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INFLUENCE OF LIPID PROFILE STATUS ON COGNITIVE FUNCTION IN PATIENTS AFTER COVID-19 INFECTION

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Abstract. One of the most acute medical and social problems of modern society for the past 2 years has been a new coronavirus infection - CoronaVirus Disease 2019 (COVID-19) - and the search for ways to adequately manage patients with this disease and its complications. Severe COVID-19 increases the risk of developing neurological symptoms and complications. Brain damage from COVID-19 may have a long-term impact on cognitive processes. Vascular and cognitive disorders represent an important medical and social problem [4,10].

Cognitive impairment is one of the most common neurological symptoms [7]. Cognitive impairment after COVID-19 may be the result of decompensation of an existing cerebral disease, such as chronic cerebral ischemia or Alzheimer's disease, or a completely new symptom in young and middle-aged patients without any history of neurological disease [6,9].

Currently, one of the most significant risk factors for the development of cerebral vascular disorders is undoubtedly dyslipidemia [11]. The study of the lipid profile is another important factor in assessing the risk of developing cognitive impairment [3].

Several studies have demonstrated that plasma lipid levels in individuals with mild cognitive impairment were higher than those with normal cognitive abilities [6]. Depressive states are also often accompanied by dyslipidemia or hypercholesterolemia [1].

Thus, the **aim** of the research is to study the effect of lipid profile on cognitive function in patients with a history of COVID-19.

Material and methods. The research included 72 patients with various cognitive impairments aged 46 to 82 years. Depending on the anamnesis, the patients were divided into 2 groups: patients with COVID-19 with and without a history. Each group included 36 patients, whose mean age was 62.1±1.06 and 61.4±1.02 years, respectively. Age data did not differ statistically significantly between the groups.

All participants were given the MMSE scale (Mini-Mental State examination). The MMSE is a commonly used 30-point scale for assessing cognitive function in the areas of orientation, registration, attention and counting, recall, language, and practice. The total score is the sum of the correct answers to all questions, with a maximum score of 30 points corresponding to the highest level of cognitive function [5].

In all patients, the levels of total cholesterol (TC), low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglycerides (TG) were studied. The study was conducted in the clinical diagnostic laboratory of the Central Clinical Hospital No. 2 according to standardized methods.

The data obtained during the study were subjected to statistical processing on a Pentium-IV personal computer using the Microsoft Office Excel-2012 software

package, including the use of built-in statistical processing functions. The methods of variational parametric and non-parametric statistics were used with the calculation of the arithmetic mean of the studied indicator (M), standard deviation (SD), relative values (frequency, %), the statistical significance of the measurements obtained when comparing the average values was determined by Student's t test (t) with the calculation of the error probability (R).

Results and discussion. According to our research, a total of more than 10 symptoms have been identified that persist in people after an acute coronavirus infection. The five most common manifestations were fatigue (93.8%), headache (88%), impaired attention (67%), hair loss (63%) and shortness of breath (34%). In 1/3 of patients at the time of discharge, cognitive and motor impairments were observed (Table 1). This is especially true as the elderly are most severely affected by COVID-19 in general. The fact that systemic inflammation contributes to cognitive decline and the development of neurodegenerative diseases makes it possible for these processes to develop in survivors of COVID-19 in subsequent years.

Table 1

The incidence of neurological disorders in the post-COVID period (n=32).

№	Symptoms	Frequency
1.	Fatigue, asthenia	93,8%
2.	Cognitive impairment	90,6%
3.	Sleep disorders	62,5%
4.	Headache	81,3%
5.	Dizziness	62,5%
6.	Smell/taste impairment	43,8%
7.	Hair loss	63,0%

An assessment was made of the clinical and neurological characteristics of patients who had a coronavirus infection and suffered from chronic cerebral ischemia. Neuropsychological examination revealed deviations from the normative indicators adopted for the elderly in all patients.

table 2

The results of neuropsychological testing in 2 groups (points; M±m).

Questionnaire	Age norm	Main group	Comparative group
MMSE	27,3±1,7	21,3±2,8*	25,7±1,3

Note: * differences are significant compared to the age norm (p<0,05).

According to the data of the conducted studies, the sensitivity and specificity of the standard scales for the detection of cognitive impairment (MMSE) were relatively low in patients of predominantly older age (>70 years) in a hospital setting. According to the MMSE scale with a cut-off of 21 points in patients with severe cognitive impairment, the sensitivity was 46%. Considering the dependence of

cognitive impairment on gender, it is worth noting that men and women scored almost the same number of points - the difference in the results is less than 1. After conducting a correlation analysis, it turned out that cognitive impairment does not depend on gender.

During the physical examination, an analysis of anthropometric parameters was carried out. The groups were comparable in age and height.

Table 3

Anthropometric parameters in the examined patients

Indicator	**Survivors of COVID-19**	**Non-survivors of COVID-19**	**P**
Number of patients -Men -Women	36 18 18	36 18 18	
Age, years	62,1±1,06	61,4±1,02	0,636
Weight, kg	86,84±1,1	80,78±1,06	0,0001
Height, cm	165,05±0,84	162,4±1,01	0,048
BMI, kg/m2	29,89±0,53	28,84±0,59	0,19

When studying lipid metabolism, all indicators of the lipid profile among the groups differed statistically significantly. So, in the group with a history of COVID-19 - total cholesterol 6.44±0.14 mmol/l, low density lipoproteins 4.46±0.11 mmol/l, high density lipoproteins 1.09±0.015 mmol/l , triglycerides 1.96 ± 0.12 mmol / l, and in the group who did not have a history of COVID-19 infection - total cholesterol 5.7 ± 0.15 mmol / l, low density lipoproteins 3.86 ± 0.11 mmol / l, high density lipoproteins 1.14±0.02 mmol/l, triglycerides 1.46±0.11 mmol/l.

Table 4

Blood lipid profile indicators

Indicator	**Survivors of COVID-19**	**Non-survivors of COVID-19**	P<
total cholesterol, mmol/l	6,44±0,14	5,7±0,15	0,002
triglycerides, mmol/l	1,96±0,12	1,46±0,11	0,05
HDL cholesterol, mmol/l	1,09±0,015	1,14±0,02	0,02
LDL-C, mmol/l	4,46±0,11	3,86±0,11	0,002
VLDL-C, mmol/l	0,89±0,05	0,67±0,05	0,002

The number of patients with hypercholesterolemia (total blood cholesterol ≥ 5 mmol/l) in the COVID-19 group in history was statistically higher compared to the

same group who did not suffer COVID-19 infection. In particular, out of 36 patients, hypercholesterolemia was detected in 30 (83.3%) patients; in group 2, hypercholesterolemia was observed in 22 (61.1%) patients. Of all (52 patients) patients with hypercholesterolemia, 58% had a history of COVID-19, the remaining 42% without a history of COVID-19.

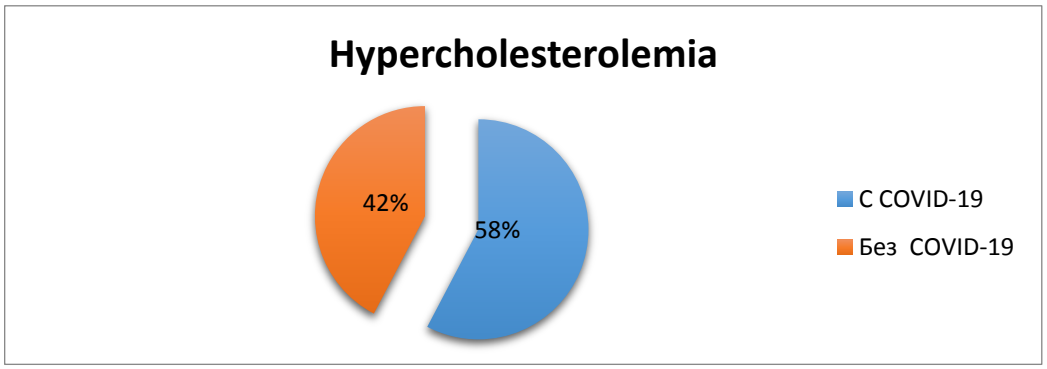

Fig.1. The presence of hypercholesterolemia in the examined

It should be noted that an elevated level of total cholesterol in the blood - hypercholesterolemia increases the risk of vascular dementia, which is an important predictor of cognitive impairment [7].

The amount of total cholesterol in the blood of all persons involved in the examination averaged 6.09±0.09 mmol/l. At the same time, in group 1, serum cholesterol was found to be within 6.44±0.14 mmol/l; in group 2, it was 5.7±0.15 mmol/l ($p<0.05$). In patients with a history of COVID-19, total cholesterol was higher by 0.74 mmol/l.

The pathophysiological mechanisms underlying the association of hypercholesterolemia with cognitive dysfunctions are still not fully understood [10]. Laboratory studies have revealed that hypercholesterolemia directly affects the activity of enzymes involved in the metabolism of amyloid precursor protein and in the synthesis of β-amyloid. Hypercholesterolemia in the blood leads to a violation of the activity of α-secretase and a decrease in the production of soluble protein - the precursor of amyloid, which triggers the amyloid "cascade" with subsequent death of neurons. In addition, it should be noted that against the background of hypercholesterolemia, changes in the properties of the membrane are noted [8].

The triglycerides in the blood averaged 1.7 ± 0.07 mmol/l. Accordingly, in groups, patients with a history of COVID-19 were higher and amounted to 1.0.12 mmol/l, and in persons without COVID-19 this the indicator was within 1.46±0.11 mmol/l. Hypertriglyceridemia was assessed based on an increase in triglyceride levels greater than 1.7 mmol/l. The prevalence of this condition was registered in 25 (34.7%) patients, while in 17 (47.2%) patients who had COVID-19 infection and in 8 (22.2%) patients without a history of COVID-19 ($p = 0.026$). The detection of this risk factor increased with the deterioration of cognitive function.

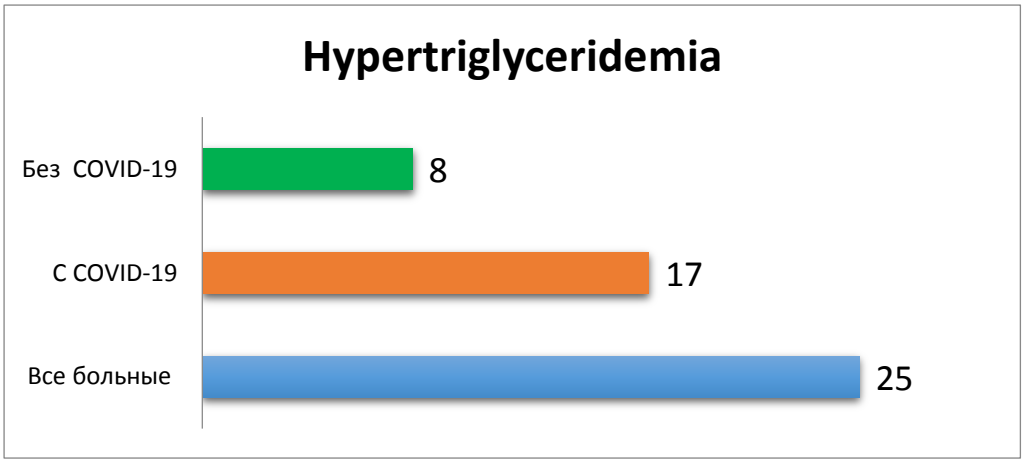

Fig.2. The presence of hypertriglyceridemia in the examined

Meanwhile, studies have shown that high triglyceride levels have been associated with a risk of cognitive dysfunction [12]. Recent molecular studies have shown that lowering triglyceride levels can increase the transport of ghrelin and insulin across the blood-brain barrier, which has a positive effect on cognitive function [13].

A decrease in the level of HDL-C in the body is a strong and independent risk factor for the development and progression of vascular atherosclerosis. The level of HDL cholesterol <1.0 mmol/l in men and <1.2 mmol/l in women is considered as a marker of an increased risk of atherogenesis progression. In turn, increased atherogenesis contributes to the progression of cognitive impairment. A decrease in the level of high-density lipoproteins (HDL) of 36 men from both groups below 1.0 mmol/l was observed in 8 (22.2%) patients; also, out of 36 women, an HDL level of less than 1.2 mmol/l was detected in 22 (61.1%) persons. In total, the prevalence of this criterion was 30 (41.67%) patients. In relation to lipid metabolism disorders by groups, the following results were revealed: in male patients who had a history of COVID-19 infection in 5 (13.9%) individuals and in females in 13 (36.1%); history without COVID-19 infection in 3 (8.3%) men (p=0.423) and 9 (25%) women (p=0.171) (Fig. 3.).

As mentioned above, in patients who had a history of COVID-19, the concentration of HDL-C in the blood was lower by 0.5 mmol / l than in patients who did not have a history of COVID-19 infection. According to the literature, it is HDL that has an important diagnostic significance for cognitive function. It was the groups of people with low levels of HDL-C in the blood that had much worse results in terms of the mental state examination (MINI-MENTAL STATE EXAMINATION) than the groups of people in whom the concentration of HDL in the blood was higher [3]. In addition, HDL-C in the blood has a positive effect on verbal episodic memory, it is this blood lipoprotein that delays the onset of Alzheimer's disease and dementia [2].

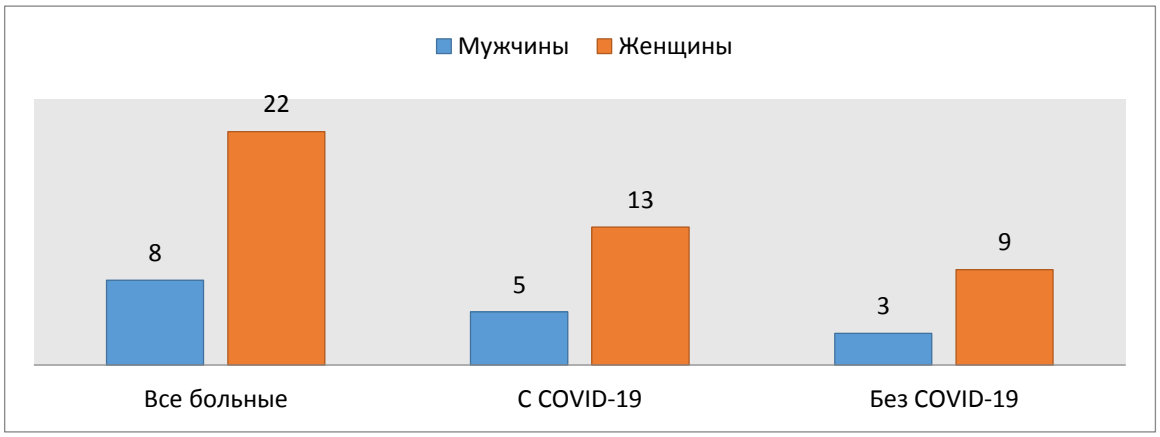

Fig. 3. Number of patients with low HDL-C

The concentration of LDL in the blood of the surveyed averaged 4.2±0.08 mmol/l. At the same time, in the group with a history of COVID-19, this indicator was 4.46±0.11 mmol/l. In persons with a history without COVID - 19 infection, the LDL index was lower and amounted to 3.86 ± 0.11 mmol / l. In accordance with the recommendations of the European Society of Cardiology (2013), for the general population, the target level of LDL-C in blood plasma should be <3 mmol/l. Of all the patients, 60 (83.3) had an increase in LDL above 3 mmol / l, while 33 (91.7%) of them belonged to the representatives of group 1 and 27 (75%) patients to group 2.

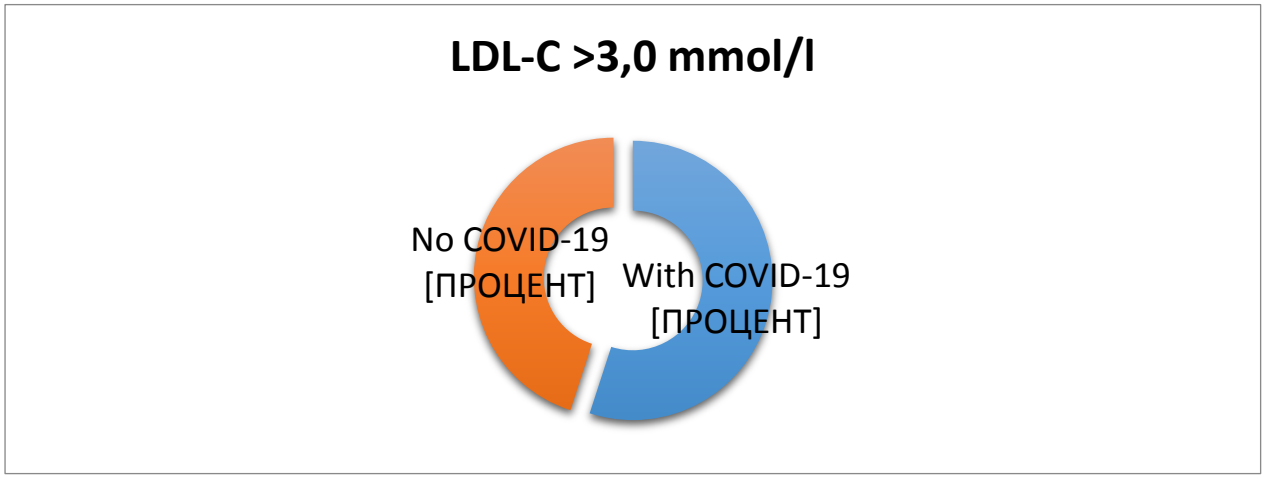

Fig.4. Number of patients with elevated levels of LDL-C

Some studies have found an association between elevated low-density lipoprotein (LDL) levels and accelerated cognitive decline [9].

An analysis of the difference in LDL values between groups revealed that in people with COVID-19 infection, this indicator is higher by 0.6 mmol/l. There is evidence that, with an increase in the concentration of LDL for every 0.259 mmol/l, the assessment of cognitive functions decreased by 0.10 points annually [8]. In addition, it is LDL that is an independent factor in faster cognitive decline in patients with Alzheimer's disease [4]

It should be noted that the results of our studies confirm the association of the lipid profile with the risk of developing mild cognitive impairment in patients who

have undergone COVID-19, which are characterized by hypercholesterolemia, hypertriglyceridemia, high levels of LDL and low levels of high-density lipoprotein (HDL) [5].

Conclusion: An analysis of the clinical and neurological examination, studies of the cognitive sphere showed that the most pronounced imbalance in lipid parameters prevailed in patients who underwent COVID 19.

Patients with higher levels of LDL, total cholesterol should be recommended strict medical lipid-lowering therapy, and HDL should be carefully monitored, increasing their blood levels to improve cognitive function and inhibit further aggravation of cognitive dysfunctions.

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