ORIGINAL ARTICLE

The Role of Interleukin 33 in patients with Allergic Diseases who has a positive result of total and specific IgE

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ABSTRACT

Background: Allergic diseases affect a large group of population and the common types were asthma, rhinitis, and urticaria and newly found that IL-33 playing an important role in the pathogenicity of allergic diseases.
Aim: To evaluate the levels of IL-33 in adult patients has real allergic diseases (asthma, rhinitis, and urticaria) through detection of both positive assays of total and specific IgE of allergic diseases.
Methods: The total and specific immunoglobulin E (IgE) and IL-33 were determined in the serum of three types of allergic patients and healthy controls.
Results: There were highly significantly higher concentrations of IgE and IL-33 in the serum of patients with allergic diseases. Serum IL-33 and total IgE concentration are clearly statistically highly significant increases in three groups of patients (Rhinitis, Asthma, Urticaria) compared with healthy control ($p< 0.001$). No significant correlation between IL-33 levels and total IgE in four groups.
Conclusion: Our results show a significantly higher concentration in serum level IL-33 of patients with three types of allergic diseases (asthma, rhinitis, and urticaria).
Keywords: interleukin 33, allergic diseases, specific IgE.

INTRODUCTION

The common types of allergic diseases are asthma, rhinitis, and urticaria and these diseases consider as hypersensitivity disorders and newly found that IL-33 playing an important role in the pathogenicity of allergic diseases[1, 2].

Interleukin (IL33) is a regulatory cytokine from IL-1 cytokine family and it consider as an alarmin that alerts the immune system, its produce by many types of cells like epithelial cells of (skin, lungs, and gastrointestinal tract that exposure to the environmental allergens), endothelial cells, osteoblast, fibroblasts, adipocytes, smooth muscle cells, macrophages and dendritic cells (DCs)[3,5] and after exposure to the exogenous antigen or allergen, IL33 released to stimulate the first line cells of the immune system such as epithelial cells[6], which activate allergic reactions through type-2 innate immunity cells[5] and promotes circulating CD34+ stem cells to proliferate and produce IL-5 and IL-13 which known as pro-allergic cytokines and stimulates mast cells, eosinophils, Th2 cells, and basophils[(7)], and recent study by Cayrol et al 2018[6] showed when human exposure to environmental allergens.

The IL33 has a protease sensor property which reveals proteolytic activities, that leads the generation of group 2 innate lymphoid cells and reduces allergic inflammation, while Chan and his colleagues 2019 [(5)] indicate that IL33 has various immune regulatory occurrences in addition to its role in the pathogenicity of allergic diseases through a combination of its blocking agents and may be interference by the synergistic characteristic in allergic and inflammatory diseases and they added that need further essential extensive clinical trials studies on allergic diseases.

The main goal of this research to evaluate the levels of IL-33 in adult patients has real allergic diseases (asthma, rhinitis and urticaria) through both positive assays of total and specific IgE of allergic diseases.

MATERIAL AND METHODS

Study group: A total of seventy-four patients (37 women, 37 men), blood samples were collected and the sera were separated and stored at –70 °C until use for serological test. Patients from with allergic diseases (24 Rhinitis patients, 26 Asthma patients, 24 Urticaria) who have a signs of one of the three types of allergic diseases who revise in the Allergic Specialized Center\Baghdad-Resafa and diagnosed by a physician and Control samples collected from twenty-eight healthy control groups with no signs of allergic diseases or any other disease (14 women, 14 men) were selected who have normal concentrations of total IgE.

Serological test: Measuring the Total IgE (which estimated by Immunoenzymetic Assay using the total IgE ELISA kit, (Euroimmum/German), and specific IgE (done by the western Immunoblotting method by using a kit has a specific IgE for 20 Inhalation allergens from Polycheck-Allergy Diagnostic/Germany).

The serum IL-33 concentrations were determined according to the manufacturer's instruction of commercial enzyme-linked immunosorbent assay (ELISA) kits (Shanghai Yehua Biological Technology /China).

Statistical analysis: The statistical was done by MINITAB Statistics version 13 software, analysis of variance (ANOVA) was achieved for comparison of variables between groups and a P-value less than 0.05 was considered statistically significant. And specific IgE results were expressed as a percentage. The experimental procedure for using human blood was obtained by informed written agreement from all subjects.

RESULT AND DISCUSSION

The patients in this study were allergic patients due to elevation of IgE and give a positive reaction with specific IgE to different allergens, where we note from the table (1) some patients will have a lot of triggers, while others may

only react to one or two items, some triggers are easier to avoid than others while grass and tree are common causes of spring allergy.

The results of specific IgE indicated a presence for one or more inhalant allergens in sera of asthma, rhinitis and urticaria patients to 20 inhalant allergens, these results indicated that the highest percentage in rhinitis patients were for Tree allergens (t2, t3, t4, t7), Grasse's allergens (g6, g12) and Weeds allergens (w6, w9) and higher in males than females, while the results of asthma patients were similar to rhinitis patients, but the proportion was higher in female than male, while the results of urticaria patients showed that the highest percentage were against mite allergens (d1,d2) and different animal allergens (e1, e2, e3, e5, e6, e82, e84)and the proportion was higher in female than male table 1, these results indicate that there is a variance in terms of the most common allergens in allergic patients. This difference may be due to several factors, including the size of the sample under study, type of allergic disease, season, age, geographical location, and housing environment (rural or city centers).

This study has shown an association of mite and animal sensitivity with urticaria due to high percentage of these two allergens, as many studies[8,9,10], and Henszel and their colleagues[10] indicate that mites effuse plenty of allergenic proteins especially mite faeces and the extracts of allergenic proteins from their purified bodies which may inflict atopic allergies (respiratory and dermal), such as bronchial asthma, rhinitis, or atopic eczema, and they added that 5% of the population is sensitive to mites allergens.

Serum IL-33 and total IgE concentration are clearly statistically highly significant increase in three groups of patients (Rhinitis, Asthma, Urticaria) in compared with healthy control ($p< 0.001$). No significant correlation between IL-33 levels and total IgE The immune environment of allergic diseases maybe not fully understood, the prevalence of allergic diseases as a chronic inflammatory disease has been rapidly increasing in last decades in the worldwide, and despite rhinitis and asthma are diseases effect on respiratory system but there were differences between two these diseases and urticaria also , in normally state there were dynamic balance between Th1 and Th2 while when an allergic disease occur due to environmental allergens cause breaking of dynamic balance between Th1 and Th2, and Th2 play a triggering role in the induction of IgE antibody-producing B cells, mast cells, and eosinophils[11,12], and these cells are found in all the tissues, especially in areas that are typical sites of allergic reactions, those sites include mouth, nose, throat, lungs, skin, and gastrointestinal (GI) tract that becomes inflamed due to an allergic reaction.

Many studies indicate IL-33 may play an important role in the allergic process, our data were in agreement with the observation of many studies as Ding and his colleagues in 2018 explained in their articles that IL-33 supports persistent structural changes, especially in airway hyper responsiveness by activating several signaling pathways and inflammatory cells in allergic asthma , while Sakashita 2008[16] and Glück 2012[17] and their colleagues found significant elevated of IL-33 in serum and consider as a marker of the disease severity, and Du[18] and his colleagues 2016 found an elevated in allergic dermatitis patients. Cayrol and Girard 2014[13] indicate that IL-33 production depends on cellular stress or cellular damage, and Oboki *et al*., 2010[14], Mjosberg *et al*., 2011[15], Khaitov *et al* 2018[11] in vivo experiments found IL-33 play crucial roles in allergic inflammation, type-2 immunity, and eosinophil homeostasis, and Chan and their colleagues 2019[5] added that IL33 liberated during cell damage and necrosis and activation of allergic inflammation through promoting production of inflammatory factors and chemotactic factors [(11)] like IL-4, IL-5, and IL-13 that progress allergic inflammation.

Many studies as Ding and his colleagues in their article said the IL-33 protein has a role in the pathophysiology of allergic diseases, by commanding the activation of various ST2-expressing cells and the production of several immune factors, more studies should be conducted for explaining the potential role of the IL-33 in allergic diseases.

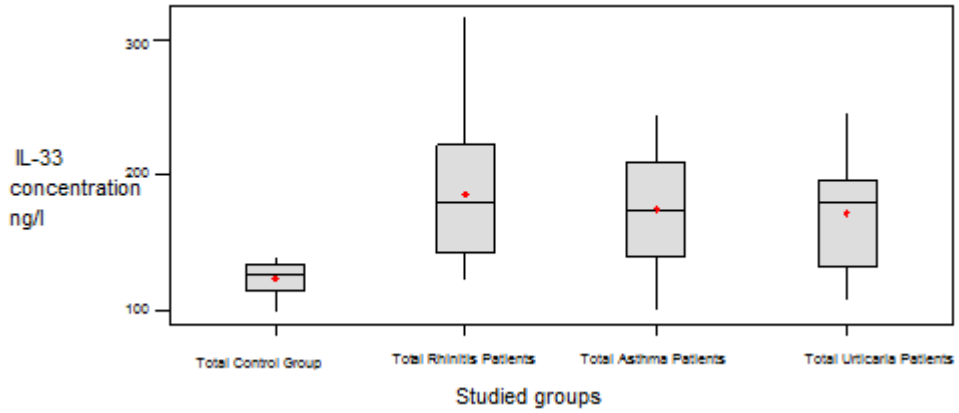
Table 1: the percentage of the type of specific IgE to inhalant allergens distributed among three allergic patients groups

Inhalant allergens	Rhinitis n = 24	Asthma n = 26	Urticaria n =24
Mite (d1,d2)			
Male	2(8.3%)	4(15.4%)	2(8.3%)
Female	5(20.8%)	3(11.5%)	3(12.5%)
Total	7(29.2%)	7(26.9%)	5(20.8%)
Tree (t2, t3, t4, t7)			
Male	10(41.7%)	4(15.4%)	1(4.2%)
Female	5(20.8%)	10(38.5%)	2(8.3%)
Total	15(62.5%)	14(53.8%)	3(12.5%)
Grasses(g6, g12)			
Male	6(25%)	4(15.4%)	0
Female	4(15.4%)	7(26.9%)	0
Total	10(41.7%)	11(42.3%)	0
Mold(m1, m2, m3, m6)			
Male	0	1(3.8%)	0
Female	3(12.5%)	1(3.8%)	2(8.3%)
Total	3(12.5%)	2(7.6%)	2*8.3%)
Weeds (w6, w9)			
Male	6(25%)	5(19.2%)	0
Female	3(12.5%)	5(19.2%)	0
Total	9(37.5%)	10(38.5%)	0
Animal (e1, e2, e3, e5, e6, e82, e84)			
Male	2(8.3%)	3(11.5%)	3(12.5%)
Female	5(20.8%)	4(15.4%)	2(8.3%)
Total	7(29.2%)	7(26.9%)	5(20.8%)

Table 2: the demographic parameters for studied groups

	Control (28) Mean ± SD	Rhinitis Pts (24) Mean ± SD	Asthma Pts(26) Mean ± SD	Urticaria Pts (24) Mean ± SD	P value groups vs. control
IL-33ng/l	124.04±13.03	185.67±48.72	174.65±42.91	172.13±38.73	0.000**
IgE	36.6±25.4	342.5±151.7	397.2±128.6	321.8±134.6	0.000**
Age	30.07±9.72	31.21±11.25	30.19±8.36	33.96±12.79	NS
Wight	69.57±16.37	71.67±12.75	79.04±13.86	73.42±10.90	NS

Fig1: The concentration of IL-33 among studied groups.



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