

METABOLIC DISORDERS IN THE ACUTE PERIOD OF COVID-19

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Abstract. *The article presents the results of studying the features of metabolic disorders in patients with COVID-19 in the acute phase of the disease. The study used data of 31 patients in the acute period of coronavirus infection caused by COVID-19. The average age of patients was 56.4 ± 12.8 years (from 32 to 80 years), among them 13 (41.9%) were men and 18 (58.1%) were women.*

The data obtained indicate that obesity and dyslipidemia, in particular, high lipid levels are more common in patients with a moderate disease course. But at the same time, some metabolic disorders are also 1.2-1.6 times more common in patients with a moderate course of coronavirus infection compared with a mild course (respectively, blood pressure $\geq 140/90$ mmHg: 23.5% vs. 14.3%; TG ≥ 1.7 mmol/L: 47.1% vs. 28.6%; HDL < 1.0 mmol/L: 64.7 vs. 28.6%; fasting glucose ≥ 6.1 mmol/L: 35.3% vs. 28.6%).

Keywords: *coronavirus, COVID-19, carbohydrate metabolism, lipid metabolism.*

Metabolic syndrome (MS) is a cluster of cardiovascular disorders, including abdominal obesity, high blood pressure, impaired glycemia, dyslipidemia, which are based on insulin resistance (IR) and compensatory hyperinsulinemia [1; 2].

According to various data, on average from 20 to 30% of the adult population in most countries suffer from MS [3; 4]. However, the range of MS prevalence varies significantly depending on the geographical region, the developmental level of the country and diagnostic criteria. For example, data on MS frequency in 10 European countries accounted for 24.3% (23.9% for men and 24.6% for women; $p < 0.001$) [5], in Turkey - 27.21% [6], in Bangladesh - 30.0% [7], in Korea - 30.52% [8], in Iran - from 13 to 37%. The prevalence of MS in the USA increased from 32.5% (2011-2012y.) to 36.9% (2015-2016y.). According to Russian data, the incidence of MS among men aged 40-55 is 44.4%, among women — 20.8% for same age group [9].

Nowadays, complications developed after the coronavirus disease in 2019 (COVID-19) represent a global problem [10; 11]. According to official statistics, 679503595 COVID-19 infection reported cases were registered throughout the world on February 25, 2023, and 250932 cases in Uzbekistan.

Although the pathophysiological mechanisms have not yet been studied, it has been observed that in most infected people the prognosis is favorable, chronic diseases usually observed in the elderly (hypertension, diabetes mellitus, cerebral vascular diseases and their predisposition states) can lead to serious clinical outcomes during prepandemia [12; 13].

In this context, MS is introduced as a common denominator of these concomitant diseases, since it is defined as a set of metabolic disorders, including insulin resistance, dyslipidemia, central obesity and hypertension, which are risk factors for the development of type 2 diabetes and cardiovascular diseases [14; 15].

Components of the metabolic syndrome, such as hypertension, type 2 diabetes and obesity, are widespread and significantly increase the risk of hospitalization and mortality in COVID-19 infected patients [16].

The aim of a research study was to determine the features of metabolic disorders in COVID-19 infected patients in the acute phase of the disease course.

Materials and methods.

The object of research were 31 patients in the acute period of coronavirus infection caused by COVID-19. The research study was conducted on the basis of the Republican Specialized Multidisciplinary Hospital "Zangiota-1" and the Republican Specialized Scientific and Practical Medical Center of Endocrinology.

The diagnosis of COVID-19 was made in accordance with the clinical course of the disease, the results of computed tomography (CT scan) of the lungs at admission, as well as a positive PCR test for SARS-CoV-2. The age of the patients ranged from 32 to 80 years (mean age was 56.4 ± 12.8 years). There were 13 (41.9%) male and 18 (58.1%) female patients. More than half of the patients (58.1%) were between 50 and 70 years old.

All patients underwent standard clinical and anamnestic examinations: anthropometric (height, body weight, calculation of body mass index (BMI)); hemodynamic (blood pressure (BP) and heart rate); laboratory examination included general and biochemical blood analysis - liver function tests (alanine aminotransferase (ALT) and aspartate aminotransferase (AST), bilirubin), coagulogram, lipid spectrum indicators (total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL), low-density lipoproteins (LDL)), as well as fasting blood glucose levels, HbA1c, fasting insulin, with determination of HOMA-IR index, urea, creatinine with GFR calculation and C-reactive protein.

The blood lipid spectrum examination was carried out by photometric method using reagent kits by the company "Human" (Germany). Glucose determination test was carried out by the glucose oxidase method using kits by the company "Human" (Germany). Glycosylated hemoglobin (HbA1c) was determined by the turbidimetric method with a set of reagents by the company "Human" (Germany). The insulin level was determined by electrochemiluminescence (ECL) method on an Elecsys and tobas immunochemical analyzer using standard sets of Cobas Roche (Germany).

The HOMA IR insulin resistance index was calculated using the formula: $HOMA-IR = \text{fasting insulin} * \text{fasting glucose} / 22.5$. Insulin resistance was established when $HOMA-IR > 2.5$.

Statistical processing of the results was carried out using the SPSS Statistics 23 program. The initial data were evaluated for compliance with the normal distribution according to the Kolmogorov-Smirnov criterion. The results are presented as median (Me) [interquartile range Q25; Q75]. The differences were considered statistically significant at $p < 0.05$.

Research results and their discussion

More than half (58.1%) of the patients had a combined concomitant pathology. Concomitant pathologies are arterial hypertension (51.6%), obesity (45.2%), respiratory system diseases (19.4%), diabetes mellitus (12.9%), chronic kidney diseases (12.9%), GIT diseases (11.3%). In a cohort study, the COVID-19 course was mild (45.2%) and moderate (54.8%). The main complaints included weakness (51.6%), cough (45.2%), increased blood pressure (35.5%), excessive sweating (32.3%), shortness of breath and a feeling of lack of air (29.0%), joint pain (25.8%).

The average age of patients was 56.4 ± 12.8 years, BMI – 30.0 ± 5.3 kg/m² (Table 1).

During the analysis, it was found that 35.5% of patients are overweight, and 45.2% are obese. The average indicators of SBP and DBP exceed the normal values, while the level of SBP ≥ 130 mmHg and DBP ≥ 70 mmHg is found in 51.6% and 64.5% of cases, respectively.

Table 1

Hemodynamic and biochemical parameters of coronavirus infected patients in the acute period of disease course

Test results	Me; Q25; Q75	Test results	Me; Q25; Q75
Age, years old	60,0; 46,5-66,5	ALT, Units/l	22,9; 18,2-32,1
BMI, kg/m ²	29,4; 27,5-33,8	AST, Units/l	23,6; 20,1-29
SBP, mm Hg.	130,0; 110,0-140	Bilirubin, μ mol/l	16,7; 12,3-20,3
DBP, mmHg.	80,0; 70,0-100	Urea, mmol/l	5,6; 4,8-7,0
Heart rate, beats/min	82,0; 77,0-89,5	Creatinine, mmol/l	78,4; 72,9-94,9
CRP, mg/l	65,4; 55,7-77,1	GFR, ml/min/1.73m ²	95,7; 81,1-111,8

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GFR, glomerular filtration rate.

In all patients, the CRP level was significantly higher than the reference values (0-5 mg/l). ALT and AST levels above the reference values were observed in 16.1% and 9.7% of patients, respectively.

Using data mining, Jiang X. et al. [17] revealed that a slightly elevated level of the liver enzyme alanine aminotransferase is the most prognostic clinical biomarker in newly infected patients with SARS-CoV-2 for the subsequent development of acute respiratory distress syndrome (ARDS). A number of meta-analyses note that abnormally high levels of hepatic aminotransferases (ALT and AST) are more common in severe cases of COVID-19 [18; 19; 20]. These results are crucial because liver diseases are very closely associated with MS, prediabetes and DM.

To assess the filtration capacity of the kidneys, urea, creatinine and GFR levels were analyzed. On average, these indicators were increased, but within the reference values. Calculated GFR data indicate a slight (GFR 60-89 ml/min) decrease in kidney function in 25.8% of patients during the acute period of coronavirus infection.

According to the literature, blood clotting dysfunction may be one of the important problems in patients with COVID-19. The analysis of clinical and laboratory data on COVID-19 showed that patients with severe disease course often had PTT prolongation, elevated D-dimer levels, low fibrinogen levels and DIC syndrome [21; 22; 23].

Coagulation dysfunction is noted in patients who have had a coronavirus infection. The mechanism of hypercoagulation is presumably associated with pronounced endothelial dysfunction and induction of platelet aggregation (the endothelium contains APF2 receptors, that is a target for the virus) [24].

In general, the coagulogram test results were within the reference values (Table 2).

Table 2

Coagulogram test results of coronavirus infected patients in the acute period of disease course

Test results	Me; Q25; Q75	Test results	Me; Q25; Q75
PTI, %	115,0; 108,8-123,5	Fibrinogen, g/l	5,1; 4,5-5,8
INR	0,9; 0,8-1,0	PTT, sec	9,9; 9,4-12,0
APTT, sec	24,0; 21,9-25,5	TT, sec	18,3; 17,5-20,3

PTI, prothrombin index; INR, International Normalized Ratio; APTT, activated partial thromboplastin time; PTT, prothrombin time; TT, thrombin time,

However, in 16.1% of patients, the level of fibrinogen and in 22.6% of patients, PTT did not significantly exceed the upper limit of the reference range. Moreover, most of them have carbohydrate metabolism disorder and are overweight or obese.

Carbohydrate metabolism disorder such as increased fasting glucose levels was detected in 6 (19.4%) patients, especially older than 50 years with concomitant hypertension, overweight and obesity. In 4 patients with a history of type 2 diabetes, the duration of the disease averaged 6.8 ± 1.7 years.

In most patients, fasting glucose levels were in the range of normal values (on average 4.4 ± 0.7 mmol/L). The HbA1c index above the reference interval was observed in 32.3% of patients. Figure 1 shows the distribution of patients depending on the indicators of carbohydrate metabolism.

When analyzing insulin resistance parameters, elevated insulin levels were noted in 22.6% of cases, HOMA IR ≥ 2.7 was found in 35.5% of patients, predominantly with moderate coronavirus infection course.

On average, the indicators of lipid metabolism were within the reference limits (TC - 4.33 ± 1.31 mmol/l; TG - 2.0 ± 1.06 mmol/l; HDL - 1.09 ± 0.33 mmol/l; LDL - 2.56 ± 0.83 mmol/L).

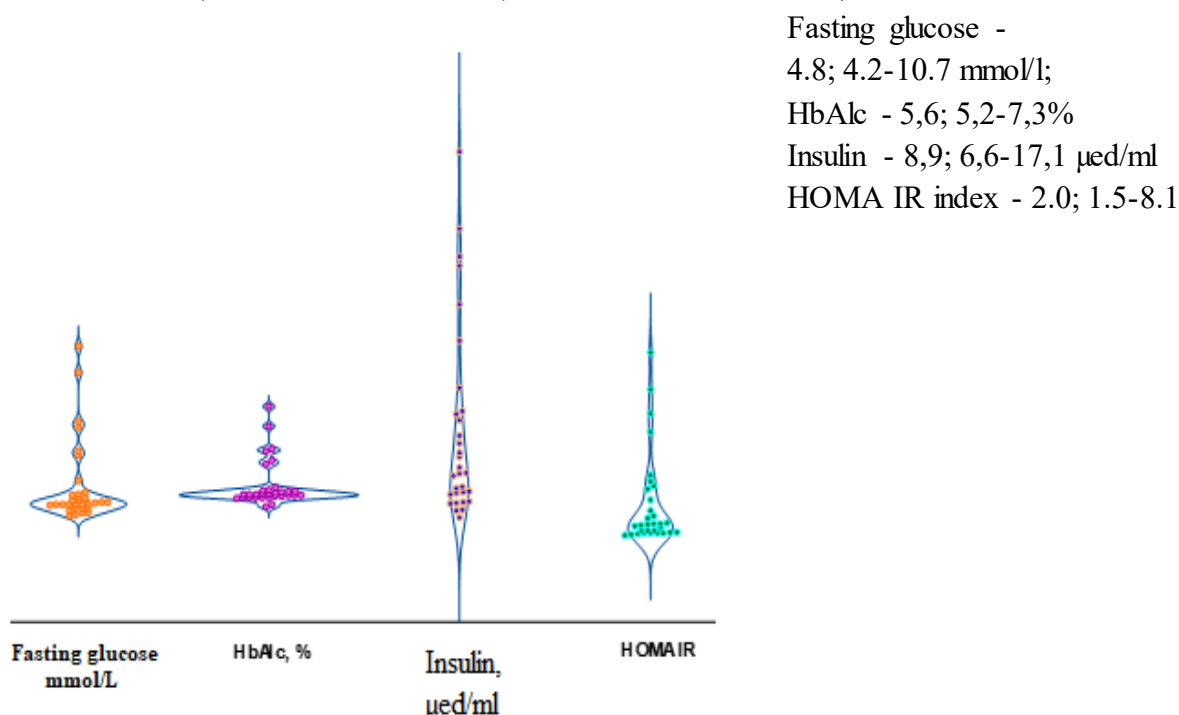


Fig. 1. Indicators of carbohydrate metabolism in patients in the acute period of COVID-19

Figure 2 shows the distribution of patients depending on the parameters of lipid metabolism.

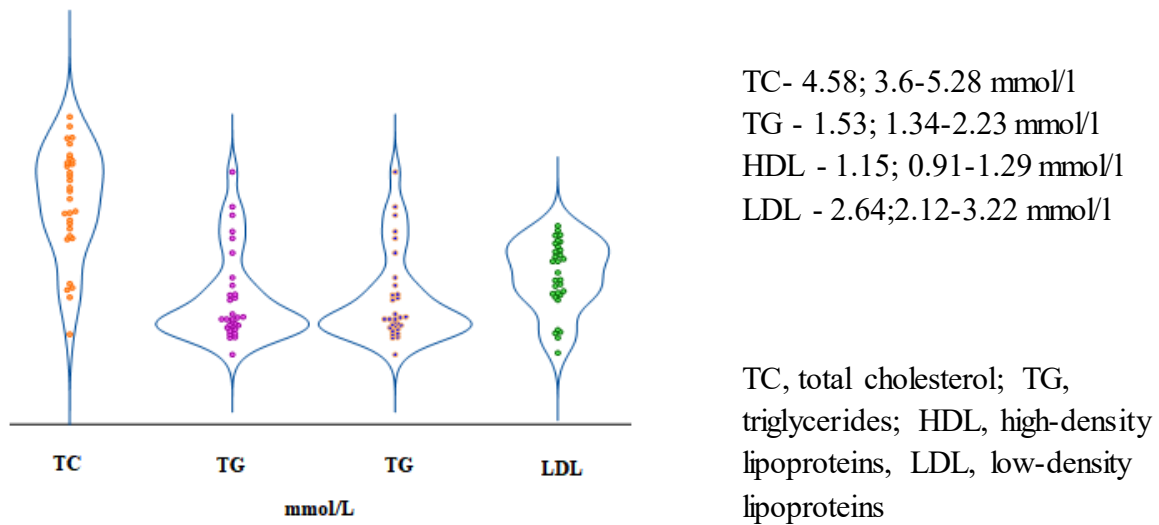
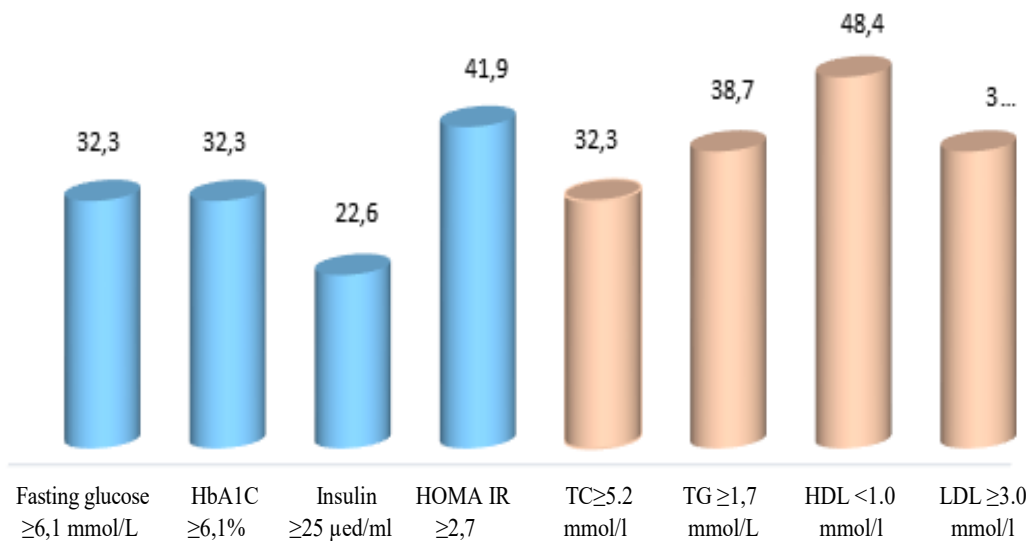


Fig. 2. Lipid spectrum in patients in the acute period of COVID-19

Nevertheless, the proportion of patients with the level of $TC \geq 5.2$ mmol/l was 32.3%, $TG \geq 1.7$ mmol/l - 38.7% and $LDL \geq 3.0$ mmol/l - 38.7%. The frequency of $HDL < 1.00$ mmol/l was also significant - 48.4% (Fig. 3.).

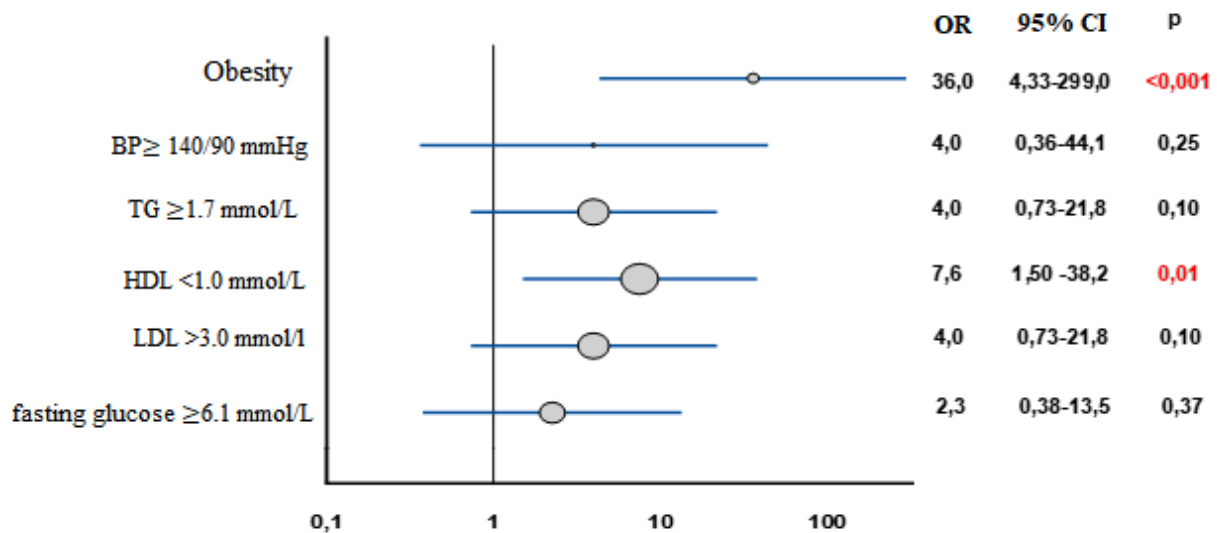


TC, total cholesterol; TG, triglycerides; HDL, high-density lipoproteins, LDL, low-density lipoproteins

Fig. 3. The frequency of occurrence of metabolic profile parameters differing from the reference values

It should be noted that this cohort study included patients with a moderate form of COVID-19 with concomitant pathologies such as overweight and obesity, arterial hypertension and impaired carbohydrate metabolism.

Next, we analyzed the frequency of occurrence of metabolic disorders depending on the severity of COVID-19 (Fig. 3.).



BP, blood pressure; TG, triglycerides; HDL, high-density lipoproteins, LDL, low-density lipoproteins

Fig.4. Comparative analysis of metabolic syndrome components incidence depending on the severity of coronavirus infection.

The data obtained indicate that obesity and LDL levels >3.0 mmol/l are significantly more common in the group with a moderate course of the disease course.

Moreover, other metabolic disorders are also 1.2-1.6 times more common in the group with a moderate course of coronavirus infection compared with a mild course (respectively, blood pressure ≥ 140/90 mmHg: 23.5% vs. 14.3%; TG ≥ 1.7 mmol/L: 47.1% vs. 28.6%; HDL < 1.0 mmol/L: 64.7 vs. 28.6%; fasting glucose ≥ 6.1 mmol/L: 35.3% vs. 28.6%).

Conclusion

Thus, the presence of metabolic disorders, such as obesity, hypertension, dyslipidemia, impaired carbohydrate metabolism, are associated with a more severe course of coronavirus infection disease. At the time of admission, there were more combined underlying diseases in the group with a moderate course of coronavirus infection than in patients in the group with a mild course.

Conflict of Interest: The author declares that there is no conflict of interest regarding the study.

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