

# Central Asian Journal of Medicine

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Volume 2020 | Issue 2

Article 6

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7-3-2020

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### Recommended Citation

Mavlyanova, Shakhnoza Z.; Mullakhanov, Javlon B.; Alimukhamedova, Yulduz A.; and Ismagilov, Abdumalik I. (2020) "CYTOKINE STATUS IN PATIENTS WITH URTICARIA," *Central Asian Journal of Medicine*: Vol. 2020 : Iss. 2 , Article 6.

Available at: <https://uzjournals.edu.uz/tma/vol2020/iss2/6>

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## CYTOKINE STATUS IN PATIENTS WITH URTICARIA

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### ABSTRACT

**Research objective.** The present research evaluates some indicators of cytokine status in patients with urticaria for evaluation of the clinical course.

**Material and methods.** 93 patients with urticaria at the age from 14 to 88 years were examined. The severity of the clinical course was assessed according to the Urticaria activity score-7. The determination of total IgE and IL-4, IL-6 and IL-10 was performed by ELISA. The digital material is processed by the method of variational statistics.

**Results.** In patients with urticaria in cytokine status, there is an increase in anti-(IL-4, IL-6) and proinflammatory (IL-10) cytokines against a background of hyperproduction of total IgE.

**Conclusion:** In patients with chronic urticaria there is a predominance of IL-6 production against the background of hyperproduction of total IgE and IL-10, causing a pronounced secondary immunological failure and decompensatory form.

**Key words:** urticaria, interleukins, immunoglobulin E.

### INTRODUCTION

Significant scientific-practical interest to problem of urticaria is noted in recent years in view of its high frequency among the population especially among children. An increase of morbidity with allergodermatoses observed among which urticaria ranks third its distribution after allergic rhinitis and bronchial asthma [8,

11, 14, 15], which raises a number of questions for clinicians in terms of an early diagnosis and maintaining an adequate therapy. According literature data every third person on Earth for once in life suffered an episode of urticaria [5, 10].

Of great interest is studying clinical course of chronic urticaria that is multifactorial disease. Transformation of acute urticaria in chronic one that reflects allergic memory in organism of patient was established in every third patient both among children and adults. Chronic forms of urticaria differ in persistent course and great durability of disease – from 6 weeks up to a few decades.

It should be noted that emergence and subsequent course of allergic skin disease including urticaria largely determined by sensitization not only to nutritional, medicinal factors but also to pollen, fungal, bacterial and other allergens [1, 6, 12]. At the same time, the result of implementation of any allergic process is formation of effector immune mechanisms, determining clinical picture and symptoms of dermal pathology process.

The given scientific studies show that the main role in allergic reactions belongs to immunity humoral link – common immunoglobulin E (IgE), that remains the main immunologic marker [2, 3, 4, 9]. Diversity of immune answer creates conditions for imbalance in the synthesis of common IgE that presents an important value for decryption of pathogenic aspects of allergic reactions of organism. So, synthesis of IgE and other immunoglobulins is the end result of immune reactions in which implementation an active part take interleukins (IL). In this regard determination of their participation in intercellular cooperation is important for disclosure mechanisms of immunoregulation in allergic diseases in particular in urticaria.

**The aim of the research was to** study of some indications of cytokine status in urticarial patients to estimate peculiarities of clinical course.

## **MATERIAL AND METHODS**

Ninety-three patients with urticaria aged from 14 to 88 were examined. Among them were 57 (61,3%) female and 36 (38,7%) male persons. All the

patients were undergoing clinical, immunological researches. All the patients have been consulted by the therapist, neuropathologist, infectionist and endocrinologist. To estimate a degree of severity of clinical course was used questionnaire Urticaria activity score-7 (UAS-7). Activity of urticaria has been determined by two basic clinical indications of dermatosis: a number of blisters and expression of itching every two hours during 7 days. Criteria of expression of clinical manifestations were estimated on a scoring system from 0 up to 3 points. From 0 up to 6 points was well-controlled urticaria, 7-15 points was light severity, 16-27 – the average degree of severity and over 28 points – severe severity.

Determination of a level of cytokines IL-4, IL-6 and IL-10 in blood serum was carried out by means of solid-phase variant of enzyme immunoassay (EIA, for this purpose were used test-systems worked out in “Vector-Best” (Novosibirsk). Results were estimated by means of multi-channel spectrophotometer Multiscan «Labsystems» (Finland) at a wave length of 450 nm.

Research of level of common IgE in blood serum was carried out by indirect solid-phase immunosorbent method (ELISA) commercial test-systems of NPO «Diagnostical systems» (Nijniy Novgorod), by means of multi-channel spectrophotometer Multiscan «Labsystems» (Finland).

Statistical processing of results was carried out by means of program Statistika V.55A using criterion Shapiro-Uilk (2006).

## RESULTS AND DISCUSSION

Acute urticaria in its clinical form was diagnosed in 42 patients that formed 45,2%, and its chronic form in 51 (54,8%) of cases. An acute urticaria most frequent was diagnosed in female persons 25 (59,5%), and in male persons in 17 (40,5%) respectively. The same picture was noted in chronic form urticaria, it was registered in 32 females (62,7%), and in 19 males (37,3%). In according to UAS-7 scale easy degree of urticaria was revealed in 27 (29,03%), average severity in 49 (52,7%) and severe severity in 17, that formed 18,3% a scale.

Results of IFA research of concentration of common IgE in urticaria patients showed an increase of its concentration in blood serum 2,5 times as compared with indicators in a group of control health persons and formed on average  $182,2 \pm 6,1$  ME/ml ( $P < 0,05$ ). According literature data a significant increase of common IgE was also noted in parasitic infestations, in this connection the patients were examined for the presence of helminthes infestation. Parasitic helminthes infection was revealed in 21 patients that formed 22,5% of cases: in 3 patients (3,2%) with acute form of urticaria and with chronic form – in 18, that formed 19 % of cases.

Investigation of common IgE in urticaria patients depending on a presence of helminthes invasion exhibited that a level of common IgE averaged  $191,1 \pm 5,05$  ME/ml whereas in patients with urticaria without parasitic infection its level was  $182,2 \pm 6,1$  ME/ml. Based on literature data a high level of IgE in absence of signs of helminthosis with high probability indicates development of allergic process in organism (7, 13).

A level of common IgE was analyzed by us depending on clinical form of morbidity (Table 1). So, in acute form of urticaria a level of common IgE exceeded 2,4 times indicators in control group ( $P < 0,05$ ), in chronic form – 2,6 times ( $P < 0,05$ ) (Table 1).

**Table 1.**

**Indicators of concentration of common IgE in urticaria patients with different clinical forms (ME/ml)**

Indicators	Healthy n=70	Acute form	Chronic form
Common IgE	$72,1 \pm 1,1$	$176,1 \pm 6,15^*$	$188,2 \pm 6,01^*$

Note: \* -  $p < 0,05$  compared to control.

Indicators of common immunoglobulin were analyzed according to sex of patients (Table 2).

**Table 2.****Indicators of common IgE in urticaria patients according to their sex (ME/ml)**

Indicator	Healthy n=70	Acute form	Chronic form
IgE	72,1±1,1	182,5±5,7 <sup>a</sup> 169,7±6,6 <sup>a</sup>	195,7±3,0 <sup>b</sup> 180,7±9,01 <sup>b</sup>

Note: \* - in the numerator is male data, in the denominator is female.  $p < 0,05$ .

a-compared to control, b – compared to patients with acute form of urticaria.

As follows from the Table 2, a level of common IgE in acute form of urticaria 1,07 times exceeded indicators in group of patients with chronic form of urticaria. ( $p < 0,05$ ).

According to literature data hyperproduction of common IgE was adjusted by production of interleukins, that differentiated predecessors of B-lymphocytes in marrow caused the proliferation of pro-activated lymphocytes as well as induced the ability of B-lymphocytes to introduce antigen. So, studies of anti- and pro-inflammatory cytokines in blood serum of urticaria patients showed imbalance in production of cytokines status against the background of hyperproduction of common IgE (Tabl. 3).

**Table 3****Indicators of anti- and pro-inflammatory cytokines (IL-4, IL-6, IL-10) in patients with urticaria (pg/ml)**

Group	IL-4	IL-6	IL-10
Healthy, n=70	4,2±1,1	4,2±0,8	10,2±1,2
Patients, n=93	12,7±0,25*	15,5±0,3*	14,3±0,21*

Note: \*  $p < 0,05$  - compared to control.

As follows from the Table 3, the concentration of IL-4 in blood serum of urticaria 3,02 times exceeded indicators of health persons ( $P < 0,05$ ). Such picture can be also traced in indicators IL-6 and IL-10, that 3,7 and 1,4 times exceeded

indicators of control persons ( $p < 0,05$ ). Data on the content of interleukins in patient with various forms of urticaria are presented in the Table 4.

**Table 4**

**Indicators of cytokine status in urticaria patients according to clinical form (pg/ml)**

Group	IL-4	IL-6	IL-10
Healthy, n=70	4,2±1,1	4,2±0,8	10,2±1,2
Acute, n=42	19,3±0,4 <sup>a</sup>	6,4±0,18 <sup>a</sup>	13,3±0,2 <sup>a</sup>
Chronic, n=51	6,05±0,11 <sup>b</sup>	24,7±0,5 <sup>b</sup>	15,3±0,21 <sup>b</sup>

Note:  $p < 0,05$ . a – compared to control, b – compared to patients with acute form of urticaria.

As follows from the Table 4, the concentration of IL-4 in acute form of urticaria 3,2 times exceeded indicators of groups of patients with chronic form of urticaria ( $P < 0,05$ ). Concentration of IL6 1,5 times exceeded indicators of healthy persons ( $P < 0,05$ ), however compared with indicators of group of patients with chronic form it was 3,8 times lower ( $P < 0,05$ ). IL-10 in patients both with acute and chronic form of urticaria increased as compared with indicators of healthy persons 1,3 and 1,5 times respectively.

Regularity of immune system functioning is that different mechanisms of immunity are mutually antagonistic. In our studies a sharp hyper production of IL-4 in acute form of urticaria inhibits the synthesis of IL-6 that evidenced formation ability of Tx2 cells and switching of B-cells for production of common IgE causing the development of acute allergic reaction in organism. Whereas lower production of IL-4 in chronic form of urticaria characterizes decompensatory reaction against a background of hyperproduction of common IgE, that, in our opinion, evidenced development of hypersensitivity to specific IgE.

IL-6 significantly 3,8 times increased in chronic form of urticaria as compared with acute form causing development of long, chronic inflammatory, autoimmune process in organism of patients. Data obtained can play a role in determining degree of severity and tactics of therapy.

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## CONCLUSION

1. An increase of anti- (IL-4, IL-6) and pro-inflammatory (IL-10) cytokines against a background of common IgE was fixed in cytokines status in urticaria patients.
2. In acute form, there is an increase in the level of total IgE with hyperproduction of cytokines with a predominance of IL-4 production ( $p<0,05$ ).
3. In the chronic form, the production of IL-6 predominates against the background of overproduction of total IgE and IL-10, which leads to pronounced secondary immunological deficiency and the development of a decompensatory form.

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