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# Evaluation of Humoral and Cell Immunity in Asthma

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**ABSTRACT**

***Background:*** *Asthma is a chronic inflammatory airway disease that universally penetrates the globe, across all societies, ages, genders, health statuses, and social statuses. The IgE as a humoral immunity has an essential role in asthma which is caused by the activation of particular IgE receptors expressed by airway structural cells (airway epithelium cells and airway smooth muscle cells) as well as immune-inflammatory cells (mast cells, eosinophils, basophils, and dendritic cells), so that the recent studies have shown a relationship between serum IgE levels, blood parameter, and airway responsiveness.* ***Method:*** *The blood specimens of 42 patients suffering from asthma and 40 healthy controls were collected during the period between June and September (2023). The level of IgE in the specimens was measured by ELISA and blood parameters (Complete Blood Count) were determined by a hematology analyzer (Beckman Coulter C32).* ***Result****: In this study, several variables were identified, including age, gender, IgE, and CBC, and found there was no significant (P= 0. 0. 65) differences between the age groups; and the percentage of female patients (n=25, 59.5 %) is insignificant (P=0.64) more than male (n=17, 40.5%). Patients with a family history were significantly (P value= 0.002) higher (64.3%) than cases without a family history of asthma (35.7%). The percentage of smokers was 76.2% and non-smokers was 23.8% but without significant differences. In this study, the level of white blood cells, both total, granulocytes, and non-granulocytes, were significantly (P=0.001) higher in patients than in controls. The average of IgE was significantly higher (296.64±67.85) in asthma patients than in the control group (32.22± 4.59). However, there are no significant (P=0.067) differences in the IgE level between males (263.7±74.2) and females (295.8±73.9). The relationship between IGE and white blood cells was determined, and there were no significant differences between them (except lymphocyte in control, P=0.001) but there is a positive correlation with total WBC, basophile, neutrophil, monocyte, lymphocyte in patients; and basophile and lymphocyte in control.* ***Conclusion:*** *Asthma occurrence is significantly related to family history, humoral immunity (IgE level) and cellular immunity (total WBC and differential WBC); and insignificantly affected by age and gender kind.*

**Keywords: IgE, ELISA, Asthma, Blood parameters.**

**Article Information**

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## INTRODUCTION

Asthma is a chronic, inflammatory respiratory condition that affects people of all ages, genders, and socioeconomic backgrounds worldwide. Over 360 million individuals worldwide have been identified as having asthma syndrome, a vast array of conditions characterized by symptoms such as dyspnea, chest discomfort, wheezing, and coughing that fluctuate in severity over time (1).


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A defining and crippling aspect of the illness is its protracted nature, which is typically linked to reversible airway blockage that responds to bronchodilators and steroid inhalation therapy. However, over the course of their lives, about 10-15% of patients gradually lose their ability to breathe permanently (2). Although many asthmatics can manage their symptoms with the help of available treatments, a small percentage of asthmatics experience severe and frequently progressive disease, sometimes leading to multiple yearly exacerbations. Even with high-intensity therapy, severe asthmatics still have frequent symptoms (3). Asthma symptoms can arise spontaneously or as a response to environmental exposures. They are characterized by intermittent episodes of symptoms and variable airflow obstruction (4).

The current treatment modalities are based on our understanding of allergen-induced airway responses and, when used properly, reduce the daily variability of asthma and significantly enhance quality of life (5). But even in this case, asthmatics still have episodes of worsening their condition. Viral respiratory infections are often the cause of these exacerbations, and the efficacy of current treatment modalities is limited during these episodes. 1-3 This suggests that asthma attacks have a distinct immunopathogenesis, underscoring the necessity of figuring out the pathways involved to treat them more effectively (6).

Biomarkers are potential therapeutic targets because they enable early diagnosis, prognosis, and identification. Serum IgE levels, CBC/blood eosinophils count (7) and eosinophil counts are frequently employed in asthma diagnosis (8). None of these can be considered as established biomarkers (s) of asthma (9). To improve asthma diagnosis and treatment, it is critical to investigate changes in cellular or molecular mechanisms related to asthma (10). In standard clinical practice, the patient's plasma and sera are examined to make a diagnosis. Analysis of biological fluids is considered a better tool to identify any change in the body's physiology. Any change in body physiology is reflected in variations in the composition of body fluids (11).

High IgE levels are a hallmark of type 1 hypersensitivity, although the mechanisms governing IgE production remain poorly understood. The two main biosynthetic pathways thought to be involved in IgE synthesis are "sequential" switching from IgM to IgG1 and then from IgG2 to IgE, or "direct" class-switch recombination (CSR) from IgM in germinal center B-cells (12). The commonality of the atopic disorder’s allergic rhinitis, atopic dermatitis, and asthma in people with noticeably elevated IgE antibody levels is a common thread connecting them (13). In pedigree analyses, high IgE levels are also correlated with bronchial hyperresponsiveness (BHR), the increased propensity for bronchial smooth muscle contraction seen in asthmatic patients (14). IgE levels are linked to a physician's diagnosis of asthma in cohorts of children with asthma (15). The classic immediate hypersensitivity reaction is triggered by the release of preformed vasoactive mediators, transcription of cytokines, and de novo synthesis of prostaglandins and leukotrienes when IgE bound to mast cells cross-links through the high-affinity IgE receptor (FcϵRI) using a polyvalent allergen (16).

These mediators quickly cause bronchial mucosa edema, mucus production, and smooth muscle constriction in the airway, and they ultimately draw in an inflammatory infiltrate (17). Studies show that allergic asthma, accounting for more than 60% of all asthma cases, is the most common phenotype (18). Furthermore, in allergic asthma, the immune system is activated through the type 2

inflammatory pathway, which includes Th2 and ILC2 and is mediated by related effective cells like mast cells and eosinophils. An important part of the pathobiology of allergic asthma is played by immunoglobulin E (IgE) (19). There are two different kinds of IgE. The first is called classical IgE, and it is characterized by allergens attaching to IgE-on-IgE receptors on correlated inflammatory cells (like mast cells), which generates proinflammatory mediators. Another mechanism is called cytokinetic IgE, which is formed without the presence of an allergen. The IgE receptor is activated by IgE produced by B cells that have transitioned to the IgE class, and interleukins then spread the IgE receptor further. Allergen avoidance is ineffective in this pathway. (20). Specific IgE receptors expressed by immune-inflammatory and airway structural cells are activated in response to specific IgE stimuli, which facilitates the pleiotropic effects of IgE (21).

This process involves the regulation of inflammatory mediators by neutrophils and eosinophils, two types of inflammatory cells that cause tissue damage through the secretion of enzymatic products, such as myeloperoxidase in neutrophil cells and eosinophil peroxidase in eosinophil cells, which generate highly effective free radicals (22). This study aimed to identify the association between certain blood parameters and/or IgE with asthma susceptibility in Iraqi patients.

## MATERIAL AND METHOD

### Subject

A total of 42 blood spacemen were collected from asthma patients attending the Allergy Center in Al-Sadr Hospital, during the period between June and September (2023), moreover, 40 healthy controls were included in the current study.

### Sample collection

Vein punctures were used from 9 a.m. to 1 p.m. to obtain approximately 5 milliliters of blood per control and patient. Blood was transferred into two tubes: an EDTA tube for hematology testing and an immunological test serum tube. The serum tube was allowed to stand at room temperature for one minute. Following the formation of a clot, the blood was centrifuged at 3000 rpm for five minutes using a microcentrifuge. A 2.5 ml volume of yellow serum was separated and used directly for testing; the remaining serum was frozen until the necessary time to finish the other test.

### Exclusion criteria's

The patient with lung diseases, corticosteroid drugs administrative and pregnant women were excluded from this study.

### Complete Blood Count

This fully automated hematology analyzer, the Beckman Coulter C32, was used in the hematology lab to estimate the complete blood count (CBC) on EDAT anticoagulated blood to perform the hematological parameters on EDTA blood.

### IgE Estimation

IgE was determined by the enzyme-linked immunosorbent assay (ELISA) from Elabscience (USA).

## STATISTICAL ANALYSIS

Statistical analysis was carried out by using statistical software (IBM SPSS Statistics 26). The Chi-square test was used to determine the statistical differences in qualitative results among different groups. Also, the person Chi correlation was used to find the correlation relationship between parameters, whereas, quantitative data was given as mean ± SD, and the differences were tested by t-test. The probability of ($P \leq 0.05$) was measured to be significant statistically (Cesana, 2018).

## RESULT

### Demographic information of asthma patients

The age of asthma patients was range from 15 years to 55 years. An almost unequal number of male (n=17, 40.5%) and female patients (n=25, 59.5 %) were included in the study. While the number of smokers was 32 (76.2%) and non-smokers was 10 (23.8%). Almost (64.3%) of the patients reported significantly (P=0.002) having asthmatic family members whereas 35.7% of cases their relatives are nonsuffering from asthma as shown in the Table (1).

### Hematological profile of asthma patients

In this study, it was found that that was a change in the average of the blood cells between asthma patients and the control group. Where was the average eosinophil in asthma patients is significantly (P=0.001) elevated (4.67±0.58) than in the control group (2.65±0.85). There was a significantly (P=0.001) low level of basophile cells in the patient (3.28± 1.27) comparison control group (5.77± 1.64). The average of neutrophils in the patient group was significantly (P=0.001) more (83.02±6.95) than in the control group (61.64±4.83).

The average of monocyte cells in the patient group (7.39±1.43), while there was a noticeable significant (P=0.001) decrease in the rate in the control group (0.53±0.21). The study showed that the average of lymphocytes in patient (47.85±5.07) was significantly (P=0.001) higher than in the control group (32.22±4.59). The Table (2) shows significant differences between parameter blood.

### The IgE level according to age and gender in asthma patients

The average of IgE was significantly (P=0.001) higher (296.64±67.85) in asthma patients than in control group (32.22± 4.59). Moreover, the IgE level in asthma patients was measured according to age and gender. It was found that the IgE level in the age group of (15-25) was insignificantly highest for IgE, Table (3). The study found that the mean level of IgE of males (263.7±74.2) was higher than that of females (295.8±73.9).

### The correlation between values of IgE and white blood cells in patients

The relationship between IGE and white blood cells was determined, and there were no significant differences between them whether in patient or in control (except lymphocyte in control, P= 0.001) but there is a positive correlation with total WBC, basophile, neutrophil, monocyte, lymphocyte in patients; and basophile and lymphocyte in control, Table (4).

**Table (1): Socio-demographic characteristics of the study population.**

| Variables | | Groups | | | | Statistical test type | P values |
|---|---|---|---|---|---|---|---|
| | | patients N= 42 | | Control N= 40 | | | |
| | | No. | % | No | % | | |
| Age Group | 15-25 | 10 | 23.8 | 12 | 24 | $X^2$ = 1.85 *df* = 3 | 0.6 NS |
| | 26-35 | 10 | 23.8 | 10 | 25 | | |
| | 36-45 | 10 | 23.8 | 9 | 22.5 | | |
| | 46-55 | 12 | 28.5 | 9 | 22.5 | | |
| Family history | Yes | 27 | 64.3 | 2 | 5 | $X^2$ =27.51 *df* =1 | 0.002 Sig |
| | No | 15 | 35.7 | 38 | 95 | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Gander** | **Male** | **17** | **40.5** | **19** | **47.5** | $X^2 = 0.22$ $df = 1$ | **0.64 NS** |
| | **Female** | **25** | **59.5** | **21** | **52.5** | | |
| **Smoking** | **Yes** | **32** | **76.2** | **25** | **62.5** | $X^2 = 0.18$ $df = 1$ | **0.73 NS** |
| | **No** | **10** | **23.8** | **15** | **37.5** | | |

**$X^2$: Chi-square, df: degree of freedom, Ns: not significant, sig: Significance.**

## Table (2): Association of IgE level and white blood cells in subject.

| Variables | Groups | | t-test | P value |
|---|---|---|---|---|
| | Patient | Control | | |
| | Mean± SD N=42 | Mean± SD N=40 | | |
| **Eosinophil** | **4.67± 0.58** | **2.65± 0.83** | **12** | **0.001 Sig** |
| **Basophile** | **3.28± 1.27** | **5.77± 1.64** | **7** | **0.001 Sig** |
| **Neutrophil** | **83.02 ±6.95** | **61.64 ±4.83** | **16** | **0.001 Sig** |
| **Monocyte** | **7.39± 1.43** | **0.53± 0.21** | **29** | **0.001 Sig** |
| **Lymphocyte** | **47.85 ±5.07** | **32.22 ±4.59** | **14** | **0.001 Sig** |
| **WBC** | **12.63 ±0.91** | **6.58 ±2.21** | **16** | **0.001 Sig** |

**IgE: Immunoglobulin E, SD: standard deviation; N=(82); sig: significance; T-independent test.**

## Table (3): Level of IgE in asthma patients according to age and gender.

| Variables | | Number | IgE | Statistical test type | P value |
|---|---|---|---|---|---|
| | | | Mean± SD | | |
| **IgE** | **Patient** | **42** | **296.64±67.85** | **t-test** | **0.001** |
| | **Control** | **40** | **32.22 ±4.59** | | |
| **Age** | **15-25** | **10** | **229.20± 43.3** | **ANOVA** | **0. 65** |
| | **26-35** | **10** | **209.20 ± 37.65** | | |
| | **36-45** | **10** | **214.60± 42.3** | | |
| | **46-55** | **12** | **211.33± 33.5** | | |
| **Gander** | **Male** | **17** | **263.7 ± 74.2** | **t-test** | **0.067** |
| | **Female** | **25** | **295.8 ± 73.9** | | |

## Table (4): correlation between values of IgE and white blood cells in patients and control.

| Subject | Statics | WBC | Eosinophil | Basophile | neutrophil | Monocyte | Lymphocyte |
|---|---|---|---|---|---|---|---|
| **Patient** | **Pearson Correlation** | **0.003** | **-0.187** | **0.20** | **0.03** | **0.04** | **0.15** |
| | **p-value** | **0.98** | **0.23** | **0.20** | **0.80** | **0.78** | **0.31** |
| **Control** | **Pearson correlation** | **-0.04** | **-0.01** | **0.186** | **-0.20** | **-0.25** | **1.00** |
| | **P-value** | **0.78** | **0.94** | **0.250** | **0.21** | **0.10** | **0.001** |

## DISCUSSION

The age and sex-related variations among Iraqi patients suffering from severe asthma is provided by this analysis. There are over 339 million asthmatics globally, with prevalence ranging from 6% in some to 18% in others (23). Asthma prevalence varies significantly by gender; males under the age of fifteen have a higher prevalence of the condition (23.8%), but adult women have higher rates than men (24).

This change in the prevalence of asthma in men and women over time points to different access points in developing versus developed nations for resources (such as nutrition and air quality), comorbidities, and medical care (25).

Genetic differences between males and females with asthma, including in gene expression and epigenetic modifications, are the basis for all these factors (26). Women are more likely than men to experience asthma during their lifetime, and the type of asthma they do have is more severe (27). More women than men will likely develop asthma during their lifetime, and the type of asthma they will likely have will be more severe (28). In developed nations, greater healthcare use is positively correlated with increased prevalence across age groups (higher among women and 15–20year old boys) (29).

An important part of the onset and progression of asthma is the activated eosinophils (30,31). By releasing cationic granule proteins, such as eosinophil cationic protein, eosinophils can cause harm to the airway epithelium and hasten airway remodeling (32,33). The most effective profibrotic cytokine is also primarily derived from eosinophils (34). Eosinophils are primarily responsible for laminin creation in epithelial cells, while macrophages are involved in the fibroblasts' tenascin production (35,36). Additionally, eosinophils and macrophages can work in concert because eosinophil products like TGF and ECP inhibit the growth of fibroblasts and the production of matrix proteins (37). Both of them thicken the laminin and tenascin layers, which facilitates airway remodeling (38).

According to Al-Ahmad *et al*. (2024), exposure to ambient tobacco smoke over time increases bronchial (39). There is no guarantee that asthmatic smokers with higher eosinophil counts than non-smokers (40). Al-Qerem et al. (2024), reported that smokers were characterized by increased macrophages and decreased eosinophil numbers in the bronchial airway walls (41). According to a study, individuals who have smoked or who have quit smoking have a noticeably higher chance of developing asthma than people who have never smoked (42,43). More recent research has demonstrated that asthmatics also experience an accelerated decline in lung function over time (44,45). smokers with asthma experience a faster rate of lung function decline than nonsmokers with asthma (46).

High levels of IL-5, IL-8, and proinflammatory mediators are linked to neutrophils in asthmatic patients' sputum and bronchial lavage (47). Activated macrophages or epithelial cells can produce IL-8, which can attract neutrophils from various sources of severe acute asthma and cause diffuse bronchial inflammation (48). A diagnosis of asthma was linked to a decreased mortality rate in people who specifically had an eosinophilic endotype. Comparing to all asthma cases, eosinophilic asthma makes up about 50% and is associated with the type 2 inflammatory response (49). While elevated blood eosinophils in isolation may misclassify the asthma phenotype, in combination with other biomarkers they have a high positive predictive value for type 2 inflammation (50).

Serum total IgE levels have been linked to the asthmatic response to treatment (51). Immunoglobulin E (IgE), a proinflammatory cytokine, is a key modulator of allergic reactions and increases inflammation of the airways (52). The use of medicines that weaken the inflammatory activities of IgE has emerged as a viable method in the treatment of asthma (53). There has been evidence of a connection in the general population between serum total IgE levels and airway responsiveness (54). Eosinophil is recognized as a pro-inflammatory granulocyte concerned in protection touching parasitic infections and plays a potential role in allergic illnesses such as bronchial asthma, allergic rhinitis, and atopic dermatitis (55). Asthma is recognized as a condition characterized by IgE-mediated allergic reactions. High levels of IgE are connected with inflammation, which is commonly detected in patients (56). They also induce inflammation by releasing lipid mediators, oxygen metabolites, and cytokines increasing vascular permeability. The standard range of eosinophil is 0–6% (57). Anti-IgE monoclonal antibodies like omalizumab can inhibit IgE from attaching to effector cell membrane receptors, hence reducing the pathologic processes associated with IgE-mediated inflammation (58). It was reported that inhibiting the effects of IgE reduced both early and late-phase responses to inhaled allergens. Specifically, anti-IgE therapy lowered serum-free IgE concentration, raised the amount of allergen required to provoke an early asthmatic response, and reduced the mean maximal decrease in forced expiratory volume (59). IgE and eosinophils both take part in a complicated process, though they have distinct functions. It is possible to argue that eosinophilia develops as a result of the entire process, whereas IgE is the cause of allergic asthma (60). IgE is mainly in charge of both the acute and chronic phases of inflammation that are typical of BA, at least in allergic forms, due to its capacity to affect the activity of various immune and structural cells of the bronchial wall. This character makes IgE an ideal target in the management of asthma (61).

## CONCLUSION

Asthma disease is vulnerable in different forms to some risk factors and leads from the effect of humoral and cell immunity, this finding is indicated by the fact that asthma occurrence is significantly related to family history and significantly associated with high levels of IgE, total WBC, and differential WBC; and insignificantly affected by age and gender kind.

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