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A.I. Yakovleva, L.D. Olesova, E.D. Okhlopkova

LIPID IMBALANCE IN YAKUTSK RESIDENTS WHEN INFECTED WITH THE SARS-COV-2 VIRUS AND IN THE POST-COVID PERIOD

YAKOVLEVA Alexandra Ivanovna – researcher, Laboratory of Biochemical and Immunological Research, DENCD, FSBSI Yakut Science Centre for Complex Medical Problems, sashyak@mail.ru; **OLESOVA Lyubov Dygynovna** – external researcher, Laboratory of Biochemical and Immunological Research, DENCD, FSBSI YSC CMP, oles59@mail.ru; **OKHLOPKOVA Elena Dmitrievna** – senior researcher, Laboratory of Biochemical and Immunological Research, DENCD, FSBSI YSC CMP. elena_okhlopkova@mail.ru.

A study of lipid metabolism was carried out in 161 residents of Yakutsk aged 20 to 72 years who had a disease with a new coronavirus infection SARS-CoV-2 from 3 to 12 months ago. The aim of the work was to assess the lipid profile after recovery from COVID-19, depending on the post-COVID period and severity of the disease, as well as the level of total cholesterol in inpatients at admission, discharge and in the post-COVID period. According to the results of the study, when infected with the SARS-CoV-2 virus, lipid metabolism is disturbed: in the acute period of infection, the level of total cholesterol decreases, in the post-COVID period, its level significantly increases. The most pronounced shift in the lipid profile towards atherogenicity occurs in patients who recovered from COVID-19 three months ago due to a decrease in the antiatherogenic fraction of lipids. Dyslipidemia is most pronounced in patients who have had an infection with severe lung damage (50-75%) due to an increase in atherogenic lipid fractions that create a risk of atherosclerosis.

Keywords. SARS-CoV-2, COVID-19, lipids, dyslipidemia.

Introduction. SARS-CoV-2 coronavirus infection does not manifest as severe acute respiratory syndrome in all infected people. In most cases, COVID-19 is asymptomatic or leads to a mild form of the disease. Some patients need intensive hospital treatment and respiratory support, especially the elderly, patients with obesity, diabetes, cardiovascular disease and hypertension, as they are at risk of severe infection, often fatal.

Scientific studies have shown that the SARS-CoV-2 virus causes a violation of metabolic processes in the body, including lipid metabolism. Lipids not only constitute the basic structure of membranes, but also play an important role as intercellular signaling agents and energy sources [3]. But it should be noted that lipids also facilitate the penetration of viruses through the host cell membrane. Viruses use and modify lipid metabolism in favor of virus replication [10].

In the acute phase of infection with SARS-CoV-2, a change in cholesterol (CH) metabolism was revealed, which is the cause of a decrease in circulating cholesterol in the blood serum [10]. An analysis of data from 1411 hospitalized patients with COVID-19 showed that low levels of the anti-atherogenic fraction (HDL-C - high-density lipoprotein cholesterol), high levels of triglycerides (TG) before infection and on admission are significant predictors of disease severity [2]. Correlations of these parameters with higher levels of D-dimer and ferritin indicate the role of acute inflammation in lipid metabolism disorders. Another large study found a decrease in low-density lipoprotein cholesterol (LDL-C) levels as the disease progressed [5].

Since lipid metabolism disorders caused by COVID-19 can persist in the post-COVID period, causing the development of cardiovascular complications, the study of the lipid profile during infection with the SARS-CoV-2 virus and after recovery is relevant.

The purpose of the study: to study changes in lipid fractions in patients who underwent COVID-19 depending on the duration and severity of the disease.

Material and methods. The study, conducted at the Clinic of the Yakut Scientific Center for Complex Medical Problems (YSC CMP), included 161 people who had a laboratory-confirmed COVID-19 infection with varying degrees of lung damage. The age of the examined patients ranged from 20 to 72 years. The mean age was Me 53.0 [41.5; 61.7] years, men - 50.5 [40.0; 61.7], women - 53.0 [42.0; 61.5] years. The percentage of men was 37.1% (60 people), women 62.7% (101 people), respectively. The exclusion criterion from the group was patients with signs of acute respiratory viral infections and active COVID-19 infection at the time of the study.

All subjects were divided into 4 groups depending on the time since recovery: group 1 - up to 3 months, group 2 - 3-6 months, group 3 - 6-9 months, group 4 - 12 months ago and the severity of lung damage (Table 1). Another 4 groups were divided according to the severity of lung damage: CT 0 (zero) - no lung damage was detected; CT 1 (mild) - damage to less than 25% of the lung volume, CT 2 (moderate-severe) 25-50%, CT 3 (severe) 50-75% (Table 1).

The study was approved by the decision of the ethical committee of the Federal State Budgetary Scientific Institution "Yakutsk Scientific Center for Complex Medical Problems", Protocol No. 52 dated March 24, 2021, and was performed with the informed consent of the subjects in accordance with the ethical standards of the Declaration of Helsinki (2000). The material of the study was blood serum from the cubital vein, taken on an empty stomach.

All biochemical studies were carried out on a Labio-200 automatic biochemical analyzer (Mindray, China) using Biocon reagents. The determination of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) was carried out by the enzymatic method. Low-density lipoprotein cholesterol (LDL-C) and very-low-density lipoprotein cholesterol (VLDL-C) were calculated using the formula of Friedewald et al., the atherogenic coefficient (C_a) was calculated using the formula proposed by A.N. Klimov.

To determine the frequency of lipid metabolism disorders, the Russian recommendations of the 7th revision of 2020, compiled taking into account the European recommendations of 2019, were used. Hypercholesterolemia (HCH) was taken as the level of total cholesterol ≥5.0 mmol/l, taking into account the risk of cardiovascular death according to the SCORE scale, an elevated level of LDL cholesterol >3.0 mmol/l, a reduced level of HDL cholesterol - the level of HDL cholesterol ≤1.0 mmol/l in men and 1.2 mmol/l in women. Hypertriglyceridemia (HTG) was classified as a TG level of >1.7 mmol/l.

In 29 patients who received inpatient treatment, a statistical analysis of the content of only total cholesterol at admission, discharge and in the post-COVID period was carried out, since the assessment of the complete lipid profile in patients at admission and discharge from the hospital was not included in the protocol of mandatory laboratory tests.

Data on the degree of ground-glass lung damage were assessed by the results of X-ray computed tomography (CT).

Statistical processing of the obtained data was carried out using the SPSS Statistics 19 statistical program. The descriptive analysis data are presented in tables as Me (median), Q1 and Q3 (quartiles 25 and 75%). The significance of differences was assessed using Student's t-test and ANOVA, for independent samples with a normal distribution and the Mann-Whitney test with an abnormal distribution. The critical value of the level of statistical significance of differences (p) was taken equal to 5%. The data in the table are presented as M±m, where M is the mean, m is the standard error of the mean. Correlation analysis of the data was carried out according to the method of Pearson and Spearman.

Results and discussion. The results of our study revealed changes in the level of total cholesterol in patients on admission and discharge. Median total cholesterol at admission was 4.10 [3.60; 5.18] mmol/l, at discharge 4.50 [3.70; 4.75] mmol/l. It was found that at admission in men, cholesterol was lower by 11% than in women: Me 3.85 [3.35; 4.87] and 4.30 [3.61; 5.28] mmol/l, respectively.

In the post-COVID period, the value of the median total cholesterol exceeded the reference value, reaching 5.42 [4.70; 6.04] mmol/l and was statistically significantly higher by 32% than at admission (p=0.000) and 20% higher than at discharge (p=0.001) (Fig. 1).

Our analysis of the state of the lipid profile in the blood serum depending on the post-COVID period showed that at all times after recovery from infection with SARS-CoV-2, the level of total cholesterol, LDL cholesterol and C_a value did not correspond to the values recommended by the Russian Society of Cardiology.

The level of TG in all terms after recovery was within the reference values and had no significant differences; over time, there is a slight decrease in indicators. The highest level of total cholesterol was observed in group I (up to 3 months after the infection), exceeding the norm by 9.6% (5.48±0.22 mmol/l). In groups in which the period after COVID-19 was from 3 to 12 months, there was a trend towards a decrease in the level of total cholesterol, but still the indicators remained above the normative values up to 12 months.

The content of HDL cholesterol was

reduced, especially in groups I and III: 0.87±0.04 and 0.98±0.04 mmol/l, respectively. In groups II and IV, the level of HDL cholesterol is close to the minimum limit value. A statistically significant difference was found between HDL cholesterol levels in groups I and II (terms after COVID-19 up to 3 months and 3-6 months) (p = 0.002) (Table 2).

The anti-atherogenic fraction of lipids LDL-C at all times exceeded the norm (<3.0 mmol/l) and its level was higher (3.94±0.19 mmol/l) in group I (in those who recovered 3 months ago).

The average content of LDL cholesterol in the post-COVID period was increased by 20-24% of the norm. A higher rate was noted in group I (in those who recovered 3 months ago), remaining at a high level up to 12 months (Table 1).

As a result of an imbalance in the lipid profile, the value of the atherogenic coefficient (C_a) was the highest in group I (in those who had been ill three months ago) (5.48±0.43), exceeding the norm by 82%. A significant difference in the value of C_a was revealed when comparing the indicators of groups I and II (p=0.047). Over time, there is a downward trend, however, in all groups, C_a remains high, even after 12 months (Table 2).

The results of the analysis of the lipid spectrum, depending on the indicators of the degree of lung damage, showed a tendency to increase the level of total cholesterol, triglycerides, LDL cholesterol, C_a from CT 0 to CT 3, and vice versa, the antiatherogenic fraction of lipids - HDL cholesterol remained at a reduced level regardless of the severity of lung damage. The content of TG at CT 3 increases by 32%, the level of LDL cholesterol increases by 7% compared with CT 0 (Fig. 2). At the same time, the content of HDL cholesterol was reduced by 10% of the standard values. As the severity of the lesion increased, the value of Ka increased and in the group with severe lung damage (CT 3) C_a was the highest - 4.51±0.40.

Correlation analysis showed a direct relationship between the degree of lung damage (CT) and the level of total cholesterol (r=0.192; p=0.015), TG (r=0.258; p=0.001) and VLDL cholesterol (r=0.246; p=0.002). This confirms the dependence of changes in the lipid profile on the severity of lung damage in COVID-19, which indicates the impact of the development of infection on lipid metabolism. The revealed decrease in the level of total cholesterol in patients upon admission to the hospital does not contradict the literature data. During the period of acute SARS-CoV-2 infection, the lev-

Table 1

Distribution of the median of patients who recovered from COVID-19 by age groups depending on the post-COVID period and the severity of the disease, Me [Q25; Q75]

Groups	Post-COVID period	Average age	Severity of lung injury	Mean age
Group I n=15	Up to 3 months	51 (42.0; 62.0)	KT 0. n=27	46 (37.0; 56.0)
Group II n=75	3-6 months	53 (41.0; 62.0)	KT 1. n=60	47 (39.0; 58.7)
Group III n=49	6-9 months	54 (39.0; 62.0)	KT 2. n=42	60 (49.7; 63.0)
IV group n=22	6-12 months	51 (42.0; 61.0)	KT 3. n=32	57(42.2; 64.7)

Note. n is the number of patients.

Table 2

Average lipid values depending on the post-COVID period

Groups by term	Total number of studied	M±m	Standard deviation	95% CI	P
Triglycerides					
I	15	1.36±0.18	1.36	0.96-1.76	-
II	75	1.39±0.11	0.98	1.16-1.61	0.921
III	49	1.14±0.10	0.69	0.94-1.35	0.099
IV	22	1.23±0.14	0.66	0.93-1.50	0.598
Total cholesterol					
I	15	5.48±0.22	0.87	4.99-5.96	
II	75	5.47±0.13	1.21	5.18-5.73	0.976
III	49	5.42±0.14	0.97	5.13-5.69	0.837
IV	22	5.36±0.17	0.83	5.00-5.73	0.645
HDL cholesterol					
I	15	0.87±0.04	0.17	0.07-0.97	
II	75	1.09±0.04	0.40	0.99-1.17	0.002^{1-2}
III	49	0.98±0.04	0.32	0.88-1.07	0.091^{1-3}
IV	22	1.02±0.07	0.34	0.88-1.18	0.098^{1-4}
LDL cholesterol					
I	15	3.94±0.19	0.76	3.52-4.36	
II	75	3.75±0.12	1.05	3.50-3.99	0.418^{1-2}
III	49	3.92±0.12	0.84	3.67-4.16	0.930^{1-2}
IV	22	3.75±0.15	0.76	3.444.10	0.475^{1-4}
VLDL cholesterol					
I	15	0.62±0.08	0.33	0.43-0.80	
II	75	0.63±0.05	0.45	0.52-0.73	0.937^{1-2}
III	49	0.51±0.04	0.31	0.43-0.61	0.296^{1-3}
IV	22	0.56±0.06	0.30	0.42-0.68	0.599^{1-4}
C_a					
I	15	5.48±0.34	1.34	4.73-6.22	
II	77	4.59±0.25	2.20	4.10-5.10	0.047^{1-2}
III	48	4.94±0.25	1.81	4.45-5.50	0.228^{1-3}
IV	22	4.86±0.49	2.29	3.81-5.79	0.320^{1-4}

Note. Group I - recovered from COVID-19 3 months ago; Group II - recovered from COVID-19 6 months ago; Group III - those who recovered from COVID-19 9 months ago; Group IV - recovered from COVID-19 12 months ago.

el of circulating cholesterol in the blood decreases [11]. Perhaps this is also due to alimentary reasons, depletion of the body and a number of other factors. In a study by N.J. Wierdsma et al., one in five patients admitted to the hospital with COVID-19 suffered severe drastic weight loss, and 73% were at high risk of sarcopenia. Moreover, almost all patients had one or more nutritional complaints. Of these complaints, the predominant nutritional complaints were decreased appetite, feeling full, dyspnea, altered taste, and loss of taste. These symptoms have serious implications for nutritional status [9].

The SARS-CoV-2 coronavirus, like other enveloped viruses, enters host cells via endocytosis, interacting with lipid rafts within the cell membrane. Lipid rafts are subdivisions of the cell membrane rich in glycosphingolipids and cholesterol. They contain many molecules such as dynamin, caveolin, and clathrin, which may be important for viral infiltration [4, 8]. Cholesterol levels directly affect the permeability of lipid rafts; therefore, a higher concentration of cholesterol in the membrane promotes endocytosis. Conversely, lower levels of membrane-bound cholesterol reduce virus entry. Perhaps this is a protective reaction of the body from the destruction of cell membranes by the virus. At the same time, according to other researchers, low cholesterol is a risk factor for poor prognosis not only in COVID-19, but also in other critical illnesses, such as sepsis. In a study by H. Chen et al., patients with sepsis had significantly lower levels of cholesterol, HDL-C and LDL-C compared with patients without sepsis [10].

HDL cholesterol is known to exhibit anti-atherosclerotic, anti-inflammatory, anti-apoptotic, and anti-thrombotic properties [1]. The pleiotropic effects of HDL cholesterol are directly related to the immune system and host defense mechanisms against pathogens. HDL cholesterol transports acute phase proteins associated with inflammation and regulation of the component system. HDL-C particles interact with key cells of the immune system, such as macrophages, dendritic cells, megakaryocytes, T-cells and B-cells, and therefore regulate immune signaling [6].

LDL cholesterol transports most of the cholesterol contained in the circulatory system [7]. They are considered more proatherogenic due to their long retention in circulation in the blood, easy penetration into arterial walls, and greater susceptibility to oxidation. Anti-inflammatory cytokines induced by viral infection

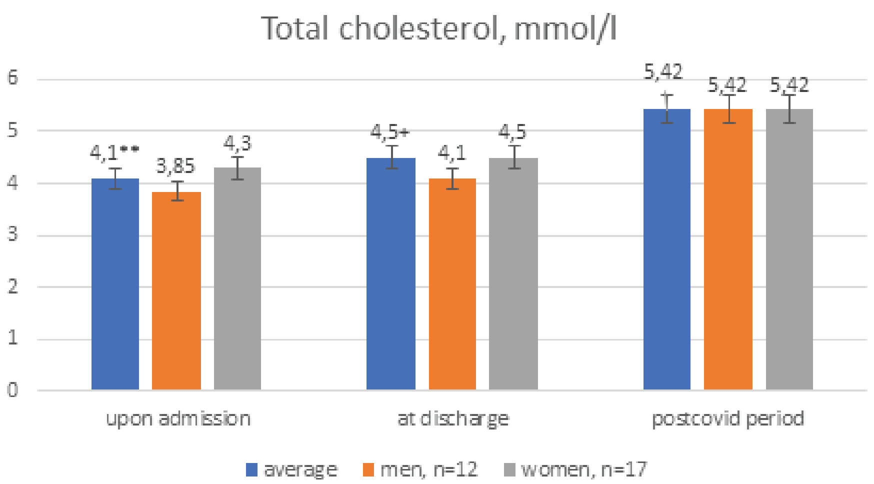

Fig.1. Median total cholesterol in blood serum in patients with COVID-19 during different periods of the disease and after recovery

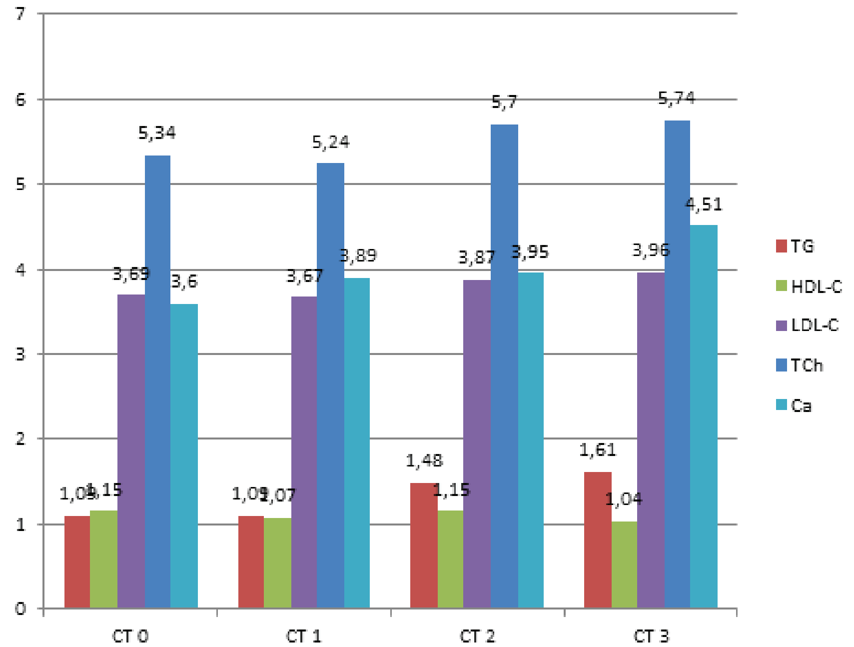

Fig.2. Lipid profile of patients with COVID-19 in blood serum depending on the severity of CT

modulate lipid metabolism, including the oxidation of LDL-C by reactive oxygen species released to facilitate clearance of LDL-C [2]. This indicates the prevalence of pro-oxidative processes after the disease for 12 months.

Thus, those who recovered from COVID-19 three months ago are at the highest risk of developing cardiovascular complications. The risk of developing cardiovascular complications persists for up to a year.

Conclusion. In patients with COVID-19 who received treatment in a hospital during the acute period of the disease, there is a decrease in total cholesterol and its increase in the post-COVID period. Patients who recovered from COVID-19 three months ago have a high risk of developing cardiovascular complications, as evidenced by a high atherogenic coefficient, which is 1.8 times higher than the normal value. The imbalance of the lipid profile increases depending on the severity of lung damage, which manifests itself in an increase in the level of total cholesterol, triglycerides, low-density lipoprotein cholesterol, which persists for up to 12 months. A pronounced shift in the lipid profile with a significant increase in the value of Ka is observed in the group of patients with severe damage to the lung volume (CT 3), which requires closer long-term medical and biological monitoring of these patients in order to prevent and prevent cardiovascular complications, including myocardial infarctions and strokes.

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E.D. Okhlopkova, Z.N. Alekseeva, L.I. Konstantinova, S.D. Efremova, A.I. Yakovleva

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NEUROSTEROID HORMONES AND PSYCHO-EMOTIONAL STATE OF INDIGENOUS MEN (YAKUTIA)

A survey of 56 practically healthy men from among the indigenous inhabitants of Yakutia (yakuts-34, evenks-22) was carried out. The average age of men was 40.1±1.58 years. The purpose of this study was to assess the psycho-emotional state and the level of neurosteroid hormones in men of the indigenous population of the Republic of Sakha (Yakutia). The results of a psycho-emotional study of men showed that good psychological adaptation was noted in 64.3% (37), of which the «health» level was 28.6% (16) and optimal adaptation was 35.7% (20).

Non-pathological maladaptation was detected in 16.1% (9), and severe pathological maladaptation - in 19.6% (11) (pathological mental maladjustment - 8.9% (5) and probably a disease state - 10.7% (6)). Depression (D) was absent in 35.7% (20), mild depression was noted in 17.8% (10), moderate in 28.6% (16) and severe in 17.8% (10), severe depression not identified. An analysis of the degree of aggression showed that in 42.9% (24) of the surveyed, the aggression index (IA) was normal, in 53.6% (30) it was low and in 3.6% (2) it was high. An increase in the level of neurosteroid hormones in indigenous men is a protective reaction of the body in ensuring homeostasis and adaptation to the conditions of the North. The concentration of steroid hormones in men decreases with the deterioration of the psycho-emotional state.

Keywords: testosterone, cortisol, dehydroepiandrosterone sulfate, serotonin, depression, neuropsychological adaptation, Yakutia.

The process of adaptation and maintenance of homeostasis in residents living in extreme climatic conditions of the North, under the influence of man-made, socio-economic factors is accompanied by activation of metabolism (metabolism), changes in the endocrine and nervous systems [8; 7; 6]. Constant exposure to stress-limiting factors can lead to depletion of the body's reserve capabilities, disrupt homeostasis and provoke «oxidative stress», thereby increasing morbidity and mortality of the working-age population [13; 4, 1, 16]. Manifestations of stress reactions in residents of Northern latitudes in more than 60% of practically healthy people are expressed in psychoemotional and endocrine changes [5, 15]. There was an increase in psychoemotional tension by 19.4% and the level of the stress hormone cortisol by two times, compared with healthy residents of the middle latitudes [14]. A relatively frequent occurrence of anxiety-depressive states was noted in residents of Southern Yakutia (Neryungri) [12].

Hormones of the hypothalamic-pituitary-adrenal system regulate not only neuroendocrine function, but also affect behavior, thinking, sleep cycle regulation, memory, depression, anxiety and aggression [21]. Aggression is one of the most common ways to solve problems that arise in complex and difficult (frustrating) situations that cause mental tension. It is essential that aggressive actions used to overcome difficulties and relieve tension are not always adequate to the situation. Aggressive actions act as: 1) means of achieving some significant goal; 2) methods of mental discharge, replacement of satisfaction of blocked needs and switching activities; 3) satisfaction of the need for self-realization and self-affirmation.

Sex steroids are involved in the formation of cognitive functions, reduce the clinical manifestations of depression and other mental disorders. Understanding the effect of nonsteroidal hormones on the development and functioning of the central nervous system in different periods of men's lives is extremely rele-

Yakut science centre of complex medical problems: **OKHLOPKOVA Elena Dmitrievna** – PhD in Biology, senior researcher at the Laboratory of Biochemical and Immunological Research, FSBSI YSC CMP, elena_ohlopkova@mail.ru; **ALEKSEEVA Zinaida Nikolaevna** – junior Researcher of the Laboratory of Neurodegenerative Diseases, FSBSI YSC CMP, gzinaida@mail.ru; **KONSTANTINOVA Lena Ivanovna** – researcher at the Laboratory of Biochemical and Immunological Research, FSBSI YSC CMP; konstanta.l@mail.ru; **EFREMOVA Svetlana Dmitrievna** – junior researcher at the Laboratory of Biochemical and Immunological Research, FSBSI YSC CMP, esd64@mail.ru; **YAKOVLEVA Alexandra Ivanovna** – researcher at the Laboratory of Biochemical and Immunological Research, FSBSI YSC CMP, sashyak@mail.ru