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## CLINICAL AND IMMUNOLOGICAL FEATURES OF VARIOUS FORMS OF GLOMERULONEPHRITIS

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### Abstract

**Background.** Glomerulonephritis is characterized by marked clinical heterogeneity, largely determined by dysregulation of cytokine-mediated immune responses. **Objective.** To investigate cytokine profile features in patients with different clinical forms of glomerulonephritis and to assess their pathogenetic significance. **Materials and Methods.** A total of 103 patients with glomerulonephritis (latent, nephrotic, hypertensive, and mixed forms) were examined; serum levels of IL-1 $\beta$ , IL-8, IL-10, IFN- $\gamma$ , and RaIL-1 $\beta$  were measured by ELISA, with statistical significance set at  $p < 0.05$ . **Results.** Patients with glomerulonephritis demonstrated a significant increase in IL-1 $\beta$  (6.5-fold), IFN- $\gamma$  (8.6-fold), and RaIL-1 $\beta$  (7.2-fold) compared with controls ( $p < 0.05$ ). The nephrotic form showed the highest IL-1 $\beta$  ( $107.1 \pm 21.6$  pg/ml) and RaIL-1 $\beta$  ( $780.3 \pm 24.6$  pg/ml) levels, with a more than 4.5-fold elevation of the IL-1 $\beta$ /RaIL-1 $\beta$  ratio relative to controls ( $p < 0.05$ ). **Conclusion.** Cytokine imbalance in glomerulonephritis varies significantly according to clinical form, indicating distinct immunopathogenetic mechanisms underlying disease progression.

**Keywords:** Glomerulonephritis, cytokines, IL-1 $\beta$ , IFN- $\gamma$ , immune inflammation, clinical forms.

**Xulosa:** Dolzarbligi. Glomerulonefrit klinik shakllarining xilma-xilligi immun javobni tartibga soluvchi sitokin tizimidagi buzilishlar bilan chambarchas bog'liq. Tadqiqot maqsadi. Glomerulonefritning turli klinik shakllarida sitokin profili xususiyatlarini o'rganish va ularning patogenetik ahamiyatini baholash. Materiallar va usullar. Glomerulonefrit bilan kasallangan 103 bemor (latent, nefrotik, gipertonik va aralash shakllar) tekshirildi; IL-1 $\beta$ , IL-8, IL-10, IFN- $\gamma$  va RaIL-1 $\beta$  darajalari IFA usuli bilan aniqlanib,  $p < 0,05$  darajasida baholandi.



Natijalar. Glomerulonefritli bemorlarda nazorat guruhiga nisbatan IL-1 $\beta$  6,5 barobar, IFN- $\gamma$  8,6 barobar va RaIL-1 $\beta$  7,2 barobar yuqori ekanligi aniqlandi ( $p < 0,05$ ). Nefrotik shaklda IL-1 $\beta$  ( $107,1 \pm 21,6$  pg/ml) va RaIL-1 $\beta$  ( $780,3 \pm 24,6$  pg/ml) maksimal darajada bo'lib, IL-1 $\beta$ /RaIL-1 $\beta$  ko'rsatkichi nazoratga nisbatan 4,5 barobardan ortiq oshgan ( $p < 0,05$ ). Xulosa. Glomerulonefritda sitokin disbalansi klinik shakliga bog'liq holda o'zgarib, kasallik patogenezida immun-yallig'lanish mexanizmlarining turlicha faolligini aks ettiradi.

**Kalit so'zlar:** glomerulonefrit, sitokinlar, IL-1 $\beta$ , IFN- $\gamma$ , immun yallig'lanish, klinik shakllar.

### **Relevance**

The immune system is a highly organized, multi-level regulatory network that maintains the body's homeostasis. According to the World Health Organization (WHO), up to 70% of chronic inflammatory and metabolic diseases are accompanied by immune regulation disorders, highlighting the key role of immune mechanisms in the pathogenesis of various diseases. Disturbances at any stage of immune response development can initiate or exacerbate the development of a pathological process [2, 5, 8, 12].

Despite the diversity of clinical manifestations, many diseases, including endocrine ones, share common pathogenetic links associated with immune dysfunction. In this context, the functional interaction of the immune and endocrine systems is particularly important. Their close integration determines the systemic nature of the body's adaptive and pathological responses [1,3,9,11].

It has been established that the immune and endocrine systems are subject to bilateral regulation at all levels of ontogenesis. The thymus plays a key role in the formation of neuroendocrine structures in the early stages of embryonic development, and neuroendocrine hormones are capable of modulating the immune response and the activity of thymus factors. Immunocompetent cells synthesize a wide range of mediators—lymphokines, interferons, and interleukins—which have pronounced hormone-like properties. The



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hypothalamic-pituitary-adrenal axis is involved in the regulation of antibody formation and controls the release of mature B-lymphocytes from the bone marrow. The presence of receptors for neuropeptides on immune system cells confirms the possibility of a direct endocrine effect on immunoreactivity. This indicates a profound functional relationship and mutual regulation of these systems [4, 6, 10, 14].

Under pathogenic conditions, activation of the innate and adaptive immune systems is accompanied by the initiation of a cytokine cascade, which is closely linked to endocrine regulatory mechanisms. Concurrent with increased production of proinflammatory mediators, the hypothalamic-pituitary-thyroid axis is activated. This process is considered an adaptive response aimed at maintaining the body's internal balance. This integrative activation ensures an adequate response to external stressors, including infectious agents and psychoemotional stress [7, 13, 15].

Thus, immune-endocrine interaction plays a key role in the formation of adaptive and compensatory reactions during the development of pathological conditions.

### **The purpose of the study:**

Study of the role of pro- and anti-inflammatory cytokines in the development of various forms of glomerulonephritis.

### **Materials and methods of research:**

As part of an in-depth study of hormonal, immune, and cytokine status, 103 patients with glomerulonephritis were selected from a general cohort. Participants aged 18 to 60 years were included in the study, having signed voluntary informed consent in accordance with the principles of the Declaration of Helsinki. The clinical trial had an open, standardized design.

Depending on the clinical form of glomerulonephritis, patients were divided into four groups: latent (n=28), nephrotic (n=25), hypertensive (n=25), and mixed (n=25). Inclusion criteria were a confirmed diagnosis of glomerulonephritis, age 18–60 years, and written informed consent. Patients with endocrine pathology,



secondary forms of glomerulonephritis, immunodeficiency states, and signs of renal failure were excluded from the study. Pregnant women and individuals over 60 years of age were also excluded.

All participants underwent ultrasound examination of the kidneys and thyroid gland using an SSD system from Aloka (Japan). Serum levels of immunobiochemical markers, including pro- and anti-inflammatory cytokines, were determined using enzyme-linked immunosorbent assay (ELISA) using the Vector-Best and ElisaKid test systems.

Statistical data processing was performed using MS Excel 16.0. The significance of differences was assessed using the t-test; values at  $p < 0.05$  were considered statistically significant.

### **Research results:**

The average age of the examined patients at the time of diagnosis was  $35.0 \pm 4.7$  years. The causes of the disease were such factors as viral infections - acute respiratory viral infections, influenza, viral hepatitis ( $10.3 \pm 0.7\%$ ); tonsillitis, chronic tonsillitis ( $6.7 \pm 0.6\%$ ); pregnancy, childbirth ( $8.7 \pm 1.2\%$ ); hypothermia ( $3.8 \pm 0.4\%$ ); hemorrhagic vasculitis ( $2.3 \pm 0.4\%$ ); bronchitis, pneumonia ( $2.1 \pm 0.3\%$ ); streptoderma, staphyloiderma ( $0.5 \pm 0.2\%$ ); vaccination ( $0.3 \pm 0.1\%$ ). In general, in  $24.8 \pm 0.7\%$ , a connection between the occurrence of GN and infection was observed. In addition to 746 patients ( $51.4 \pm 1.23\%$ ), in whom this kidney pathology was subclinical throughout the observation period, among patients with other forms of GN, in  $10.21 \pm 0.64\%$  of patients (in 18 patients with nephrotic GN, in 86 patients with the hypertensive form and 9 patients with the mixed form of GN), the disease in the early stages also proceeded asymptotically with only laboratory changes, and on average after  $15.1 \pm 2.1$  months it transitioned to other forms of the disease (hypertensive, mixed, nephrotic).

56 ( $4.1 \pm 0.51\%$ ) patients were treated for diseases other than GN, although blood tests already showed changes indicating glomerular renal disease. This fact was established retrospectively during the study of outpatient card data. According to the retrospective analysis, patients in this group had changes in urine tests (proteinuria -  $0.5 \pm 0.01$  g / l, microhematuria or macrohematuria (in 2 patients) -



9.3±0.9 erythrocytes in the field of view) several months before the clinical manifestation of the disease and the diagnosis of GN. The patients in this group were predominantly young men (under 25 years old) who consulted an otolaryngologist about ENT infections (tonsillitis, chronic tonsillitis, chronic pharyngitis). The average duration of the subclinical course of the disease was 21.2±1.3 months. During this period, patients were treated with a non-renal diagnosis.

The classic manifestation with a cyclical course of the disease, with the manifestation of a triad of syndromes (edematous, hypertensive, urinary) was observed only in 31 patients (3.4%).

The distribution of various clinical forms of the disease varied across age groups. Among patients aged 18 to 25, renal involvement with urinary syndrome was prevalent (69%). This form of GN also predominated in the 25 to 45 age group (57%), with an increased proportion of the nephrotic form (15%) and hypertensive (7%). In patients over 45, the hypertensive form was more common (43%). With increasing age, an increase in the proportion of glomerular renal involvement leading to nephrosclerosis was noted. While it was not detected at all in the first age group (under 25), it was observed in 1.8% of patients in the second group, and in 17% in the third.

Of the total number of patients observed, 103 patients with GN were selected for participation in this study. The examined patients were divided into 4 groups depending on the predominant syndromes of disease manifestation (Table 1).

Group I included 28 patients with a latent (urinary) form of the disease, which is known to be an oligosymptomatic form of glomerulonephritis. The patients had no subjective sensations of the disease. Objective signs were scant. In most patients, blood pressure was within the normal range. In 3 patients, short-term increases in blood pressure were observed from time to time (systolic up to 145 mm Hg, diastolic up to 95 mm Hg). Edema was absent. Proteinuria fluctuated from 0 to 2 g / L in different patients. More often, only traces of protein (< 0.03 g / L) were detected. Erythrocyturia was also weakly expressed (from 1 to 60 in the field of view) and inconstant. The content of hyaline casts in urine fluctuated within 1-3 in the field of view, granular and waxy casts were not detected at all.



Renal concentrating capacity remained unchanged: tubular reabsorption was 97-100%. No nitrogen retention was observed in the blood: serum creatinine levels ranged from 60 to 120  $\mu\text{mol/L}$ . SCF values, determined by the clearance method, ranged from 65-90 ml/min. Patient ages ranged from 18 to 53 years. Disease duration ranged from 1 month to 29 years.

**Table 1 Characteristics of the study groups**

Indicators	Groups of patients with GN			
	Group I	Group II	Group III	Group IV
	latent form	nephrotic form	hypertension-Czech form	mixed form
Number of patients:				
General	28	25	25	25
With acute course of GN	6 (21%)	6 (24%)	7 (28%)	7 (28%)
With chronic course of GN	22 (79%)	19 (76%)	18 (72%)	18 (72%)
Men	16 (57%)	15 (60%)	14 (56%)	14 (56%)
Women	12 (43%)	10 (40%)	11 (44%)	11 (44%)
Age (years)	33.1 $\pm$ 10.1	34.2 $\pm$ 6.9	35.4 $\pm$ 7.2	33.1 $\pm$ 8.1
Duration diseases (years)	11.5 $\pm$ 1.4	7.1 $\pm$ 0.5	9.0 $\pm$ 4.8	6.1 $\pm$ 1.8

The next group (Group II) included 25 patients with nephrotic GN. As the patients themselves noted, the development of edema syndrome was gradual: initially, puffiness under the eyes and ankle swelling appeared in the mornings, later the swelling became constant, spreading to the trunk. In some patients, physical and instrumental examination revealed hydrothorax, ascites, and hydropericardium. At this stage, dry skin appeared, its elasticity decreased, and muscle atrophy developed. Blood pressure did not increase. Proteinuria was recorded at levels from 3.0 to 7.0 g/L, erythrocyturia - from 2 to 50 in the field of view, cylindrical cytoplasm - from 2 to 4 in the field of view. Tubular function did not change: tubular reabsorption ranged from 98 to 100% in different patients in the group. SCF values in different patients within the group ranged from 62 to 85 ml/min.



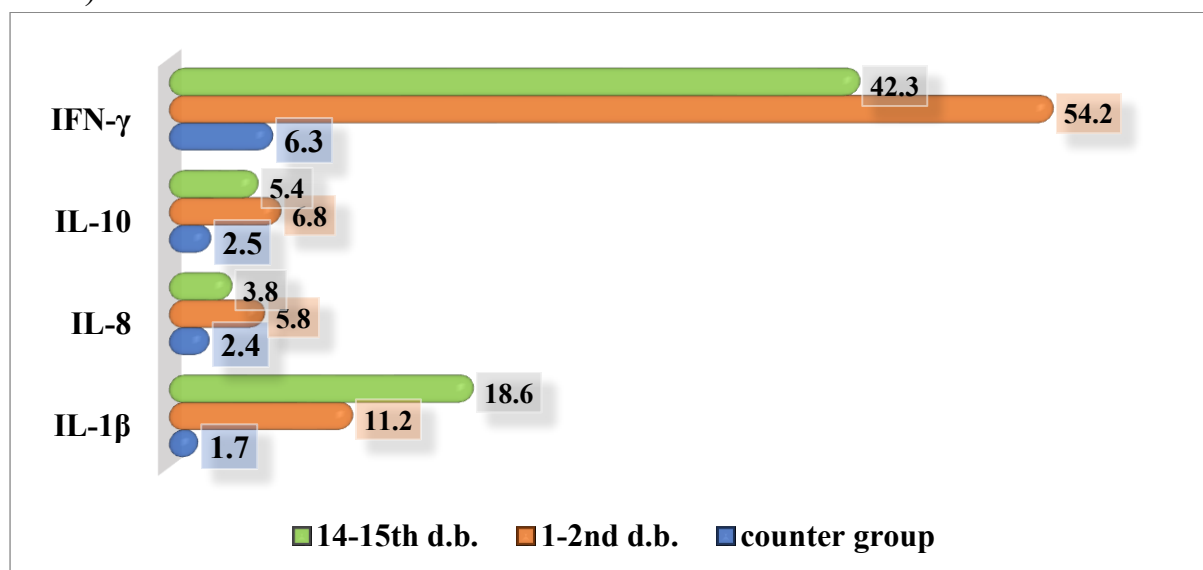


Disease duration ranged from 1 month to 7 years.

Group III included 25 patients with the hypertensive form. Arterial hypertension was the dominant clinical symptom in this group. Edema was absent in most patients, although mild and intermittent edema was present in two patients. Urine changes were minor: all patients had urine protein levels less than 0.03 g/L, no more than 1 cast per field of view, and the number of red blood cells in the urine ranged from 10 to 50 per field of view. Disease duration ranged from 1 month to 15 years in different patients, and age ranged from 18 to 26 years.

Group IV included patients with a mixed form of GN. Most patients presented with progressive hypertension and edema of varying severity (ranging from facial puffiness to widespread and cavitory edema) from the onset. Urinary tract infection was characterized by significant nonselective proteinuria (more than 2 g/day), with micro- or macrohematuria. Hypoalbuminemia, hypercholesterolemia, and hypercoagulability were observed. Disease duration ranged from 2 months to 9 years in different patients.

To identify the pathogenetic role of various immunological factors in the pathogenesis of GN, we determined the level of a number of different cytokines (IL-1 $\beta$ , IL-8, IL-10, IFN- $\gamma$ ) in the blood serum of patients with GN during inpatient treatment (1-2nd and 14-15th days) and practically healthy people (Fig. 3.2.1).



**Fig. 1. Serum cytokine content in patients with GN (pg/ml)**



A comparative analysis of patients with GN upon admission to hospital revealed a difference in the levels of the studied cytokines compared to the control group. (Table 1). Differences were observed in all the cytokines studied: IL-1 $\beta$  – 6.5 times, IL-8 – 2.4 times, IL-10 – 2.7 times, IFN- $\gamma$  – 8.6 times. The level RAIL-1 $\beta$  was also elevated, differing 7.2-fold from the control group. This cytokine level trend persisted until the end of inpatient treatment (days 14-15). RAIL-1 $\beta$  and IFN- $\gamma$  levels showed a significant decrease over the course of inpatient treatment.

**Table 2. Serum cytokine levels in patients with GN**

Cytokines, pg/ml	Days of illness	Control group n=20	Patients with GN n=103	R
IL-1 $\beta$	1-2nd	1.7 $\pm$ 0.2	11.2 $\pm$ 1.4	<0.05
	14-15th		18.6 $\pm$ 2.1	<0.05
IL-8	1-2nd	2.4 $\pm$ 0.3	5.8 $\pm$ 1.7	>0.05
	14-15th		3.8 $\pm$ 1.2	>0.05
IL-10	1-2nd	2.5 $\pm$ 0.8	6.8 $\pm$ 1.3	>0.05
	14-15th		5.4 $\pm$ 1.1	>0.05
RA IL-1 $\beta$	1-2nd	43.2 $\pm$ 6.7	312.3 $\pm$ 27.8	<0.05
	14-15th		289.3 $\pm$ 34.1	<0.05
IFN- $\gamma$	1-2nd	6.3 $\pm$ 0.7	54.2 $\pm$ 7.6	<0.05
	14-15th		42.3 $\pm$ 6.1	<0.05

The next step of our study was to examine the cytokine status of patients depending on the clinical form of GN (Table 2). A comparison was made between the parameters of one specific form and the parameters of a composite group comprising all other forms of GN. Thus, Table 2 presents the parameters of patients with the latent form and a composite group including nephrotic, hypertensive, and mixed forms of GN.

The latent form of GN was characterized by low levels of proinflammatory cytokines - IL-1 $\beta$ , its receptor antagonist and IL-8 both at the beginning and at the end of treatment, and the initial levels of anti-inflammatory cytokines (IL-10 and IFN- $\gamma$ ) were at a fairly high level. In the latent form of GN, the level of





expression of IL-1 $\beta$  and RAIL-1 $\beta$  increased in a unidirectional manner, which can be judged by the integral indicator, which is equal to the ratio of these cytokines (IL-1 $\beta$ /RAIL-1 $\beta$ ) within the control values, as well as in patients of the comparison group, that is, in the combined group of other forms of GN, an increase in the level of IL-1 $\beta$  predominated over the degree of RAIL-1 $\beta$  production, and as a result, the average value of this integral indicator - IL-1 $\beta$ /RAIL-1 $\beta$  was 2.89 times higher than this indicator in the control group. During inpatient therapy in patients with latent GN, no significant changes in cytokine status were observed.

**Table 3 Cytokine levels in patients with latent GN**

Cytokines, pg/ml	Days of illness	Control group n=20	Latent form of GN n=28	Other forms of GN n=75	R
IL-1 $\beta$	1-2nd	1.7 $\pm$ 0.2	10.8 $\pm$ 1.6	19.2 $\pm$ 2.5	<0.05
	14-15th		7.1 $\pm$ 1.1	24.6 $\pm$ 3.1	<0.05
IL-8	1-2nd	2.4 $\pm$ 0.3	2.5 $\pm$ 1.1	5.1 $\pm$ 2.1	>0.05
	14-15th		2.8 $\pm$ 1.2	5.6 $\pm$ 1.2	>0.05
IL-10	1-2nd	2.5 $\pm$ 0.8	4.8 $\pm$ 1.7	3.8 $\pm$ 1.5	>0.05
	14-15th		2.7 $\pm$ 1.4	3.7 $\pm$ 1.1	>0.05
RA IL-1 $\beta$	1-2nd	43.2 $\pm$ 6.7	380.3 $\pm$ 24.6	412.9 $\pm$ 31.8	<0.05
	14-15th		367.4 $\pm$ 27.5	379.3 $\pm$ 31.8	<0.05
IFN- $\gamma$	1-2nd	6.3 $\pm$ 0.7	83.1 $\pm$ 23.5	51.2 $\pm$ 8.6	<0.05
	14-15th		54.7 $\pm$ 26.7	52.4 $\pm$ 6.4	<0.05

Notes: P- here and in Table 3.2.1 – reliability (<0.05) of differences in indicators in patients relative to control values

In patients with the nephrotic form of GN, changes in cytokine levels were opposite to those found in patients with the latent form of the disease: levels of IL-1 $\beta$ , RAIL-1 $\beta$ , and IL-8 were higher than in patients with other forms of GN, while the level of IL-10 was lower (Table 3). The content of IFN- $\gamma$  in patients with the nephrotic form of GN at the end of treatment was lower compared to the value of this cytokine in patients with other forms of the disease.



**Table 4 Cytokine levels in patients with nephrotic GN**

Cytokines, pg/ml	Days of illness	Control group n=20	Nephrotic form of GN n=25	Other forms of GN n=78	R
IL-1 $\beta$	1-2nd	1.7 $\pm$ 0.2	107.1 $\pm$ 21.6	11.2 $\pm$ 2.5	<0.05
	14-15th		72.1 $\pm$ 19.1	12.4 $\pm$ 3.1	<0.05
IL-8	1-2nd	2.4 $\pm$ 0.3	6.8 $\pm$ 1.2	4.1 $\pm$ 1.8	>0.05
	14-15th		5.7 $\pm$ 1.1	3.9 $\pm$ 1.2	>0.05
IL-10	1-2nd	2.5 $\pm$ 0.8	2.8 $\pm$ 0.7	4.1 $\pm$ 1.5	>0.05
	14-15th		2.7 $\pm$ 1.1	2.9 $\pm$ 1.1	>0.05
RA IL-1 $\beta$	1-2nd	43.2 $\pm$ 6.7	780.3 $\pm$ 24.6	462.9 $\pm$ 31.8	<0.05
	14-15th		567.4 $\pm$ 27.5	393.3 $\pm$ 31.8	<0.05
IFN- $\gamma$	1-2nd	6.3 $\pm$ 0.7	73.1 $\pm$ 33.5	75.2 $\pm$ 12.6	<0.05
	14-15th		44.7 $\pm$ 26.7	52.4 $\pm$ 6.4	<0.05

In patients in the general group, the increase in IL-1 $\beta$  and RAIL-1 $\beta$  levels was equivalent, resulting in the integrated indicator (IL-1 $\beta$ /RAIL-1 $\beta$ ), reflecting their balance, not exceeding control values. In patients with nephrotic GN, this integrated indicator was more than 3.2 times higher than in the general group and 4.5 times higher than in the control group.

Patients with the hypertensive form of GN were characterized by low levels of IL-8 and IL-10 before treatment and a high level of Ra-IL-1 $\beta$  (Table 5).

**Table 5 Cytokine levels in patients with hypertensive GN**

Cytokines, pg/ml	Days of illness	Control group n=20	Hypertensive form of GN n=25	Other forms of GN n=78	R
IL-1 $\beta$	1-2nd	1.7 $\pm$ 0.2	14.1 $\pm$ 21.6	14.2 $\pm$ 2.5	<0.05
	14-15th		22.3 $\pm$ 11.5	25.7 $\pm$ 3.1	<0.05
IL-8	1-2nd	2.4 $\pm$ 0.3	4.7 $\pm$ 1.2	5.2 $\pm$ 1.8	>0.05
	14-15th		5.2 $\pm$ 1.1	3.8 $\pm$ 1.3	>0.05
IL-10	1-2nd	2.5 $\pm$ 0.8	2.8 $\pm$ 0.7	4.6 $\pm$ 1.5	>0.05
	14-15th		2.7 $\pm$ 1.1	2.9 $\pm$ 1.1	>0.05
RA IL-1 $\beta$	1-2nd	43.2 $\pm$ 6.7	512.3 $\pm$ 24.6	442.9 $\pm$ 31.8	<0.05
	14-15th		767.4 $\pm$ 27.5	386.3 $\pm$ 31.8	<0.05
IFN- $\gamma$	1-2nd	6.3 $\pm$ 0.7	58.1 $\pm$ 33.5	65.2 $\pm$ 12.6	<0.05
	14-15th		57.7 $\pm$ 26.7	52.4 $\pm$ 6.4	<0.05



The mixed form of GN was characterized by high levels of IL-8 before treatment and high levels of IL-1 $\beta$ , IFN- $\gamma$ , and IL-10 after treatment compared to the overall group. A decrease in IL-8 expression was also observed with an increase in the integral indicator. IL-1 $\beta$ /RAIL-1 $\beta$  after treatment (Table 6).

**Table 6 Cytokine levels in patients with mixed GN**

Cytokines, pg/ml	Days of illness	Control group n=20	Mixed form of GN n=25	Other forms of GN n=78	R
IL-1 $\beta$	1-2nd	1.7 $\pm$ 0.2	24.1 $\pm$ 21.6	14.2 $\pm$ 2.5	<0.05
	14-15th		37.3 $\pm$ 11.5	18.7 $\pm$ 3.1	<0.05
IL-8	1-2nd	2.4 $\pm$ 0.3	8.7 $\pm$ 1.2	5.1 $\pm$ 1.8	>0.05
	14-15th		5.4 $\pm$ 1.1	3.9 $\pm$ 1.3	>0.05
IL-10	1-2nd	2.5 $\pm$ 0.8	3.9 $\pm$ 0.8	4.2 $\pm$ 1.5	>0.05
	14-15th		4.7 $\pm$ 1.1	2.9 $\pm$ 1.1	>0.05
RA IL-1 $\beta$	1-2nd	43.2 $\pm$ 6.7	507.3 $\pm$ 21.6	462.9 $\pm$ 21.8	<0.05
	14-15th		467.4 $\pm$ 22.5	376.3 $\pm$ 19.8	<0.05
IFN- $\gamma$	1-2nd	6.3 $\pm$ 0.7	38.1 $\pm$ 13.5	55.2 $\pm$ 12.6	<0.05
	14-15th		62.7 $\pm$ 16.7	48.4 $\pm$ 6.4	<0.05

The next stage of our study was to evaluate the cytokine status of patients with various clinical forms of GN (Table 7). Analysis of the presented data revealed that each clinical form was characterized by dynamic activity of a specific cytokine. Thus, the nephrotic form was characterized by the lowest IL-8 levels, while the highest levels of this cytokine were observed in the mixed form. The latent form was characterized by the highest IL-10 level, while the lowest values for this cytokine were observed in the nephrotic and hypertensive forms. High levels of IL-1 $\beta$  and RAIL-1 $\beta$  were observed in the nephrotic form of GN, while low levels were observed in the urinary form of GN. IFN- $\gamma$  levels differed only in the latent form of GN and were higher than in patients with other forms of the disease.



**Table 7 Cytokine levels in patients with various forms of GN**

Cytokines, pg/ml	Days of illness	Latent form of GN n=28	Nephrotic form of GN n=25	Hypertension- Czech forms of GN n=25	Mixed form of GN n=25
IL-1 $\beta$	1-2nd	10.8 $\pm$ 1.6	107.1 $\pm$ 21.6	14.1 $\pm$ 21.6	24.1 $\pm$ 21.6
	14-15th	7.1 $\pm$ 1.1	72.1 $\pm$ 19.1	22.3 $\pm$ 11.5	37.3 $\pm$ 11.5
IL-8	1-2nd	2.5 $\pm$ 1.1	6.8 $\pm$ 1.2	4.7 $\pm$ 1.2	8.7 $\pm$ 1.2
	14-15th	2.8 $\pm$ 1.2	5.7 $\pm$ 1.1	5.2 $\pm$ 1.1	5.4 $\pm$ 1.1
IL-10	1-2nd	4.8 $\pm$ 1.7	2.8 $\pm$ 0.7	2.8 $\pm$ 0.7	3.9 $\pm$ 0.8
	14-15th	2.7 $\pm$ 1.4	2.7 $\pm$ 1.1	2.7 $\pm$ 1.1	4.7 $\pm$ 1.1
RA IL-1 $\beta$	1-2nd	380.3 $\pm$ 24.6	780.3 $\pm$ 24.6	512.3 $\pm$ 24.6	507.3 $\pm$ 21.6
	14-15th	367.4 $\pm$ 27.5	567.4 $\pm$ 27.5	767.4 $\pm$ 27.5	467.4 $\pm$ 22.5
IFN- $\gamma$	1-2nd	83.1 $\pm$ 23.5	73.1 $\pm$ 33.5	58.1 $\pm$ 33.5	38.1 $\pm$ 13.5
	14-15th	54.7 $\pm$ 26.7	44.7 $\pm$ 26.7	57.7 $\pm$ 26.7	62.7 $\pm$ 16.7

## Conclusion

When comparing cytokine levels before and after treatment in patients with the latent form, no significant dynamics were found in the levels of any cytokines during treatment. The most pronounced cytokine profile dynamics were observed in patients with the nephrotic form of the disease, who showed decreased levels of IL-8, IL-10, IFN- $\gamma$ , and RAIL-1 $\beta$ . In the mixed variant, IL-8 production decreased, as in patients with the nephrotic form of the disease, but, unlike the latter, the IL-1 $\beta$ /RAIL-1 $\beta$  ratio significantly increased. In the group of patients with hypertensive GN, RAIL-1 $\beta$  levels increased, while IL-10 levels decreased slightly.

Regarding the final cytokine levels, it should be noted that patients with nephrotic GN maintained the minimum levels of IL-1 $\beta$ , RAIL-1 $\beta$ , and IL-8 found at the beginning of treatment. In patients with the nephrotic form, only IL-10 levels remained elevated for a long time; the mean value, as at the beginning of treatment, was minimal compared to other patient groups. Furthermore, nephrotic GN had the lowest IFN- $\gamma$  levels at the end of treatment.

Thus, the cytokine profile of patients with the hypertensive form at the end of treatment, as in patients with nephrotic GN, showed a reduced IL-2 level relative to other patient groups. In mixed GN, high levels of IL-1 $\beta$ , IL-10, IFN- $\gamma$ , and IL-1 $\beta$ /RAIL-1 $\beta$  were detected.



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