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ROLE OF INTERLEUKIN-6 AND INTERLEUKIN-25 IN THE DEVELOPMENT OF RESPIRATORY ALLERGY THAT AFFECTED BY HOUSE MITES ALLERGEN IN IRAQ

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Abstract

House Dust Mite allergy is type of respiratory allergic disease that is related to phylum Arachnid. A large proportion of patients with both of Allergic Rhinitis, and Allergic Asthma are sensitized to mites species, which are found in dark humid areas. This study aims was design to shed light on the relations of interleukin (IL-6 and IL-25) in the development of Allergic Rhinitis and Allergic Asthma that Sensitized to Dust Mites allergen. The sample patients was collected from specialized center of Allergy in Baghdad / Al-Resafa during the period from October 2017 to march 2018. A total 90 of house mite allergy patients and healthy volunteer were identified belonging to 3 groups as follows : [30] of allergic asthma (12 males and 18 females) with age between (15-50) year, [30] patients sample with allergic rhinitis, in gender (10 males and 20 females) with age between (20-45) year, this group for patient sensitized to house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), other groups of [30] healthy volunteer in gender (14 males and 14 females) with age between (22- 45) year. This type of allergy was diagnosed by Pulmonary Function Test, Skin Prick test for house dust mite, detected of Eosinophil count, measured serum level of Interleukins IL-6 and IL-25 . There is a highly significant difference between studied groups ($p=0.0064$), ($p<0.01$) in IL-6, and There is no significant difference between studied groups ($p=0.547$) in IL-25. In this study the level interleukins play important role as indicator for dust mites allergy.

***Keywords*:** Dust Mites, Interleukin-6, Interleukin-25, Allergic Rhinitis, Allergic Asthma.

Introduction

Mites allergy is a type of respiratory allergic disease that are able to sensitize and induce allergic disease (Fernández *et al.*, 2014) such as allergic asthma and allergic rhinitis (Arshad, 2010; Blomme *et al*., 2013). Asthma is chronic disease associated with immune system inflammation (Athari *et al*., 2016; Chaparzadeh *et al*., 2016), which leads to distinct structural and functional changes, including Airway Hyper Responsiveness (AHR) and remodeling (Holgate, 2012), associated with an increased risk factor, exacerbation reduce quality of life, reduced productivity increased health care utilization and debilitation (Demoly *et al*., 2012).

Asthma is a characteristic of different phenotypes of chronic airway inflammation, including allergic asthma (extrinsic) which caused by inhalation of environmental allergens like house dust mite (Bunyavanich and Schadt, 2015; Calderón *et al*., 2015) and non allergic asthma (intrinsic) often develops later with no family history of allergy.

Allergic Rhinitis (AR) is allergic disease of the nasal mucosa that are related to the type-I hypersensitivity. Different factors cause the development of rhinitis pathogenesis like environmental and genetic factors (Greiner *et al*., 2011; Li *et al*., 2015). Mites are generally be divided into two groups; house dust mites group for example *Dermatophagoides pteronyssinus* and *Dermatophagoides farina* ,which live in textile of pillows and carpets and storage mites groups like *Glycyphagus domesticus*, that live in storage facilities of some storage grains like, hay, corn and wheat (Radauer *et al*., 2014).

Interleukin -6 is a glycoprotein that is produced from innate immune system cells like Mast Cells (MCs), and Dendritic Cells (DCs), is secreted from a number of malignant cells, endothelial cells, fibroblasts a strictest , and epithelial cells (Hirano, 1998). Interleukin-6 is important in patients suffering from (AA) with accounts about (50%) in all asthmatics state (Neveu *et al*., 2010).

Interleukin -25 (an IL-17 cytokine family member) can enhance and induce the production of Th2 cell expansion and cytokines of Th2 like IL-4 or IL-5 (Iwakura *et al*., 2011; Morita *et al*., 2015). Elevated expression of IL-25 occur in tissues of patients with asthma, atopic dermatitis, and chronic rhino sinusitis, that means a possible link between the functions of IL-25 and the exacerbation of allergic disorders (Angkasekwinai *et al*., 2007; Corrigan *et al*., 2011; Hvid *et al*., 2011; Shin *et al*., 2015). Skin tests are methods that are considered to be the standard for diagnosing of specific IgE-mediated HDM allergen sensitization (Prescott and Tang, 2005; Pawankar *et al*., 2012). It is performed in vivo because this test is fast, safety, inexpensive and widely used for the detection of IgE associated with allergies (Krouse and Mabry, 2003). The major aim of study to investigate the role of IL-6 and

IL-25 in the Development of Respiratory Allergy that Sensitized to Mites allergen in Iraq.

Material and Methods

The sample patients divided in three groups: [30] of allergic asthma (12 males and 18 females) with age between (15-50) year, [30] patients sample with allergic rhinitis, in gender (10 males and 20 females) with age between (20-45) year, and [30] healthy volunteer (14 males and 14 females) with age between (22- 45) year. This groups for house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farina*). The sample patients groups was collected from specialized center of Allergy in Baghdad /Al-Resafa ,with diagnoses by , medical history and physical examination were obtained include, pulmonary function test (PFT), skin prick test, detected the differential WBCc and Eosinophil counts and investigation the development of respiratory allergy that sensitized to Mites allergen in Iraq by serum level IL-6 and IL-25 level.

Statistical Analysis

The Statistical Analysis System- SAS (2012), program was used to effect of difference factors in study parameters. Chi-square test was used to significant compare between percentage and Least significant difference –LSD test (ANOVA) was used to significant compare between means in this study. Genotype frequencies were analysed statistically by the chi-square test. The Hardy-Weinberg equilibrium was estimated using the x^2 test.

Results and Discussion

The results in studied groups were compared to the WBC count; allergic asthma [(7913.33 ±287.82)], allergic rhinitis is [(7559.33 ±408.69)] and healthy control [(6020.00 ±322.86)] as shown in Table (1) below. There are highly significant differences between them (p=0.0004), (P<0.01).

Table 1 : Distribution of allergic patients with allergy mites according to WBCs in comparison with healthy control.

Hematological assay		No.	Mean	P – value	
				ANOVA test	LSD test
WBCs Count (X 1000)	Asthma	30	7913.33 ±287.82 a	P=0.0004 Highly sign. (P<0.01).	965.74 **
	Rhinitis	30	7559.33±408.69 a		
	control	30	6020.00±322.86 b		
	Total	90			

The results in studied groups were compared to the Eosinophil Cell (%) ; allergic asthma [(6.03 ± 0.32)] , allergic rhinitis is [(5.93 ± 0.36)] and healthy control [(2.40 ± 0.17)], Figure (2). There are highly significant differences between studied groups (p=0.0001), (P<0.01).

Table 2 : Distribution of allergic patients with allergy mites according to Eosinophil cell count in comparison with healthy control.

Hematological assay		No.	Mean	P – value	
				ANOVA test	LSD test
Eosinophil count (%)	Asthma	30	6.03 ± 0.32 a	P=0.0001 Highly sign. ** (P<0.01)	
	Rhinitis	30	5.93 ± 0.36 a		0.841 **
	control	30	2.40 ± 0.17 b		
	Total	90			

The results of studied groups when compared to the Interleukins-6 (IL-6); allergic asthma was (27.03 ± 4.87), allergic rhinitis is (15.47 ± 1.59) and healthy control was (14.47 ± 0.99). There is a highly significant difference between studied groups (p=0.0064), (p<0.01) as shown in Table (3)

Table 3 : Distribution of allergic patients with allergy mites according to IL-6 levels (pg/ml) in comparison with healthy control.

Immunological assay		No.	Mean	P – value	
				ANOVA test	LSD test
IL-6 (ng/ml)	Asthma	30	27.03 ± 4.87 a	P=0.0064 Highly Sign. (p<0.01)	8.479 **
	Rhinitis	30	15.47 ± 1.59 b		
	control	30	14.47 ± 0.99 b		
	Total	90			

The results in studied groups were compared to the Interleukins-25 ; allergic asthma [(16.75 ± 3.56)] , allergic rhinitis is [(18.33 ± 3.32)] and healthy control[(13.87 ± 1.22)]. There is no significant difference between studied groups (p=0.547) as shown in Table (4) below .

Table 4 : Distribution of allergic patients with allergy mites according to IL-25 levels (pg/ml) in comparison with healthy control.

Immunological assay		No.	Mean	P – value	
				ANOVA test	LSD test
IL-25 (ng/ml)	Asthma	30	16.75 ± 3.56	P=0.547 NS: Non-Significant	
	Rhinitis	30	18.33 ± 3.32		8.161 NS
	control	30	13.87 ± 1.22		
	Total	90			

The results of WBC count were in agreement with many studies in Iraq such as (Ava and Wasima, 2013) who showed the significant difference in total WBC count in allergic asthma and rhinitis patients when compared with control. Other studies of WBC count (Wahhab, 2013; Al-Yasiri, 2014) in Iraq recorded that there are no significant differences between allergic patients and control.

Allergic disease leads to increase the WBC count and eosinophils, basophils during allergic mechanism. White Blood Cell count is considered as an important component of cell that may release high amounts of (Histamine) especially in airway disease. So the higher level of (WBCs) is an indicator that is associated with (Histamine) and other inflammatory markers (Ava and Wasima, 2013).

The results of Eosinophile cell count % were in agreement with several Iraqi studies such as (Abd-Alwahaab, 2007; Brakhas *et al*., 2015; Rasheed *et al*., 2016) in Iraq which have high significant differences in eosinophil count mean in allergic rhinitis patients when compared with control. Hassan (2015) and Brakhas *et al*., (2016) recorded the increase in Eosinophil Cell Count (%) in allergic asthma and rhinitis. (Wahhab, 2013) reported the significant

difference in Eosinophil Cell Count (%) in allergic asthma patients when compared with control.

This study about IL-6 agrees with (Lajunen *et al*., 2016) who reported a significant association of the IL- 6 with the risk of adult-onset asthma, and especially with the atopic adult onset asthma. In (Rincon and Irvin, 2012) showed the increased level of IL-6 in many airway disorders .It is related to product of ongoing inflammation of lungs. (Yokoyama *et al.,* 1995) showed the elevated IL-6 level into plasma or serum of patient suffering from Allergic Asthma. IL-6 a cytokine produced by inflammatory cells is also produced by primary lung epithelial cells in response to a variety of different stimuli including allergens. Interleukin -6 Level was founded with increased level of inflammation disorder. This Interleukin also secreted from non leukocytes like, Endothelial cell, Fibroblasts Astrocytes, Epithelial cell, and a numbers of malignant cells (Hirano, 1998). This study about IL-25 is in disagreement with [36] who showed a significant elevation of concentrations of IL-25 in the Development of Allergic Rhinitis Sensitized to House Dust Mite , and they suggested that IL-25 may be involved in the development of Th2 immune response in HDM-induced AR. (Saenz *et al*., 2008; Mjösberg *et al*., 2011; Kouzaki *et al*., 2016), IL 25, is critical regulators of innate and adaptive immune responses associated with Th2 cytokine mediated inflammation at nasal mucosal tissues and Allergic Rhinitis. Other studies in (Cheng *et al*., 2014) identified IL-25 measurements with distinct asthma phenotypes, cause interleukin 25 that plays an important role to induce immune response (type two); in addition, this interleukin was expressed from Bronchial epithelial cells as determinant for (type two) response activation of Allergic Asthma, and the level of this Interleukin were increased Allergic Asthma. Allergic disease and Allergic Asthma have association with IL-25, which have function for promoting type two of immunity in mucous epithelial surface cells and for protects from helminthes Infection of intestine canal (Petersen *et al*., 2012). Interleukin -25 receptors, relate as, mediator innate and adaptive pulmonary type two immune response. Other reports have demonstrated that eosinophils produce IL-25 (Dolgachev *et al*., 2009; Terrier *et al*., 2010). Eosinophilia state linked with Interleukin -25 plays a role to induce allergy response (Petersen *et al*., 2012).

References

Abd-Alwahaab, Y.B. (2007). Study of the relationship between certain disease in Immunological indicators and severity of people with asthma. Master Thesis. College of Science. University of Baghdad.

Al-Yasiri, M.Y.K. (2014). Study some Immunological and Haematological changes upon workers of Vegetable Oils factory in Baghdad suffering from Hypersensitivity Type -1. MSc thesis, Collage of Sciences for Women. University of Baghdad.Iraq, pp.1-101.

Angkasekwinai, P.; Park, H.; Wang, Y.-H.; Wang, Y.-H.; Chang, S.H.; Corry, D.B. and Dong, C. (2007). Interleukin 25 promotes the initiation of proallergic type 2 responses. The Journal of Experimental Medicine, 204(7): 1509–1517.

Arshad, S.H. (2010). Does exposure to indoor allergens contribute to the development of asthma and allergy? Current Allergy and Asthma Reports, 10(1): 49-55.

Athari, S.S.; Pourpak, Z.; Folkerts, G.; Garssen, J.; Moin, M.; Adcock, I. M.; and Mortaz, E. (2016). Conjugated Alpha-Alumina nanoparticle with vasoactive intestinal peptide as a Nano-drug in treatment of allergic asthma in mice. European Journal of Pharmacology, 791(3): 811–820.

Ava, D. and Wasima, J. (2013). A Study of The Hematological Profile In Relation To Some Allergic Diseases (A Hospital Based Study). International Journal of Basic and Applied Physiology (IJBAP), 2(1): 35-40.

Blomme, K.; Tomassen, P.; Lapeere, H.; Huvenne, W.; Bonny, M.; Acke, F. and Gevaert, P. (2013). Prevalence of allergic sensitization versus allergic rhinitis symptoms in an unselected population. International Archives of Allergy and Immunology, 160(2): 200–207.

Brakhas, S.; Abrar, J. H. and A.N. Jasim (2016).Study of total Immunoglobulin E and Eosinophil count in allergic disease. Baghdad Science Journal, 13(2): 298-304.

Brakhas, S.A.; Atia, M.R.; Aziz, Y.J. and AL-Sharqi, S.A.H. (2015). Study of total IgE levels and eosinophil count according to age and gender in patients with allergic rhinitis. World J Pharm Res., 4(1): 295-303.

Bunyavanich, S. and Schadt, E.E. (2015). Systems biology of asthma and allergic diseases: A multiscale approach. Journal of Allergy and Clinical Immunology, 135(1): 31–42.

Calderón, M.A.; Kleine-Tebbe, J.; Linneberg, A.; De Blay, F.; Hernandez Fernandez de Rojas, D.; Virchow, J.C. and Demoly, P. (2015). House Dust Mite Respiratory Allergy: An Overview of Current Therapeutic Strategies. Journal of Allergy and Clinical Immunology: In Practice, 3(6): 843–855.

Chaparzadeh, N.; Yavari, B. and Athari, S.S. (2016). Benefit Non-Enzymatic Antioxidant Effects on Allergic Asthma. Advances in Bioresearch, 7(4): 1-11.

Cheng, D.; Xue, Z.; Yi, L.; Shi, H.; Zhang, K.; Huo, X. and Zhen, G. (2014). Epithelial interleukin-25 is a key mediator in Th2-high, corticosteroid-responsive asthma. American Journal of Respiratory and Critical Care Medicine, 190(6): 639–648.

Corrigan, C.J.; Wang, W.; Meng, Q.; Fang, C.; Eid, G.; Caballero, M.R. and Ying, S. (2011). Allergen-induced expression of IL-25 and IL-25 receptor in atopic asthmatic airways and late-phase cutaneous responses. Journal of Allergy and Clinical Immunology, 128(1): 119–124.

Demoly, P.; Annunziata, K.; Gubba, E. and Adamek, L. (2012). Repeated cross-sectional survey of patient-reported asthma control in europe in the past 5 years. European Respiratory Review, 21(123): 66–74.

Dolgachev, V.; Petersen, B.C.; Budelsky, A.L.; Berlin, A.A. and Lukacs, N.W. (2009). Pulmonary IL-17E (IL-25) production and IL-17RB+ myeloid cell-derived Th2 cytokine production are dependent upon stem cell factor-induced responses during chronic allergic pulmonary disease. Journal of Immunology, 183(9): 5705–5715.

Fernández-Caldas, E.; Puerta, L. and Caraballo, L. (2014). Mites and allergy. In: Bergmann K, Ring J, editors. History of allergy, Chem immunol allergy, vol. 100. Basel: Karger; 234–242.

Greiner, A.N.; Hellings, P.W. and Rotiroti, G. (2011). Allergic rhinitis. The Lancet, 378(9809): 2112-2122.

Hassan, A.J. (2015). Levels of Interleukin IL-17A,IL-33and Heat Shock Protein 70 in Some Allergic Diseases. collage of science . University of Baghdad.

Hirano, T. (1998). Interleukin 6 and its receptor: ten years later. International reviews of immunology, 16(4): 249-284.

Hirano, T. (1998). Interleukin 6 and its receptor: ten years later. International reviews of immunology, 16(4): 249-284.

Holgate, S. T. (2012). Innate and adaptive immune responses in asthma. Nat. Med.; 18(5): 673–683.

Hvid, M.; Vestergaard, C.; Kemp, K.; Christensen, G. B.; Deleuran, B. and Deleuran, M. (2011). IL-25 in atopic dermatitis: a possible link between inflammation and skin barrier dysfunction? The Journal of Investigative Dermatology, 131(1): 150–157.

Iwakura, Y.; Ishigame, H.; Saijo, S. and Nakae, S. (2011). Functional Specialization of Interleukin-17 Family Members. Immunity, 34(2): 149-162.

Kim, D. W.; Kim, D.-K.; Eun, K. M.; Bae, J.-S.; Chung, Y.-J.; Xu, J.; and Mo, J.-H. (2017). IL-25 Could Be Involved in the Development of Allergic Rhinitis Sensitized to House Dust Mite. Mediators of Inflammation, 2017(4): 1–8.

Kouzaki, H.; Matsumoto, K.; Kato, T.; Tojima, I.; Shimizu, S. and Shimizu, T. (2016). Epithelial Cell-Derived Cytokines Contribute to the Pathophysiology of Eosinophilic Chronic Rhinosinusitis. Journal of Interferon & Cytokine Research, 36(3): 169–179.

Krouse, J. H. and Mabry, R. L. (2003). Skin testing for inhalant allergy 2003: Current strategies. Otolaryngology - Head and Neck Surgery, 129(4): 212-222.

Lajunen, T. K.; Jaakkola, J. J. K. and Jaakkola, M. S. (2016). Interleukin 6 SNP rs1800797 associates with the risk of adult-onset asthma. Genes and Immunity, 17(3): 193–198.

Li, J.; Zhang, Y. and Zhang, L. (2015). Discovering susceptibility genes for allergic rhinitis and allergy using a genome-wide association study strategy. Current Opinion in Allergy and Clinical Immunology, 15(1): 33-40.

Mjösberg, J. M.; Trifari, S.; Crellin, N. K.; Peters, C. P.; Van Drunen, C. M.; Piet, B. and Spits, H. (2011). Human IL-25-and IL-33-responsive type 2 innate lymphoid cells are defined by expression of CRTH2 and CD161. Nature Immunology, 12(11): 1055–1062.

Morita, H.; Arae, K.; Unno, H.; Toyama, S.; Motomura, K.; Matsuda, A.; and Nakae, S. (2015). IL-25 and IL-33 contribute to development of eosinophilic airway inflammation in epicutaneously antigen-sensitized mice. PLoS ONE, 10(7): 30-52.

Neveu, W.A.; Allard, J. L.; Raymond, D. M.; Bourassa, L.M.; Burns, S. M.; Bunn, J.Y. and Rincon, M. (2010). Elevation of IL-6 in the allergic asthmatic airway is independent of inflammation but associates with loss of central airway function. Respiratory Research, 11(3): 2-17.

Pawankar, R.; Canonica, G.; Holgate, S. and Lockey, R. (2012). white book on allergy. Pediatriya, 52(2): 55–58.

Petersen, B.C.; Budelsky, A.L.; Baptist, A.P.; Schaller, M.A. and Lukacs, N.W. (2012). Interleukin-25 induces type 2 cytokine production in a steroid-resistant interleukin-17RB + myeloid population that exacerbates asthmatic pathology. Nature Medicine, 18(5): 751–758.

Prescott, S. L. and Tang, M. L. K. (2005). The Australian Society of Clinical Immunology and Allergy position statement: Summary of allergy prevention in children. Medical Journal of Australia, 182(9): 464–467.

Radauer, C.; Nandy, A.; Ferreira, F.; Goodman, R.E.; Larsen, J.N.; Lidholm, J. and Breiteneder, H. (2014). Update of the WHO/IUIS Allergen Nomenclature Database based on analysis of allergen sequences. Allergy: European Journal of Allergy and Clinical Immunology, 69(4): 413-419.

Rasheed, S.M.H. (2016).Role of Total and Specific IgE in Identification of Inhalant Allergens and their Association with HLA-DRB1 Alleles in AL-Najaf province. University of Kufa. Journal University of Kerbala, Vol. 14 No.4 Scientific. /College of Medicine.

Rincon, M. and Irvin, C.G. (2012). Role of IL-6 in asthma and other inflammatory pulmonary diseases. International Journal of Biological Sciences, 8(9): 1281–1290.

Saenz, S.A.; Taylor, B.C. and Artis, D. (2008). Welcome to the neighborhood: Epithelial cell-derived cytokines license innate and adaptive immune responses at mucosal sites. Immunological Reviews, 226(1):172-190.

SAS. (2012). Statistical Analysis System, User's Guide. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N.C. USA.

Shin, H.-W.; Kim, D.-K.; Park, M.-H.; Eun, K. M.; Lee, M.; So, D.; … Kim, D. W. (2015). IL-25 as a novel therapeutic target in nasal polyps of patients with chronic rhinosinusitis. The Journal of Allergy and Clinical Immunology, 135(6): 1476–1485.

Terrier, B.; Bièche, I.; Maisonobe, T.; Laurendeau, I.; Rosenzwajg, M.; Kahn, J.-E. and Saadoun, D. (2010). IL-25: a cytokine linking eosinophils and adaptative immunity in Churg-Strauss syndrome. Blood, 4523–4531.

Wahhab, R.S. (2013). Investigate Role of IL-17 and Its Relationship Some Immunological Indicators and Severity in Patients of Allergic Asthma, AL-Mustansiriya University ,College of Basic Education.