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ABSTRACT

FEATURES OF NEUROCOGNITIVE AND AUTONOMIC DISORDERS AND PAIN IN PATIENTS IN THE ACUTE PHASE OF COVID-19

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Introduction. The WHO emphasizes that the COVID-19 pandemic has a negative impact on mental health, with approximately 20% of patients who have had COVID-19 experiencing mental disorders.

Research objective was to investigate gender and age characteristics of psychopathological symptoms in patients in the acute phase of SARS-CoV-2 respiratory infection.

Materials and methods. A total of 66 patients aged 8 to 92 years with COVID-19 undergoing inpatient treatment with confirmed lung damage were examined. Clinical, clinical-psychopathological, psychometric, and statistical data processing methods were used to assess the mental status of patients.

Results. A high frequency of autonomic symptoms was found among the examined patients. The presence of autonomic dysfunction syndrome correlates with female gender, age, the presence of depression, anxiety, and the presence of concomitant diseases. The data obtained indicate greater autonomic reactivity in women, especially young women. Patients in the acute phase of COVID-19 showed cognitive impairment according to the MMSE results. Among women, disturbances in time orientation, writing, and reading were more pronounced. The presence and deepening of cognitive impairment correlates with age, the presence of concomitant diseases, and the presence of depression.

Analysis of pain sensations using the Paindetect questionnaire revealed the presence of neuropathic pain in 25.8% of respondents: 87.5% of women and 58.3% of men. Neuropathic pain in Covid-19 patients correlates with female gender, age over 50, lack of a partner, depression, anxiety, and autonomic dysfunction syndrome. Women mostly complained of headaches, pain in the arms, neck, and back; men were more bothered by pain in the legs, lumbar region, and joints. At the

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same time, widespread pain was more common in men. The highest intensity of neuropathic pain was found in the 46–60 age group.

Discussion and conclusions. COVID-19 affects the autonomic nervous system, neurocognitive processes, and pain sensitivity.

The data obtained will be useful in developing personalized approaches to the diagnosis and support of patients with COVID-19.

Keywords: COVID-19, SARS-CoV-2, autonomic dysfunction, cognitive impairment, neuropathic pain.

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ОСОБЛИВОСТІ НЕЙРОКОГНІТИВНИХ, ВЕГЕТАТИВНИХ РОЗЛАДІВ ТА БОЛЮ У ПАЦІЄНТІВ В ГОСТРІЙ ФАЗІ COVID-19

Вступ. За даними ВООЗ 20% хворих, що перенесли COVID-19 мають психічні розлади.

Мета дослідження. Дослідити гендерні та вікові особливості психопатологічної симптоматики у пацієнтів в гострій фазі респіраторної інфекції SARS-CoV-2.

Матеріали та методи дослідження. Всього обстежено 66 пацієнтів віком від 8 до 92 років, хворих на COVID-19, які перебували в стаціонарі з підтвердженим ураженням легень. Для оцінки психічного статусу пацієнтів були використані клінічний, клініко-психопатологічний, психометричний метод та методи статистичної обробки даних.

Результати. Результати продемонстрували високу частоту виникнення вегетативних симптомів під час гострої фази COVID-19. Наявність синдрому вегетативної дисфункції корелює з жіночою статтю, віком, наявністю депресії, тривоги, наявністю супутніх захворювань. Отримані дані свідчать про більшу вегетативну реактивність у жінок, особливо молодого віку. У пацієнтів, які перебували в гострій фазі COVID-19, виявлено когнітивні порушення згідно з результатами MMSE. Серед жінок більш вираженими були порушення орієнтування в часі, письма та читання. Наявність і поглиблення порушень когнітивних функцій корелює з віком, наявністю супутніх захворювань, наявністю депресії.

Аналіз больових відчуттів за допомогою опитувальника Paindetect засвідчив наявність нейропатичного болю у 25,8% респондентів: у 87,5 % жінок та 58,3 % чоловіків. Невропатичний біль у хворих на Covid-19 корелює з жіночою статтю, віком за 50 років, відсутністю партнера, наявністю депресії, тривоги та синдрому вегетативної дисфункції. При чому жінки скаржились здебільшого на головний біль, біль в руках, біль у шиї та у спині; чоловіків турбував більшою мірою біль в ногах, поперековій зоні та суглобах. При цьому поширена локалізація болю була більш характерна для чоловіків. Найбільша інтенсивність нейропатичного болю виявлена у віковій групі 46–60 років.

Обговорення та висновки. COVID-19 впливає на вегетативну нервову систему, нейрокогнітивні процеси та больову чутливість.

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Отримані дані будуть корисні при розробці персоналізованих підходів до діагностики й підтримки пацієнтів з COVID-19.

Ключові слова: COVID-19, SARS-CoV-2, вегетативна дисфункція, когнітивний дефіцит, нейропатичний біль.

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INTRODUCTION

The WHO emphasizes that the COVID-19 pandemic had a significant negative impact on mental health: approximately 20% of people who have suffered from the disease experience mental disorders. During the pandemic, acute stress, anxiety, and depressive symptoms are quite common – about 45% of respondents reported some symptoms of mental disorders. Severe COVID-19 is often accompanied by complications such as delirium, delusions, and psychomotor agitation [1].

About a third of patients experience anxiety, asthenia, sleep disturbances, and depressed mood for a long period after discharge from the hospital. Individuals who have had prolonged respiratory distress syndrome and required mechanical ventilation often report impaired concentration, slowed thinking, neurocognitive disorder, and the “brain fog” phenomenon [2].

Complex immunological processes that are triggered by SARS-CoV-2 infection, on the one hand, cause chronic inflammation in the form of myalgic encephalomyelitis and, as a consequence, chronic fatigue, fibromyalgia, autonomic disorders, and neurocognitive disorder [3, 8]. On the other hand, disorders of the blood coagulation systems increase the risk of pulmonary embolism and cerebrovascular accident, triggering a hypoxic effect on the CNS [3]. In addition, the COVID-19 pandemic was negatively impacting psychological well-being worldwide through negative media content, changes in the mode of study, social isolation, and fear for one's own life and well-being, which caused acute stress. The above symptoms tend to become chronic and are described in the literature as Long Covid [4, 5, 6, 7, 8]. Such an impact implies a new paradigm for understanding the etiopathogenesis of COVID-19-associated mental disorders as a biopsychosocial model, where the systemic effect is due to a combination of factors (psychogenic, hypoxic, neurotoxic, and inflammatory). The results of our previous studies showed that during inpatient treatment, 60.6% of patients had symptoms of depression, and 66.1% of patients had symptoms of anxiety [7]. The dependence of mental disorder severity and polymorphism on the age and gender of patients has been established [1, 2, 5, 7]. The above-mentioned determined the relevance of our research.

Objective of the study: to investigate the pathopsychological characteristics of patients in the acute phase of SARS-CoV-2 respiratory infection depending on age and gender. The study was conducted at Municipal Non-Profit Enterprise of Sumy Regional Council "Sumy City Clinical Hospital No. 5", Municipal Non-Profit Enterprise of Sumy Regional Council "Sumy Regional Infectious Clinical Hospital named after Z. Y. Krasovytsky", Municipal Non-Profit Enterprise of Sumy Regional Council "Sumy Regional Clinical Hospital of War Veterans" during inpatient treatment of COVID-19 acute respiratory infection confirmed by laboratory tests, in compliance with the principles of bioethics and medical deontology. The research data collection period is from 2020 to 2022. All study participants provided written informed consent in accordance with the Law of Ukraine "On Psychiatric Care" dated February 22, 2000.

MATERIALS AND METHODS

We examined a total of 66 patients with COVID-19, aged 8 to 92 years, who were treated in a hospital and had 30 to 70% lung damage confirmed by X-ray within 20 days of disease onset. Analysis of patients' socio-demographic, clinical, and anamnestic data showed the following. The patients were evenly divided by gender: 33 women and 33 men (50%/50%). By age, the patients were distributed as follows: 8 to 18 years – (3.03 ± 2.13)% (n=2), 19 to 30 years – (18.2 ± 4.78)% (n=12), 31 to 50 years – (24.2 ± 5.32)% (n=16), 51 to 70 years – (25.8 ± 5.42)% (n=17), 71 to 92 years – (28.8 ± 5.62)% (n=19). At the same time, patients aged 50 years or older accounted for more than half (54.5%, n=36). The average age of patients was (53±5.18) years. Among the subjects, (54.5±6.18)% (n=36) had concomitant diseases. Somatic pathology was represented in (30.6±4.62)% (n=11) of patients by hypertension, in (22.2±4.05)% (n=8) – by diabetes mellitus, in (8.33±2.58)% (n=3) – by chronic peptic ulcer disease, in (8.33±2.58)% (n=3) – by osteochondrosis, in (30.6±4.62)% (n=11) – by other diseases. Marital status of patients: (42.4±6.13)% (n=28) were not married, while (57.6±6.13)% (n=38) had a partner.

To achieve the set goal, we used clinical, psychopathological, and psychometric methods, including the following questionnaires to assess psychopathological symptoms within the framework of psychiatric screening upon admission to the hospital.

The Mini-Mental State Examination (MMSE), developed by M. F. Folstein, S. E. Folstein, and P. R. Hugh in 1975, is a 30-item questionnaire used to screen for cognitive impairment, particularly dementia. The interpretation of the results is as follows: a score of 28–30 – normal cognitive functions; 24–27 – mild cognitive impairment; 20–23 – mild dementia; 11–19 – moderate dementia; 0–10 – severe dementia. Wayne Test (A. M. Wayne, 1998) is used to quantify the subjective and objective manifestations of autonomic disorders. It helps detect impairments even in the absence of chief complaints and determine their severity. A score of more than 25 points indicates autonomic dysfunction syndrome, and a score of more than 50 points indicates significant autonomic disorders.

The Paindetect test (M. Roland, R. Morris, 1983) is a self-questionnaire aimed at detecting neuropathic pain in certain patients. 0 to 12 points indicates that a neuropathic component of pain is unlikely; 12 to 18 points indicates that the result is uncertain, but the presence of a neuropathic component of pain is possible; 19 to 38 points indicates that a neuropathic component of pain is highly likely.

Statistical processing of the obtained data (Sydorenko E. V., 2001) was performed on a personal computer using Microsoft Excel (Microsoft Office 2016 Professional Plus, Open License 67528927). The mean value and its error were calculated, as well as the percentage and its error, the Student's test (t) and the significance of the differences (p), and the correlation between the parameters and their significance (r).

RESULTS AND DISCUSSION

A study of autonomic dysfunction using the Wayne questionnaire showed (see Fig. 1) that among the surveyed COVID-19 patients, 34.8% (n=23) did not have autonomic dysfunction syndrome secondary to the disease, while 56.1% (n=43) of patients had autonomic dysfunction syndrome. Among them, 9.09% (n=6) had pronounced autonomic disorders. Mean index (M) according to Wayne was 28.19, presence of autonomic dysfunction syndrome, m=1.767.

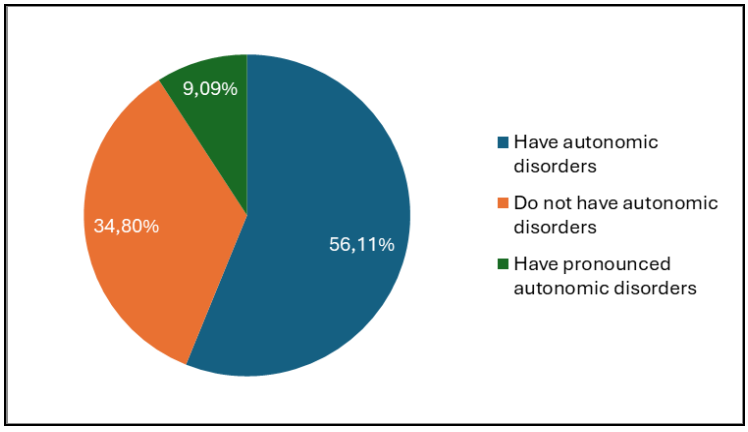

Figure 1 – The distribution of autonomic disorders according to the Wayne questionnaire in patients with COVID-19

Gender analysis of autonomic dysfunction showed the following: 83.3% (n=55) of patients complained of decreased working capacity, of which 28 were women and 27 were men; 74.2% (n=49) – of headache, of which 27 were women and 22 were men; 66.7% (n=44) – of increased sweating, of which 19 were women, 25 were men; 65.2% (n=43) – of sleep disturbances, of which 19 were women, 24 were men; 51.5% (n=34) – of redness/pallor of the face, of which 21 were women and 13 were men; 45.5% (n=30) – of gastrointestinal dysfunction, of which 14 were women and 16 were men; 40.9% (n=27) – of numbness/coldness of fingers/toes, of which 17 were women and 10 were men; 39.4% (n=26) – of palpitations or “heart sinking", of which 16 women and 10 men; 37.9%, (n=25) – for a feeling of difficulty breathing, of which 16 women and 9 men; 19.7 (n=13) – of a change in the color of the fingers/toes, of which 7 women and 6 men; 19.7% (n=13) – of fainting, of which 12 women and 1 man (Fig. 2).

Therefore, we can conclude that women mainly reported symptoms such as redness or paleness of the face, numbness or a feeling of coldness in the fingers and toes, a change in the color of the fingers and toes, palpitations, a feeling of “heart sinking", difficulty breathing, fainting, headache, and decreased working capacity. Men were more likely to experience increased sweating, gastrointestinal disturbances, and sleep

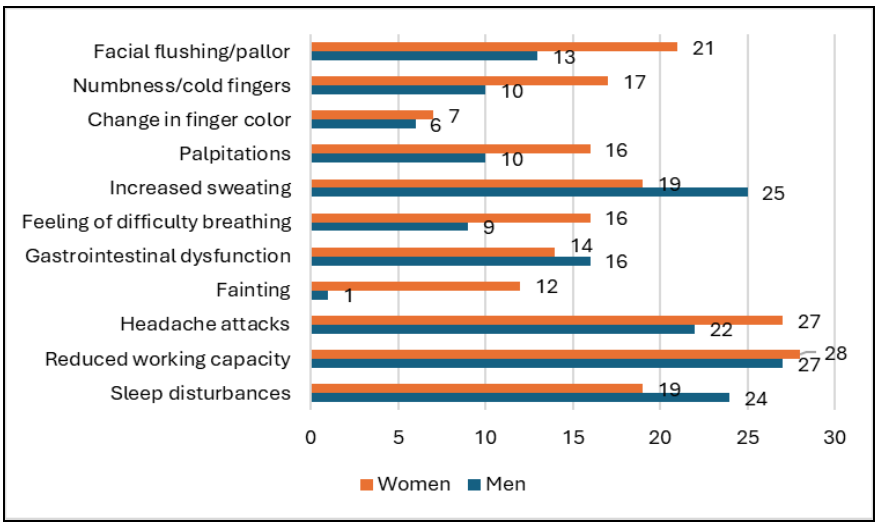

Figure 2 – Gender-specific characteristics of autonomic disorders according to the Wayne questionnaire in patients with COVID-19

disorders. The intensity of autonomic disorders gradually increased with the age of the patients ($p \leq 0.01$), as shown in Figure 3.

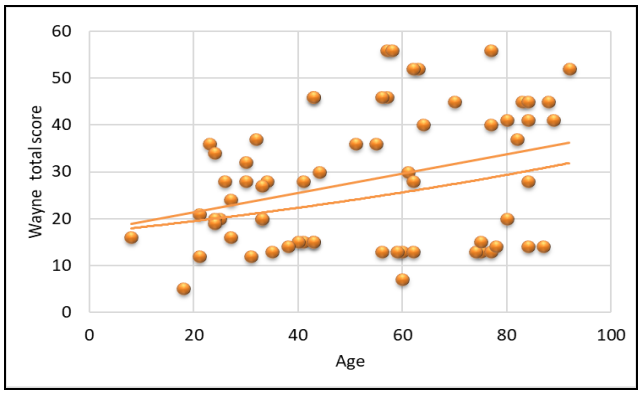

Figure 3 – Dot plot of the relationship between the severity of autonomic disorders according to the Wayne questionnaire and age in patients with COVID-19

A study of cognitive functions in patients with moderate to severe COVID-19 acute respiratory infection showed that this disease negatively affected cognitive functioning (see Fig. 4). According to the results of MMSE testing, it was found that among COVID-19 patients, 60.6% (n=40) had no cognitive impairment, 21.2% (n=14) had mild impairment, 13.6% (n=9) had moderate impairment, 3.03% (n=2) had mild dementia, and 1.52% (n=1) had moderate dementia. The average MMSE score was 28.424 points, corresponding to mild cognitive impairment (m=0.352). Analysis by gender showed that among women, 63.6% (n=21) had no cognitive impairment, 18.2% (n=6) had mild cognitive impairment, 12.1% (n=4) had moderate cognitive impairment, 3.03% (n=1) had mild dementia, and 3.03% (n=1) had moderate dementia. Among men, 57.6% (n=19) had no cognitive impairment, 24.2% (n=8) had mild cognitive impairment, 15.2% (n=5) had moderate cognitive impairment, and 3.03% (n=1) had mild dementia (see Fig. 5).

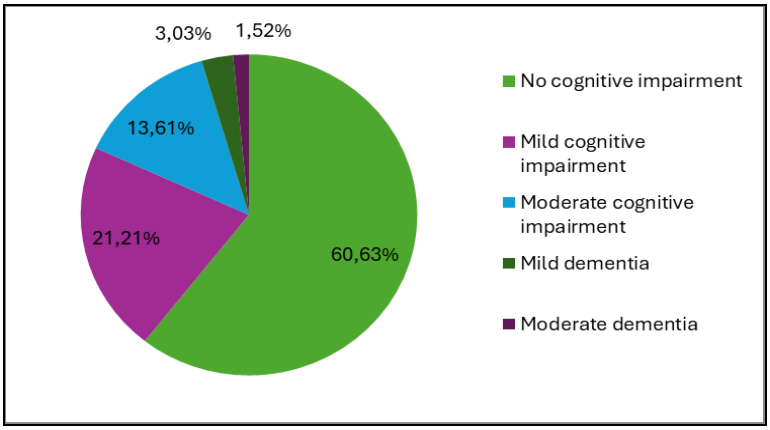

Figure 4 – Severity of cognitive impairment according to MMSE in patients with COVID-19

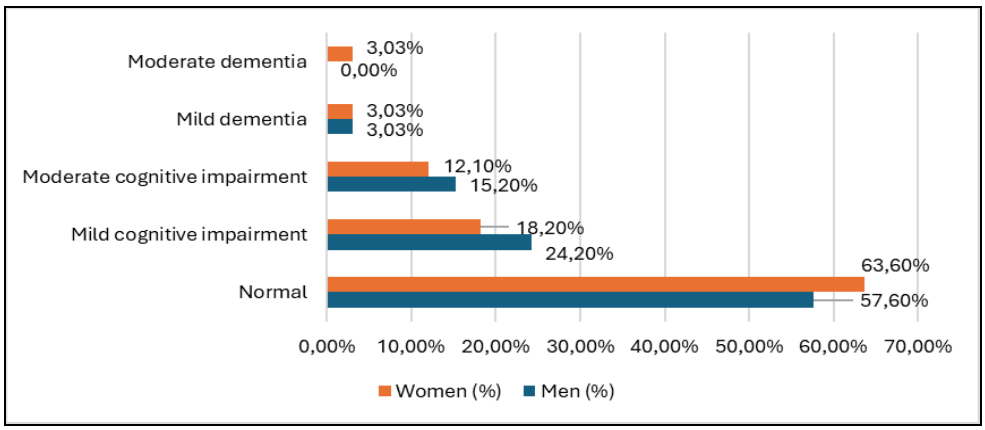

Figure 5 – Gender-specific severity of cognitive impairment according to MMSE in patients with COVID-19

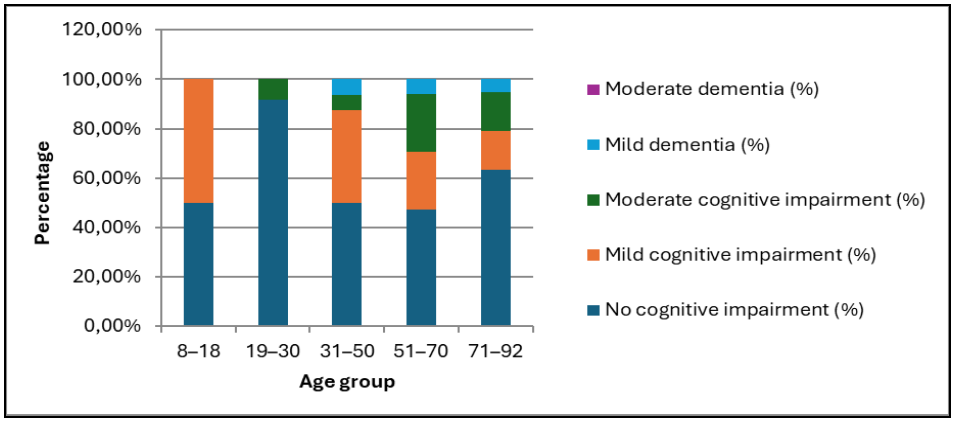

Figure 6 – Age-specific severity of cognitive impairment according to MMSE in patients with COVID-19

The results of the age-specific analysis of the COVID-19 impact on cognitive function status are shown in Figure 6. Among patients aged 8–18, 50% (n=1) had no cognitive impairment and 50% (n=1) had mild cognitive impairment. In the group aged 19 to 30, 91.7% (n=11) had no cognitive impairment, 8.33% (n=1) had moderate cognitive impairment. Among patients aged 31 to 50 years, 50% (n=8) had no cognitive impairment, 37.5% (n=6) had mild cognitive impairment, 6.25% (n=1) had moderate cognitive impairment, and 6.25% (n=1) had mild dementia. Among patients aged 51 to 70 years, 47.1% (n=8) had no cognitive impairment, 23.5% (n=4) had mild cognitive impairment, 23.5% (n=4) had moderate cognitive impairment, and 5.88% (n=1) had moderate dementia. In the group of patients aged 71 to 92 years (n=19), 63.2% (n=12) had no cognitive impairment, 15.8% (n=3) had mild cognitive impairment, 15.8% (n=3) had moderate cognitive impairment, and 5.26% (n=1) had mild dementia. Thus, it was found that the occurrence and progression of cognitive impairment in patients with COVID-19 was associated with age (average correlation level r=0.671; among women: r=0.139, among men: r=0.259) (see Fig. 7). In terms of gender, the structure of cognitive disorders had certain differences: in women, the disturbances of temporal orientation ($p \leq 0.01$), writing, and reading ($p \leq 0.1$) were significantly more pronounced (see Table 1).

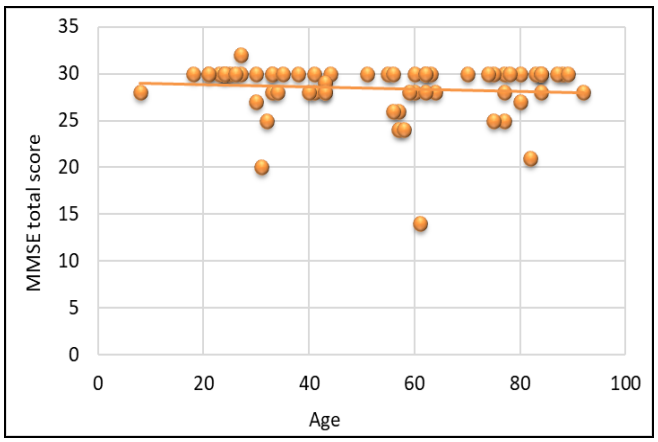

Figure 7 – Dot plot of the relationship between the severity of cognitive impairment according to the MMSE and age in patients with COVID-19

Table 1 – Gender-specific structure of cognitive impairments in COVID-19 patients

Indicator	Average score	Women	Men	P
Temporal orientation (0–5 points)	4.55±2.58	4.57±3.69**	4.51±3.67**	0.01
Spatial orientation (0–5 points)	4.82±2.66	4.81±3.78	4.81±3.78	0
Memorization (0–3 points)	2.86±2.07	2.87±2.95	2.84±2.94	0.007
Attention and calculation (0–5 points)	3.98±2.43	4.15±3.52	3.81±3.38	0.007
Recall (0–3 points)	2.47±1.93	2.51±2.76	2.42±2.71	0.02
Language (0–3 points)	2.7±2.01	2.75±2.89	2.63±2.83	0.003
Three-step task (0–3 points)	2.44±1.91	2.57±2.80	2.3±2.65	0.07
Reading (0–1 point)	0.83±1.13	0.94±1.71	0.73±1.5	0.09
Writing (0–1 point)	0.82±1.12	0.94±1.71*	0.7±1.47*	0.1
Copying (0–1 point)	1±1.23	1±1.76	1±1.76	0
Average score (0–30 points)	28.4±5.59	28.2±7.96*	28.6±7.99*	0.1

Note: probability of differences at the level *p≤0.1; **p≤0.01

At the same time, patients of both sexes had noticeable attention and calculation disorders. Analysis of the neuropathic component of pain using the PainDETECT questionnaire showed that it was present in 25.8% (n=17) of respondents, while it was absent in 74.2% (n=49). The mean value according to the PainDETECT scale was 7.681 (m=0.672), indicating a low probability of neuropathic pain (see Fig. 8). A study of pain localization showed that patients most often complained of headache (40.9%; n=27) and chest pain (36.4%; n=24). Less frequently, they reported pain in the legs (16.7%; n=11), arms (16.7%; n=11), lumbar region (13.6%; n=9), neck (7.58%; n=5), back (6.06%; n=4), and joints (4.55%; n=3). In general, it can be noted that women more often complained of headaches, pain in the arms, neck, and back, while men were more likely to experience pain in the legs, lower back, and joints. At the same time, a more diffuse localization of pain was more typical among men (see Fig. 9). A study of average values in women and men showed the following results. In women, the average score (M) according to the MMSE test (28.24 points) corresponded to mild cognitive impairment; according to the Wayne test (35.12 points), to autonomic dysfunction syndrome; according to the PainDetect test (9.06 points), to the unlikely presence of a neuropathic component of pain.

In men, the average score (M) according to the MMSE test (28.60 points) corresponded to mild cognitive impairment; according to the Wayne test (21.27 points) – to the absence of autonomic dysfunction syndrome and a presence of mild anxiety; according to the Paindetect test (6.303 points) – to the unlikely presence of a neuropathic component of pain.

Thus, the analysis of gender-specific psychopathological symptoms of patients with COVID-19 showed the following.

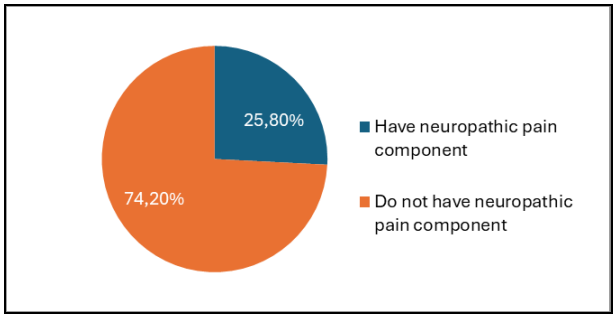

Figure 8 – Severity of neuropathic pain according to the PainDetect questionnaire in COVID-19 patients

Most women with COVID-19 had mild cognitive impairment, autonomic dysfunction syndrome, and were unlikely to have a neuropathic component of pain. Most men had mild cognitive impairment, no autonomic dysfunction syndrome, and were unlikely to have a neuropathic component of pain.

Correlation analysis demonstrated the following patterns. The presence of autonomic dysfunction syndrome correlated with female gender ($p \leq 0.001$), age ($p \leq 0.01$), depression ($p \leq 0.001$), anxiety ($p \leq 0.001$),

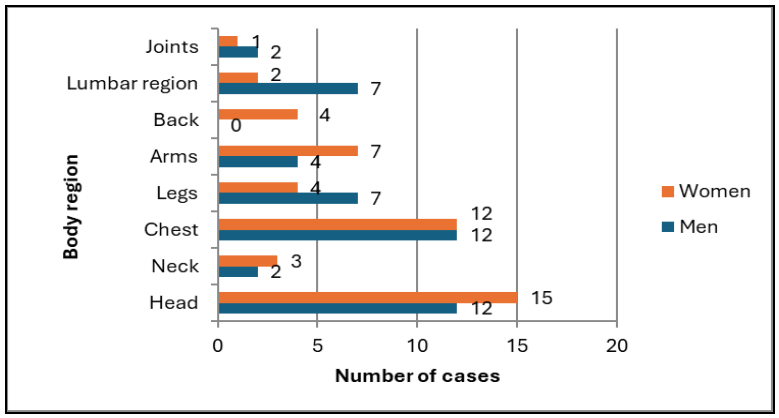

Figure 9 – Gender-specific severity of neuropathic pain according to the PainDetect questionnaire in patients with COVID-19

and comorbidities ($p \leq 0.001$). Cognitive impairments correlated with age ($p \leq 0.01$), comorbidities ($p \leq 0.001$), and depression. The presence of a neuropathic component of pain in COVID-19 patients correlated with female gender, age over 50 years ($p \leq 0.05$), lack of a partner ($p \leq 0.001$), depression ($p \leq 0.01$), anxiety ($p \leq 0.001$), and autonomic dysfunction syndrome ($p \leq 0.001$).

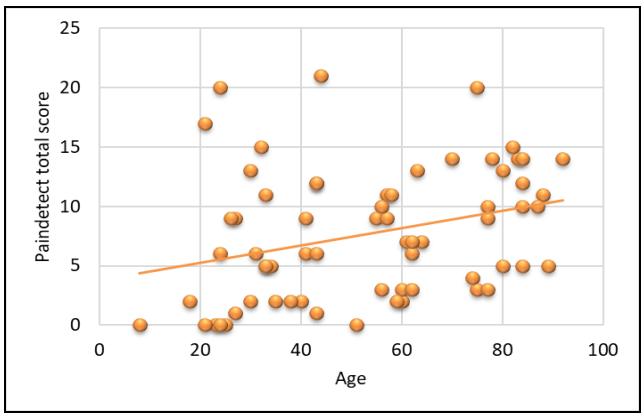

Figure 10 – Dot plot of the relationship between the severity of neuropathic pain according to the PainDetect questionnaire and age in patients with COVID-19

Analysis of the data obtained confirmed the multisystemic impact of COVID-19 infection on the nervous system, manifested through a combination of autonomic, cognitive, and sensory disorders. The high frequency of autonomic dysfunction syndrome (56.1%) is consistent with the hypothesis of immune-mediated damage to the autonomic nervous system. In terms of gender, higher Wayne scores in women (35.12 versus 21.27 in men) indicate a lower threshold of vegetative resistance. Women's complaints of palpitations and shortness of breath may be associated with the development of post-COVID tachycardia, while the predominance of gastrointestinal disorders in men suggests the involvement of the enteric nervous system. The progressive deterioration of autonomic status with age ($p \leq 0.01$) is explained by a decrease in the body's adaptive reserves and the presence of comorbid conditions (cardiovascular diseases, diabetes). Although the average MMSE score (28.4) formally was within the normal range, the presence of cognitive impairment in 39.4% of patients indicated significant neurotropic activity of the virus. Attention and calculation disorders found in patients of both sexes are typical markers of neurotoxic encephalopathy, characteristic of an acute infectious process, the so-called "brain fog" symptom. More pronounced disturbances of temporal orientation and writing skills in women ($p \leq 0.01$) could be a consequence of the stronger influence of systemic inflammation (cytokine storm) on the hippocampus and parietal cortex. The high correlation coefficient ($r=0.67$) confirmed that elderly patients were at the highest risk of irreversible neurodegenerative changes after COVID-19. The detection of neuropathic pain in 25.8% of patients indicated direct or indirect damage to peripheral nerves (small fibers). The close correlation of pain with partner absence ($p \leq 0.001$), anxiety, and depression demonstrated that the limbic system largely modulates the intensity of pain syndrome in COVID-19. Social isolation and psychological stress acted as amplifiers of pain. The predominance of headache and arm pain in women vs. leg and joint pain in men indicated the need for a differentiated approach to prescribing anticonvulsants and antidepressants in the treatment regimen.

Thus, COVID-19 provokes a gender- and age-specific neurosymptom complex. Women demonstrated higher autonomic and emotional lability, while men are prone to somatization and diffuse pain syndromes.

CONCLUSIONS

COVID-19, an acute respiratory infection, affects the autonomic nervous system, cognitive functions, and pain perception.

During inpatient treatment, the majority of examined patients had a high prevalence of autonomic symptoms. It was found that autonomic dysfunction syndrome was associated with female gender (p≤0.001), age (p≤0.01), depression (p≤0.001), anxiety disorders (p≤0.001), and comorbidities (p≤0.001). Women mainly reported symptoms such as face redness or paleness, numbness or coldness in the fingers and toes, a change in fingers and toes color, palpitations, a feeling of “heart sinking", difficulty breathing, fainting, headache, and decreased working capacity. Complaints of increased sweating, gastrointestinal disorders, and sleep disturbances predominated in men. The results indicated a more pronounced autonomic reactivity in women, especially in younger women.

Neurocognitive impairment was also identified in patients in the acute phase of COVID-19. In particular, women had significantly more pronounced disorders of temporal orientation (p≤0.01), as well as writing and reading difficulties (p≤0.1). The risk of developing and worsening cognitive impairment in COVID-19 was associated with age (average correlation level r=0.67), comorbidities (p≤0.001), and depressive states.

Neuropathic pain was recorded in 25.8% of respondents (among them, 87.5% of women and 58.3% of men). It was found that the presence of a neuropathic component of pain in patients with COVID-19 was associated with female gender, age over 50 years (p≤0.05), lack of a partner (p≤0.001), depression (p≤0.01), anxiety (p≤0.001), and autonomic dysfunction syndrome (p≤0.001).

Women most often reported headaches, as well as pain in the arms, neck, and back. Men were more likely to report pain in the legs, lower back, and joints, and to have widespread pain. The highest level of neuropathic pain intensity was observed in the age group of 46–60 years.

PROSPECTS FOR FUTURE RESEARCH

The data obtained will be useful in developing a personalized approach to diagnosing and supporting patients with COVID-19. The study emphasizes the need to include neuroprotective and autonomic-stabilizing therapies during inpatient treatment.

ETHICAL CONSIDERATIONS

All study participants provided written informed consent in accordance with the Law of Ukraine "On Psychiatric Care" dated February 22, 2000. The study was approved by the Bioethics Committee at the Medical Institute of Sumy State University (protocol No. 5/05 dated 05/18/2026).

AUTHOR CONTRIBUTIONS

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

ARTIFICIAL INTELLIGENCE DISCLOSURE

The authors state that artificial intelligence was not used to write the article.

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