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Immune Metabolic Stress In Purulent Inflammatory Diseases. Pyelonephritis.

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ABSTRACT

The article reports on the study devoted to the clinical manifestations of pyelonephritis and possible options of its diagnostics. The study included findings of over 120 patients with 6 variations of pyelonephritis. Based on the analysis of the patients' findings the authors have demonstrated: an opportunity to diagnose variations of the immune metabolic status using non-specific methods with further formalization of signaling tests as formulas; to specify the effect of clinical peculiarities of the disease based on the typical laboratory findings; to correlate immunologic and metabolic mechanisms of purulent inflammatory pathology of the urinary tract.

Keywords: immune-metabolic disorders, pyelonephritis, immunologic parameters, metabolic parameters.

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INTRODUCTION

Pyelonephritis is a non-specific inflammatory process with prevailing damage of the renal tubular system, mostly of the bacterial etiology. There are known three major types of pyelonephritis – acute, chronic, chronic with exacerbation. The compromised immune system appears to be a specific factor leading to the onset of the disease. The disease is difficult to diagnose, since it has diverse manifestations and sometimes occurs in the latent form.

The aim of the study was to validate objective assessment of typical changes of the laboratory status using non-specific methods and to document functional relations between variations of immunologic and metabolic parameters (metabolic immunity) in different variations of pyelonephritis[1].

MATERIALS AND METHODS

Acute and chronic pyelonephritis, combinations of chronic pyelonephritis with chronic cystitis, chronic salpingo-oophoritis, kidney stone disease, benign prostatic hyperplasia (BPH) were selected as clinical models of purulent inflammatory kidney disorders. Research subjects and healthy donors were categorized into 7 randomized groups,20-25 patients in each group, based on their gender, age, and a form of the disease.

The number of leukocytes, lymphocytes, mature and immature granulocytes (stabs and segmentonuclear cells), monocytes and erythrocyte sedimentation rate (ESR) were assessed in all patients using routine techniques. Clones and subclones of lymphocytes (T-cells, T-helpers, T-cytotoxic, T-regulatory, T-active, T-dependent natural killers, regulatory natural killers, B-lymphocytes) were identified in the immunological study by the NAVIOS Beckman Coulter flow cytofluorometry using monoclonal antibodies CYTO-STATtetraCHROM. Phagocytic absorbing and oxygen-producing capacity (phagocytic index, phagocytic number, nitro blue tetrazolium spontaneous (NBT_{spont}), nitro blue tetrazolium activated (NBT_{activ})) was also detected. The content of circulating immune complexes (CIC), serum immune globulins of the main classes (IgM, IgG, IgA), medium weight molecules (MWM), pro- and anti-inflammatory cytokines (interleukins IL-2, 4, 6, 8, 10, TNF)was determined by the immunoenzyme method using sets of reagents of the “Protein contour” company (“Proteinovyikontur” – Russian version) [2, 9].

Spectrophotometry methods, fluorescence techniques, reactions with 2-thiobarbituric acid and others [5-8, 10] allowed specifying the following parameters: free radical oxidation parameters of lipids and proteins – diene conjugates, ketodienes, malondialdegyde (MDA), bi-tyrosine linkages, Schiff’s bases, – and parameters of the antioxidant defense system – superoxide dismutase (SOD), catalase, vitamin E, systemic thiols, protein thiols, non-protein thiols, plasma anti-oxidative activity.

Validity of the results obtained was supported by application of the modern panel of planning methods - randomization, representativeness of the sample - according to L.E. Kholodov, V.P. Yakovlev formula [2], statistical analysis of the obtained parameters using parametric (Student’s) and non-parametric (Wilcoxon-Mann-Whitney) criteria depending on the normal distribution of the parameters. Signaling tests were determined using coefficient of diagnostic consideration (Kj) calculated on the formula,

$$Kj = \frac{2 \cdot (\delta_1^2 + \delta_2^2)}{(M_2 - M_1)^2},$$

where $^2_1$ и δ^2_2 – mean root square deviations, M_1, M_2 – mean values of the parameters of the compared groups; they were interpreted as follows: the lower was the Kj module, the higher was the level of parameters deviations from the target level.

Key parameters were formalized into the standard formulas of the immune system disorders and metabolic disorders calculated with reference to normal values in healthy people. Association of the key immunologic and metabolic parameters was characterized by determining the number of strong correlations of formulas summands and a coefficient > 0.6. [2].

Summarized (Σ), stimulated (+), suppressed (-) variations were grouped by the methods of parameter investigations – hematologic, immunologic, metabolic – and by the components of the immunity system – cellular, B-dependent, phagocytic, cytokine, as well as by the parameters of free radical oxidation and the antioxidant defense system. Integral assessment of the variations was ranked on the scale into insignificant

(the 3rd rank) under the relevant variation of the parameter value in 0-33% of patients, average (the 2nd rank) - in 34-66% of patients, significant (the 1st rank) – in more than 66% [3].

RESULTS

The frontal analysis of variation of hematologic inflammatory markers given in Table 1 was qualitatively similar in all variations of purulent inflammatory diseases and demonstrated leukocytosis, monocytosis, accelerated ESR; accumulation of mature granulocytes, eosinophilia and limphopenia were registered in all cases except for acute pyelonephritis. Quantitatively, modification of 100% of parameters was observed in patients with chronic pyelonephritis + BPH, chronic pyelonephritis + chronic cystitis, chronic pyelonephritis; modification of 86% of parameters was observed in patients with chronic pyelonephritis + kidney stone disease,; modification of 57% of parameters was observed in patients with acute pyelonephritis.

Qualitative analysis of immunologic markers in acute cystitis revealed minimal changes. In patients with chronic pyelonephritis, chronic pyelonephritis + chronic cystitis, chronic pyelonephritis + chronic salpingo-oophoritis, chronic pyelonephritis + kidney stone disease, chronic pyelonephritis + BPH the level of T-cells, operative and reserve metabolism of neutrophils in the context of stimulation of B-cells, IgM, auto-aggressive CIC, MWM, anti-inflammatory IL6 and IL8 decreased and was absolute, except for patients with chronic pyelonephritis + BPH. Variations of regulatory T-cell subpopulations appeared to be variously directed and dependent on the clinical forms of purulent inflammatory disorders. Thus, the number of T-helpers decreased in 5 variations of the disease, except chronic pyelonephritis, where stimulation was observed; the number of T-cytotoxic decreased in chronic pyelonephritis, chronic pyelonephritis + chronic cystitis, and increased in chronic pyelonephritis + chronic salpingo-oophoritis, chronic pyelonephritis + kidney stone disease, chronic pyelonephritis + BPH. Phagocytic index was positive in patients with acute and chronic pyelonephritis, and negative in combination of chronic pyelonephritis with salpingo-oophoritis and benign prostatic hyperplasia. Anti-inflammatory cytokines (IL2, IL4) were mostly reduced, and anti-inflammatory TNF α – increased.

Generally, relative resulting vectors of stimulation/suppression of T-dependent parameter variations from the norm level were close in patients with 6 variations of the purulent inflammatory diseases and were equal 42 and 32%; relative resulting vectors of stimulation/suppression of humoral parameters were characterized by the activation prevailing over inhibition – 75 and 14%; relative resulting vectors of stimulation/suppression of phagocytic and cytokine tests were 28 and 42%, 36 and 22% correspondingly.

Therefore, patients with purulent inflammatory diseases of the urinary tract developed relevant reaction of 72% of the investigated immunologic parameters to the pathological process; of these, 45% of parameters were with the stimulating vector, 28% of parameters were with the suppressing vector (Table 1).

Proportion of metabolic parameters significantly different from the norm level of healthy people demonstrated that in patients with pyelonephritis this number constituted 46%, in patients with combination of chronic cystitis with kidney stone disease or BPH this number constituted 69%, in patients with chronic pyelonephritis, chronic pyelonephritis and chronic cystitis, chronic pyelonephritis and chronic salpingo-oophoritis this number constituted 85%. The vector of decreased values prevailed in calculating the proportion of stimulated and suppressed laboratory parameters.

Frontal qualitative analysis of differences of metabolic parameters in patients with 6 variations of purulent kidney diseases compared to the norm level of healthy people was performed; general tendency of free radical oxidation parameters activation and anti-oxidant defense system parameters suppression with certain variations of specific tests depending on clinical findings of pathological processes was revealed. Thus, for instance, the MDA level appeared to be suppressed in all cases; the ketodienes level appeared to be suppressed in acute and chronic pyelonephritis and their combination with cystitis or benign prostatic hyperplasia; the Schiff's bases level appeared to be suppressed in chronic pyelonephritis and its combination with kidney stone disease or chronic salpingo-oophoritis. The concentration of diene conjugates, at the same time, was decreased in chronic pyelonephritis, chronic pyelonephritis + chronic cystitis, chronic pyelonephritis + kidney stone disease, chronic pyelonephritis + BPH, and increased in chronic pyelonephritis + chronic salpingo-oophoritis; the concentration of bi-tyrosine linkages was decreased in acute pyelonephritis, chronic pyelonephritis + chronic cystitis, and increased in pyelonephritis + BPH, chronic pyelonephritis + chronic salpingo-oophoritis.

As for non-enzymatic summands of the anti-oxidant defense, the decreased plasma anti-oxidant activity was observed in all nosoforms; the decreased level of systemic thiols was observed in chronic pyelonephritis, chronic pyelonephritis + kidney stone disease, chronic pyelonephritis + BPH, chronic pyelonephritis + chronic salpingo-oophoritis; the decreased level of non-protein thiols was observed in chronic pyelonephritis, chronic pyelonephritis + chronic cystitis, chronic pyelonephritis + chronic salpingo-oophoritis; the decreased level of protein thiols was observed in chronic pyelonephritis + chronic cystitis, chronic pyelonephritis + BPH, chronic pyelonephritis + chronic salpingo-oophoritis. Variations of vitamin E concentrations were suppress-directed in acute pyelonephritis, chronic pyelonephritis + chronic cystitis, chronic pyelonephritis + chronic salpingo-oophoritis, and stimulation-directed in chronic pyelonephritis, chronic pyelonephritis + kidney stone disease, chronic pyelonephritis + BPH. Changes of the anti-oxidant defense system enzymatic mechanism tended to decrease but not in all patients. Thus, the content of superoxide dismutase and catalase was suppressed in chronic pyelonephritis, chronic pyelonephritis + kidney stone disease,chronic pyelonephritis + chronic salpingo-oophoritis and acute pyelonephritis; the ceruleoplasmin level was activated in chronic pyelonephritis, chronic pyelonephritis + kidney stone disease,chronic pyelonephritis + BPH and suppressed in chronic pyelonephritis + chronic cystitis. These data proved certain affinity of the free radical oxidation and the anti-oxidant defense system response and certain variability dependent on clinical peculiarities – the stage and combination of the disease.

Summarized data of the formalized assessment of the immune metabolic parameters variations in patients with pyelonephritis are given in Table 3.

The formalized analysis of laboratory findings detected two regularities: general decreased expressiveness of the parameter changes in patients with acute pyelonephritis compared to other variations of the disease, and monotonous (typical) variations of the studied parameters, with the exception of suppressed tests, the level of pro- and anti-inflammatory cytokines, and the number of strong intersystemic correlative links of parameters in patients with various kidney diseases. They are given in bold in Table 3.

Thus, the decreased proportion of summarized – hematologic, immunologic, metabolic - parameters was relevant in patients with chronic pyelonephritis + chronic cystitis or BPH; in all other cases this number was insignificant. Significant changes of the cytokine level of the 1st rank were registered in the combined pathologies – chronic pyelonephritis + chronic cystitis, chronic pyelonephritis + kidney stone disease, chronic pyelonephritis + BPH; moderate changes of the cytokine level of the 2nd rank were registered in the combination of chronic pyelonephritis + chronic salpingo-oophoritis; insignificant changes of the cytokine level of the 3rd rank were observed in mono-diseases – acute and chronic pyelonephritis. Based on the number of relevant correlations the most activity was detected in combination chronic pyelonephritis + salpingo-oophoritis (8 associations), then – in kidney stone disease or BPH (6 associations each, next – in chronic pyelonephritis + chronic cystitis (5 associations each) and in acute pyelonephritis and chronic pyelonephritis (3 associations each).

The decreased total rank of parameter variations from the target level in patients with different purulent inflammatory diseases was as follows: chronic pyelonephritis + chronic cystitis, chronic pyelonephritis + chronic salpingo-oophoritis; chronic pyelonephritis + kidney stone disease, chronic pyelonephritis + BPH; chronic pyelonephritis, acute pyelonephritis.

Detalization of the key metabolic parameters calculated using a coefficient of diagnostic value was formalized in the formulas, see Table 4.

Quantitative distribution of the signaling immunologic and metabolic parameters in typical formulas of disorders in patients with 6 variations of purulent inflammatory diseases was as follows: the immunity cellular component in the formula of the immune system disorders included 22% of tests, the humoral and non-specific – 39% each; the free radical oxidation component in the formula of metabolic disorders included 61% of tests, the anti-oxidant defense system – 39% of tests.

Qualitative comparison of the formulas in patients with specific nosoforms reported that, relating immunologic parameters, considering order of location, vector and degree of changes, variations were registered in 2-3 parameters out of three; relating metabolic parameters – in three out of three.

In particular, patients with **acute pyelonephritis** revealed: stimulation of the phagocytic index level, molecule weight mass, T cytotoxic suppressors and – the decreased content of catalase, plasma anti-oxidative

activity, vitamin E. Patients with **chronic pyelonephritis** revealed accumulation of B-cells, MWM, Schiff's bases, MDA against inhibition of the neutrophil and superoxide dismutase metabolism. In combination **chronic pyelonephritis and chronic cystitis,** the leading position was taken by leukocytosis, T-cells deficiency, phagocytic number combined with the increased concentration of ketodienes, MDA, and SOD insufficiency. In combination **chronic pyelonephritis with chronic salpingo-oophoritis**, patients revealed monocytosis, the excess of B-lymphocytes, the decreased content of the NBT test, with stimulation of bi-tyrosine linkages, decrease of SOD and protein thiols. Combination of **chronic pyelonephritis with kidney stone disease** resulted in the activation of formation of B-lymphocytes, CIC, T-cytotoxic suppressors, MDA, Schiff's bases with the decreased plasma anti-oxidative activity. In combination **chronic pyelonephritis with BPH** patients revealed insufficiency of T-cytotoxic cells, overproduction of CIC, deficiency of anti-inflammatory IL6, diene conjugate, MDA, system thiols.

Qualitative analysis of correlations of the key immune metabolic parameters gives evidence of the simultaneously revealed peculiarities and differentiation of concrete mechanisms of the metabolic immunity in various purulent inflammatory diseases.

Thus, patients with **acute pyelonephritis** demonstrated association of the phagocytic absorbing capacity with factors of the substrate free radical oxidation (MDA, Schiff's bases), and MWM – with plasma anti-oxidative activity. Patients with **chronic pyelonephritis** revealed converse dynamics – B cells were connected with one free radical oxidation parameter (MDA), and MWM – with 2 tests of the anti-oxidant defense (vitamin E and SOD). The combination **chronic pyelonephritis + chronic cystitis** provided correlation of leukocytosis with diene conjugates; T-cells with Schiff's bases, SOD; the phagocytic number with catalase and non-protein thiols. In **chronic pyelonephritis + chronic salpingo-oophoritis** the number of monocytes depended on the level of non-enzymatic anti-oxidant defense mechanisms (vitamin E, non-protein thiols); the number of B-lymphocytes depended on markers of the lipid and protein free radical oxidation (MDA, bi-tyrosine linkages), enzymes of the anti-oxidant defense system (catalase, SOD); the operative oxygen-dependent metabolism of neutrophils depended on the free radical oxidation and anti-oxidant defense system factors (ketodienes and ceruleoplasmin). In patients with **chronic pyelonephritis + kidney stone disease** the number of B-cells consistently changed with 2 parameters of the free radical oxidation (Schiff's linkages, MDA), and 2 parameters of the anti-oxidant defense system (plasma anti-oxidative activity, catalase); CIC concentration consistently changed with non-enzymatic mechanisms of the anti-oxidant system (ceruleoplasmin and systemic thiols). In patients with complex pathology **chronic pyelonephritis + BPH** the content of T-cells correlated with three free radical oxidation tests (ketodienes, MDA, bi-tyrosine linkages); the content of auto-active CIC correlated with ceruleoplasmin activity; the content of anti-inflammatory IL2 – with mechanisms of the free radical oxidation and anti-oxidant defense system (ketodienes and plasma anti-oxidative activity).

Table 1. Frontal analysis of the relevant variations of laboratory findings from the norm level in patients with pyelonephritis

Parameters	Acute pyelonephritis	Chronic pyelonephritis	Chronic pyelonephritis + chronic cystitis	Chronic pyelonephritis + chronic salpingo-oophoritis	Chronic pyelonephritis + kidney stone disease	Chronic pyelonephritis + BPH
Leukocytes	+	+	+	+	+	+
Lymphocytes		-	-	-	-	-
Stabs	+	+	+			+
Segmentonuclear		+	+	+	+	+
Eosinophils		+	+	+	+	+
Monocytes	+	+	+	+	+	+
Erythrocyte sedimentation rate (ESR)	+	+	+	+	+	+
T-cells		-	-	-	-	-
T-helpers	-	+	-	-	-	-
T-cytotoxic		-	-	+	+	+

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T-regulatory		+	-	+	+	-
T-activated	+	+	+	+		
$NK_{T\text{-dependent}}$	+		+	+	+	
$NK_{regulatory}$	-	+	+			+
$NK_{cytotoxic}$	+		+		+	+
B		+	+	+	+	+
IgM	+	+	+	+	+	+
IgG		+	+	-	+	-
IgA			+	-	-	-
Circulatingimmune complexes (CIC)	+	+	+	+	+	+
Medium weight molecules (MWM)	+	+	+	+	+	+
CD11b		+				-
CD18	+					
Phagocytic index (PhI)	+	+	+	-	+	-
Phagocyticnumber (PhN)	+		+	-	+	+
Nitro Blue Tetrozolium spontaneous (NBT_{spont})	-	-	-	-	-	-
Nitro Blue Tetrozolium activated (NBT_{activ})		-	-	-	-	-
IL2			-	-	-	
IL4			-		-	-
IL6		+	+	+	+	+
IL8		+	+	+	+	
IL10					-	-
Tumor necrosis factor (TNF)	+		+		+	+
Malondialdegyde (MDA)	+	+	+	+	+	+
Diene conjugates		-	-	+	-	-
Ketodienes	+	+	-			+
Schiff's bases		+		+	+	
Bi-tyrosine linkages	-		-	+		+
Plasma anti-oxidative activity	-	-	-	-	-	-
Vitamin E	-	+	-	-	+	+
Superoxide dismutase (SOD)		-		-	-	-
Ceruleoplasmin	+	+	-		+	
Systemic thiols		-		-	-	
Non-protein thiols			-	-		
Protein thiols			-	-		-
Catalase	-	-	-	-	-	

Notes: +/- relevantly stimulated/ suppressed parameters compared to the normal level.

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Table 2. Parameters of the metabolic immunity in pyelonephritis

Parameters	Norm	Acute pyelonephritis	Exacerbation of chronic pyelonephritis	Exacerbation of chronic pyelonephritis + exacerbation of chronic cystitis	Exacerbation of chronic pyelonephritis + kidney stone disease	Exacerbation of chronic pyelonephritis + BPH	Exacerbation of chronic pyelonephritis + exacerbation of chronic salpingo-oophoritis
Free radical oxidation of lipids and proteins							
MDA, µM/l	1.36±0.1	1.4±0.3*	2.3±0.11*	1.87±0.2*	2.6±0.3*	2.9±0.3*	3.0+_1.2*
Diene conjugates, relative density unit/ml	30.3+0.04	29. 5±0.12	28.5±0.03*	27.8±0.06*	29.0±0.05*	24.5+0.3*	35.4±0.3*
Ketodienes «-«	19.2+0.02	21.6±0.03*	22.2±0.06*	25.6±0.5*	20.5±1.0	24.5±1.2*	20.4±1.3
Schiff's bases «-«	30.04+2.9	31.9±2.7	48.9±4.8*	32.3±2.5	45.1±2.9*	32.3±3.8	39.7±4.5*
Bi-tyrosine linkages, relative units/ml	0.3±0.02	0.29±0.05*	0.31±0.2	0.34±0.05*	0.33±0.03	0.4±0.01*	0.44±0.2*
The anti-oxidant system							
Plasma anti-oxidative activity, µM/l	65.3±1.3	32.2±1.5*	25.6±0.4*	45.2±2.1*	20.4±0.9*	28.1±0.9*	30.0±1.8*
Vitamin E,µM/l	20.9±3.8	16.6±2.7*	33.5±2.2*	14.7±1.5*	33.7±3.1*	34.6±0.4*	14.9+_1.5*
SOD,µM/ml	0.9±0.03	0.83±0.08	0.4±0.1*	0.6+_0.01	0.8±0.02*	0.8±0.02*	0.3±0.01*
Ceruleoplasmin,µM/l	264.2+29.9	275.9±17.0	301.8±10.6*	238.9±31.1*	340.5±31.0*	300.7±-21.1*	272.1±20.9
Systemic thiols, mM/l	44.52+0.85	46.9±5.0	35.2±2.1*	45.8±1.3	29.9±0.77*	29.8±0.6*	31.3±0.9*
Non-protein thiols, mM/l	23.86+0.71	24.5±0.6	20.8±3.2	17.5±0.4*	22.2±1.9	24.3±1.0	19.5±0.6*
Protein thiols, mM/l	38.8±0.82	40.4±1.7	37.4±1.8	30.2±0.7*	39.5±1.4	34.1±2.5*	21.3±1.7*
Catalase,µM/l*min	31.1±1.43	22.4±1.7*	27.5±1.3*	25.5±1.8*	25.0±1.2*	26.7±4.8	25.4±1.1*

Notes: *significance of deviations from the norm, P<0.05.

Table 3. Formalized rank assessment of total variations of the immune-metabolic parameters from the norm in patients with pyelonephritis

Parameter	Frontal analysis			Grouped parameters									CL	Sum of ranks	variations
	Σ	+	-	H	I	M	Detailed values								
							C	B	Ph	Cy	F	A			
Acute pyelonephritis	2	3	**3**	2	2	2	2	2	1	**3**	2	2	**3/4**	29	IV
Chronic pyelonephritis	1	2	**3**	1	1	1	1	1	1	**3**	1	1	**3/4**	20	III
Chronic pyelonephritis + chronic cystitis	1	2	**2**	1	1	1	1	1	1	**1**	1	1	**5/3**	17	I

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Chronic pyeloneph ritis + chronic salpingo-oophoritis	1	2	**3**	1	1	1	1	1	1	**2**	1	1	**8/1**	17	I
Chronic pyeloneph ritis + kidney stone disease	1	2	**3**	1	1	1	1	1	1	**1**	2	1	**6/2**	18	II
Chronic pyeloneph ritis + BPH	1	2	**2**	1	1	2	1	1	1	**1**	1	2	**6/2**	18	II

Notes: the numerator denotes the number of strong links, the denominator – rank of differences; Σ/+/- sum/stimulating/suppressed parameters; H-hematologic, I-immunologic, M-metabolic, C-cellular, B - B-dependent, Ph – phagocytic, Cy – cytokine, F – free radical oxidation, A – antioxidant defense system – grouped parameters; CL – correlation links of the cellular component of the immunity to the free radical oxidation parameter; 1/2/3 – sufficient/moderate/insufficient rank of variations; I-IV – decreasing total levels of parameter variations.

Table 4. Signaling tests of the key formulas of the immune metabolic disorders and their correlations in patients with pyelonephritis

Disorder	Formula of the immune system disorders	Formula of metabolic disorders	Correlations
Acute pyelonephritis	$PhI^{+}_{2}MWM^{+}_{3}Tcyt^{+}_{3}$	$C^{-}_{1}PAA^{-}_{2}VE^{-}_{1}$	PhI^{+}_{2}-**MDA,+ScB;** MWM^{+}_{3}-**PAA**
Exacerbation of chronic pyelonephritis	$B^{+}_{3}MWM^{+}_{3}NBTsp^{-}_{2}$	$ScB^{+}_{2}SOD^{-}_{2}MDA^{+}_{3}$	B^{+}_{3}**+MDA**; MWM^{+}_{3}-**VE,-SOD**;
Exacerbation of chronic pyelonephritis + exacerbation of chronic cystitis	$L^{+}_{3}T^{-}_{3}PhN^{-}_{3}$	$KD^{+}_{2}MDA^{+}_{2}SOD^{-}_{2}$	L^{+}_{3}**+DC**; T^{-}_{3}+**ScB,-SOD**; PhN^{-}_{3}-C**,-NPT**
Exacerbation of chronic pyelonephritis + exacerbation of chronic salpingo-oophoritis	$M^{+}_{3}B^{+}_{3}NBTsp^{-}_{2}$	$BL^{+}_{2}SOD^{-}_{2}BL^{-}_{2}$	M^{+}_{2}-**VE,-ST**; B^{+}_{3} **–MDA,-BL**,-C**, +SOD**; $NBTsp^{-}_{2}$+**KD,-CP**
Exacerbation of chronic pyelonephritis + kidney stone disease	$B^{+}_{3}CIC^{+}_{3}Tcyt^{+}_{2}$	$MDA^{+}_{3}ScB^{+}_{2}PAA^{-}_{3}$	B^{+}_{3}-**ScB,+PAA,+MDA,-C**; CIC^{+}**CP,-ST**
Exacerbation of chronic pyelonephritis + BPH	$Tcyt^{-}_{3}CIC^{+}_{3}IL6^{-}_{2}$	$DC^{-}_{2}MDA^{-}_{1}ST^{-}_{3}$	$Tcyt^{+}_{3}$ **+KD.-MDA,+BL**;CIC^{+}_{3}-**CP;**IL^{-}_{2}-**KD,+PAA**

Notes: parameters that have valid correlations are given **in bold**; other designations are as follows: Tc – T cytotoxic, IgM - immune globulins of class M, MWM - medium weight molecules, Th – T-helpers, IgA – immune globulins of class A, IL8 – interleukins 8, L – leukocytosis, T – T-cells, PhN – phagocytic number, Tac – T active, NBTactiv – Nitro Blue Tetrazolium activated, AOD – anti-oxidant defense system, C – catalase, SOD –

superoxide dismutase, CP – ceruleoplasmin, ST – systemic thiols, PAA – plasma anti-oxidative activity, KD – ketodienes, MDA – malondialdegyde, BL – bi-tyrosine linkages, VE – vitamin E, DC – diene conjugate, ScB – Schiff's bases, NPT – non-protein thiols.

CONCLUSIONS

1. Application of non-specific methods of assessment of immunologic (population, sub-populations of lymphocytes, immune globulins, MWM, CIC, absorbing, metabolic capacity of phagocytes, pro- and anti-inflammatory cytokines) and metabolic parameters (the substrate free radical oxidation, the anti-oxidant defense system) gave an opportunity to characterize and formalize changes of the immune metabolic status in patients with pyelonephritisin diagnostic formulas.

2. Six clinical variations of pyelonephritis were proved to have a determinating influence on typical changes of the metabolic immunity in patients with pyelonephritis.

3. Correlative analysis of strong links of signaling laboratory tests allowed specifying the phenomenon of interaction of specific immunologic and metabolic mechanisms in various purulent inflammatory diseases.

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