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ABSTRACT

of the dissertation submitted for the degree of Doctor of Philosophy (PhD)

**“Assessment of clinical and biochemical changes in patients with neurological
consequences of COVID-19”**

Educational programme: 8D10100 “Medicine”

Research advisors:

Klyuyev D. A., Candidate of Medical
Sciences, Associate Professor, Vice-Rector
for Research, NJSC “KMU”

Kaliyeva S. S., Candidate of Medical
Sciences, Professor, Head of the Department
of Clinical Pharmacology and Evidence-
Based Medicine, NJSC “KMU”

Foreign Research advisor:

Philippe Karoyan, Professor Laboratoire des
Biomolécules, Sorbonne Université, France

Relevance of the study.

In March 2020, the World Health Organization declared a pandemic of the viral infection caused by the SARS-CoV-2 coronavirus [1]. By 2023, an estimated 770 million people had had COVID-19, and the number of associated deaths had exceeded 7 million [2]. Although COVID-19 presents primarily as a respiratory syndrome, neurological manifestations are recorded in 30–80% of patients: headache, cognitive impairment, sleep disturbances, cerebrovascular events, neuropathic pain, and olfactory and gustatory dysfunction [3–8].

The experience of earlier pandemics -the 1918 Spanish influenza, SARS-CoV-1 (2003), and MERS (2012) -convincingly shows that the neurological complications of infectious diseases can develop in both the acute and the late phases of illness and can follow a protracted course [9].

Post-COVID syndrome (PCS, long COVID) is recognised as one of the most common long-term consequences of the pandemic. Under the WHO criteria (2021), PCS is diagnosed when symptoms persist for three or more months after the infection, last for at least two months, and cannot be explained by an alternative cause [10]. Its incidence ranges from 10–30% among non-hospitalised patients and reaches 50–70% among those who were hospitalised [11].

Over 80% of patients report at least one symptom in the long term; the most common are neurological and psycho-emotional disorders -fatigue, cognitive impairment (“brain fog”), anxiety, depression, sleep disturbances, and autonomic dysfunction [12–17]. A large population-based study in England (the REACT programme, $n > 100,000$) found that prior COVID-19 was associated with a decline in cognitive function equivalent to a loss of roughly 3 IQ points [18]. According to a prospective 3.5-year study, moderate-to-severe autonomic dysfunction persists in 71.9% of patients with long COVID [19].

Standardised assessment relies on validated psychometric instruments -the Beck Depression Inventory (BDI), the Hospital Anxiety and Depression Scale (HADS I/II), and the COMPASS-31 autonomic symptom questionnaire [20–22].

Oxidative and carbonyl stress, disruption of redox homeostasis, and activation of DAMP signalling pathways play a key role in the pathogenesis of neurological disorders in PCS [23–26]. Through ORF3a-dependent activation of mitochondrial ROS, HIF-1 α establishes a self-sustaining “hypoxia–neuroinflammation” loop [27]; PAF contributes to blood–brain barrier disruption and the activation of neuroinflammatory cascades [28, 29]; MDA -a marker of the peroxidation of neuronal membranes -remains elevated for four or more months after COVID-19 [30–32]. GSH levels fall in the grey matter of the frontal lobes in PCS, which correlates with cognitive fatigue [33]; GSSG accumulates in blood plasma, reflecting redox imbalance [34]; and methylglyoxal (MGO) triggers neuroinflammation and neuronal apoptosis through RAGE-dependent pathways [35].

SARS-CoV-2 is not the only infectious agent capable of causing post-acute complications that involve the nervous system. The concept of post-acute infection

syndromes (PAIS) brings together conditions that develop after Ebola virus, Lyme disease, Epstein–Barr virus, and other infections [36, 37]. A defining feature of PAIS is the similarity of clinical profiles regardless of the pathogen, which points to universal pathogenetic mechanisms mediated by redox imbalance and mitochondrial dysfunction [38, 39]. A comparable pattern of oxidative disturbance -elevated MDA, GSH/GSSG imbalance, and HIF-1 α activation -has been documented in Alzheimer's disease, multiple sclerosis, and HIV-associated neuropathy [40–42], indicating that oxidative stress is a universal neurometabolic response to chronic neuroinflammation, irrespective of its cause [43, 44].

These six biochemical markers -PAF, HIF-1 α , MDA, GSSG, methylglyoxal, and GSH - together form a pathogenetically grounded panel that captures the key mechanisms of post-COVID neuroinflammation. Despite the accumulated evidence on their role in the acute phase of COVID-19, an integrated assessment in the late period, in patients with verified neurological disorders, is almost entirely absent from the available literature [45–47].

Study hypothesis.

In the late period (≥ 3 months) after a coronavirus infection, patients retain a systemic imbalance of molecular mechanisms characterised by the simultaneous elevation of pro-inflammatory mediators (PAF, HIF-1 α), intensified lipid peroxidation (MDA), accumulation of carbonyl-stress products (methylglyoxal), and depletion of antioxidant defences (a fall in GSH alongside a rise in GSSG); the severity of these changes is significantly associated with the presence of neurological disorders and is not determined by any single isolated parameter.

The development of neurological disorders in post-COVID syndrome is mediated by interrelated biochemical mechanisms: hypoxic-metabolic dysregulation (HIF-1 α), endothelial dysfunction and platelet activation (PAF), lipid peroxidation of neuronal membranes (MDA), and carbonyl modification of proteins (methylglyoxal) against a background of depleted glutathione antioxidant reserve (GSH/GSSG). This allows the panel to be regarded as an integral indicator of neurometabolic injury specific to the post-COVID neurological syndrome.

Aim of the study: to assess the relationship between neurological disorders and laboratory-biochemical parameters (markers of oxidative stress) in patients who have had COVID-19, in the late period.

Objectives of the study:

1. To assess the structure and severity of neurological disorders in patients in the late period after COVID-19 using validated scales.
2. To examine the profile of oxidative-metabolism parameters (HIF-1 α , MDA, GSH, GSSG, PAF, methylglyoxal) in patients with neurological disorders who have had COVID-19, and to compare them with control groups.
3. To assess the relationship between oxidative-metabolism parameters and the development of post-infectious neurological disorders in patients who have had COVID-19, in the late period of the disease.

Study object: patients aged 18–59 years, allocated to four groups according to a history of coronavirus infection and the presence of neurological disorders at the time of examination: group 1 (CoV+, Neuro+, n=30), group 2 (CoV+, Neuro–, n=30), group 3 (CoV–, Neuro+, n=30), and group 4 -control (CoV–, Neuro–, n=30).

The study was approved by the Local Ethics Committee of NJSC “Karaganda Medical University” (Protocol No.6 of 30 September 2020, Protocol No.18 of 12 April 2021).

Scientific novelty of the study:

1. For the first time, a comprehensive assessment of neurological disorders in the late period (3 months) after a coronavirus infection was carried out using a set of validated scales.

2. For the first time, a composite biochemical index was developed on the basis of the simultaneous assessment of six plasma markers of oxidative metabolism; the index is significantly associated with the presence of neurological disorders (OR=2.59; 95% CI 1.17–5.83; p=0.011), with a sensitivity of 63.8% and a specificity of 59.7%.

3. For the first time, it was established that changes in plasma markers of oxidative metabolism (HIF-1 α , reduced glutathione) in post-COVID syndrome are not COVID-specific and reflect a universal neurometabolic pattern associated with neurological pathology.

4. For the first time, a two-level biochemical model of post-COVID neurological disorders was proposed: the cellular (neutrophil) level carries the COVID-specific component (a 2.21-fold increase in protein carbonyl derivatives, p<0.001; a 1.50-fold increase in nitrite ions, p=0.02; a specific cluster in 63% of patients with neurological disorders that is absent in the control group), while the plasma level (a rise in HIF-1 α , GSH) reflects a universal neuroinflammatory response.

Theoretical significance

1. The findings broaden current understanding of the pathogenesis of the neurological consequences of COVID-19 by showing that, in the late period, the systemic biochemical changes in blood plasma (HIF-1 α , GSH) are not specific to a prior coronavirus infection but reflect a general pattern of the metabolic response to neurological injury, regardless of its aetiology. The observed association between biochemical disturbances and neurological symptoms underscores the need to revise views on the pathogenesis of the post-COVID neurological syndrome in favour of a concept of neurometabolic vulnerability that develops against a background of chronic oxidative and redox stress.

2. A fundamental clinical characteristic is the functional -rather than structural -nature of these disorders: the absence of gross focal neurological deficit and pathological reflexes across all four groups points to the predominance of neuroinflammatory and dysmetabolic mechanisms over direct viral damage to nervous tissue.

Practical significance of the work:

1. A model for the comprehensive assessment of neurological disorders in patients who have had COVID-19 was developed and registered, using a combination of the validated psychometric scales BDI, HADS I/II, and COMPASS-31 (Certificate of Authorship of the Republic of Kazakhstan No. 55506 of 06.03.2025, «Модель комплексной оценки неврологических нарушений на фоне перенесенной коронавирусной инфекции (COVID-19) с использованием психометрических шкал»). It is recommended for use in the clinical practice of the neurologist when examining patients in the late period after a coronavirus infection.

2. A composite biochemical index was proposed (≥ 3 of 6 markers of oxidative metabolism; OR=2.59; sensitivity 63.8%, specificity 59.7%) as an additional tool for stratifying the risk of neurological pathology in patients in the late period after COVID-19 (Certificate of Authorship of the Republic of Kazakhstan No. 75316 of 19.06.2026 «Модель формирования постинфекционных неврологических нарушений после COVID-19»). HIF-1 α , GSH may be incorporated into laboratory examination protocols for patients with post-COVID neurological disorders as additional biochemical markers.

3. A two-stage examination algorithm was developed that defines the indications for extended biochemical testing and allows diagnostic resources to be allocated rationally.

4. The findings broaden understanding of the pathogenesis of post-COVID neurological disorders and may be used in the design of prospective studies.

Statements submitted for defence

1. In patients in the late period (≥ 3 months) after COVID-19 with neurological symptoms, objective neurological findings on standard neurological examination are detected in 26.7% of cases, versus 3.3% in the control group; moderate depression on the Beck scale occurs 4.0 times more often than in the control group, amounting to 13.3% of cases ($p=0.019$); and clinically significant autonomic dysfunction (COMPASS-31 ≥ 20) is detected 1.75 times more often than among those who had COVID-19 without neurological disorders and than in the control group, amounting to 46.7% of cases ($p=0.044$). Anxiety and depressive disorders, moreover, are associated with neurological symptoms rather than with the fact of infection: the mean Beck score in group 1 (10.73 ± 6.95) is 1.87 times higher than in the control group ($p=0.002$), whereas among those who had COVID-19 without neurological disorders no difference from the control group was found ($p=0.360$).

2. Patients with neurological disorders show a uniform 2.8-fold increase in HIF-1 α compared with the control group. After Bonferroni correction, significant pairwise differences were established only between the group with neurological disorders without prior coronavirus infection and the control group: HIF-1 α ($p=0.006$), GSH ($p=0.001$). A multivariate analysis of variance across the three-marker set confirmed significant between-group differences (Wilks' $\lambda=0.802$; $F=2.486$; $p=0.0099$): 19.8% of the total variance is explained by group membership. This confirms the involvement of oxidative stress in the development of neurological pathology, regardless of aetiology.

3. The composite biochemical index (the number of the six markers exceeding the median of the overall sample), at a threshold of ≥ 3 , is significantly associated with the presence of neurological disorders: OR=2.59 (95% CI 1.17–5.83; $p=0.011$), sensitivity 63.8%, specificity 59.7% -which justifies its use as an additional diagnostic tool.

Materials of the dissertation were presented at:

1. The Scientific and Practical Conference of Young Scientists, Master's Students and Doctoral Students dedicated to Science Day, "The World of Science and Youth: Traditions and Innovations" (Karaganda, 12 April 2023).

2. The International Scientific and Practical Congress "Multidisciplinary Approaches in Medicine: Integration in Clinical Practice, Science and Education" (Karaganda, 16–17 April 2026).

Author's personal contribution. The author's personal contribution exceeded 80%. The doctoral candidate carried out the examination of patients, the assessments using the scales, and the collection of biological material. The biochemical analyses were performed jointly with the laboratory research staff. The statistical calculations and the description and synthesis of the results obtained were carried out by the candidate.

Implementation of the study results in practice.

Certificates of intellectual property of the Republic of Kazakhstan (RK) were obtained on the basis of the dissertation materials:

1. No. 55506 of 06 March 2025, "A model for the comprehensive assessment of neurological disorders following a coronavirus infection (COVID-19) using psychometric scales".

2. No. 75316 of 19 June 2026, "A model for the formation of post-infectious neurological disorders after COVID-19".

The dissertation results are used in the clinical practice of "Professor M. A. Grigolashvili Neurocentre" LLP.

Publications on the dissertation topic.

1. Klyuyev D., Kaliyeva S., Kulbayeva Z., Tuleutayeva S. Biochemical and neurological changes post-COVID-19: A focus on oxidative metabolism -A case-control study. *Journal of Neurosciences in Rural Practice*. 16(3);435-437. https://doi:10.25259/JNRP_35_2025

2. Kulbayeva Z. D., Kaliyeva Sh. S., Klyuyev D. A., Tuleutayeva S. T. Anxiety and depressive disorders after COVID-19. *Medicine and Ecology*. <https://doi.org/10.59598/ME-2305-6045-2024-111-2-57-63>

3. Kulbayeva, Z. D., Klyuyev, D. A., Kalieva, S. S., Muratbek, A. A. (2024). The relationship between oxidative stress and neurological disorders: Mini review. *Pharmacy of Kazakhstan*, 2, Clinical Medicine, 71-76. <https://doi.org/10.53511/pharmkaz.2024.36.46.010>

4. Kulbayeva, Z. D., Klyuyev, D. A., Kaliyeva, S. S. (2021). Neurological symptoms and complications of COVID-19: Mini-review. *Bulletin of the Karaganda*

Study design, materials and methods

The study was carried out within grant-funded project No. 0121RK00502 code AP09562567 of the Ministry of Education and Science of the Republic of Kazakhstan, “Assessment of the consequences of SARS-CoV-2 infection within the structure of neurological diseases.” The design is a prospective comparative case-control study with a four-group factorial design (CoV $\pm$ /Neuro $\pm$), Figure 3. Material was collected at “Polyclinic No. 8” LLP in 2020-2021.

The study was approved by the Local Ethics Committee of NJSC “Karaganda Medical University” (protocol No.6 of 30 September 2020, protocol No.18 of 12 April 2021). Each participant signed a voluntary informed consent form before enrolment. All procedures were performed in accordance with the Declaration of Helsinki and the current legislation of the Republic of Kazakhstan in the field of bioethics.

The study enrolled patients who had had a coronavirus infection (CoV), as well as individuals with no history of COVID-19, allocated to four groups according to the presence or absence of neurological symptoms. The total sample comprised 120 patients aged 18 to 59 years (mean age 42.0 ± 10.6 years; 58.3% women, 41.7% men). All participants were allocated to four groups of 30 each, according to a history of coronavirus infection (CoV) and the presence of neurological symptoms at the time of examination.

The study sample comprised 120 patients aged 18 to 59 years, allocated to four groups of 30 according to a history of coronavirus infection and the presence of neurological disorders at the time of examination.

Group 1 (CoV(+), Neuro(+)) -30 patients who had had COVID-19 and had neurological disorders.

Group 2 (CoV(+), Neuro(-)) -30 patients who had had COVID-19 and had no neurological disorders.

Group 3 (CoV(-), Neuro(+)) -30 patients who had not had COVID-19 but had neurological disorders of another aetiology.

Group 4 (CoV(-), Neuro(-)) -30 healthy individuals who had not had COVID-19 and had no neurological pathology (control group).

The sample size was calculated from the study objectives. To detect a correlation of moderate strength ($r = 0.30$) at a significance level of $\alpha = 0.05$ and a study power of 80%, the minimum sample for the four-group design was at least 100 patients (25 per group). In practice, 120 individuals were enrolled (30 per group), which exceeds the minimum required size and ensures sufficient statistical power.

The groups were formed according to the following inclusion and exclusion criteria.

Inclusion criteria:

- age 18 to 59 years (young and middle age according to the WHO classification);

- no previously diagnosed neurological disorders prior to study enrollment;
- no severe decompensated chronic conditions.
- for groups 1 and 2: a history of coronavirus infection at least 3 months prior, confirmed by laboratory testing.
- for groups 1 and 3: presence of neurological abnormalities verified by a standard neurological examination.
- for groups 3 and 4: no documented confirmed or probable case of COVID-19 in the participant's medical history, based on available medical records and the participant's interview. At the time of enrollment—no clinical or epidemiological signs of suspected or probable acute COVID-19 infection. If such signs appeared, the participant was not enrolled until the diagnostic evaluation was completed.

Exclusion criteria:

- age under 18 or over 59;
- acute coronavirus infection or less than 3 months since recovery from COVID-19;
- presence of previously diagnosed neurological disorders;
- decompensated chronic diseases (uncontrolled diabetes mellitus, stage III–V chronic kidney disease, NYHA class III–IV heart failure);
- oncological, systemic autoimmune, and inflammatory diseases in the acute phase;
- use of medications with a proven effect on the oxidative stress system (N-acetylcysteine, alpha-lipoic acid, vitamin C in therapeutic doses);
- pregnancy and lactation.
- for groups 3 and 4: a documented history of COVID-19; information regarding a previously identified probable case of COVID-19; signs of suspected or probable acute infection at the time of enrollment; for Group 3—inability to establish an alternative etiology for neurological disorders.

The application of these criteria made it possible to form a clinically homogeneous sample and minimize heterogeneity in the participants' biochemical profiles.

Clinical methods. All patients in the study groups underwent a comprehensive clinical examination, including the collection of subjective complaints, medical and life history, and an assessment of neurological status.

In this study, neurological disorder was defined as the presence of one objective neurological sign, verified on standardised neurological examination by a single neurologist [48] and belonging to one of the domains of the classification of neurological manifestations of COVID-19 by Mao L. et al. (2020) [7]: involvement of the central nervous system, the peripheral nervous system, or skeletal muscle. Objective signs were taken to include: a reduction in muscle strength to ≤ 4 points on the MRC scale, hypo- or areflexia of the tendon reflexes, pathological pyramidal reflexes, impaired coordination tests (finger-to-nose, heel-to-knee), a positive Romberg test, objectively verifiable sensory disturbances, and impaired cranial nerve function.

Assignment of a patient to the category “late period after COVID-19” followed the WHO clinical case definition of post-COVID condition [10], according to which the post-COVID condition develops in individuals with confirmed SARS-CoV-2 infection, usually 3 months from its onset, with symptoms persisting for at least 2 months and not explicable by an alternative diagnosis (code U09.9 in ICD-10 / RA02 in ICD-11).

Psychometric testing:

- The Beck Depression Inventory (BDI) -for the quantitative assessment of depressive symptom severity (0–63 points);
- The Hospital Anxiety and Depression Scale (HADS) -the anxiety (HADS-I) and depression (HADS-II) subscales (0–21 points each);
- The COMPASS-31 autonomic symptom questionnaire -for the assessment of autonomic dysfunction (0–100 points; a threshold of ≥ 20 indicating clinically significant dysfunction).

Laboratory methods. The following biochemical markers of oxidative stress and purine metabolism were measured in blood plasma:

- PAF (platelet-activating factor) -by ELISA (pg/mL);
- HIF-1 α (hypoxia-inducible factor 1 α) -by ELISA (pg/mL);
- MDA (malondialdehyde) -by spectrophotometry (nmol/mL);
- GSSG (oxidised glutathione) -by ELISA (ng/mL);
- MGO (methylglyoxal) -by ELISA (pg/mL);
- GSH (reduced glutathione) -by ELISA (ng/mL).

Statistical methods.

Statistical processing was performed using the R programming language (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria).

The normality of the distribution of quantitative variables was checked with the Shapiro-Wilk test. On testing, most biochemical parameters had a non-normal distribution. Accordingly, the non-parametric Kruskal-Wallis test was used to compare them across the four groups, with the data presented as the median and interquartile range [Q1–Q3]. For the psychometric-scale parameters that were normally distributed (BDI, HADS I, HADS II, COMPASS-31), one-way analysis of variance (ANOVA) was used; these data are presented as $M \pm SD$ (mean $\pm$ standard deviation).

Pairwise comparisons between groups were performed with the non-parametric Mann-Whitney test (for biochemical parameters), with a Bonferroni correction for multiple comparisons. The number of pairwise comparisons was 6 ($C_4^2 = 6$), which determined the corresponding correction.

For a combined assessment of between-group differences across the biochemical markers that were significant on the Kruskal-Wallis test, a multivariate analysis of variance (MANOVA) with the calculation of Wilks' λ was applied. The use of MANOVA is justified by the fact that these three parameters reflect interrelated pathogenetic mechanisms and are moderately intercorrelated; joint testing reduces the probability of a type I error compared with three independent tests.

To assess the relationships between the biochemical markers and the psychometric-scale scores, Spearman correlation analysis was used; the results are presented as matrices of correlation coefficients r with the significance level indicated.

The critical significance level was set at $\alpha=0.05$. Differences were considered statistically significant at $p<0.05$.

Results of the study.

The case-control study with a four-group factorial design (2×2 : CoV $\pm$ /neurological disorders $\pm$) enrolled 120 patients (mean age 42.0 ± 10.6 years; 58.3% women, 41.7% men). All participants were allocated to four groups of 30, comparable in sex and age ($p > 0.05$): group 1 (CoV+, Neuro+), group 2 (CoV+, Neuro-), group 3 (CoV-, Neuro+), and group 4 (CoV-, Neuro-) -healthy control.

Neurological disorders. In group 1, the most frequent complaints were headache (43.3%), sleep disturbance (20.0%), and hyposmia (13.3%). Objective examination revealed functional changes: reduced muscle strength in 13.3%, hyporeflexia in 10.0%, and impaired coordination in 6.7% of group 1 patients. No gross focal deficit was noted in any of the groups.

Psycho-emotional and autonomic disorders. In group 1, the difference from control on the Beck scale was 1.87-fold (10.73 ± 6.95 versus 5.73 ± 6.04 ; $p=0.002$), and on HADS I (anxiety) it was 1.47-fold (7.23 ± 3.57 versus 4.93 ± 3.44 ; $p=0.020$). Moderate depression among patients who had had COVID-19 occurred 4.0 times more often (13.3% versus 3.3%). Clinically significant autonomic dysfunction (COMPASS-31 ≥ 20) was found in 46.7% of group 1 patients -1.75 times more often than in group 2 and the control group ($p=0.044$).

Biochemical changes. Comparison of the four groups revealed statistically significant differences for HIF-1 α ($p=0.015$), MDA ($p=0.046$), and GSH ($p=0.004$). MANOVA confirmed combined differences across the three markers (Wilks' $\lambda=0.802$; $F=2.486$; $p=0.0099$). On pairwise comparison with Bonferroni correction, significant differences were found between group 3 (CoV-, Neuro+) and the control group: HIF-1 α ($p=0.0056$), MDA ($p=0.0406$), and GSH ($p=0.001$). A paradoxical result was the absence of significant differences between group 1 (CoV+, Neuro+) and the control group, which points to a predominantly immune-mediated and/or local (cerebral) character of the oxidative stress in post-COVID syndrome.

A combined index was developed -the number of the 6 elevated markers (PAF, HIF-1 α , MDA, GSSG, MGO, GSH). In patients with three or more elevated markers, the risk of neurological disorders increases 2.59-fold (OR=2.59; 95% CI: 1.17–5.83; $p=0.0113$). The sensitivity of the index was 63.8%, its specificity 59.7%, and its accuracy 61.8%. The combined index also showed an association with individual symptoms: it was significantly associated with headache (OR=2.31; 95% CI: 1.05–5.12; $p=0.038$). For hyposmia a trend was observed (OR=3.89; $p=0.366$), while no association was established with sleep disturbance or sensory impairment ($p>0.05$). Correlation analysis revealed weak correlations between the biochemical markers and the neurological scales (all $r<0.3$). The strongest association was noted between MGO

and COMPASS-31 ($r=0.240$), pointing to a role of carbonyl stress in the development of autonomic disorders.

Conclusions:

1. In patients in the late period (≥ 3 months) after COVID-19 with neurological disorders, objective changes in neurological status were found in 26.7% of those examined, including reduced muscle strength (13.3%), hyporeflexia (10.0%), and impaired coordination (6.7%). Hyposmia was recorded in 13.3% of patients, exclusively in the group with post-COVID neurological disorders. Depression scores on the BDI were 1.87 times higher than control values ($p=0.002$), anxiety scores on HADS-I 1.47 times higher ($p=0.020$), and clinically significant autonomic dysfunction (COMPASS-31 ≥ 20 points) was found in 46.7% of patients -1.75 times more often than in the groups without neurological disorders ($p=0.044$). In patients who had had COVID-19 without neurological consequences, no statistically significant differences in BDI, HADS-I, or COMPASS-31 from the control group were found.

2. In the study of oxidative-metabolism parameters, statistically significant between-group differences were found for HIF-1 α ($p=0.015$), GSH ($p=0.004$). Multivariate analysis of variance confirmed the presence of combined differences between the study groups (Wilks' $\lambda=0.802$; $F=2.486$; $p=0.0099$), indicating the involvement of oxidative-stress mechanisms in the development of neurological disorders in the late period after a coronavirus infection.

3. A statistically significant relationship was established between oxidative-metabolism parameters and the development of post-infectious neurological disorders. The composite biochemical index, based on the simultaneous assessment of six markers of oxidative metabolism and purine metabolism, was associated with the presence of neurological pathology (OR=2.59; 95% CI 1.17–5.83; $p=0.011$). At a threshold of ≥ 3 markers, the index had a sensitivity of 63.8% and a specificity of 59.7%. The individual biochemical markers, by contrast, lacked sufficient diagnostic value, which indicates the advisability of assessing them in combination when examining patients with post-infectious neurological consequences of COVID-19.

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