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RESEARCH ARTICLE

Study of serum interleukin 33 and heat shock protein70 in allergic disease

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Abstract

Allergic and hypersensitivity reactions are the results of immune response to allergens; this response is mediated by IgE antibody specific to the allergen. Mast cells, basophiles are activated after IgE bindings, starting a serious of cellular and molecular events that results in the clinical manifestation of allergic diseases. Type I reactions underlie atopic disorders (eg, allergic asthma, rhinitis, urticaria). Type I reactions develop < 1 h after exposure to antigen. The present study was aimed to evaluate the levels of interleukin 33 and heat shock protein 70 in allergic disease. interleukin 33 and heat shock protein 70 were done for 73 patients with allergic disease (allergic asthma, allergic rhinitis, and urticaria) their age between (10-70) years and 15 healthy control their age between (16-54) years collected from Allergy Specialized Center in Baghdad /AL-Resafa, during the period from April 2014 to September 2014. A highly significantly ($p<0.001$) increased in the mean level of serum interleukin 33 in patients with, allergic asthma, rhinitis, and urticaria (42.01 ± 4.67 , 39.94 ± 6.07 , 27.49 ± 2.90 pg/ml) respectively as compared with healthy controls (18.73 ± 2.73 pg/ml) while the levels of shock protein 70 was increased significantly ($P < 0.05$) only in asthmatic patients (32.51 ± 3.85 ng /ml), as compared with healthy control (15.94 ± 4.27 ng /ml). Allergic disease associated with increased of serum IL-33 while HSP70 increased only in asthmatic patients. From this we can deduce that elevation of IL-33 is associated with allergic disease and HSP70 is associated with allergic asthma and may be a marker of the disease severity and potential therapeutic targets.

INTRODUCTION

Type I reactions (immediate hypersensitivity) are IgE-mediated. Allergen binds to IgE that is bound to tissue mast cells and blood basophils, triggering release of preformed mediators (eg, histamine, proteases, chemotactic factors) and synthesis of other mediators (eg, prostaglandins, leukotrienes, platelet-activating factor, cytokines). These mediators cause vasodilation, increased capillary permeability, mucous hypersecretion, smooth muscle spasm, and tissue infiltration with eosinophils, type 2 helper T (T_H2) cells, and other inflammatory cells [1]. Asthma is a chronic allergic disorder of the airways in which many cells and cellular elements play a role in particular mast cells .The inflammation causes recurrent symptoms of breathlessness, wheezing, chest tightness and cough usually there is a widespread airflow obstruction with these episodic symptoms which is reversible to varying degrees either spontaneously or with treatment[2]. Allergic rhinitis is an acute IgE mediated type I hypersensitivity reaction of nasal mucosa in response to antigenic substances (allergens) associated with episodic attacks of sneezing, watery rhinorrhea and watering of the eyes, patients also present tightness of chest due to subclinical bronchospasm [3] . Urticaria (hives) is a common disorder, occurring in 15- 25% of individuals at some point in life, It is characterized

by recurrent, pruritic (itchy), pink-to-red edematous (swollen) lesions that often have pale centers (wheals) . The lesions can range in size from a few millimeters to several centimeters in diameter, and are often transient, lasting for less than 48 hours [4]. Interleukin (IL)-33 is a new member of the IL-1 superfamily of cytokines that is expressed by mainly stromal cells, such as epithelial and endothelial cells, and its expression is upregulated following pro-inflammatory stimulation [5,6] . IL-33 strongly induces Th2 cytokine production from these cells and can promote the pathogenesis of Th2-related disease such as asthma, rhinitis and urticaria [7] . Heat shock proteins (HSPs) are molecular chaperones essential for maintaining cellular functions by preventing misfolding and aggregation of nascent polypeptides and by facilitating protein folding [8,9] . Hsp70, have also been reported to play important roles in antigen presentation, activation of lymphocytes and macrophages, and activation and maturation of dendritic cells (APCs). Thus, it has been suggested that HSPs provide the link between innate and adaptive immune systems and that their presence in the circulation serves as danger signals to the host [10].

Material and methods

The study was carried out at the allergy specialized center in Baghdad/AL-Resafa from April 2014 to September 2014. 73 patients with allergic disease were classified into three groups, (28 asthma, 20 rhinitis, and 25 urticaria) , and 15 individual as a healthy control. Both physical and clinical examinations were done for each subject and the information was recorded in a data sheet. 5 ml blood samples were collected for estimation of serum interleukin 33 by ELISA using kit from PEPROTEACH (USA), and serum heat shock protien 70 by ELISA using kit from CUSABIO (china).

Statistical Analysis

The Statistical Analysis System- SAS (2012) was used to effect of different factors in study parameters. Least significant difference –LSD test was used to significant compare between means. Estimate of correlation coefficient between difference parameters in this study (SAS, 2012) .

Results:

In the present study, 28 patients with allergic asthma, 11 (39.29%) males and 17 (60.71%) females, their mean age was (34.80± 1.59) years, 20 patients with allergic rhinitis, 11 (55%) males and 9 (45%) females, their mean age was (34.58± 2.04) years 25 patients with urticaria, 16 (64%) males and 9 (36%) females, their mean age was (29.20± 3.98) years, as compared to 15 healthy control group, 8(53.33%) males and 7(46.66%) females, their mean age was (36.44± 1.99) years. The general characteristics of the studied groups are presented in table (1).

Table (1): General characteristic of the studied groups.

Parameters	Controls	Allergic asthma	Allergic rhinitis	urticaria
Total number	15	28	20	25
Male	8(53.33%)	11(39.29%)	11(55%)	16(64%)
Female	7(46.66%)	17(60.71%)	9(45%)	9(36%)
Age(mean±SE)	(36.44± 1.99)	(34.80± 1.59)	(34.58± 2.04)	(29.20± 3.98)

A highly significantly ($p<0.001$) increased in the mean levels of serum IL-33 in patients with allergic asthma (42.01 ± 4.67 pg/ml),allergic rhinitis (39.94 ± 6.07pg/ml),and urticaria (27.49 ± 2.90pg/ml), as compared with healthy controls (18.73 ± 2.73 pg/ml) as shown in table (2).

Table (2) The concentration of IL-33 in studied groups

study Group	NO.	Minimum	Maximum	IL-33(pg/ml) Mean ± SE
Allergic asthma	28	12.5	90.7	42.01 ± 4.67**
Allergic rhinits	20	13.56	520.7	39.94 ± 6.07**
Allergic urticaria	25	12.5	110.6	27.49 ± 2.90**
Control	15	12.5	32.5	18.73 ± 2.73
LSD value	**14.632 ****			
P-value	**0.0071**			

**** (P≤0.01)**

Table (3) showed that patient with allergic asthma (32.51 ± 3.85 ng/ml) have significantly ($p<0.05$) elevated in the mean of serum HSP70 as compared with healthy controls (15.94 ± 4.27 ng/ml), while there was no change in the level of HSP70 in patients with allergic rhinitis (19.51 ± 2.19 ng/ml) and urticaria (19.63 ± 3.76 ng/ml) as compared with healthy control(15.94 ± 4.27 ng/ml)

Table (3) Comparison between groups in HSP70

Group	NO.	Minimum	Maximum	HSP70 (ng/ml) Mean ± SE
Allergic asthma	28	10.3	79.4	**32.51 ± 3.85***
Allergic rhinits	20	7.5	37.6	**19.51 ± 2.19**
Allergic urticaria	25	2.7	64.3	**19.63 ± 3.76**
Control	15	7.8	41.7	**15.94 ± 4.27**
LSD value	**12.976 ***			
P-value	**0.0207**			

*** (P≤0.05),** NS: Non-significant.

there was a significant ($p<0.05$) positive correlation between IL-33 and HSP70 in asthmatic patients.While no significant correlation was observed in patients with allergic rhinitis and urticaria as presented in table (4).

Table 4. Correlation coefficient between IL-33 and HSP70 in allergic disease

Allergic groups	Correlation coefficient (r)	Level of sig.
asthma	**0.23**	*
rhinitis	**0.09**	**NS**
urticaria	**0.13**	**NS**
* (P≤0.05).		

Discussion

Allergic diseases are characterized by the IgE-dependent release of mast cell-derived mediators and cellular infiltration particularly of activated eosinophils and T-lymphocytes [1]. These data in agreement with previous studies who reported that serum IL-33 level may be elevated in certain allergic disease conditions, the present result like the study by Prefontaine *et al*,(2010) [12] when found The levels of IL-33 are higher in lung smooth muscle or epithelial cells from asthmatic patients than from healthy control subjects.

Our present findings are in agreement with previous study by Yashimoto and Matsushita (2014) [13] showed that both endogenous IL-33 and pollen -specific Th2 immunity contribute to the nasal accumulation of basophils in allergic rhinitis. IL-33 protein is constitutively expressed in the nucleus of nasal epithelial cells and is promptly released into nasal fluids in response to nasal exposure to pollen, that leads to development of sneezing and the nasal accumulation of eosinophils and basophils by increasing histamine release and inducing the production of chemo attractants from FcεRI+ mast cells and basophils, respectively. Hsu *et al*,(2010)[14] showed differences in the baseline levels of IL-33 within the skin in urticaria.

Allergic asthma patients showed a significant($P < 0.05$) increase in level of HSP70 as compared with the control. This result was compatible with studies done by Tamási *et al*,(2010)[15] and Changchun*et al*,(2011)[16] who suggested that HSP70 concentrations are elevated in asthma patients and supports a potential role for HSP70 as a new biomarker for asthma. the finding of mean value of serum HSP70 concentrations for allergic rhinitis and urticaria indicates that there is at no significantly (NS) level in patient compared to healthy controls, that results was

disagree with what have been for Lisi *et al*, (2003)[17] who found It was concluded that the elevated HSP70 level in peripheral lymphocytes of the allergic rhinitis patients might contribute to the development of allergic rhinitis.

Many studies reported that their was positive correlation among serum interleukin 33 level and heat shock protein 70 in allergic asthma, but their was no associated between allergic rhinitis, urticaria and HSP70 . Luzina *et al*,(2013)[18] and Dickel *et al.*,(2010)[19] was reported that IL-33 was found to increase the expression of several heat shock proteins (HSPs) significantly, and in particular HSP70, which is known to be associated with asthma. While there is no correlation among its in rhinitis and urticaria.

Conclusions: This study provided evidence that IL-33 is associated with allergic disease and HSP70 is associated with allergic asthma and may be a marker of the disease severity and potential therapeutic targets.

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