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HEMATOLOGICAL BLOOD PARAMETERS IN RESIDENTS OF YAKUTSK RECOVERED FROM CORONAVIRUS INFECTION COVID-19

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The study is devoted to a comparative analysis of the results of the effect of COVID-19 coronavirus infection on hematological blood parameters in patients who have been ill after three, six, nine and twelve months. Monitoring of hematological parameters is important for the identification and control of patients who have undergone COVID-19, who need additional assistance, and stratification of the risk of severe course of the disease. The study involved 161 residents of Yakutsk aged 20 to 72 years who had suffered COVID-19 in different periods of the pandemic. The study of hematological parameters showed that the average indicators of the morphological composition of red and white blood in people who have had COVID-19 correspond to generally accepted standards, with the exception of the tendency to increase monocytes, basophils, ESR and a slight decrease in MCHC indicators, which indicates a recently transmitted infectious disease.

Keywords: coronavirus infection, COVID-19, SARS-CoV-2, blood test, hematological parameters of blood.

Despite the fact that the COVID-19 pandemic is currently considered over, according to WHO and a number of authors, up to 1 million cases of this disease are observed in the world every month [2, 14]. In this regard, intensive study of the clinical and epidemiological features of the disease, the development of new means of its treatment and prevention is still ongoing. The most common clinical manifestation of a new variant of coronavirus infection is bilateral pneumonia (viral diffuse alveolar injury with microangiopathy).

Numerous studies indicate that the new coronavirus infection has a different effect on the human body, causing various symptoms and complications, and also causes disorders in the blood clotting system. Some patients develop hypercoagulation syndrome with thrombosis and thromboembolism, other organs and systems are also affected (central nervous system, myocardium, kidneys, liver, gastrointestinal tract, endocrine and immune systems).

Based on the results of the analysis of publication activity, one of the most relevant in the study of this infection are hematological parameters that play an important role in the early diagnosis of the disease. The total number of leukocytes, the differential number of neutrophils, lymphocytes, eosinophils and monocytes, the number of platelets, the average volume of platelets and certain ratios of these parameters can be used as markers of inflammation in patients with COVID-19. The usual hematological changes observed in COVID-19 are: anemia, leukocytosis or leukopenia, neutrophilia, low levels of eosinophils or eosinophilia, thrombocytopenia and rarely thrombocytosis [11].

The purpose of this study is to study the effect of the new COVID–19 coronavirus infection on hematological blood parameters, depending on the duration and severity of the disease.

Materials and methods: The examination was carried out in the clinic of the Yakut scientific center for complex medical problems. 161 residents of Yakutsk, who suffered COVID-19 in different periods of the pandemic, aged from 20 to 72 years (including young people (20-44 years), were examined they were 56 people (34.8%); average (45-59 years old) – 53 people (32.9%); elderly (60-74 years old) – 51 people (31.7%) and senile (75-90 years old) – 1 person (0.6%) of age, respectively). There were 60 men (37.3%), 101 women (62.7%). All study participants gave voluntary informed consent to participate in the study according to the ethical standards of the Helsinki Declaration, which was approved by the decision of the local Ethics committee at the Yakut scientific center for complex medical problems, protocol No. 52 of March 24, 2021.

Four groups were formed, depending on the duration of the disease: the 1st group - up to 3 months, the 2nd group – up to 6, the 3rd group – up to 9, the 4th group - up to 12 months ago and according to the degree of lung damage by the type of "frosted glass", which were evaluated by the results of computed tomography (CT) obtained from discharge epicrisis: CT0 (zero) – absence of lung damage; CT1 (mild) – lung volume damage less than 25%; CT2 (moderate) – prevalence 25-50%; CT3 (severe) – 50-75%.

The material for the study was blood taken from the ulnar vein in the morning on an empty stomach. A general blood test was performed on a hematological analyzer "Sysmex KX-21N" (Japan), using reagents "CELLPACK" (Japan). The erythrocyte sedimentation rate (ESR) was determined by the Panchenkov method.

The analysis of the indicators was carried out as part of a one-stage study. Statistical processing of the results of the study was carried out using the Statistica 27 software package. The significance of the differences was assessed using the Student's t-test and ANOVA for independent samples with normal distribution and the Mann-Whitney test with abnormal distribution. A significance level of $p<0.05$ was established for all parameters. Correlation analysis of the data was carried out using the Pearson method.

Results and discussion. Hematological studies have shown that the average indicators of the morphological composition of red and white blood in people who have had COVID-19 correspond to generally accepted standards, with the exception of a tendency to increase monocytes, basophils, ESR and a slight

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decrease in MCHC indicators, which indicates a recently transmitted infectious disease.

According to the data obtained by us, depending on the duration of the disease, the platelet count was within the normal range, however, a statistically significant increase in platelet levels was noted only in group 4 in comparison with groups 1, 2 and 3 (p=0.001, p=0.044, p=0.010, respectively) (table 1). A direct correlation between the platelet level and the level of leukocytes (r=0.527; p<0.000), rod-shaped and segmented neutrophils (r=0.239; p<0.042 and r=0.278; p<0.007) and an inverse relationship with MCV and MCH (r=-0.239; p<0.022 and r=-0.266; p<0.010), with lymphocytes (r=-0.320; p<0.002) and monocytes (r=-0.23; p<0.027). According to literature data, after an infection, pronounced changes are determined by the content of platelets in peripheral blood. After a covid infection, there is a natural decrease in the content of platelets in peripheral blood during the first three months. Then there is a slow increase in their number. The number of these cells in the peripheral blood that is safe against hemorrhagic complications is achieved within 6 months of the postcovid period. It should be noted that normalization of platelet count is not achieved even after a year [1]. Thrombocytopenia is moderate, but more pronounced in the group of patients with severe course and subsequently died from COVID-19 [3, 8, 16].

A number of studies have shown that an informative criterion for identifying patients with severe forms of new coronavirus infection is the level of lymphocytes in the general blood test [12, 16]. The most frequent and characteristic feature is lymphopenia [3, 8]. According to the data obtained by us, the level of lymphocytes at all terms was within the normal range (Table 1). An inverse correlation was revealed with platelets (r=-0.320; p<0.002), leukocytes (r=-0.286; p<0.000), rod-shaped and segmented neutrophils (r=-0.189; p<0.038 and r=-0.786; p<0.000, respectively).

Comparative analysis of erythrocyte levels at all times revealed a significant increase in the first group in comparison with the 2nd, 3rd and 4th groups (p=0.06, p=0.042, p=0.021, respectively), however, the readings of erythrocytes were within the reference values (Table 1). Correlation analysis showed a direct relationship with hemoglobin (r=0.705; p<0.000) and leukocytes (r=0.295; p<0.00) and

Table 1

Hematological blood parameters depending on the duration of the disease

Indicator	I group up to 3 months	II group up to 6 months	III group up to 9 months	VI group up to 12 months	Significance
Leukocytes (4.0-9.0 x 10^9/l)	5.33 ± 0.34 n=15	6.13 ± 0.22 n=77	5.83 ± 0.24 n=49	5.84 ± 0.25 n=22	-
Erythrocytes (M. 4.0-5.1 x 10^{12} units/l, W. 3.7-4.7 x 10^{12} units/l	4.88 ± 0.09 n=15	4.68 ± 0.05 n=75	4.63 ± 0.05 n=49	4.56 ± 0.08 n=22	$p=0.06^{1-2}$ $p=0.042^{1-3}$ $p=0.021^{1-4}$
Hemoglobin (M. 132-164, W. 115-145)	140.73 ± 3.14 n=15	137.08 ± 1.56 n=75	134.35 ± 2.33 n=48	138.18 ± 2.34 n=22	-
Hematocrit, % (M. 40-48, W. 36-42)	44.45 ± 0.90 n=15	43.54 ± 0.43 n=75	43.14 ± 0.61 n=48	43.39 ± 0.65 n=22	-
MCV, fl (M. 81-93, Ж. 82-96)	92.26 ± 0.83 n=15	93.19 ± 0.58 n=75	92.72 ± 0.90 n=48	95.15 ± 0.67 n=22	$p=0.066^{3-4}$
MCH, pg (27-33)	29.21 ± 0.39 n=15	29.35 ± 0.23 n=75	28.94 ± 0.38 n=48	30.26 ± 0.27 n=22	$p=0.016^{3-4}$
MCHC, % (32,6-36,2)	31.65 ± 0.20 n=15	31.48 ± 0.11 n=75	31.12 ± 0.18 n=48	31.82 ± 0.12 n=22	$p=0.053^{2-3}$ $p=0.007^{3-4}$
Platelets, (150-400 x 10^9/l)	227.75 ± 5.83 n=48	259.69 ± 9.68 n=51	240.00 ±12.79 n=19	293.00 ±13.53 n=13	$p=0.001^{1-4}$ $p=0.044^{2-4}$ $p=0.010^{3-4}$
RDW-CV, % (11,5-14,5)	13.47 ± 0.12 n=15	13.44 ± 0.11 n=75	13.79 ± 0.22 n=48	13.25 ± 0.13 n=22	$p=0.064^{3-4}$
ESR, mm/h (M. 1.00-10.0, W. 2.0-15.0)	13.20 ± 1.59 n=15	18.91 ± 1.54 n=75	18.10 ± 1.59 n=48	15.86 ± 2.14 n=22	-
Basophils, % (0-1)	0.53 ± 0.40 n=15	0.23 ± 0.08 n=75	0.37 ± 0.12 n=49	0.14 ± 0.07 n=22	-
Eosinophils, % (0-5)	3.00 ± 0.44 n=12	3.37 ± 0.27 n=69	3.56 ± 0.46 n=43	3.76 ± 1.03 n=21	-
Stick - core, % (1-6)	2.41 ± 0.61 n=12	2.38 ± 0.28 n=55	1.89 ± 0.19 n=37	3.21 ± 0.67 n=14	$p=0.046^{3-4}$ $p=0.028^{3-4}$
Segmentonuclear, % (45-70)	53.07 ± 3.11 n=15	55.04 ± 0.84 n=75	54.52 ± 1.32 n=48	54.14 ± 1.66 n=22	-
Lymphocytes, % (18-40)	33.73 ± 2.39 n=15	30.29 ± 0.76 n=75	31.10 ± 1.03 n=48	30.23 ± 1.46 n=22	-
Monocytes, % (2-9)	8.73 ± 0.93 n=15	10.21 ± 053 n=75	9.52 ±.048 n=48	10.32 ± 0.84 n=22	-

Note. In Tables 1-2, n is the number of people who have been ill, p is the level of statistical significance.

feedback with MCV and MCH (r=-0.350; p<0.000 and r=-0.205; p<0.000) and the term of the transferred COVID-19 (r=-0.172; p0,029).

The average hemoglobin content at all terms was within the normal range and had no significant differences, but in the 2nd, 3rd and 4th groups there was a tendency to decrease this indicator (Table 1). According to literature data, the causes of a decrease in hemoglobin levels may be damage to the erythrocyte membrane by the SARS-CoV-2 virus due to the presence of angiotensin and proteins interacting with ACE2 on the surface of erythrocytes, a direct attack by the heme virus, a violation of the regulation of iron metabolism, blood loss that occurred during renal replacement therapy and gastrointestinal bleeding in patients with or without the use of anticoagulants, autoimmune hemolytic anemia during a cytokine storm [5, 13].

The hematocrit level was within the upper limit of the norm and did not differ depending on the duration of the disease (Table 1).

According to the MCV data obtained by us, MCH RDW-CV in the fourth group of patients significantly increased (p=0.066, p=0.016 and p=0.064) in comparison with the third group, but were within normal values (Table 1). The detection of RDW-CV in a patient above the normal range reflects the presence of anisocytosis, probably associated with the presence of small and/or large erythrocytes, whereas a decrease in the value of this indicator, as a rule, has no clinical significance [4, 15].

The MCHC level is slightly reduced at all times. Significant differences were revealed when comparing the indicators of the second and third groups (p=0.053) and the third and fourth groups (p=0.007) (Table 1). In rare cases, a decrease in this indicator is associated with infectious processes in the acute phase.

The results of the obtained data revealed that the average values of white blood in people who have had COVID-19 are within acceptable normal values. According to the data obtained by us, the leukocyte level was within the normal range regardless of the time after recovery (Table 1). According to the literature, the leukocyte level in most patients is within the normal range, a third has leukopenia [3, 7, 8]. The level of leukocytes had a direct correlation with hemoglobin (r=0.256; p<0.001), with platelets (r=0.527; p<0.000), rod-shaped and segmented neutrophils (r=0.232; p<0.011 and r=0.271; p<0.000, respectively) and an inverse relationship with RDW-CV (r=-0.214; p<0.006), lymphocytes (r=-0.286; p<0.000) and monocytes (r=-0.176; p<0.025).

When calculating the number of monocytes as a percentage of all leukocytes, there was a tendency to increase in the second, third and fourth groups (Table

Table 2

Hematological blood parameters depending on the severity of CT

Indicator	CT 0	CT 1	CT 2	CT 3	Significance
Leukocytes (4.0-9.0 x 10^9/l)	5.43 ± 0.32 n=27	5.90 ± 0.19 n=60	6.03 ± 0.31 n=42	6.23 ± 0.31 n=32	-
Erythrocytes (M. 4.0-5.1 x 10^{12} units/l, W. 3.7-4.7 x 10^{12} units/l	4.66 ± 0.08 n=27	4.62 ± 0.05 n=60	4.61 ± 0.05 n=42	4.84 ± 0.07 n=32	$p=0.013^{1-3}$ $p=0.011^{2-3}$
Hemoglobin (M. 132-164, W. 115-145)	135.81 ± 2.42 n=27	134.03 ± 1.97 n=60	136.46 ± 1.76 n=42	143.03 ± 2.46 n=32	$p=0.045^{0-3}$ $p=0.011^{1-3}$ $p=0.03^{2-3}$
Hematocrit, % (M. 40-48, W. 36-42)	43.18 ± 0.72 n=27	49.42 ± 6.54 n=60	43.31 ± 0.49 n=42	45.08 ± 0.61 n=32	-
MCV, fl (M. 81-93, W. 82-96)	92.77 ± 0.84 n=27	92.92 ± 0.78 n=60	94.01 ± 0.59 n=42	93.19 ± 0.93 n=32	-
MCH, pg (27-33)	29.19 ± 0.36 n=27	29.10 ± 0.34 n=60	29.61 ± 0.23 n=42	29.54 ± 0.35 n=32	-
MCHC, % (32,6-36,2)	31.44 ± 0.16 n=27	31.27 ± 0.16 n=60	31.49 ± 0.11 n=42	31.68 ± 0.18 n=32	-
Platelets, (150-400 x 10^9/l)	250.89 ± 26.05 n=9	251.93 ± 9.95 n=29	252.87 ± 9.26 n=32	275.19 ± 17.72 n=21	-
RDW-CV, % (11,5-14,5)	13.55 ± 0.21 n=27	13.57 ± 0.17 n=60	13.38 ± 0.15 n=42	13.57 ± 0.14 n=32	-
ESR, mm/h (M. 1.00-10.0, W. 2.0-15.0)	15.33 ± 1.77 n=27	18.27 ± 1.43 n=60	20.17 ± 2.24 n=42	15.53 ± 1.94 n=32	-
Basophils, % (0-1)	0.67 ± 0.27 n=27	0.28 ± 0.08 n=60	0.19 ± 0.12 n=42	0.09 ± 0.05 n=32	$p=0.049^{0-1}$ $p=0.021^{0-2}$ $p=0.009^{0-3}$
Eosinophils, % (0-5)	4.45 ± 0.83 n=22	3.28 ± 0.30 n=56	2.89 ± 0.28 n=37	3.73 ± 0.72 n=30	-
Stick - core, % (1-6)	1.89 ± 0.25 n=18	2.36 ± 0.32 n=44	2.54 ± 0.33 n=33	2.30 ± 0.41 n=23	-
Segmentonuclear, % (45-70)	52.85 ± 1.71 n=27	55.47 ± 0.98 n=60	54.78 ± 1.46 n=42	54.09 ± 1.41 n=32	-
Lymphocytes, % (18-40)	32.29 ± 1.61 n=27	30.15 ± 0.84 n=60	31.15 ± 1.12 n=42	30.56 ± 1.21 n=32	-
Monocytes, % (2-9)	9.88 ± 0.59 n=27	9.80 ± 0.62 n=60	9.82 ± 0.63 n=42	10.09 ± 0.61 n=32	-

1). The level of monocytes had an inverse correlation with platelets (r=-0.231; p<0.027), with leukocytes (r=-0.176; p<0.025), with rod-shaped and segmented neutrophils (r=-0,232; p<0.011 and r=-0.477; p<0.000).

The average content of rod-shaped and segmented neutrophils in the postcovid period was within the normal range. A significant difference was revealed when comparing the indicators of rod-shaped neutrophils in the third and fourth groups (p=0.028) (Table 1).

Erythrocyte sedimentation rate (ESR) is one of the oldest non-specific markers of quantitative determination of the inflammatory process. An increase in ESR is observed in the 3rd and 4th groups (Table. 1), which does not contradict the literature data [3, 8]. The erythrocyte sedimentation rate had an inverse correlation with erythrocytes (r=-0.390; p<0.000), hemoglobin (r=-0.414; p<0.000) and MCHC (r=-0.171; p<0.029).

The results of red blood tests – platelet, erythrocyte, hemoglobin, hematocrit levels, depending on the degree of lung tissue damage, also varied within the reference values. However, there was a tendency of an unreliable increase in platelet levels depending on the degree of lung damage. The level of erythrocytes in persons with T3 was increased in comparison with the data at K 1 (p=0.013) and KT2 (p=0.011). The hemoglobin content of COVID-19 patients with CT3 was also increased in comparison with CT0 (p=0.045), CT1 (p=0.011) and CT2 (p=0.03) (Table 2). Correlation analysis showed that the hemoglobin level had a direct relationship with the degree of lung damage (r=0.185; p<0.019). This confirms the dependence of hemoglobin changes on the severity of lung tissue damage in a new coronavirus infection [7, 10]. In addition, hemoglobin had a direct relationship with MCV, MCH, MCHC (r=0.354; p<0.000; r=0.528; p<0.000; r=0.670; p<0.000, respectively), as well as an inverse relationship with RDW-CV (r=-0.486; p<0.000). The hematocrit level changed unreliably.

According to the data obtained by us, the level of leukocytes, regardless of the degree of damage to the lung tissue of SARS-CoV-2, was within the normal range and had no significant differences (Table 2).

The average content of basophils varied within the reference values, but depending on the CT level, there was a decrease in CT1, CT2 and CT3 compared to CT0 (p=0.049, p=0.022 and p=0.009, respectively) (Table 2).

In our study, the level of the largest and most lysosomally filled phagocytes of the granulocyte series – monocytes was higher than normal in all groups and did not depend on the degree of lung tissue damage, but had no statistically significant differences (Table 2).

The erythrocyte sedimentation rate in patients with COVID-19, depending on the CT level, was increased in all groups, while the greatest increase was observed with CT1 and CT2, but had no statistically significant differences (Table 2). The increased erythrocyte sedimentation rate is another inflammatory biomarker that is increased with COVID-19 [2]. The exact reason is not known. However, since ESR depends on changes in the size, shape of red blood cells and plasma concentration, it is assumed that COVID-19 can cause a change in the characteristics of red blood cells or plasma, which leads to an increase in ESR [9].

Thus, in the individuals we examined after COVID-19, almost all hematological blood parameters were within the reference values and did not significantly differ from the duration of the disease and the degree of lung damage of SARS-CoV-2. Depending on the duration of the new coronavirus infection, there was a significant decrease in platelet levels after 3, 6 and 9 months compared to 12 months, which is a positive sign and indicates the recovery of the body. However, in all patients with a new coronavirus infection, inflammatory processes remained at a low level, since the level of monocytes and ESR remained elevated in all, regardless of the duration of the disease and the degree of lung damage. Also, a low MCHC content, most pronounced after 9 months, indicates signs of hypochromic iron deficiency anemia.

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