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Characteristics of hematological parameters in military patients with post-Covid cardiac syndromes

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Abstract: Today, the world is actively identifying new markers that characterize the severity of the condition after suffering from COVID-19. For a more detailed understanding of what changes the SARS-CoV-2 virus causes in the human body and what is associated with the long-term persistence of symptoms after a new coronavirus infection, it is necessary to evaluate the relationship between patients with post-Covid cardiac syndromes and clinical blood test parameters.

Keywords: post-Covid cardiac syndrome (PCCS), chronic persistent myoendocarditis (CPME), chronic fibrinous pericarditis (CFP), chronic heart failure (CHF), PLR, NMR, LMR, SII, arterial hypertension combined with dyslipidemia,

Introduction. Coronavirus disease 2019 (COVID-19), originated from Wuhan, China, has rapidly spread throughout the world, with the number of cases increasing exponentially from 2019 to 2022 [1, 4]. Currently, healthcare systems around the world are faced with another important problem, namely the consequences caused by the SARS-CoV-2 virus on the human body. Most patients with post-Covid syndrome require dynamic monitoring, and therefore in 2020 Klok F.A. et al. developed an ordinal scale for ranking patients after COVID-19 in order to highlight significant criteria and combine them into categories - the Post COVID-19 Functional Status Scale (PCFS) [7]. At the same time, to characterize the reaction of the immune system, it is more objective to use the results of a clinical blood test, more precisely the leukocyte formula and various coefficients and indices that have previously shown themselves to be good in predicting the course of acute COVID-19. The most obvious coefficients are NLR (granulocyte to lymphocyte ratio), PLR (platelet to lymphocyte ratio), LMR (lymphocyte to monocyte ratio), MLR (monocyte to lymphocyte ratio), as well as the systemic immune inflammation index SII (calculated based on blood parameters - platelets, granulocytes and lymphocytes) [10].

The aim of this study was to evaluate the potential relationship between post-Covid cardiac syndromes (PCCS) and chronic inflammation ratios such as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), lymphocyte/monocyte ratio (LMR), systemic immune inflammation index (SII), which can be obtained from a complete blood count.

Material and methods. Clinical examination of patients was carried out at the bases of the Military Medical Academy (Military Hospital). The study included 170 patients with cardiac post-Covid syndromes (average age 42±4.2 years), which developed 2-3 weeks after suffering from COVID-19 at various stages, pneumonia with lung damage. Lung involvement up to 70% was noted in 12 (7.0%), lung

involvement up to 40% in 45 (26.5%) and lung involvement up to 15% in 58 (34.0%) patients. And in 55 (32.3%) patients there was no lung damage. The diagnosis of COVID-19 was confirmed by PCR. Patients who had no previous pathology of the cardiovascular system.

The control group consisted of 35 practically healthy patients. Of these, n=164 (80%) men with an average age of 43±2.8 years and n=41 (20%) women with an average age of 40±2.0. Of the total number of patients examined, 35 developed chronic fibrinous pericarditis (CFP) (average age 40±2.8 years), 57 had arterial hypertension combined with dyslipidemia (average age 38±2.3 years), and 65 had chronic persistent myoendocarditis (CPME) (average age 28±3.4 years) and 18 with chronic heart failure (CHF) (average age 48±3.2 years).

Table. 1.

Characteristics of blood parameters in patients with post-Covid cardiac syndromes

J.	Indicators	CFP (n=35)	AH+ dyslipidemia (n=57)	CHF (n=18)	CPME (n=65)	Control group (n=35)
1.	Total red blood cell count (RBC)	4,17±1,0	5,30±1,60	4,67±1,20	5,41±1,80	4,87±0,90
2.	Hemoglobin (Hb)	12,4±1,30	15,0±2,3	14,10±3,0	14,10±2,8	12,50±2,0
3.	Hematocrit (Ht)	36,5±3,20	45,4±4,0	42,0±3,60	43,7±3,30	43,9±2,80
4.	Absolute reticulocyte count	58,4±2,90	86,0±4,0 ***°°°	72,9±3,90**°°	88,5±4,50***°°°	55,0±4,20
5.	Difference in hemoglobin content in reticulocyte and mature erythrocyte	5,40 ±0,70*	7,30±1,20**	6,60± 0,50*	9,10±1,20***°°	3,40±0,90
6.	Erythrocyte sedimentation rate (ESR)	11,0± 2,20	10,0±1,20	14,0±1,50*	18,0±2,10**°	9,0±1,20
7.	Total platelet count	236, 0±5,60***	360,0± 6,90***°°°	262,0 ±4,90*	345,0± 7,20***°°°	295,0±6,90
8.	Thrombocrit	0,31 ±0,02	0,32±0,04	0,38± 0,04	0,46±0,08	0,32±0,03
9.	Immature platelets	1,50 ±0,06	2,20±0,08	6,60± 1,30**°°°	8,10±1,0***°°°	3,90±0,50
10.	Total white blood cell count	7200 ±325***	9500±652***°°	8400± 523***	10500± 652***°°°	5200±225
11.	Lymphocytes %	45,0 ±4,90**	49,0±3,80***	43,0± 6,30**	48,0±7,0***	28,0±4,80
12.	Absolute reactive lymphocytes	0,20 ±0,01**°°	0,60±0,08***°°	0,03± 0,01	0,80±0,02 ***°°°	0,01±0,002
13.	Reactive lymphocytes %	0,40 ±0,06	2,0±0,90 ***°°°	0,40± 0,02	7,0±0,60***°°°	0,20±0,03

14.	Absolute neutrophil count	3,37 ±0,60	5,29±1,0**	4,70± 0,80*	8,28±1,0***°	2,84±0,50
15.	Neutrophils	63,1 ±3,2	46±3,0	60,5± 4,3	67,6±3,8	54,6±4,2
16.	Immature granulocytes %	0,70 ±0,02**	1,10±0,30***°°°	0,30± 0,02	0,20±0,01	0,20±0,04
17.	Absolute monocyte count	0,41 ±0,02	2,25±0,50***°°°	0,65± 0,02*	0,82±0,05 **°°	0,35±0,01
18.	Monocytes %	7,70 ±1,50	6,90±1,80	8,40± 1,20*	9,60±1,90**°°	6,70±2,20
19.	Absolute eosinophil count	0,08 ±0,01	0,19±0,03	0,12± 0,02	0,06±0,01	0,19±0,05
20.	Eosinophils %	1,50 ±0,50	1,70±0,30	1,50± 0,40	0,50±0,08	3,70±0,90
21.	Basophils %	1,30 ±0,09**	1,50±0,05**	1,25± 0,05**	1,80±0,08***	0,80±0,04

*Note: *p<0.05, **p<0.01, ***p<0.001 – significant difference with the control group. °p<0.05, °°p<0.01, °°°p<0.001 – significance of the difference between groups*

Leukocytes and their structural composition are the most important indicators for calculating complex indicators of inflammation. The total number of leukocytes in the group of patients with CPME was increased by 49.52% (p<0.001) compared to the control group. And in patients with arterial hypertension combined with dyslipidemia, it was increased by 42.50% (p <0.001). The level of immature platelets (IPF) in the blood of patients with CPME compared to the control group was higher by 48.14% (p<0.001), compared with patients with arterial hypertension combined with dyslipidemia by 27.16% (p<0.001).

There was a pronounced increase in one of the markers of inflammation, the indicator of the difference in hemoglobin content in a reticulocyte and a mature erythrocyte (Delta-He), in patients with CPME compared to the control group by 2.6 times (p<0.001). And in patients with arterial hypertension, combined with dyslipidemia, it was increased by 2.2 times (p<0.01), in the group of patients with CFP by 1.6 times (p<0.05). Also, the level of immature platelets in the blood was significantly increased in patients with CHF compared to the control group by 45.50% (p <0.001). Lymphocytosis and monocytosis were observed in all groups of patients (p<0.001). The absolute number of reticulocytes in the blood was increased in patients with CPME in comparison with the control group by 62.14%, and in patients with CHF by 60.0% and in patients with arterial hypertension combined with dyslipidemia by 57.0% (p <0.001).

In all groups of patients, moderate basophilia was noted (p <0.001), which was a predictor of the development of immune-inflammatory processes in patients after suffering from COVID-19. Erythrocyte sedimentation rate (ESR) is one of the oldest nonspecific markers for quantifying the inflammatory process [5,7]. In this study, ESR was significantly higher in groups of patients with CPME compared to the control group by 50.0%. And in patients with CHF by 44.0% (p<0.01).

Iron homeostasis and the inflammatory process are closely linked through the action of hepcidin - in addition to suppressing the acute inflammatory response, it also reduces the availability of iron for erythropoiesis cells, retaining iron in

macrophages and suppressing iron absorption in the intestine. In patients with post-Covid syndrome, redistribution of iron in plasma quickly causes hypoferremia, as well as a decrease in Ret-He, leading to a drop in Delta-He. Inflammation inhibits erythropoiesis, reduces the availability of iron in the body and is accompanied by an increase in serum iron, and is also a risk marker for the development of an inflammatory process in the cardiovascular system, which leads to a number of conditions for the development of complications. Such as inflammatory damage to the walls of the vascular bed, including the coronary arteries (coronaritis), arterial hypertension, atherosclerosis and myoendocarditis [4,8].

Thus, hematological parameters related to inflammation, immature platelets, absolute reticulocyte count, difference in hemoglobin content of reticulocyte and mature erythrocyte (Delta-He), monocytosis and lymphocytosis are closely related to inflammation in the body in patients with PCCS.

Table.2.

Characteristics of chronic inflammation coefficients in patients with post-Covid cardiac syndromes

	Indicators	CFP (n=35)	AH+ dyslipidemia (n=57)	CHF (n=18)	CPME (n=65)	Control group (n=35)
.	Platelet index lymphocytes (PLR)	188,0±5,90***	172,0±4,60***	205,0±7,20***°°	250,0±5,80***°°°	110,0±4,90
.	Neutrophil/lymphocyte index (NLR)	3,80±0,60*	4,10±0,80*	5,0±0,90**	5,20±0,70**	2,50±0,50
.	Systemic immune inflammation index (SII)	645,0±22,0**	644,0±18,0**	638,0±13,0**	937,0±20,0***°°°	433±11,0
.	Lymphocyte/ monocyte index (LMR)	3,60±0,70	1,70±0,60**°°	1,40±0,20**°°°	1,70±0,40**°°	5,20±1,0

*Note: *p<0.05, **p<0.01, ***p<0.001 – significant difference with the control group. °p<0.05, °°p<0.01, °°°p<0.001 – significance of the difference between groups*

The next stage of the study was to assess complex indicators of inflammation and determine the types of immune response in patients with post-Covid cardiac syndromes. The platelet-to-lymphocyte ratio (PLR) in patients with CPME compared to the control group was higher by 44.0% (p<0.001), and in patients with CHF it was higher by 34.20% (p<0.001). Comparisons between the groups of patients with CPME and those with CAF, the level of PLR was significantly higher in patients with CPME by 75.20%, which was a high significant value (p < 0.001). The neutrophil/lymphocyte index (NLR) was significantly higher in patients with CPME compared to the control group by 48.0%, in patients with CHF by 46.0% (p<0.01), as well as in patients with arterial hypertension combined with dyslipidemia higher by 30.0% (p<0.05).

The value of the systemic immune inflammation index (SII) in the group of patients with CPME in comparison with the control group was 2.2 times higher ($p < 0.001$). And in patients with CFP, the SII score was 1.5 times higher ($p<0.01$). In comparison between the groups, the index of systemic immune inflammation with patients with CPME and a patient with CFP was 1.5 times higher, which was significant ($p < 0.001$). The LMR coefficient in comparison with the control group in patients with CHF was 3.7 times lower, and in patients with CPME it was also 3.1 times lower ($p < 0.001$). This means that patients with post-Covid cardiac syndromes had a reduced protective reaction in the body.

Thus, according to immunolaboratory tests, it was revealed that all patients had an increased marker of the inflammatory process, NLR, PLR, LMR, SII can be useful for early prediction of the development of PCCS. It is emphasized that among these LMR indicators, SII may be the best independent variable that can be used to predict PCCS.

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