen is combined with a monoclonal biotinylated antibody, a reaction between the two occurs, creating an antibody-antigen complex. The unbound antigen is isolated from the antibody-antigen bound fraction. An enzyme-labelled antibody-antigen biotinylated-antibody complex is created when another antibody labelled with the enzyme is added. To create colour, that can be measured using a spectrophotometer, a substrate is added.

Procedure

A sandwich enzyme linked immunosorbent assay (ELISA) kit (Accubind, CA, USA) was used to determine the total serum IgE (IU/ml) in 200 Healthy controls and 200 asthma patients. The manufacturer's instructions were followed in the preparation of all reagents and working standards. An ELISA reader (BIO-RAD) with dual filters set to 450 nm and 630 nm was used to measure the absorbance. Every sample was thawed just once and subjected to two separate analyses.

Statistical Analysis

The Student's t-test for continuous variables were used to assess the differences in the distribution of clinical characteristics between the two study groups (patients and HC). Mean $\pm$ Standard Deviation (SD) was used to express clinicodemographic variables. For factors like age, gender, PFT, and IgE, were segregated based on the mild, moderate and severe asthmatics and healthy individuals.

The IgE analysis and one-way analysis of variance (ANOVA) using SPSS were conducted and the model with the greatest significant area under the curve (AUC) was taken into consideration.

Results

Table 1: Categorization of Asthma cases based on severity

Groups	Number of Subjects (%) (N=200)
Normal	25 (12.5%)
Mild asthma	142 (71%)
Moderate asthma	27 (13.5%)
Severe asthma	6 (3%)

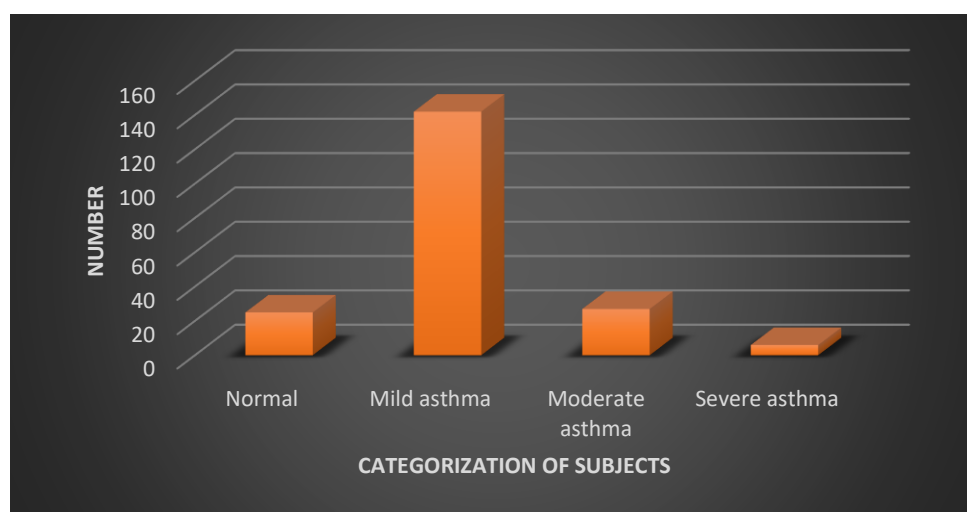


Figure 1. Distribution of subjects (N=200) based on asthma severity. The bar graph categorizes subjects into four groups: Normal, Mild asthma, Moderate asthma, and Severe asthma. The length of each bar represents the number of subjects in each category, with the majority classified under Mild asthma.

The asthmatics in this study were divided into four groups according to the Global Initiative for Asthma (GINA) guidelines: Normal, mild, moderate, and severe of which 25 patients (12.5%) had normal IgE levels, 142 patients (71%) were with Mild asthma, 27 patients (13.5%) moderate asthma and 6 patients (3%) severe asthma respectively (Table 1, Fig 1).

Table 2: Demographic characteristics of healthy controls and different groups of asthma patients.

Characteristics	Healthy Controls (N=200) Mean±SD	Normal(N=25)	Mild asthma (N=142)	Moderate asthma (N=27)	Severe asthma (N=6)
Age (Mean±SD)	33.39±11.26	36.36±14.99	40.648±14.640	39.37±13.483	35.57±13.82
Gender- (Male/ Female)	116(58%)/84(42%)	11(44%)/14(56%)	61(42.9%)/81(57%)	12(44%)/15(55.5%)	4(66.6%)/2(33.3%)
FEV1/FVC Post (Mean±SD)	85.52±16.09	91.6±15.99	88.423±19.35	92.481±15.37	84.429±13.83
Total Serum IgE IU/mL (Mean±SD)	232.3±132.7	52.089±27.017	286.59±106.98	540.09±0.45	636.04±20.49

A total of four hundred subjects were employed for this investigation which included 200 healthy controls (116 males and 84 females) and 200 asthmatics (88 males and 112 females). Table 2 shows the comparison between clinical and demographic features of asthma patients with elevated serum IgE and those with normal serum IgE. Among the study group, the number of mild asthma group was predominant with 42.9% males and 57% females. The mean age of mild asthmatics was 40.648±14.640 and the mean

PFT forced expiratory volume 1/forced vital capacity (FEV1/FVC Post) values was found to be 88.423 ± 19.35 . The findings indicate that among all groups, asthma patients exhibited significantly elevated serum IgE levels with mild cases showing 286.59 ± 106.98 IU/L, compared to other groups.

ANOVA

Table 3: One-way ANOVA analysis for clinical parameters within the four groups of asthma patients (Normal, Mild, Moderate and Severe)

Variable	Comparisons	Sum of squares	Degrees of Freedom	Mean Square	F statistic	P-value
Age	Between groups	527.845	3	175.948	0.828	0.480
	Within groups	41858.165	197	212.478	-	-
	Total	42386.010	200	-	-	-
Gender	Between groups	0.541	3	0.180	0.724	0.539
	Within groups	49.051	197	0.249	-	-
	Total	49.592	200	-	-	-
FEV1/FEV post	Between groups	679.822	3	226.607	0.674	0.569
	Within groups	66193.103	197	336.006	-	-
	Total	66872.925	200	-	-	-
IgE	Between groups	3906138.700	3	1302046.233	157.006	0.000
	Within groups	1633712.474	197	8292.957	-	-
	Total	5539851.174	200	-	-	-

A one-way ANOVA was carried out to relate the differences between the means of the variables among the groups, normal, mild, moderate and severe asthma patients. In the present study, serum IgE levels were found to be statistically significant among the groups at $p < 0.05$. [$F(3,197) = 157.006$, $p < 0.000$]. There was a significant difference in the IgE mean levels across the groups, according to an ANOVA with post hoc test for comparisons using the Tukey HSD and Bonferroni test used for all the markers. (Table 3)

ROC curve analysis

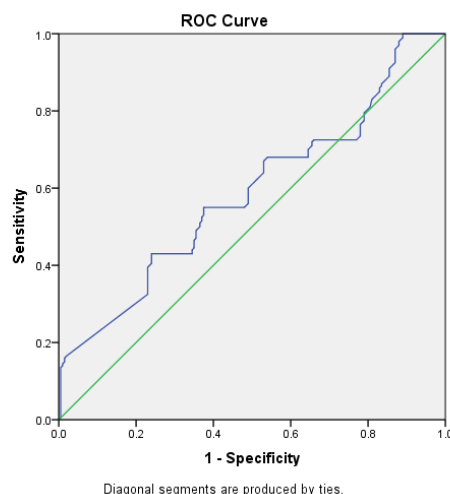


Fig 2: Receiver operating characteristic plot of IgE serum levels in comparing control (HC) with asthma patient's groups.

Table 4: ROC curve: A comparison between the control (HC) and asthma patient groups for IgE serum levels.

Values (IU/mL)	AUC	Std error	95% CI	P-Value	Cut-off (IU/mL)	Sensitivity (IU/mL)	Specificity (IU/mL)
IgE	0.587	0.028	0.532-0.643	0.003	232.50	58 %	51%
AUC- Area Under Curve, 95% C.I. Confidence Interval, $P < 0.01$ considered to be significant							

To compare the total IgE levels in asthma patients with healthy controls, ROC curves were created. With a statistically significant result at $P < 0.005$, the IgE test was determined to be good with an AUC of 0.587 (95% CI: 0.532–0.643) (Figure 2). For the serum levels, the cut-off value was 232.50, and the sensitivity and specificity were 58% and 51%, respectively. Subjects with an IgE level below 232.50 were considered to be high risk, but those with an IgE level over this cutoff were considered low risk. (Table 4)

Discussion

Airway hyperresponsiveness and periodic airflow restriction are characteristics of asthma, a complicated chronic respiratory disease. This hypersensitivity reaction is Type 1⁹. IgE is responsible for certain allergic responses including airway irritation. Since IgE levels have been associated to asthma, IgE may influence the severity of asthma. It has been demonstrated that nonspecific bronchial hyperresponsiveness and reported respiratory symptoms together accurately identify patients with severe asthma¹⁰. Elevated IgE-dependent processes, the function of the immune system, and related events may be the cause of elevated serum IgE levels in asthma. These factors are all essential for the pathophysiology of asthma. High Immunoglobulin E levels indicate an underlying disease development involving airway inflammation and a potential genetic predisposition (atopy)¹¹.

The current study investigated the levels of total serum IgE and asthma severity along with the clinicodemographic characteristics such as age, sex and PFT values in both asthmatics and healthy controls. Our results demonstrated that the mean age of mild asthmatics was 36.36 when compared to healthy controls. In consistent with our investigation, the mean age was found to be <40 years in German population¹² and Indian population⁹. Among all the study groups, female patients were more prominent than males when compared to HC's in the present investigation. Similarly, in Chinese study, females were more prone to asthma when compared to males¹³ and in contrast to our investigation, the disease was found to be more prominent in men when compared to women^{9,10}. With regards to FEV1/FVC Post, the mean value of asthma patients was high when compared to healthy controls. Similar studies demonstrated the significant increase in FEV1/FVC values in asthmatics when compared with healthy controls^{11,14}. Contrary to these studies, the FEV1/FVC values have found to be significantly decreased in asthmatics when compared to healthy individuals in Chinese¹³ and German population.¹² Asthmatics serum IgE levels were considerably higher than those of HC, and elevated IgE levels in patients may be an inflammatory marker of the disease. The study conducted by Ahmed MA et al, in Pakistan investigated children of different ages and segregated them in mild, moderate and severe asthma groups and found that mean IgE concentration reaching its highest levels in severe asthma patients¹⁰. A previous study in China had reported that compared to patients with mild asthma, those with moderate asthma had greater IgE levels among asthmatics¹³. In contrast to those with low IgE, a high percentage of people with greater IgE levels had moderate-to-severe asthma in a Mexican population¹⁴. K.M.Beeh et al. reported that low serum IgE levels were significant in German population. Similarly, in the present study, the mild asthma group were more predominant in clinical and demographic characteristics when compared to other groups¹².

Snehalatha et al explained in her study that elevated IgE levels have a major impact on the severity and course of asthma symptoms, particularly in individuals with the Th2 inflammatory phenotype. In children, mean IgE values were significantly greater in severe cases compared to mild cases¹⁵. Additionally, in the Chinese population, the study observed that there was a 1.8 times higher rate of IgE levels in patients with uncontrolled asthma¹⁶. A study conducted in Barabanki region and in the city of Bangalore, India, observed that compared to normal individuals, asthmatics had higher serum immunoglobulin E levels. The severity of asthma was found to be positively correlated with serum IgE levels^{2,17}. Since, asthma patients have considerably higher serum IgE levels than healthy controls (HCs), it can serve as a biomarker to distinguish between asthmatics and non-asthmatics¹⁸. A similar investigation conducted in Iraq(2008) and Italy(2023) demonstrated that serum IgE levels were predictive in asthma and may help distinguish asthmatic individuals from non-asthmatics when used alongside other biomarkers^{19,20}. IgE can enhance antibody responses to specific antigens, leading to increased airway inflammation and remodeling, creating a feedback loop that perpetuates asthma severity²¹. In the current investigation, IgE levels were substantially greater in asthmatics compared to healthy controls, suggesting that elevated IgE levels may influence inflammation in the disease.

Conclusion

According to our study findings, serum IgE levels increased significantly as asthma severity progressed from mild to severe and were greater in asthmatics than in healthy individuals. It facilitates an in-depth understanding the fundamental characteristics of the disease and how it develops and highlighting IgE's role in triggering asthma and its early involvement in the inflammatory cascade. Further research could pave the way for novel asthma therapies.

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Conflict of interest declaration

The authors declare that there are no conflicts of interest.

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