8. Essamedin MN, Eman SE, Shahenda GB, AL ZM, Aya M, El S et al. Analysis of cumulative antibiogram reports in intensive care units at an Egyptian University Hospital Journal of Infection and Public Health. 2023 (16);1220–1229. https://doi.org/10.1016/j.jiph.2023.05.032
9. Krishnamoorthy SG, Raj V, Viswanathan B, Dhanasekaran GP, Palaniappan D, Borra SS. Enhancing the empiric antibiotic selection by introducing an antibiogram toolkit in a tertiary care hospital in Southern India – A prospective study. J Clin Pharm Ther. 2022 Apr;47(4):507–516. doi: 10.1111/jcpt.13571.
10. Sakai T, Morimoto Y. The History of Infectious Diseases and Medicine. Pathogens. 2022 Oct 4;11(10):1147. doi: 10.3390/pathogens11101147.
11. Simner PJ, Hindler JA, Bhowmic.k T, Das S, Johnson JK, Lubers BV et al. What's New in Antibiograms? Updating CLSI M39 Guidance with Current Trends. J Clin Microbiol. 2022 Oct 19;60(10):e0221021. doi: 10.1128/jcm.02210-21.
12. Truong WR, Hidayat L, Bolaris MA, Nguyen L, Yamaki J. The antibiogram: key considerations for its development and utilization. JAC Antimicrob Resist. 2021 May 25;3(2):dlab060. doi: 10.1093/jacamr/dlab060.
13. WHO Regional Office for Europe and European Centre for Disease Prevention and Control. Surveillance of antimicrobial resistance in Europe, 2020 data. Executive Summary. Copenhagen: WHO Regional Office for Europe; 2021: 1–5.

Стаття надійшла 9.03.2023 р.

DOI 10.26724/2079-8334-2024-1-87-31-35
UDC 616-036.21:371.711-08

O.O. Belov, N.G. Pshuk, A. M. Skrypnikov[1], L. O. Herasymenko[1] R.I. Isakov[1]
National Pirogov Memorial Medical University, Vinnytsia
[1]Poltava State Medical University, Poltava

DYNAMICS OF PSYCHOPATHOLOGICAL SYMPTOMS IN THE POST-COVID-19 PERIOD

e-mail: oleksbelov@gmail.com

The dynamics of post-COVID-19 psychopathological manifestations in 31 men and 33 women were studied. It was established that fatigue (75 %), anxiety (70 %), cognitive dysfunction (69 %) and low mood (63 %) dominate the structure. The dynamics of depressive and anxiety changes were more pronounced in the first 6 months (from 63 % to 34 % and from 70 % to 48 %), and fatigue, cognitive impairment and insomnia – after 12 months (from 63 % to 28 %, from 63 % to 23 % and from 33 % to 22 %). In the early period, clinically defined depressive disorders were found in 36 % of patients, in the late period – in 8 %. The prevalence of psychopathological symptoms other than irritability was non-significantly higher among women; they were also found to have higher levels of depression and anxiety. Two years after COVID-19, symptoms of fatigue, cognitive dysfunction, dyssomnia, depression, and anxiety were present in 22 %, 17 %, 16 %, 14 %, and 13 %, respectively. Depression and anxiety rates normalized 12 months after COVID-19, faster in men than in women.

Key words: COVID-19, post-COVID-19 period, depression, anxiety, fatigue, cognitive dysfunction

О. О. Белов, Н. Г. Пшук, А. М. Скрипніков, Л. О. Герасименко, Р. І. Ісаков

ДИНАМІКА ПСИХОПАТОЛОГІЧНОЇ СИМПТОМАТИКИ В ПОСТКОВІДНОМУ ПЕРІОДІ

Досліджено динаміку постковідних психопатологічних проявів у 31 чоловіка і 33 жінок. Встановлено, що у структурі постковідних психопатологічних проявів домінують втома (75 %), тривога (70 %), когнітивна дисфункція (69 %) та знижений настрій (63 %). Динаміка депресивних і тривожних змін у постковідному періоді була більш виражена у перші 6 місяців (з 63 % до 34 % і з 70 % до 48 %), а втоми, когнітивних порушень та безсоння – після 12 місяців (з 63 % до 28 %, з 63 % до 23 % і з 33 % до 22 %). У ранньому постковідному періоді клінічно оформлені депресивні розлади виявлені у 36 % пацієнтів, у пізньому – у 8 %. Поширеність психопатологічних симптомів, крім дратівливості, була незначуще вищою серед жінок; у них також виявлено вищі рівні депресії і тривоги. Через два роки після COVID-19 симптоми втоми, когнітивної дисфункції, диссомнії, депресії і тривоги були наявні у 22 %, 17 %, 16 %, 14 % та 13 % відповідно. Показники депресії і тривоги нормалізувалися через 12 місяців після COVID-19, у чоловіків швидше, ніж у жінок.

Ключові слова: COVID-19, постковідний період, депресія, тривога, втома, когнітивна дисфункція

The study is a fragment of the research project "Structural and dynamic concepts of affective pathology in modern society (clinical phenomenology, pathopsychological criteria, complex treatment)", state registration No. 0121U113294.

Monitoring the effects of COVID-19 has revealed a wide range of long-term disorders after the resolution of respiratory symptoms. These disorders have been referred to as "long COVID-19", "post-acute COVID-19", "long-haul COVID-19", but the term "post-COVID-19 syndrome" is most often used. The National Institute for Health and Care Excellence guidelines define the post-COVID-19 syndrome as "signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis" [6]. Total prevalence of post-COVID-19 syndrome estimated to 35 % in the general population and up to 85 % in previously hospitalized patients [9].

Mental disorders occupy an important place among the symptoms of post-COVID-19 syndrome. The most common psychiatric symptoms of the long-COVID-19 syndrome included depression, anxiety, fatigue, post-traumatic stress disorder, cognitive disturbances and insomnia [3, 7, 8]. The causes of these disorders are associated with the persistence of the virus in the nervous system, hypoxia, hyperinflammation, cytokine release syndrome, adverse respiratory distress syndrome, immuno-inflammatory dysregulation; the long COVID-19 syndrome can be due to several aetiopathogenetic factors is too [10, 13]. Many researchers have studied the characteristics of the psychiatric consequences of COVID-19, but information on gender different is limited; it is also necessary to expand research into the dynamics of psychopathological changes in patients over a long term [11, 14, 15]. These studies are important for managing the psychiatric consequences of post-COVID-19 syndrome and improving psychiatric and psychological care for people who have recovered from coronavirus infection.

The purpose of the study was to establish the features of psychopathological symptoms in the post-COVID-19 period, taking into account gender factor.

Materials and methods. We tracked the dynamics of psychopathological symptoms in 64 patients (31 men and 33 women) who sought psychiatric help or consultation in connection with psychiatric symptoms after suffering from COVID-19 in the Vinnytsia Regional Psychoneurological Hospital and at the Department of Medical Psychology and Psychiatry of National Pirogov Memorial Medical University, Vinnytsia, from June 2020 to September 2023. None of the patients included in the study had previously sought psychiatric help or had mental disorders before contracting COVID-19. The first examination was carried out when seeking psychiatric help (consultation) in the first three months after COVID-19, repeated in 6, 12 and 24 months after the disease. The average age of all patients was 39.4±16.2 years, of the men 40.7±16.2 years, and 38.1±16.5 years for women (p=0.357). The examination included a clinical interview to identify the spectrum and severity of psychopathological symptoms, assessment of the severity of depression and anxiety using the Hamilton Rating Scale for Depression – HRDS [4] and Hamilton Anxiety Rating Scale – HARS [5] respectively. All patients gave informed consent to participate in the study. The procedures of this study complied with the provisions of the Declaration of Helsinki concerning research on Human participants. The Ethics Committee of National Pirogov Memorial Medical University approved this study. Statistical analysis of the data was performed using the licensed application package Statistica (Stat-SoftInc., USA). The nature of the distribution of quantitative traits was assessed using the Shapiro-Wilk test. Intergroup analysis of differences was performed using a nonparametric Mann-Whitney test and Fisher's exact criteria. The level of statistical significance of differences $p<0.05$ was considered acceptable.

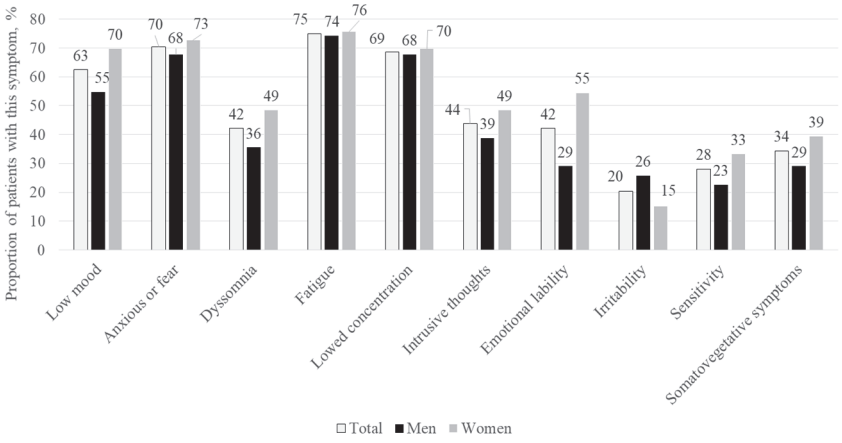

Fig. 1. Structure of psychopathological symptoms in the first three months after COVID-19

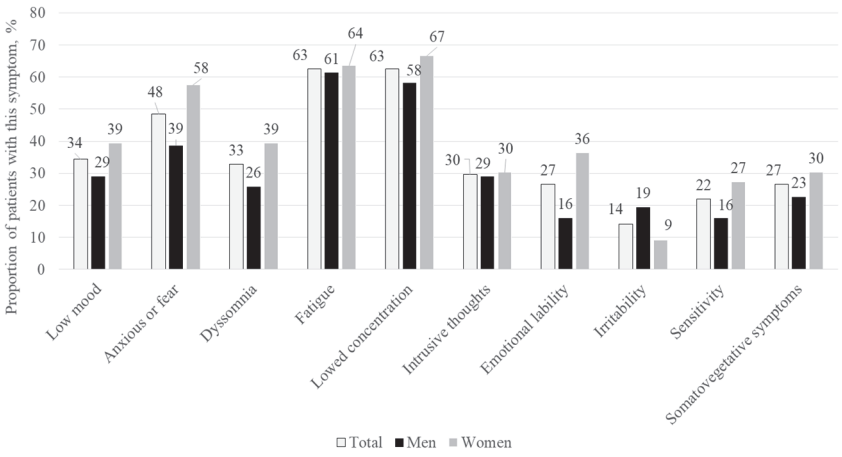

Fig. 2. Structure of psychopathological symptoms 6 months after COVID-19

Results of the study and their discussion. The prevalence of psychopathological symptoms was greatest in the first three months after COVID-19. The most common symptoms immediately after COVID-19 were fatigue, anxious or fear, low concentration and low mood (Fig. 1).

Six months after COVID-19, the incidence of anxiety and depression decreases, while fatigue and cognitive impairment remain at a high level (Fig. 2).

A year after COVID-19, fatigue remains the main complaint of patients, cognitive impairment and anxiety are significantly reduced, and depressive symptoms decrease slowly (Fig. 3).

Two years after COVID-19, the prevalence of different symptoms varies less, and the structure of psychopathological manifestations was dominated by manifestations of asthenia and cognitive dysfunction (Fig. 4).

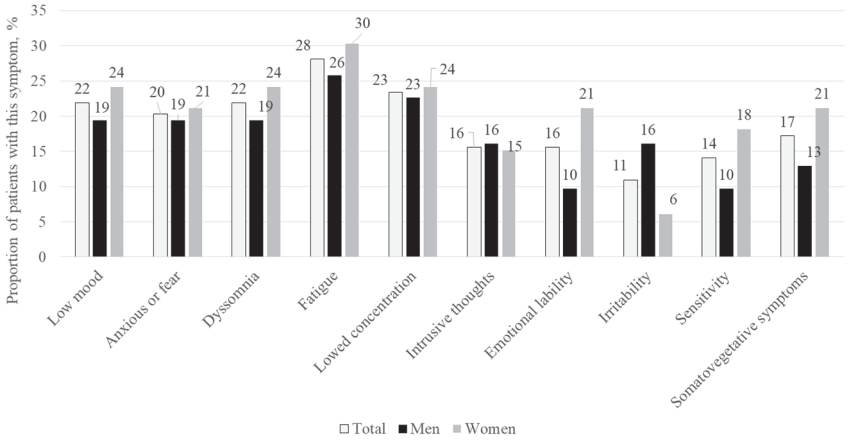

Fig. 3. Structure of psychopathological symptoms 12 months after COVID-19

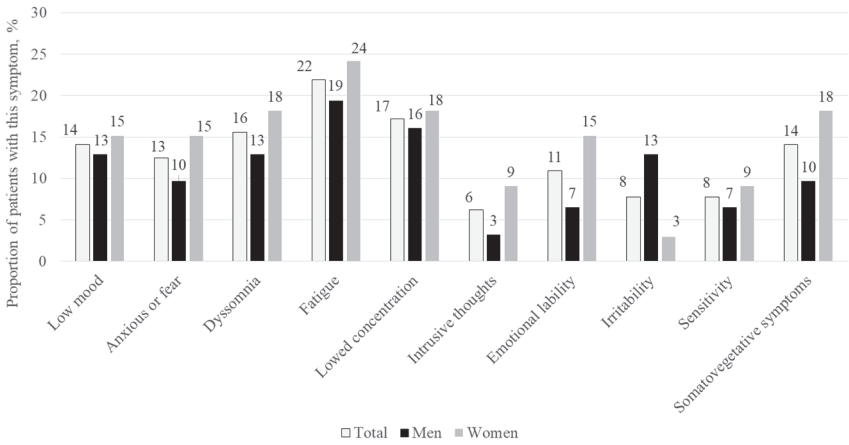

Fig. 4. Structure of psychopathological symptoms 24 months after COVID-19

Differences when comparing the prevalence of symptoms in the first three months and after 6 months are statistically significant for low mood (p=0.001), anxious or fear (p=0.010) and emotional lability (p=0.047); when comparing after 6 and 12 months – for low mood (p=0.084), anxious or fear (p=0.001), fatigue (p=0.001), low concentration (p=0.000), intrusive thoughts (p=0.045); when compared after 12 and 24 months differences are not significant (p>0.05).

The prevalence of psychiatric complaints gradually decreased over follow-up, although the decrease was uneven across symptoms. Low mood and anxiety decreased most rapidly in the first 6 months after the COVID-19, and subsequently the dynamics slowed down. Dyssomnias, fatigue and cognitive impairment were more persistent and the greatest changes occurred after 12 months. Fatigue and cognitive impairment were the most common symptoms after two years of follow-up. Emotional lability, irritability, sensitivity and somatovegetative symptomatic were characterized by more uniform dynamics.

In women, the prevalence of all symptoms except irritability was higher, but the differences were not statistically significant, with the exception of emotional lability in the first three months after COVID-19 (p=0.035).

At the first visit, 36 % of patients met diagnostic criteria for depression (32 % of men and 39 % of women, p=0.370), 6 months after COVID-19 – 20 %, 16 % and 24 % respectively (p=0.311), 12 months after COVID-19 – 11 %, 10 % and 12 % respectively (p=0.536), after 24 months – in 8 %, 7 % and 9 % respectively (p=0.530).

These results are confirmed by analysis of the depression scores (Table 1).

When comparing indices in the first three months and after 6 months after COVID-19, statistically significant differences (p<0.01) were found for all indicators except somatic anxiety (p=0.371). When comparing indices after 6 months and after 12 months, statistically significant differences were found for total score of HDRS (p=0.001), adynamic depression (p=0.023), total score of HARS (p=0.001), psychical anxiety (p=0.001), somatic anxiety (p=0.001); the differences are not statistically significant for agitation depression (p=0.074), depression with fear (p=0.134) and undifferentiated depression (p=0.074). At 12 months and at 24 months, the differences were statistically significant for depression with fear (p=0.008), undifferentiated depression (p=0.016), total score of HARS (p=0.001), psychical anxiety (p=0.001), and not statistically significant significant for total score of HDRS (p=0.055), adynamic depression (p=0.052), agitation depression (p=0.149) and somatic anxiety (p=0.546).

Table 1

Depression scores in the post-COVID-19 period

Indices	Level, M±SD, points			p men vs women
	Total, n=64	Men, n=31	Women, n=33	
In the first three months				
Total score	11.11±5.75	9.42±5.47	12.70±5.62	0.017
Adynamic depression	7.53±4.20	5.97±4.09	9.00±3.80	0.004
Agitation depression	5.36±2.77	4.81±2.70	5.88±2.78	0.091
Depression with fear	3.52±2.08	2.84±1.90	4.15±2.06	0.008
Undifferentiated depression	2.48±1.93	1.68±1.49	3.24±2.00	0.001
After 6 months				
Total score	8.14±4.12	7.26±4.06	8.97±4.07	0.059
Adynamic depression	5.38±2.88	4.55±2.83	6.15±2.75	0.016
Agitation depression	4.14±2.30	3.74±2.31	4.52±2.27	0.127
Depression with fear	2.83±1.70	2.32±1.62	3.30±1.65	0.010
Undifferentiated depression	1.98±1.44	1.42±1.18	2.52±1.48	0.003
After 12 months				
Total score	7.88±4.21	6.94±4.16	8.76±4.12	0.054
Adynamic depression	5.23±2.93	4.39±2.92	6.03±2.76	0.013
Agitation depression	4.03±2.36	3.61±2.36	4.42±2.32	0.108
Depression with fear	2.77±1.72	2.26±1.65	3.24±1.66	0.009
Undifferentiated depression	1.91±1.40	1.32±1.14	2.45±1.42	0.002
After 24 months				
Total score	7.34±4.05	6.68±3.97	7.97±4.08	0.099
Adynamic depression	4.84±2.74	4.32±2.86	5.33±2.58	0.056
Agitation depression	3.81±2.27	3.45±2.19	4.15±2.33	0.142
Depression with fear	2.55±1.62	2.19±1.62	2.88±1.58	0.044
Undifferentiated depression	1.70±1.29	1.26±1.09	2.12±1.34	0.009

The level of anxiety decreased more slowly, and in the first 12 months corresponded to a mild anxiety disorder. Two years later, anxiety levels remained elevated, close to the borderline of mild anxiety disorder. There were no significant differences in anxiety levels between men and women (Table 2).

Table 2

Anxiety scores in the post-COVID-19 period

Indices	Level, M±SD, points			p men vs wonem
	Total, n=64	Men, n=31	Women, n=33	
In the first three months				
Total score	17.67±8.57	16.52±8.55	18.76±8.57	0.326
Psychical anxiety	11.72±5.34	10.35±4.65	13.00±5.69	0.077
Somatic anxiety	5.95±3.95	6.16±4.22	5.76±3.73	0.803
After 6 months				
Total score	17.02±8.41	15.65±7.92	18.30±8.77	0.273
Psychical anxiety	11.13±5.30	9.61±4.23	12.55±5.84	0.042
Somatic anxiety	5.89±3.87	6.03±4.07	5.76±3.73	0.824
After 12 months				
Total score	14.45±5.91	13.90±5.97	14.97±5.90	0.527
Psychical anxiety	8.91±3.13	8.13±2.69	9.64±3.37	0.049
Somatic anxiety	5.55±3.44	5.77±3.63	5.33±3.29	0.671
After 24 months				
Total score	14.08±5.51	13.58±5.79	14.55±5.29	0.505
Psychical anxiety	8.66±2.76	7.90±2.45	9.36±2.87	0.035
Somatic anxiety	5.42±3.45	5.68±3.81	5.18±3.13	0.782

The mean level of depression in the examined patients corresponded to mild depression. At the same time, the level of depression in women was significantly higher than in men. Women also had higher rates of adynamic depression, depression with fear and undifferentiated depression. In the first 6 months, the level of depression decreased and generally corresponded to the lower limit of mild depression, and in men – to the upper limit of normal. After 12 months, the depression score in all patients and in men corresponded to the upper limit of the norm, and in women – to the lower limit of mild depression. After 24 months, depression scores had decreased slightly and were below the mild depression limit in all groups. There were significant differences in depression levels between men and women only at the first examination.

Our results are generally consistent with the data of other studies (Calabria M. et al. [2], Chen A.K. et al. [3], Ohira M. et al. [7], Paez A.F. et al. [8], Stallmach A. et al. [12], Zakia H. et al. [14],) that identified the most common psychopathological symptoms in the post-COVID-19 period are fatigue (10.6 – 93.2 %), depression and anxiety (22.0 % – 81.3 %), sleep disturbances (13.3 % – 50.0 %) and cognitive dysfunction (23.5 % – 73.2 %). Our study confirmed the data of Boiko D.I. et al. (2022) who found that COVID-19 caused a greater predisposition to the development of circadian rhythm disorders, in particular delayed sleep phase disorder, and increased levels of both trait and state anxiety [1].

The peculiarity of our study was that we observed patients for two years after Covid-19, and differentiated symptoms depending on gender. Also, there were no psychiatric patients in our sample, which made it possible to exclude the influence of mental disorders before COVID-19 and to assess the impact of coronavirus infection on the psyche over a long period.

Limitations of this study were the small sample size and no adjustment for patient age.

Conclusions

1. In the post-COVID-19 period, long-term mental disorders persist, the most common among them were chronic fatigue, cognitive dysfunction, depression, anxiety and sleep disorders.

2. The greatest dynamics of depressive and anxiety disorders in the post-COVID-19 period was observed in the first 6 months after infection, and cognitive dysfunction and fatigue – after 12 months.

3. The most persistent psychopathological symptoms in the post-COVID-19 period were fatigue, low concentration and dyssomnia, which persisted in 15 % – 20 % of patients even two years after COVID-19.

References

1. Boiko DI, Skrypnikov AM, Shkodina AD, Hasan MM, Ashraf GM, Rahman MH. Circadian rhythm disorder and anxiety as mental health complications in post-COVID-19. Environmental science and pollution research. 2022; 29: 28062–28069. http://repository.pdmu.edu.ua/handle/123456789/18560

2. Calabria M, García-Sánchez C, Grunden N. Post-COVID-19 fatigue: The contribution of cognitive and neuropsychiatric symptoms. J. Neurol. 2022; 269: 3990–3999. doi: 10.1007/s00415-022-11141-8.

3. Chen AK, Wang X, McCluskey LP. Neuropsychiatric sequelae of long COVID-19: Pilot results from the COVID-19 neurological and molecular prospective cohort study in Georgia, USA. Brain Behav. Immun. Health. 2022; 24: 100491. doi: 10.1016/j.bbih.2022.100491.

4. Hamilton M. A rating scale for depression by Max Hamilton. Journal of Neurology, Neurosurgery, Psychiatry. 1960; 23: 56–62. doi: 10.1136/jnnp.23.1.56.

5. Hamilton M. The assessment of anxiety states by rating. British Journal of Medical Psychology. 1959; 32: 50–55. doi: 10.1111/j.2044-8341.1959.tb00467.x.

6. National Institute of Clinical Excellence (NICE) COVID-19 Rapid Guideline: Managing the Long-Term Effects of COVID-19. National Institute of Clinical Excellence; London, UK: 2022.

7. Ohira M, Sano T, Takao M. Clinical features of patients who visited the outpatient clinic for long COVID in Japan. eNeurologicalSci. 2022; 28: 100418. doi: 10.1016/j.ensci.2022.100418.

8. Paez AF, Nicolalde B, Esquetini-Vernon C, Lara-Taranchenko Y, Zambrano K, Ocampo J, et al. Psychiatric disorders in Post-acute COVID-syndrome (PDPACS): Recommendations for health care professionals. Eur Neuropsychopharmacol. 2022; 58: 100–102. doi: 10.1016/j.euroneuro.2022.03.003.

9. Pavli A, Theodoridou M, Maltezou HC. Post-COVID Syndrome: Incidence, Clinical Spectrum, and Challenges for Primary Healthcare Professionals. Arch. Med. Res. 2021; 52: 575–581. doi: 10.1016/j.arcmed.2021.03.010.

10. Penninx BWJH. Psychiatric symptoms and cognitive impairment in “Long COVID”: The relevance of immunopsychiatry. World Psychiatry. 2021; 20: 357–358. doi: 10.1002/wps.20913.

11. Sampogna G, Di Vincenzo M, Giallonardo V, Perris F, Volpicelli A, Del Vecchio V, et al. The Psychiatric Consequences of Long-COVID: A Scoping Review. J Pers Med. 2022; 12(11): 1767. doi: 10.3390/jpm12111767.

12. Stallmach A, Kesselmeier M, Bauer M. Comparison of fatigue, cognitive dysfunction and psychological disorders in post-COVID patients and patients after sepsis: Is there a specific constellation? Infection. 2022; 50: 661–669. doi: 10.1007/s15010-021-01733-3.

13. Stefano GB, Ptacek R, Ptackova H, Martin A, Kream RM. Selective Neuronal Mitochondrial Targeting in SARS-CoV-2 Infection Affects Cognitive Processes to Induce ‘Brain Fog’ and Results in Behavioral Changes that Favor Viral Survival. Med. Sci. Monit. 2021; 27: e930886. doi: 10.12659/MSM.930886.

14. Zakia H, Pradana K, Iskandar S. Risk factors for psychiatric symptoms in patients with long COVID: A systematic review. PLoS One. 2023. 18(4): e0284075. doi: 10.1371/journal.pone.0284075.

15. Zawilska JB, Kuczyńska K. Psychiatric and neurological complications of long COVID. J Psychiatr Res. 2022. 156:349-360. doi: 10.1016/j.jpsychires.2022.10.045.

Стаття надійшла 15.03.2023 р.