Kirkuk Journal of Medical Sciences

REVIEW ARTICLE

Serum IgE Antibody Level in Iraqi Patients with Various Atopic Respiratory Diseases: A Narrative Review

Ikram Khazal Al-Hasso [1,*], Asmaa Zaki Shetawi [1], Niam Basheer Alyuzbaki [1]

[1]*Microbiology Department, College of Medicine, University of Mosul, Mosul, Iraq*

[*]*Corresponding author email: ikramhassow@uomosul.edu.iq*

Received: 26 March 2024
Accepted: 03 August 2024
First published online: 01 October 2024

*DOI:*10.32894/kjms.2024.148238.1102.

ABSTRACT

Immunoglobulin E (IgE) is an antibody class that is unique to mammals, it is regarded as the last of the five classes of human immunoglobulins which was discovered in 1968 and it is widely linked to various numbers of allergic illnesses. Basophils, intestinal epithelial cells, antigen presenting cells, tissue mast cells as well as airway epithelial cells all express IgE receptor on its surface. The cell-degranulation signal, release of inflammatory allergic mediators and hypersensitivity responses, all begin with the cross-linking of allergen to receptor-bound IgE. IgE plays an important role in type I hypersensitivity, which is demonstrated as allergic asthma and various allergenic disorders, for example, sinusitis and chronic urticaria. In non-allergic people, serum IgE levels are relatively low (0.05 mg/ml). Remarkably, there is evidence of a relationship between whole IgE values and environmental and host variables. Regardless of sensitivity to frequent allergies or other allergy manifestations, population studies have found a link between the frequency of various allergies and serum total IgE levels.

Key words: Atopic diseases; Asthma; Eosinophil count; Serum IgE.

©Authors;
licensed under Creative Commons Attribution 4.0 International (CC BY 4.0)

INTRODUCTION

Immune responses induced by IgE are referred to as "immediate hypersensitivity" responses. This description emphasizes each of the IgE systems' extraordinary sensitivity to antigens and the immune response's significant rapidity. Atopic dermatitis, asthma, and allergic rhinitis are all associated with increased IgE production [1].

In this review, we will cover the previous studies on the IgE values in Iraqi atopic individuals and show the relation of IgE level with the risk factors of these diseases. The review will be based on data gathered and summarized from articles authored by the Iraqi researchers from north to south. These studies were collected from Google Scholar and academic journals from Iraq.

IgE History

Immunoglobulin E (IgE) was the fifth class of humans immunoglobulins which was observed in 1968, and is closely related to allergic illness different symptoms [2]. However, its significance in evolutionary development appears to provide a defense mechanism against parasites [3].

IgE was identified decades after IgG, IgM, IgD, and IgA because It is the least prevalent immunoglobulin type in the blood, IgE represents 50-300 ng/mL of total antibodies in the serum, while IgG represents 10 mg/mL [4]. Because of the small proportion of B lymphocytes specialized to IgE manufacturing, along with the quick uptake of IgE in tissues where it is strongly linked by FcϵRI to mast cells, there is a paucity of IgE in the blood and a comparatively brief half-life (one to two days, in contrast to three-weeks for IgG) [5].

The Structure of IgE

IgE is a 188 kDa monomeric immunoglobulin; serum IgE levels are very low in comparison to the other immunoglobulin isotypes; yet, basophiles and mast cells express a high-affinity IgE-specific receptor, resulting in IgE saturation. Serum IgE is thought to account for around half of total body IgE, with the remainder linked to basophils besides mast cells via their IgE Fc receptors having strong affinity [6]. The overall design of the IgE monomer varies more dramatically compared to IgG in terms of the "extra" heavy chain constant region, as well as the lack of a hinge area in the epsilon chain (ϵ-chain) [7]. IgE seems to have a longer Y-shaped architecture than IgG due to the additional domain pair [8]. The isotype-dependent activities of IgE, involving interplay with its cellular and extracellular receptors, are conferred by a constant region consisting of four constant epsilon (Cϵ) repeats in the heavier chains' C-terminal regions [9].

The binding activities of receptors of IgE are distinct; FcRI, which is physically similar to other components of the FcR group, and FcRII/CD23, a fellow of the C-type (Ca2+-dependent) lectin-identical subfamily, various immune cells express FcRI as basophiles beside mast cells [10]. The sign for cells degranulation, emission of presynthesized inflammatory molecules, and an acute hypersensitive action is the bridge of allergen-definite IgE receptor-associated to basophils besides mast cells by antigens [11] .

Role of IgE and T Lymphocyte-Mediated Allergic Inflammation

Polyvalent allergens encourage the production of preexisting vasoactive messengers by bridging IgE attached to mast cells via the high-affinity IgE binding site (FcRI), Cytokine expression and de novo production of leukotrienes and prostaglandins in the classic immediate hypersensitivity reaction. These mediators induce mucus production, airway mucosal swelling, and restriction of muscle cells in the airway, and they ultimately attract an infiltration of inflammatory cells[12].

Along with mast cells and basophils via FcϵRI, IgE reacts with a variety of additional cell kinds via the lower-affinity "CD23" IgE binding site which is found on a variety of cells [13]. Sensitization to antigens in hereditarily predisposed persons is driven when Th2 and B cells are stimulated, Th2 cells can identify antigens handled by antigen-presenting cells. IgE antibody production is boosted by interleukins generated by stimulated Th2 lymphocytes (interleukin - 4 and interleukin-13)[14]. Upon the sensitization phase, antigen attaches to the IgE varying areas of neighboring two immunoglobulins on a basophil or mast cell, resulting in physical cross-linking of their receptors, degranulation and the manufacture of proinflammatory agents such as histamine, prostaglandins, and leukotrienes occur as a result of calcium ion uptake [15] .

IgE and Atopic Respiratory Diseases

Asthma, allergic conjunctivitis besides allergic rhinitis are marked by immune system stimulation. Exposure to in-

haled antigens causes rapid mast cell and basophil cell lysis triggered by IgE, resulting in swelling and airway obstruction in sensitized persons, systemic inflammatory signals are triggered by local inflammation, and peripheral blood leukocytes are further activated. IgE is widely known for playing a key part in the immunopathogenesis of asthma. The fundamental step in immediate-type and inflammatory allergic reactions, including asthma, is the cross-linking of IgE-allergen complex with FcϵRI, which mediates activation of the targeted mast cell and subsequent degranulation and mediator release [16] .

- **IgE Level in Allergic Respiratory Diseases in Iraqi Patients**

Several studies were conducted in various locations of Iraq. The first study, done in 2008 in Samara, Tikrit governorate, reported by Al Obaidi et al included 562 asthmatic patients, whom age range from (17-52) years, This research found that the average serum IgE value in asthmatic was higher (554 +/- 447 IU/ml) than in the comparison group (69 +/- 33 IU/ml), this study also showed that specific immunotherapy can reduce 36% of asthmatic patients had a high blood overall IgE concentration, and that patients who received House-dust mites immunotherapy experienced a greater reduction (47%) than those who received grasses (36%) or mould (16%) vaccinations [17] . Another study in Baghdad was done by Darwesh in 2011 [18] , in which 36 samples of asthma patients and 24 sample of control subjects were incorporated, the research demonstrated that IgE concentration was significantly increased (mean±SD: 101±35.11) in asthmatic cases compared to controls group (mean±SD: 85 ± 20.21).

In Babylon province, 2013 an immunological study was performed on 60 (27 males and 33 females) asthmatic patients and 30 (14 males and 16 females) controls. For comparability, the patients in this analysis were separated into three age groups : (1-20) ,(21-40) besides (41-60) years, The analysis indicated that there was no substantial variation in IgE average between cases and controls in the primary age category, whilst IgE values were considerably increased in the second and final age categories, reaching 74.276 and 68.106 IU/ml, correspondingly, whereas it was 31.541 and 22.807 IU/ml in controls [19] .

Additional study in Babylon, 2013, which was done by Alkhayat et al [20] to find the correlation between IgE and antioxidant level in cases minimal, medium/serious allergic rhinitis (AR) affected. Fifty cases with allergic rhinitis were sub-grouped into two categorize, minimal AR category included 20 cases, second category included 30 cases with medium/serious AR, the age range of both groups is between (20-25) years. IgE values were detected in the serum of medium/serious cases (P <0.01) and a momentous increase in IgE was found in minimal cases of AR patients in contrast to controls (P< 0.05). Further research in Babylon Governorate in 2013 done by Ali , on 25 allergic patients, showed an increased level of IgE in allergic patients (80 IU/ml) than in controls[21] .

In Diyala, Alwan et al in 2014 ,[22] conducted a case-control study in which the patients were divided into two categories, asthmatic set (190) and allergic rhinitis set (110). The average age of the individuals involved in the research was 34.34 ± 11.58 years, the serum IgE mean was much greater in asthma with normal weight category, asthmatic having obesity, asthmatic having metabolic syndrome and allergic rhinitis category than in control category; the mean was 215.873±138.5 IU/ml, 261.758±144.42 IU/ml, 207.103 ±125.515 IU/ml, 110.626±39.353 IU/ml for patients sets correspondingly and it was 82.687±34.4 IU/ml in allergic rhinitis having obesity.

In Babylon, a study conducted by Ishraq in 2015 [23] , in which a total of 87 individuals with allergies and 40 control were involved in the study, their age range was (10-69) years, the immunological parameters showed that there is a significant increase in IgE (448.75 IU/ml) compared to control group (52.11 IU/ml) in age group (10-19) and no significant increase (p> 0.05) of E-rosette test value in the allergic cases (32.6%) compared to control group (17.2%).

In AL-Najaf province, a study conducted in 2016 by Brakhas et al, on 210 cases (110 woman, 100 man) having allergic illness (asthma, urticaria, and rhinitis) with age range from ten to seventy. In asthmatics, there was a relatively marked increase in mean blood whole IgE (503.54 ± 63.49 IU/ml), Allergic rhinitis (442.77 ± 95.76 IU/ml) and urticaria (489.53 ± 69.68 IU/ml) as a compared with healthy controls (23.67 ± 5.81 IU/ml). There were a substantial (P<0.05) a rise in the mean blood amount of total IgE in cases in age category (30-39 years) with asthma (558.049±89.13pg/ml), urticaria (503.262±113.7 pg/ml) and rhinitis (513.934±72.49pg/ml), as comparison to controls (42.05±17.43pg/ml). The mean of serum total IgE levels in men rise in asthma 506.025±138.7 IU/ml, while in women rise in rhinitis 511.398±103.6 IU/ml besides urticaria 412.95 ± 91.74 IU/m [24] .

In Mosul, Bader Fathi in 2017, [25] conduct Receiver Operator Characteristic (ROC) curve study on 751 persons

(561 people suffering from numerous allergy diseases and 190 individuals who are not allergic) age varied from (10-59 year), The generated ROC curve of the whole cohort revealed that total blood IgE has intermediate reliability in allergy disorders, with a 95% confidence interval of (0.7300.022) with asthmatic having the lowest AUC (0.720 0.027).

Another study conducted in Mosul by Al-Hamadany in 2018 to demonstrate the link between Epstein-Barr Viruses (EBV) exposure and asthma, in this study 65 asthma patient (37 females and 28 males), inside the age range of (15-62 years) and 20 healthy controls were included, the study revealed that IgE level was linked to the degree of dyspnea (327.95 IU/ml) and that the elevated amount of IgE in asthmatics was in the age category (45-55years). EBV serotesting demonstrated infections by this virus increased with severity of asthma [26] .

In Anbar province, Hassan et al., 2019 conducted a study to assess overall and particular IgE values in 50 asthmatics (5-60 years) and (10 healthy subjects) as controls [27] . The findings revealed that 56% of sufferers have low or absent IgE concentrations (250 IU/ml), and that particular IgE frequencies varies amongst individuals, the highest specific IgE concentration were in Crab (21.28 IU/ ml) and it was frequent in only one patient, while the lowest concentration was found in Bermuda grass allergen (0.02 IU/ml).

A study conducted by [28] in 2019 in Kirkuk consisted of 20 males and 20 females with ages ranging between (5-65 years) and the majority of cases (37.5%) have allergic bronchitis showed that the highest age group affected was between (36-50) years, and that IgE is more common in females "the sample size is 3.721, the total numbers of females and males are 2.013 (54.1%) and 1.708 (45.9%), respectively".

An empirical cross-sectional investigation was carried out in Baghdad by Turki et al. in 2020 [29] to investigate the allergenic pattern in 653 allergic rhinitis besides 521 asthmatics for the assessment of overall and particular IgE found that the (16-45) years age group was most frequently observed in allergic rhinitis as well as bronchial asthma patients (79.1 and 75.1%, correspondingly). For overall IgE, bronchial asthma sufferers. Throughout all age categories, the amount was considerably greater than in rhinitis sufferers in both sexes. However, overall IgE amounts revealed no remarkable difference among age categories with the exclusion of bronchial asthma cases in the age category > 45 years having the smallest value of IgE (338 ± 269 IU/ml). When the sera were tested for eight allergens, molds were shown to be the most common agent in rhinitis as well as asthma subjects (8.7 and 19.6%, respectively).

Altaii and Al-Tae in Mosul in 2020 conducted a case control research to detect the role of serum overall IgE in the diagnosis of allergenic asthma, dermatitis and rhinitis; 38 asthmatic, 27 rhinitis, 46 dermatitis and 45 controls were involved. The study found that the total IgE means were 316.87 IU/ml (95% CI: 234.69 to 427.82) in allergic asthma, 262.07 IU/ml (95% CI:174.24 to 394.18) in allergic rhinitis and 270.48 IU/ml (95% CI:202.57 to 361.16) in atopic dermatitis contrasted to 16.90 IU/ml (95% CI:12.32 to 23.18) in healthy controls. Indicating that in allergic disorders, overall IgE levels were considerably higher than in controls [30] .

A retrospective case-control study was conducted in 2021 by Shaban et al [31] on 104 (50 woman and 54 man) asthmatic patients and 111 controls. There was a family history of allergies in 51.9% of the cases. In terms of antigen type, 21.2% of asthmatics tested positive for a combination of antigens. The average level of overall IgE was substantially higher in asthmatics (204.1 ng/ml) than in controls (163.3 ng/ml). The overall IgE concentration correlated strongly with illness severity. Serious forms had the greatest amount (244.9 ng/ml), whereas moderate cases had the minimum value (189.7 ng/ml). According to the type of allergen, the level of specific IgE varied across asthma patients, with seronegative subjects having the highest median (215.2 ng/ml), nonetheless, the lowest level was seen in people who tested positive for animal dander (189.3 ng/ml).

A study performed by Jebur and Saud [32] to determine IgE concentrations in the serum of 150 subjects having asthma and 50 control. Findings showed that IgE and IL-13 concentrations, additionally, the proportion of eosinophils, was substantially higher ($p < 0.001$) in cases compared to control group. In order to test IgE levels by ELISA, ALmashhadani and Jawad conducted a study in Baghdad in 2021 with 52 asthmatic patients. Twenty distinct allergens' levels of IgE were assessed in those patients; 25 individuals tested positive for Dermatophagoides farina, 22 tested positive for Birch pollen, 22 tested positive for Alder pollen, and 22 tested positive for Plantain pollen [33].

Conclusions

There is a meaningful link between respiratory allergic symptoms and a high level of total IgE and the value of total blood

IgE has a modest degree of accuracy in diagnosing different allergic disorders. Compared to healthy controls, all Iraqi allergic patients of all ages had significantly higher levels of total IgE with variations in IgE concentrations observed between males and females based on the specific allergic condition. In individuals with allergic asthma and rhinitis, the percentage count of IgE increased significantly.

ETHICAL DECLARATIONS

- **Acknowledgements**

  None.

- **Ethics Approval and Consent to Participate**

  Not required.

- **Consent for Publication**

  Not applicable.

- **Availability of Data and Material**

  No patient data are presented in the study.

- **Competing Interests**

  The authors declare that there is no conflict of interest.

- **Funding**

  Self funded.

- **Authors' Contributions**

  All stated authors contributed significantly, directly, and intellectually to the work and consented it to be published.

REFERENCES

[1] Burton OT, Oettgen HC. Beyond immediate hypersensitivity: evolving roles for IgE antibodies in immune homeostasis and allergic diseases. Immunological reviews 2011;242(1):128–143. https://doi.org/10.1111/j.1600-065X.2011.01024.x.

[2] Sutton BJ, Davies AM, Bax HJ, Karagiannis SN. IgE antibodies: from structure to function and clinical translation. Antibodies 2019;8(1):19. https://doi.org/10.3390/antib8010019.

[3] Mukai K, Tsai M, Starkl P, Marichal T, Galli SJ. IgE and mast cells in host defense against parasites and venoms. In: Seminars in immunopathology, vol. 38 Springer; 2016. p. 581–603.

[4] Shamji MH, Valenta R, Jardetzky T, Verhasselt V, Durham SR, Würtzen PA, et al. The role of allergen-specific IgE, IgG and IgA in allergic disease. Allergy 2021;76(12):3627–3641. https://doi.org/10.1111/all.14908.

[5] Oettgen HC. Fifty years later: Emerging functions of IgE antibodies in host defense, immune regulation, and allergic diseases. Journal of Allergy and Clinical Immunology 2016;137(6):1631–1645. https://doi.org/10.1016/j.jaci.2016.04.009.

[6] Ansotegui IJ, Melioli G, Canonica GW, Caraballo L, Villa E, Ebisawa M, et al. IgE allergy diagnostics and other relevant tests in allergy, a World Allergy Organization position paper. World allergy organization journal 2020;13(2):100080. https://doi.org/10.1016/j.waojou.2019.100080.

[7] Zhang X, Calvert RA, Sutton BJ, Doré KA. IgY: a key isotype in antibody evolution. Biological Reviews 2017;92(4):2144–2156. https://doi.org/10.1111/brv.12325.

[8] Drinkwater N, Cossins BP, Keeble AH, Wright M, Cain K, Hailu H, et al. Human immunoglobulin E flexes between acutely bent and extended conformations. Nature structural & molecular biology 2014;21(4):397–404.

[9] Gould HJ, Sutton BJ, Beavil AJ, Beavil RL, McCloskey N, Coker HA, et al. The biology of IGE and the basis of allergic disease. Annual review of immunology 2003;21(1):579–628. https://doi.org/10.1146/annurev.immunol.21.120601.141103.

[10] Sutton BJ, Davies AM. Structure and dynamics of IgE–receptor interactions: Fcε RI and CD 23/Fcε RII. Immunological reviews 2015;268(1):222–235. https://doi.org/10.1111/imr.12340.

[11] Bax HJ, Keeble AH, Gould HJ. Cytokinergic IgE action in mast cell activation. Frontiers in Immunology 2012;3:229. https://doi.org/10.3389/fimmu.2012.00229.

[12] Vitte J, Vibhushan S, Bratti M, Montero-Hernandez JE, Blank U. Allergy, anaphylaxis, and nonallergic hypersensitivity: IgE, mast cells, and beyond. Medical Principles and Practice 2022;31(6):501–515. https://doi.org/10.1159/000527481.

[13] Eckl-Dorna J, Villazala-Merino S, Campion NJ, Byazrova M, Filatov A, Kudlay D, et al. Tracing IgE-producing cells in allergic patients. Cells 2019;8(9):994. https:

//doi.org/10.3390/cells8090994.

[14] Kumar S, Jeong Y, Ashraf MU, Bae YS. Dendritic cell-mediated Th2 immunity and immune disorders. International journal of molecular sciences 2019;20(9):2159. https://doi.org/10.3390/ijms20092159.

[15] Nguyen SMT, Rupprecht CP, Haque A, Pattanaik D, Yusin J, Krishnaswamy G. Mechanisms governing anaphylaxis: inflammatory cells, mediators, endothelial gap junctions and beyond. International journal of molecular sciences 2021;22(15):7785. https://doi.org/10.3390/ijms22157785.

[16] Lavinskiene S, Jeroch J, Malakaskas K, Bajoriuniene I, Jackute J, Sakalauskas R. Peripheral blood neutrophil activity during Dermatophagoides pteronyssinus-induced late-phase airway inflammation in patients with allergic rhinitis and asthma. Inflammation 2012;35:1600–1609.

[17] Ahmad Al Obaidi AH, Mohamed Al Samarai AG, Yahya Al Samarai AK, Al Janabi JM. The predictive value of IgE as biomarker in asthma. Journal of asthma 2008;45(8):654–663. https://doi.org/10.1080/02770900802126958.

[18] Darwesh MF. Immunological aspects on asthmatic patients. Collage of Science, Kufa university, Iraq 2011;p. 1–6.

[19] Alaa J, Thanaa A. Immunological study of patients with asthma. Journal of Babylon University/Pure and Applied Sciences 2013;21(7):56–61.

[20] Al-Khyat THAT, Alturaihy SH, Ali ZA. The Relationship between Tumour Necrosis Factor-alpha, IgE Levels and Oxidative Stress In Iraqi Patients with Allergic Rhinitis. Medical Journal of Babylon 2013;10(4):969–975.

[21] Al-khafaji AMS. Estimation level Immunoglobulin IgE by using kit of immuno electrographic and some parameters Humeral and cellular immune response for allergy patients. Al-Qadisiyah Journal of Pure Science 2013;18(4).

[22] Alwan AH, Alobaidi AHA, Alsamarai AM. Leptin, obesity and IgE in patients with asthma and allergic rhinitis 2014;http://148.72.244.84:8080/xmlui/handle/xmlui/8764.

[23] ALmaamory I. Estimation of Specific Immunoglobulins E, A Antibodies and E-rosette in Allergic Patients. Journal of the University of Babylon 2015;23(2):779–785.

[24] Brakhas SA, Hassan AJ, Jassim AN. Study of total Immunoglobulin E and Eosinophil count in allergic disease. Baghdad Science Journal 2016;13(2):0298–0298. http://dx.doi.org/10.21123/bsj.2016.13.2.0298.

[25] Bader Fathi H. Receiver Operating Characteristic Curve of Total Serum IgE in Allergic Patients. Mosul Journal of Nursing 2017;5(2):77–82.

[26] Al-Hamadany AYM. Estimation of serum immunoglobulin E level in asthma and its correlation with Epstein Barr Virus (EBV) infection. Tikrit Journal of Pure Science 2018;23(9):12–15. http://dx.doi.org/10.25130/tjps.23.2018.143.

[27] AL-Alouci MM, AL-Janabi OA, AL-Haiani NN. TOTAL AND SPECIFIC (INHALATIVE) IgE IN ASTHMATIC PATIENTS IN RAMADI CITY, IRAQ. Biochemical & Cellular Archives 2019;19(1). http://dx.doi.org/10.35124/bca.2019.19.1.645.

[28] Ahmed AA, Fathala FN, Majeed DM. Measurement of IgE hypersensitivity among people attending the tertiary allergic center in Kirkuk, Iraq. Al-Kitab Journal for Pure Sciences 2019;3(2):259–267.

[29] Turki SG, Ad'hiah AH, Brakhas SA, Atiyah MR. Allergen profile of rhinitis and asthma among Iraqi patients. Clinical Epidemiology and Global Health 2020;8(2):637–642. https://doi.org/10.1016/j.cegh.2019.12.018.

[30] Altaii HA, Al-Tae FM. Investigation of serum total IgE and eosinophil levels in different allergic diseases together with the study of their correlations with various possible allergens in Mosul City. Immunological Investigations 2022;51(3):567–587. https://doi.org/10.1080/08820139.2020.1853154.

[31] Shaban SA, Brakhas SA, Ad'hiah AH. Significance of total and specific IgE in asthma of Iraqi adult patients. Tikrit Journal of Pure Science 2021;26(1):1–7. http://dx.doi.org/10.25130/tjps.26.2021.001.

[32] Jebur MS, Saud AM. Serum levels of total IgE and interleukin-13 in a sample of allergic asthma patients in Baghdad. Iraqi Journal of Science 2020;p. 3208–3214.

[33] Ola Kamal MAJ Zuhair Ibraheem ALmashhadani. Identification Of Specific Ige In Asthmatic Patients In Iraq. Systematic Reviews in Pharmacy 2020;12(1):1170–1174. http://dx.doi.org/10.31838/srp.2021.1.161.