



Serum Immunoglobulin E as A Marker of Asthma Severity: A Cross-Sectional Study in Hillah City

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Received: 01/10/2025

Accepted: 30/12/2015

Published: 30/06/2026

Keywords: Asthma severity, Immunoglobulin E, FEV1, Hillah city, Allergic asthma.



DOI:10.62472/kjps.v17.i28.1-10

Abstract

Background: Asthma is a persistent inflammatory pulmonary disease frequently was linked with elevated levels of immunoglobulin E (IgE), particularly in atopic individuals. The degree to which IgE levels correlate with asthma severity is clinically relevant for diagnostic and therapeutic strategies.

Objective: To examine the association between serum IgE concentrations and asthma severity grade.

among patients in Hillah city.

Methods: This cross-sectional study was conducted in Hillah, Iraq. Asthmatic patients are categorized into mild, moderate, and severe asthma groups based on FEV1% predicted values. Serum IgE levels were measured and stratified into two groups: <100 IU/mL and >100 IU/mL. The distribution of IgE levels across the asthma severity spectrum was analyzed.

Results: Among mild asthma patients (FEV1 > 80%), 64.3% had IgE levels <100 IU/mL and 35.7% had levels >100 IU/mL. In moderate cases (FEV1 60–80%), 55.2% had IgE >100 IU/mL. For severe asthma (FEV1 < 60%), 60.4% of patients presented with IgE >100 IU/mL. A progressive increase in elevated IgE prevalence with increased asthma severity was observed.

Conclusion: There is a clear positive association between increased IgE levels and increasing asthma severity. Monitoring serum IgE can aid in classifying asthma phenotypes and tailoring therapy.

الغلوبولين المناعي E في المصل كمؤشر على شدة الربو: دراسة مقطعية في مدينة الحلة

علا حمود وزهراء عبد العلي المظفر

الخلاصة

الربو هو مرض التهابي مزمن في الرئتين، وغالبًا ما يرتبط بارتفاع مستويات الغلوبولين المناعي (IgE) ، خاصة لدى الأشخاص المصابين بالحساسية (الأتوبيين). إن درجة ارتباط مستويات IgE بشدة الربو تُعد ذات أهمية سريرية من الناحيتين التشخيصية والعلاجية.

الهدف من الدراسة

دراسة العلاقة بين تركيز الغلوبولين المناعي E في المصل وشدة الربو لدى المرضى في مدينة الحلة.

طرق العمل

تم إجراء دراسة مقطعية شملت مرضى مصنفين إلى ثلاث مجموعات حسب شدة الربو: خفيفة، متوسطة، وشديدة، وذلك اعتمادًا على القيم المتوقعة لنسبة $FEV_1\%$ تم قياس مستويات IgE في الدم وتصنيفها إلى مجموعتين: أقل من 100 وحدة دولية/مل، وأكثر من 100 وحدة دولية/مل. تم تحليل توزيع مستويات IgE عبر درجات شدة الربو المختلفة.

النتائج

من بين مرضى الربو الخفيف ($FEV_1 > 80\%$) ، كان لدى 64.3% مستويات IgE أقل من 100 وحدة دولية/مل، بينما كان لدى 35.7% مستويات أعلى من 100 وحدة دولية/مل. أما في الحالات المتوسطة (FEV_1 بين 60–80%)، فكان لدى 55.2% مستويات IgE أعلى من 100 وحدة دولية/مل. وفي حالات الربو الشديدة ($FEV_1 < 60\%$) ، وُجد أن 60.4% من المرضى لديهم $IgE > 100$ وحدة دولية/مل. لوحظ ازدياد تدريجي في انتشار المستويات المرتفعة من IgE مع ازدياد شدة الربو.

الاستنتاج

توجد علاقة إيجابية واضحة بين ارتفاع مستويات IgE وزيادة شدة الربو. يمكن أن يساعد رصد IgE في تصنيف أنماط الربو وتوجيه العلاج بشكل أدق.

1. Introduction

Asthma is a multifaceted disease marked by fluctuating airflow restriction and airway hypersensitivity. (Lambrecht and Hammad, 2015) In allergic inflammation, immunoglobulin E (IgE) is essential mediator that contribute to bronchoconstriction and mucosal edema through mast cell activation. In Iraq and globally, asthma prevalence and its burden are rising, emphasizing the need for better biomarkers to assess severity and guide management.

Asthma exacerbation consists of two phases: Sensitized IgE antibodies generated by plasma cells initiate the first phase. Certain environmental cues trigger the immune response of these antibodies. After that, IgE antibodies bind to basophils and high-affinity mast cells. When a pollutant or pathogen is inhaled, it triggers the release of alarmines by the bronchial epithelium, which include cytokines IL-25, IL-33, and thymic stromal lymphopoietin. (Pelaia et al., 2017, Hoof et al., 2020). Both pathways are targeted by pharmacological interventions to minimize bronchoconstriction and inflammation, according the severity of the disease. Consequently, degranulation of mast cells results in secretion of histamine, prostaglandins, and leukotrienes. These mediators subsequently contract the smooth muscle, resulting in airway constriction. Immunoglobulin E is one of the five isotopes of immunoglobulin that play a major role in atopic hypersensitivity reaction including asthma. IgE is also responsible for immunological response against parasitic infection. Fraction of IgE is present in plasma but it is mainly found in body tissues bound to the effector cells; basophil and mast cells via FC receptors (R1 and R2). High affinity Fc epsilon receptor consist of five subunits expressed on the surface of mast cell and basophil. One subunit is for IgE binding and the other four subunits span the membrane. Stimulation of R1 receptor cause acute hypersensitivity reaction manifest as urticaria, oedema, sneezing, bronchospasm and sometimes end up with fatal anaphylactic cardiovascular collapse. (Hostoffer and Joseph, 2018). Th2 cells can identify antigens that have been processed by antigen-presenting cells (APCs). IgE antibody production is enhanced by interleukins (such as IL-4 and IL-13) released from activated T helper2. These antibodies subsequently bind to additional resident cells that have particular IgE receptors. A little domain (found in Fc_γ 3) of the IgE "constant" region attaches itself to the low-affinity receptor (Fcε RII, also called CD23) on the surface of eosinophils and B lymphocytes. It also binds to the high-affinity receptor (Fcε RI) on the surface of basophil or mast cells. When IgE attach to FcεRI receptor expressed on the surface of mast cells and basophils, the signaling cascade start by the release of histamine, tryptase, chymase and other preformed mediators. In the early phase of the reaction these mediators act as vasodilator that increase vascular permeability, and they upregulate adhesion molecules and result in smooth muscle contraction. In addition to that increasing level of PGD₂, LTC₄, IL-4, and IL-13 stimulate over production of mucus by goblet cells by the effect of mast cells that accumulate in bronchial submucosa. Late phase of the reaction characterized by production of specific cytokines responsible for recruitment of different immune cells. IgE receptors stimulation in bronchial smooth muscles resulting in hypertrophy, hyperplasia and hypercontractility. Finally, the effect of the hypersensitivity reaction ends by the ubiquitination of IgE-receptor complex and lysosomal degradation. In asthmatic patient, IgE is predominantly generated in a reservoir of memory IgG-positive B cells that undergo differentiation into IgE and differentiate into long-lasting plasma cells when stimulated by IL-4 and/or IL-13. (Woo et al., 2021). The severity of asthma and its association with elevated blood IgE levels in certain geographical populations, such as in Hillah city, remains underexplored. The purpose of this

study is to investigate the relationship between serum IgE levels and the severity of asthma, which will be classified based on spirometry criteria.(McDonnell et al., 2023)

2. Material and Methods

2.1.Study Design and Participants

The study is cross sectional performed at Merjan Teaching Hospital in Hillah city, Iraq. A total of 153 patients with clinically diagnosed asthma were included, categorized into three severity groups (mild, moderate and sever) according to Global Initiative for Asthma (GINA) classification using FEV1% predicted values.

2.2.Data Collection and Analysis

2.2.1. Inclusion Criteria

The study recruited participants aged 15 to 70 years, of both genders, with an inclusion criterion of asthma diagnosis based on GINA criteria, which encompasses two essential defining characteristics: A history of respiratory symptoms, including wheezing, dyspnea, cough, and chest constriction that fluctuate in both duration and severity.

2.2.2. Exclusion Criteria

lung disease other than asthma, Smoking, History of malignant disease, History of heart or renal disease and Pregnancy.

2.3.Data Collection and Analysis

Demographic and Clinical data will be collected using a specific detailed questionnaire. Around 3ml of venous blood were drawn from antecubital fossa of each individual after skin sterilization with ethanol-soaked gauze using 5ml syringes while tourniquet is placed to the upper part of the arm. The blood sample was then dispensed into gel tube and allowed to clot. To separate the serum the tubes are centrifuged at 3500 rpm for 15 minutes to remove small clots from the serum. The serum was subsequently transferred to a new 2ml Eppendorf tube and stored in a deep freeze at -20°C. (Salem et al., 2025)

2.4.Ethical Consideration

Ethical Approval Committee of kufa College of Medicine / University of Al Kufa has consented this research.

2.5.IgE Measurement

Serum IgE concentrations are measured using the VIDAS total IgE kit by BioMérieux. IgE values were grouped into two categories: <100 IU/mL(normal) and >100 IU/mL (elevated).

2.6.Pulmonary Function Testing

Spirometry was performed to assess pulmonary indices. Asthma severity is categorized according to GINA criteria as: Mild: FEV1 > 80% Predicted, Moderate: FEV1 60–80% Predicted, Severe: FEV1 < 60% Predicted, Bronchodilator reversibility test was done to confirm the diagnosis (defined as an increase in FEV1 of >12% and >200 mL from baseline after inhalation 200-400 mg albuterol for 10 minutes).

2.7.Data Analysis

Data are analyzed using descriptive statistics. The association between asthma severity and IgE levels is evaluated using Chi-square tests. A p-value <0.05 is considered statistically significant.

3. Results

3.1. Demographic and Clinical Characteristics

Asthmatic patients are categorized according to socio-demographic characteristics including (age, sex, body mass index (Kg/m^2), and disease onset). Mean age of patients is (40.99 ± 17.51) years, range between 15-83 years. Mean body mass index is $(28.61 \pm 5.38) \text{ Kg/m}^2$, range between 46.87 Kg/m^2 and 15.21 Kg/m^2 . Obese patients represent 57 patients (37.3%) as in Table1.

Table1: Distribution of Asthmatic Patients According to Socio-Demographic Characteristics

Socio-demographic characteristics	Number	%
Age		
15-25 years	34	22.2%
25-45 years	52	34.0%
45-65 years	49	32.0%
≥ 65 years	18	11.8%
Total	153	100.0%
Sex		
Male	59	38.6%
Female	94	61.4%
Total	153	100.0%
BMI (Kg/m^2)		
Normal (18.5-24.9)	36	24.7%
Overweight (25-29.9)	59	38.6%
Obese (≥ 30)	57	37.3%
Total	153	100.0%
Onset		
Early onset	75	49.0%
Late onset	78	51.0%
Total	153	100.0%

Severity of asthma according to GINA classification: According to GINA classification patient classified into in Mild (FEV1 predicted $> 80\%$, Moderate FEV1 predicted (60-80%) and Severe (FEV1 predicted $< 60\%$). Patients with Mild grade represent (N=42, 27.5%), patients with Moderate grade represent (N=58, 37.9%) and patients with Severe grade represent (N=53, 34.6%). as in Table2 and Fig.1.

Table2: Severity of Asthma According to GINA Classification

Asthma Severity	Number	%
Mild (FEV1) $> 80\%$ Predicted	42	27.5%
Moderate (FEV1) 60-80% Predicted	58	37.9%
Severe (FEV1) $< 60\%$ Predicted	53	34.6%
Total	153	100.0%

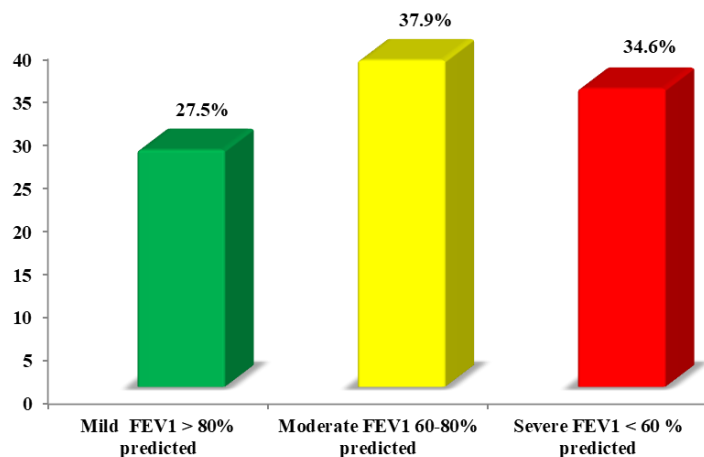


Figure1: Distribution of asthmatic patients according to severity of asthma (N=153)

3.2.The relation between IgE level and severity of asthma

There was significant relation between IgE and severity of asthma as in Table3 and Fig.2.

Table3: The Relation Between Ige (Ku/L) Level and Severity of Asthma According to FEV1

IgE (kU/l)	Severity of asthma			Total	P value
	Mild (FEV1 > 80%) N=42	Moderate (FEV1 60-80%) N=58	Severe (FEV1< 60 %) N=53		
Normal (< 100 kU/l)	27 (64.3)	26 (44.8)	21 (39.6)	74 (48.4)	0.046*
Elevated> 100 kU/l)	15 (35.7)	32 (55.2)	32 (60.4)	79 (51.6)	
Total	42 (100.0)	58 (100.0)	53 (100.0)	153 (100.0)	

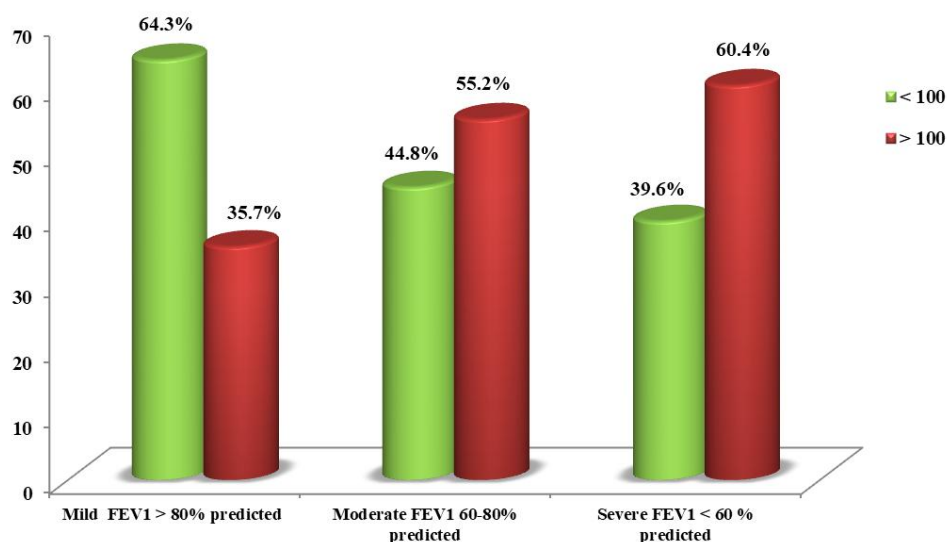


Figure2: The relation between IgE level and severity of asthma

Individuals with mild disease, 64.3% had IgE <100 IU/mL, and 35.7% had IgE >100 IU/mL. In the moderate group, the percentage of patients with IgE >100 IU/mL increased to 55.2%, while 44.8% had lower levels. Among those with severe asthma, 60.4% had IgE >100 IU/mL, compared to 39.6% with lower levels. A one-way ANOVA was conducted to assess differences in mean serum IgE levels across asthma severity groups defined by predicted FEV1/FVC ratios. Patients were categorized as Mild (>80%), Moderate (76–80%), or Severe ($\leq$ 75%). The analysis revealed a statistically significant difference ($F = 4.82$, $p = 0.011$) in IgE levels among these groups. Patients in the Mild group had the lowest mean serum IgE (143.62 kU/L), while those in the Moderate and Severe groups exhibited substantially higher IgE levels (341.37 kU/L and 350.80 kU/L, respectively). These findings support the association between elevated IgE and increased asthma severity as in Table4 and Fig.3.

Table4: The Relation Between Ige (Ku/L) Level and Severity of Asthma According to FEV1/FVC Ratios

Asthma Severity	Predicted FEV1/FVC (%)	Mean Serum IgE (Ku/L)	p-value
Mild	>80%	143.62	0.011
Moderate	76–80%	341.37	
Severe	$\leq$ 75%	350.80	

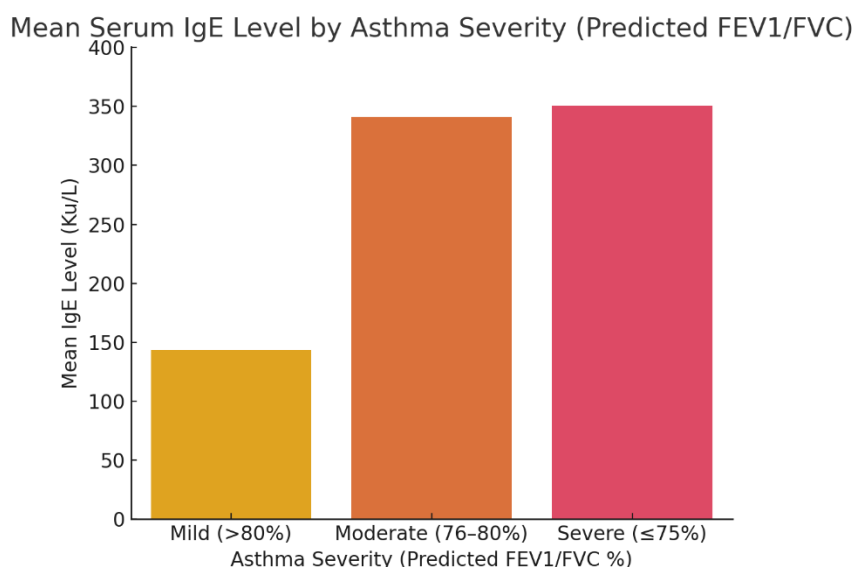


Figure3: The Relation Between Serum Ige Level and Asthma Severity Defined by Predicted FEV1/FVC Ratio.

4. Discussion

Our findings are consistent with prior studies that have reported higher IgE levels among patients with more severe asthma, particularly in atopic phenotypes. Several investigations have proposed that IgE plays a central role in the pathophysiology of allergic asthma, mediating airway inflammation through mast cell activation, eosinophil recruitment, and release of inflammatory mediators.(Gould and Sutton, 2008). This pathway not only contributes to acute bronchospasm but also to airway remodeling,(Djukanovic et al., 1990) which may account for the observed link between elevated IgE and chronic reduction in lung function.(Ayakannu et al., 2022). The clinical implications of these results are twofold. First, measuring serum IgE may offer a readily available biomarker to help stratify patients according to disease burden, particularly in settings where access to advanced inflammatory biomarkers (such as periostin, FeNO, or sputum eosinophils) is limited (Bousquet et al., 2008). Second, identifying patients with markedly elevated IgE may inform therapeutic decisions, including consideration of anti-IgE biologic therapy (e.g., omalizumab), which has shown benefit in selected severe allergic asthma patients.(Busse et al., 2001). However, our results also underscore that IgE alone should not be used in isolation to define asthma severity. A proportion of patients with mild asthma exhibited elevated IgE, and conversely, some with severe asthma had levels below 100 IU/mL. This variability may be explained by the heterogeneity of asthma phenotypes, non-allergic triggers, genetic factors influencing IgE production, and the influence of ongoing corticosteroid therapy.(Bergeron and Hamid, 2005)

The weak correlation between IgE and FEV₁/FVC% predicted observed in our study aligns with literature suggesting that lung function impairment in asthma is multifactorial. While IgE-mediated inflammation contributes to airflow limitation, other mechanisms, such as neutrophilic inflammation or fixed airway remodeling, may be independent of IgE levels.(Rengganis et al., 2018). .(Farhood et al., 2019) and (ABBAS and ALI, 2024) reported similar findings in Iraqi population, indicating that IgE is a reliable biomarker for disease progression. The role of IL-4 and periostin in promoting IgE synthesis also supports the observed correlation.(Shaban et al., 2021). While the study provides insight

into local asthma immunopathology, the relative limited sample size and absence of longitudinal follow-up are limitations for this study. Nonetheless, it reinforces the utility of IgE as a practical, low-cost tool in clinical asthma assessment. Variability in total blood IgE levels is a biomarker that may be easily collected and can be useful tool for predicting flare-ups of asthma in the future.(Yuan et al., 2021)

Conclusion

This study reveals a substantial correlation between elevated blood IgE levels and asthma severity in individuals from Hillah city. Monitoring IgE may aid in identifying high-risk patients and implementing targeted therapies. Further multicenter studies are recommended to validate these findings and explore underlying immunological pathways.

Ethical Approval

The research was approved by the scientific and ethical committee of medical college, Kufa university on 14 Feb.2024.

Conflict of Interest

The authors declare no conflict of interest.

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