

Specific IgE for Aero and Food Allergens in Adult Chronic Urticaria Patients Without Other Allergic Diseases

Osama Mohamed Abdel Latif

Allergy and Clinical Immunology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Email address:

osamalatif@med.asu.edu.eg

To cite this article:

Osama Mohamed Abdel Latif. Specific IgE for Aero and Food Allergens in Adult Chronic Urticaria Patients Without Other Allergic Diseases. *International Journal of Immunology*. Vol. 6, No. 2, 2018, pp. 25-29. doi: 10.11648/j.iji.20180602.11

Received: May 18, 2018; **Accepted:** May 31, 2018; **Published:** June 13, 2018

Abstract: Chronic Urticaria (CU) is a diseases characterized by occurrence of spontaneous wheels observed by the patient for more than 6 weeks duration. The prevalence of CU varies from 0.5-5% in adult population. This is a disease of complex etiologies with more areas to be explored by researches. The aim of the study was to detect the Prevalence of allergen sensitizations among adult chronic urticaria patients without other allergic diseases. This study is a cross-sectional case control study. 70 patients with CU without evident cause and 50 healthy control individuals were included in the study. Patients with any other allergic diseases (such as Asthma, allergic Rhinitis, Allergic Conjunctivitis, Drug Allergy, atopic Dermatitis, Anaphylaxis....), patients with other chronic or systemic Diseases (such as Cardiac, respiratory, renal, hepatic, hematological, thyroid or other skin Diseases, etc....) and smokers were excluded from the study. Each patient and control individual was subjected to full medical history, complete medical examination and routine lab test. Determination of allergen-specific IgE (for 20 separate food and 20 aeroallergens) in serum for the patients was done by using EUROLINE Atopy Screen. Each of the patients and control groups were comparable according to age and gender. There was a significant difference between the CU patients and the control group as regard the prevalence of any allergen sensitization (65.7% for CU patients and 18% in control group) $p < 0.05$. There was also a significant difference between the sensitized individual in each group as regard the number of allergens per each individual; for sensitized CU patients the mean was 3 allergens and interquartile range was (2-4), for the sensitized control individuals the mean was 2 and interquartile range was (1-2) with $p = 0.014$. The mostly frequent allergens were found in the CU sensitized patients was the house dust mite allergens (34.8% of the sensitized CU patients were sensitized to one or more of the two types of mites; dermatophagoides pteronyssinus and or dermatophagoides farinae). The study concluded that; a great prevalence of CU patients proved to be sensitized to common allergens which open the door to start a trials to examine the value of environmental control, food avoidance and specific allergen immunotherapy in this group of patients.

Keywords: Chronic Urticaria, Allergen-Specific IgE, Aero-Allergens, Food Allergy

1. Introduction

Chronic Urticaria (CU) is a disease characterized by the appearance of spontaneous wheals with or without angioedema for more than 6 weeks duration [1]. The prevalence of CU estimated to be 1% in the general population [2]. Also CU is associated with high rate of psychological consequences as poor sleep, anxiety and depression [3].

The mast cell known to be the most important effector cell in CU through releasing of its mediators; From them the histamine with its inflammatory action, stimulation of

peripheral nerves and increasing vascular permeability. Also other mediators such as leukotriene, tryptase and heparin sharing in the pathogenesis of CU [4].

The role of IgE in the activation of mast cell is well known also its role in CU as part of activation of mast cell in this disease [5]. Moreover a significant higher total serum IgE level in CU patients (34%) than the healthy control (8.6%) with a significant correlation between elevated level of serum total IgE (above 175 U/ml) with CU symptoms severity [6] were found.

On the other hand treatment with anti-IgE monoclonal antibody (Omalizumab) now known to be effective in the treatment of CU and reduction of its symptoms even in cases not responding to Anti-histamine [7-8], and decreases the need of oral corticosteroids with up to 12 months of Omalizumab use [9].

The relation between Atopic Dermatitis in early childhood (below age of 2 years) and the development of other atopic diseases has been studied and showing that there were increase incidence of developing CU in those children with ratio of proportion 2.04 (CI 1.80-2.31) [10].

There is a limited data about the cause of IgE sensitization in CU patients without any known history of other atopic diseases, this study was conducted to explore the association between IgE sensitization and CU in these type of patients.

2. Patients' Selection

This study is a cross-sectional case control study. Patients were selected from Ain Shams University Hospital; Allergy and Clinical Immunology outpatient clinic during the period from 1st of March 2017 till the end of December 2017.

Inclusion Criteria: patients with CU complaining of spontaneous wheels without evident cause observed by the patient for more than 6 weeks duration.

Exclusion criteria:

- 1- Patients with vasculitic Urticaria (the single wheal duration more than 24 hours which resolves with skin pigmentation)
- 2- Patients with any other allergic diseases (such as Asthma, allergic Rhinitis, Allergic Conjunctivitis, Drug Allergy, atopic Dermatitis, Anaphylaxis....)
- 3- Patients with other chronic or systemic Diseases (such as Cardiac, respiratory, renal, hepatic, hematological, thyroid or other skin Diseases, etc....)
- 4- Smokers

50 healthy individuals matched for the age and sex to the patients are selected as control group

3. Methods

Each patient and control individual was subjected to full medical history, complete medical examination and routine lab test (CBC, renal functions, liver functions, thyroid functions....) and any patient confirmed to have one or more of exclusion criterion was omitted.

Determination of allergen-specific IgE (for 20 separate food and 20 aeroallergens) in serum for the patients was done by using EUROLINE Atopy Screen (EUROIMMUNE-Medizinische Labordiagnostika AG; Germany).

The aeroallergen panel included (dermatophagoides farinae, dermatophagoides pteronyssinus, alternaria alternata, aspergillus fumigatus, candida albicans, cladosporim herbarum, penicillium notatum, sweet vernal grass, timothy grass, cultivated rye, alder, birch, oak, common ragweed, mugwort, orchard grass, cat, dog, cockroach and hamster)

The food panel included (egg white, egg yolk, cow milk,

chocolate, wheat flour, soybean, Baker yeast, hazelnut, peanut, orange, strawberry, banana, mango, tomato, carrot, onion, chicken, lamb's meat, codfish, and shrimp)

The patients were further classified in two groups:

Group 1 (sensitized patients with specific IgE positive to any of the allergens examined) and group 2 (non-sensitized patients with –ve results for all the examined allergens)

The control subjects were classified also in two groups:

Group 3 (sensitized control subjects with specific IgE positive to any of the allergens examined) group 4 (non-sensitized patients with –ve results for all the examined allergens)

Statistical methods: the author used mean and standard deviation for describing numerical data, number and percent for describing prevalence, student t test for calculating significance between numerical variables in two groups, ANOVA for calculating significance between numerical variables in more than two groups, Chi square for difference in Nonparametric data between two groups and Mann-Whitney test for calculating significance between Nonparametric variables in more than two groups.

4. Results

70 patients with CU and 50 healthy control individuals were included in the study, table 1 shows a statistical significant difference in the prevalence of allergen sensitization by the specific IgE in-between the patients group and the control group.

Table 1. Prevalence of allergen sensitization in-between the patients group and the control group.

	Sensitized	Non-sensitized	total
CU no. (%)	46 (65.7)	24(34.3)	70
Control no. (%)	9(18)	41 (82)	50
Significance	P<0.05 ¶, $\chi^2=26.75$		

Chi-square for calculation of statistical significance between the CU patients and the control

¶ Significant difference

Table 2 shows the distribution of gender of the four groups denoting non-significant differences between the groups.

Table 2. Gender distribution in the four groups.

	Female	Male	total
Group 1 (no.)	29	17	46
Group 2 (no.)	14	10	24
Group 3 (no.)	6	4	10
Group 4 (no.)	13	17	40
total	72	84	120
Significance	$\chi^2=0.3095$. The p-value is.958236 §		

Chi-square for calculation of statistical significance between the 4 groups according to gender and the control

§ Non-significant difference

Table 3 shows that the ages were comparable through the 4 groups without any significant differences.

Table 3. Ages were comparable through the 4 groups.

	Group 1	Group 2	Group 3	Group 4
Age:	36.739	33.167	32.3	35.65
mean(SD*)	(15.4)	(13.8)	(13.7)	(13.2)
Significance	p= 0.69 §			

*SD= Standard Deviation

Analysis by ANOVA: ANalysis Of VAriance between groups

§ Non-significant difference

Table 4 shows the comparison between the number of allergen specific IgE in each of sensitized groups of the CU patients and the control individuals denoting a statistically significant difference between the two groups with higher number of allergens per each patient in CU group than the control group.

Table 4. Number of allergens in each patient of the sensitized groups (group 1 and group 3).

	Mean	Inter-quartile range
Group 1	3	2-4
Group 3	2	1-2
Significance	P= 0.014 ¶, z= 2.45	

Comparison by Mann-Whitney test

¶ Significant difference

The prevalence of individual allergens sensitization shown in table 5 with the most prevalent allergens are the house dust mite allergens (*Dermatophagoides farinae* & *Dermatophagoides pteronyssinus*).

The no. of patients with sensitization of one or more of house dust mite allergens was 16 (34.8%) in Group 1, and the control was 3 (33.3%) p= 0.933(non-significant) $\chi^2=0.007$.

Table 5. Number of individual allergen sensitization in each sensitized group.

Aeroallergens	no.		Food allergen	no.	
	Group 1	Group 3		Group 1	Group 3
<i>Dermatophagoides farinae</i>	8	2	Egg white	3	0
<i>Dermatophagoides pteronyssinus</i>	12	2	Egg yolk	0	0
<i>Alternaria alternata</i>	6	0	Cow milk	6	1
<i>Aspergillus fumigatus</i>	9	1	Chocolate	1	0
<i>Candida albicans</i>	4	0	Wheat flour	4	1
<i>Cladosporium herbarum</i>	4	0	Soybean	4	1
<i>Penicillium notatum</i>	7	1	Baker yeast	0	0
Sweet vernal grass	4	0	Hazelnut	1	1
Timothy grass	6	3	Peanut	1	0
Cultivated rye	6	0	Orange	3	0
Alder	3	0	Strawberry	3	1
Birch	10	1	Banana	2	0
Oak	3	0	Mango	3	0
Common ragweed	3	1	Tomato	0	0
Mugwort	8	2	Carrot	1	0
Orchard grass	1	0	Onion	1	0
Cat	7	0	Chicken	0	0
Dog	4	0	Lamb's meat	0	0
Cockroach	0	0	codfish	0	0
Hamster	0	0	shrimp	2	0

5. Discussion

CU is a common dermatological disease which encounters many physical and psychological burden on the patients [11], nevertheless the etiology of CU is still unclear, even after the successful control of CU symptoms by Anti-IgE antibody (Omalizumab) which was designed primary to treat IgE mediated Asthma [12-13], the role of IgE sensitization to common aero and food allergens was not thoroughly investigated.

In the current study the author found that there was a significant difference between the patients and the control regarding the prevalence of allergen sensitization with 65.7% sensitization in the patients with CU versus 18% of control group ($P<0.05$, $\chi^2=26.75$), a lower incidence was observed in CU patients in study conducted by Zuberbier et al. 2010 who found sensitization of 39.1% of those patients by using Skin Prick Test (SPT) only and the researches in this study only performed the SPT on selected cases (69.7% of the study population) whose

presented with active disease during the study time [2], in contrast the current study used the specific IgE instead of SPT to avoid the false –ve results especially in patients with active CU who couldn't stop the anti-histaminic which alter the results of the SPT even for week after stoppage of its intake [14], Caliskaner et al. also found a rate of allergen sensitization by SPT was 27.4% in CU patients after the stoppage of anti-histaminic for 7 days although the rate was lower than the current study; they only performed SPT for aeroallergens without food allergens [15], in another study the prevalence of sensitivity to House Dust Mite (HDM) only by SPT in a group of patients with CU without any other allergic Diseases was 53% which is more consistent with the results of the current study [16], another study conducted on 88 patients with CU (from them 33% had history of other atopic diseases) found 47.7% had positive SPT to allergens used (16 for food allergens and 12 for aeroallergens) [17]; In the current study the number of allergens used was 20 for food allergens and 20

aeroallergens also the used method was specific IgE not SPT, also Liutu et al. found a positive SPT in 51.7% of 91 CU patients to 17 aeroallergens [18], a higher percent of Allergen sensitization was found by Yi Zhou et al. who found a sensitization of 95.83% of children with CU aged 4-10 years when examimnig 34 alleregens by specific IgE [19]. Furthermore Mahesh et al. found a higher prevalence of sensitization of House Dust Mite by SPT (64%) of 122 CU patients [16], which is higher than the current study (34.8% of the sensitized patients in this study had positive specifics IgE Ab to one or more of the House Dust Mite allergens; *Dermatophagoides farinae* and /or *Dermatophagoides pteronyssinus*), it was verified that the Hose Dust Mite allergen can induce skin manifestations either by introduction of the allergen through the respiratory route or direct contact with the allergen in the Atopic dermatitis model [20].

Food allergy is a common cause of Acute Urticaria (urticaria last less than 6 weeks) and the diagnosis often simple by history of appearance of urticaria symptoms after ingestion of certain type of food, also can be diagnosed by SPT and serum specific IgE levels to food allergens, but the relation between food allergy and CU is not clear [21], in the current study the author found the prevalence of food allergy by specific IgE for milk allergen was 8.6%, soy and wheat 5.7% for each and minor percent for other major food allergens.

Furthermore in a recent study on pediatric the authors found a positive allergen sensitization in 92 of the 95 children with CU; with the house dust mite, flour mite, egg yolk and egg white as the most prevalent allergens [22].

In the current study the number of allergens per individual were higher in the sensitized CU patients (3 allergens) than the sensitized control (2 allergens) with $P=0.014$, $z=2.45$, the allergen sensitization by specific IgE in healthy individual was noticed before in rate of 9.2% in 4 years old children, 14.5% at 8 years and 21.8% at 16 years old children when they examined for the presence of specific IgE for cat and dog allergens and the sensitization was a good predictor of the development of allergy symptoms on the follow up years [23].

6. Conclusions

The current cross-sectional case control study revealed a significantly higher prevalence of specific aero-allergen and food allergen sensitization in CU patients than the healthy control. That may open the door to more researches to examine the value of environmental control, food avoidance and specific allergen immunotherapy in CU patients in the future.

References

- [1] Bernstein, J. A., Lang, D. M., Khan, D. A., Craig, T., Dreyfus, D., Hsieh, F., Sheikh, J., Weldon, D., Zuraw, B., Bernstein, D. I. and Blessing-Moore, J., 2014. The diagnosis and management of acute and chronic urticaria: 2014 update. *Journal of Allergy and Clinical Immunology*, 133(5), pp. 1270-1277.
- [2] Zuberbier, T., Balke, M., Worm, M., Edenharter, G. and Maurer, M., 2010. Epidemiology of urticaria: a representative cross-sectional population survey. *Clinical and experimental dermatology*, 35(8), pp. 869-873.
- [3] Balp MM, Khalil S, Tian H, Gabriel S, Vietri J, Zuberbier T. Burden of chronic urticaria relative to psoriasis in five European countries. *Journal of the European Academy of Dermatology and Venereology*. 2018 Feb; 32(2):282-90.
- [4] Darlenski, R., Kazandjieva, J., Zuberbier, T. and Tsankov, N., 2014. Chronic urticaria as a systemic disease. *Clinics in dermatology*, 32(3), pp. 420-423.
- [5] Grattan C, Maurer M. Urticaria and angioedema. Zuberbier T, editor. Springer; 2010 Apr 30.
- [6] Kessel A, Helou W, Bamberger E, Sabo E, Nusem D, Panassof J, Toubi E. Elevated serum total IgE—a potential marker for severe chronic urticaria. *International archives of allergy and immunology*. 2010; 153(3):288-93.
- [7] Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Giménez-Arnau A, Agarwal S, Doyle R, Canvin J, Kaplan A, Casale T. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *New England Journal of Medicine*. 2013 Mar 7; 368(10):924-35.
- [8] Kaplan A, Ledford D, Ashby M, Canvin J, Zazzali JL, Conner E, Veith J, Kamath N, Staubach P, Jakob T, Stirling RG. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. *Journal of Allergy and Clinical Immunology*. 2013 Jul 1; 132(1):101-9.
- [9] Wang L, Ke X, Kavati A, Wertz D, Huang Q, Willey VJ, Stephenson JJ, Ortiz B, Paknis B, Bernstein JA, Beck LA. Real-world treatment patterns and outcomes of omalizumab use in patients with chronic idiopathic urticaria. *Current medical research and opinion*. 2018 Jan 2; 34(1):35-9.
- [10] Böhme M, Lannerö E, Wickman M, Nordvall SL, Wahlgren CF. Atopic dermatitis and concomitant disease patterns in children up to two years of age. *Acta dermato-venereologica*. 2002 Mar 1; 82(2).
- [11] Vietri J, Turner SJ, Tian H, Isherwood G, Balp MM, Gabriel S. Effect of chronic urticaria on US patients: analysis of the National Health and Wellness Survey. *Annals of Allergy, Asthma & Immunology*. 2015 Oct 1; 115(4):306-11.
- [12] Spector SL, Tan RA. Effect of omalizumab on patients with chronic urticaria. *Annals of Allergy, Asthma & Immunology*. 2007 Aug 1; 99(2):190-3.
- [13] Büyüköztürk S, Gelincik A, Demirtürk M, Kocaturk E, Colakoğlu B, Dal M. Omalizumab markedly improves urticaria activity scores and quality of life scores in chronic spontaneous urticaria patients: a real life survey. *The Journal of dermatology*. 2012 May 1; 39(5):439-42.
- [14] Heinzerling L, Mari A, Bergmann KC, Bresciani M, Burbach G, Darsow U, Durham S, Fokkens W, Gjomarkaj M, Haahela T, Bom AT. The skin prick test—European standards. *Clinical and translational allergy*. 2013 Dec; 3(1):3.
- [15] Caliskaner Z, Ozturk S, Turan M, Karaayvaz M. Skin test positivity to aeroallergens in the patients with chronic urticaria without allergic respiratory disease. *Journal of Investigational Allergology and Clinical Immunology*. 2004 Jan 1; 14(1):50-5.

- [16] Mahesh PA, Kushalappa PA, Holla AD, Vedanthan PK. House dust mite sensitivity is a factor in chronic urticaria. *Indian Journal of Dermatology, Venereology, and Leprology*. 2005 Mar 1; 71(2):99.
- [17] Kulthanan K, Jiamton S, RUTNIN NO, Insawang M, Pinkaew S. Prevalence and relevance of the positivity of skin prick testing in patients with chronic urticaria. *The Journal of dermatology*. 2008 Jun 1; 35(6):330-5.
- [18] Liutu M, Kalimo K, Uksila J, Kalimo H. Etiologic aspects of chronic urticaria. *International journal of dermatology*. 1998 Jul 1; 37(7):515-9.
- [19] Zhou Y, Sheng M, Chen M. Detection and allergen analysis of serum IgE in pediatric patients with chronic urticaria.
- [20] Tupker RA, Monchy JG, Coenraads PJ. House - dust mite hypersensitivity, eczema, and other nonpulmonary manifestations of allergy. *Allergy*. 1998 Dec 1; 53(s48):92-6.
- [21] Burks W. Skin manifestations of food allergy. *Pediatrics*. 2003 Jun 1; 111(Supplement 3):1617-24.
- [22] Zhou Y, Sheng M, Chen M. Detection and allergen analysis of serum IgE in pediatric patients with chronic urticaria. *Pakistan Journal of Medical Sciences*. 2018 Mar; 34(2):385.
- [23] Asarnoj A, Hamsten C, Wadén K, Lupinek C, Andersson N, Kull I, Curin M, Anto J, Bousquet J, Valenta R, Wickman M. Sensitization to cat and dog allergen molecules in childhood and prediction of symptoms of cat and dog allergy in adolescence: a BAMSE/MeDALL study. *Journal of Allergy and Clinical Immunology*. 2016 Mar 1; 137(3):813-21.