

До питання цілісної клінічної інтерпретації психічних розладів при пандемії SARS-CoV-2: експертна думка

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Резюме. З прогресуванням пандемії COVID-19 спостерігається зростання проблем з психічним здоров'ям, що вимагає дедалі більшої уваги клініцистів. Саме ці проблеми призводять до основних порушень соціальної адаптації, передусім через розлади, розподілені на три «кластери»: тривалу астенію (втому) з когнітивними порушеннями, тривожні розлади з розладами сну та депресії. Останні виявляються також в осіб, які не хворіли на SARS-CoV-2, та оцінюються як результат впливу стресу внаслідок пандемії. Щоб успішно подолати наслідки пандемії необхідно випрацювати цілісну клінічну інтерпретацію психічних розладів, пов'язаних із коронавірусною інфекцією COVID-19. Запропонована у нашому дослідженні модель охопила б усі вищезазначені прояви в такий спосіб: а) для загальної популяції — триадою «нозогенних реакцій» з надмірним (гіпер-), нормальним (нормо-) або ігноруючим (гіпо-нозогностичним) психологічним реагуванням на стрес, пов'язаний зі смыслом та особистою значимістю діагнозу «SARS-CoV-2» (нозосом); б) для лонг COVID: біопсихосоціальною моделлю, як типовою комбінацію нейротоксичної астенії з когнітивними порушеннями за К. Бонгофером (нейробіологічний фактор), яка посилює «нозогенну» тривогу і порушення сну (психологічний фактор), що в низці випадків провокує депресію (як фактор соціальної дезадаптації).

Ключові слова: SARS-CoV-2, лонг COVID-19, нозогенні стресові розлади, нейротоксична астенія (Бонгофера), когнітивні розлади, депресія, цілісна клінічна концептуалізація.

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Toward a cohesive clinical interpretation of mental disorders in SARS-CoV-2 pandemic: An expert opinion

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Abstract. As the COVID-19 pandemic progresses, the observed increase in mental health issues requires more and more clinical attention. Mental disorders have become a major cause for disturbances in social adjustment, primarily due to disorders that fall into three clusters: prolonged fatigue (asthenia) with cognitive impairment; anxiety disorders with sleep disorders; and depression. The last two are also found in individuals who have not contracted SARS-CoV-2; they are seen as a result of their exposure to the stress of the pandemic. Therefore, to successfully manage the consequences of the pandemic, it is necessary to develop a cohesive clinical interpretation of mental disorders related to COVID-19 infection. Our proposed model would encompass all the above manifestations as follows: a) *for the general population* – by the triad of 'nosogenic reactions' with excessive (hyper-), normal (normo-) or ignoring (hypo-nosognostic) psychological responses to stress related to the *semantics and individual significance* of the SARS-CoV-2 diagnosis (nosos); b) *for long COVID* – by the biopsychosocial model as a typical combination of neurotoxic asthenia with cognitive impairment (Bonhoeffer's neurobiological factor) that exacerbates 'nosogenic' anxiety and sleep disorders (psychological factor) and thus provokes a depressive response (as a social maladaptive factor).

Keywords: SARS-CoV-2, long COVID-19, nosogenic stress-related disorders, neurotoxic asthenia (Bonhoeffer), cognitive disorders, depression, clinical conceptualization.

The **objective** of this report is to propose an integral interpretation of the entire range of mental disorders in COVID-19 found in existing clinical studies. The authors explored the following issues: a) why COVID-19 pandemic is accompanied by a particular spectrum of mental and psychological disorders; c) which clinical interpretation of such disorders is proposed in the available studies; and (c) wheth-

er there exists a cohesive clinical rationale for these disorders, which range from anxiety and depression in the general population [1] to typical manifestations of long COVID.

Methods: the academic part comprised a review of Pubmed literature on mental disorders in the case of COVID-19, starting from January 2020, with emphasis on a) epidemi-

ological indicators in patients uninfected with COVID, who manifested typical stress-dependent psychological reactions to any information about COVID-19 diagnosis; b) mental disorders during the acute phase of the disease; c) mental disorders in long COVID.

The clinical part included: a) *in the psychotherapeutic setting* – an in-depth description of the development of stress-dependent disorders in patients who did not contract COVID-19, but were admitted as patients with complaints of anxiety, insomnia, or depression; c) *in consultations* – an analysis of manifestations of long COVID for their cohesive clinical qualification, with consideration of the published data; d) discussion of the data obtained from psychodynamic therapy and clinical consultations with a culturally independent expert psychoanalyst – Professor Alfred Pritz, Honorary Professor of Danylo Halytsky National Medical University in Lviv and our long-standing partner in educational and research projects.

Literature review: general population. Jiagi Xiong et al. (2020) who analyzed the population-based mental health studies at the *onset of the pandemic* in 7 countries pointed out relatively high levels of anxiety (6.33% to 50.9%), depression (14.6% to 48.3%), PTSD (7% to 53.8%), psychological stress (34.43% to 38%), and overall stress (8.1% to 81.9%). The risk groups for these disorders during the pandemic include women, individuals under 40, students, the unemployed, and individuals with preexisting health issues, both physical and mental; constant preoccupation with news about COVID-19 in the media *contributed to the risk* [2].

A recent longitudinal study of mental health [3] showed that the proportion of respondents with anxiety symptoms in 2020 increased to 20.1% from 17.3% in 2014-2019. Schäfer et al. (2020) [4] assessed psychopathological symptoms and adaptability before and after the outbreak of COVID-19, as well as traumatic distress associated with COVID-19 in a sample of German-speaking population: only 10% of respondents experienced a clinically significant increase in psychopathological symptoms, and 15% met the threshold criteria for traumatic distress associated with COVID-19. *More importantly*, however, two groups with *different responses to stress* were identified. The

group with an *intense* response to the stress experienced an increase in psychopathological symptoms and a decrease in adaptability, while the group with *lower levels* of response to the stress experienced reverse symptoms.

Based on the findings from 84 studies in 2021, MB Stein [5] provides the resulting data on the characteristics of psychiatric symptoms in the general population. This data does not differ significantly from the 2020 data listed above: a) distress and PTSD were present in up to 36%; b) depression – in 17%; c) distress – in 14%; d) PTSD symptoms – in 7%. The author does not summarize the data on sleep disorders and anxiety, although other studies pay special attention to these two categories. This may be due to the fact that the author views anxiety as a manifestation of distress (up to 36%).

A recent study on the epidemiology of mental disorders in the general population conducted by Castadelli-Maia JM et al. [6] indicates a significant increase in anxiety disorders (up to 18% in Asia and up to 29% outside Asia and Europe) and depression (16% in China, 26% in Europe, and 39% in other non-Asian countries). The authors believe that lower levels of depression and anxiety found in Asian countries could be culture-dependent.

Taking into account the findings of other recent reviews [7,8], it can be summarized that the incidence of anxiety, depressive disorders, stress reactions, and sleep disorders in the general population exceeds the pre-pandemic one by 2 to 2.5 times. All authors in one way or another emphasize the role of *information pressure and psychological distress* associated with severe consequences of infection, isolation, and panic.

We did not specifically analyze the **acute phase** of COVID-19, although currently available literature data [5] make it clear that all registered syndromes of mental disorders fully correspond to the well-known concept of exogenous organic syndromes by K. Bonhoeffer, 1917). As a reminder: this concept deals with typical and nonspecific syndromes undetermined by a specific cause of brain damage (infections, intoxications, tumors, etc.): *delirium; memory disorder; disturbance of attention and thinking; paroxysmal states with possible disturbances of consciousness; hallucinations;*

and asthenia. In fact, it is a case of an 'acute cerebropathic disorder' in one of the listed options or even a combination of several of them. This clinical concept does not only account for the *characteristic types* of all mental disorders in COVID-19 (as well as the entire group of SARS infections) [5] but envisages an *acute and temporary course* of the above disorders.

Long COVID. It is now clear that the pandemic is having a negative, long-term impact on the mental health of individuals who contract COVID-19. Such patients mostly seek medical help for asthenia, attention disturbances and minor short-term memory disorders, anxiety-phobic disorders, and depression. Within 14 to 90 days after being diagnosed with COVID-19, 18% of the patients sought help from a psychiatrist; in 5.8% of those cases, symptoms of asthenia, anxiety, and depression were revealed for the first time. A study conducted during the initial outbreak of COVID-19 in China found: 53.8% of respondents rated the psychological impact of the pandemic as moderate or severe; 16.5% reported moderate to severe symptoms of depression; 28.8% — moderate and severe anxiety symptoms; 8.1% — medium and significant levels of stress [1].

More recent studies focusing on long-term consequences of COVID-19 [9, 10] note that a number of patients who contracted even mild forms of COVID-19 experienced long-term mental consequences that were also associated with direct lesions of the nervous system, such as intracranial hemorrhage and ischemic stroke. Psychiatric disorders were noted in 5.8% of individuals with no history of mental illnesses. Asthenia was the most common condition: individuals who tested positive for SARS-CoV2 felt exhausted, suffered from apathy over the course of 3 to 4 months, and were unable to fully resume working. In particular, in a comparative study of neurological and mental disorders in the case of COVID-19 by Taquet M. et al. [10], it was shown that within 6 months after the acute phase of the disease, patients who had contracted COVID-19 demonstrated a highly significant increase in all types of mental disorders.

Chronic fatigue or asthenia is proved to be the most frequent long-term consequence of COVID-19 among all mental disorders found in COVID-19 (long COVID) [11]. The next most

frequent findings include anxiety and depressive disorders, as well as cognitive impairment. The authors also note that, compared to neurological disorders, common psychiatric disorders (mood and anxiety disorders) showed a weaker relationship with markers of COVID-19 severity in terms of incidence or hazard ratios. They believe that their occurrence reflects, at least partly, the influence of psychological implications on COVID-19 diagnosis – rather than being a direct manifestation of the illness.

Clinical conceptualization. In terms of clinical conceptualization of psychopathological presentations induced by the COVID-19 pandemic, only two studies involving a unified clinical interpretation of pandemic-related mental disorders can be cited [12, 13].

In one of these studies analyzing the self-assessment data of 265 patients a month after discharge from hospital (all male samples, average age of 56 years) during the «second wave» of the pandemic in 2020, authors conclude that psychiatric consequences of SARS-CoV-2 infection can be caused both by the immune response to the virus itself, *and by psychological stressors* such as social isolation, the psychological impact of a novel severe and potentially fatal illness, concerns about infecting others, and stigma [12]. However, the impact of each of these factors remains unclear.

In the other study, the authors discuss the possibility of 'infectious' triggering or even pathogenetic conditioning of all classes of mental disorders, including schizoaffective psychosis and schizophrenia [13].

Therefore, we believe that our attempt to formulate a holistic cohesive clinical interpretation of COVID-19-related psychopathology may be useful for the understanding of the full range of mental disorders observed during the pandemic.

Psychotherapeutic setting. Since January 2020, in the inpatient department of Lviv Clinical Psychoneurological Dispensary of our clinic, 22 patients (19 women, 3 men) were treated for anxiety disorders or depression by a combination of medical treatment and psychotherapy. Seven patients had contracted COVID-19, while 15 patients were uninfected. The psycho-

therapeutic diagnosis was established according to the principles of operationalized psychodynamic diagnosis (OPD-2) [14]. OPD-2 is a standardized procedure of psychodynamic diagnosing of the patients' attitude toward the disease, personality structure, and basic conflicts and relationships verified according to ICD-10 criteria. In our case, it involved an analysis of psychological factors that may trigger anxiety or depressive reactions to COVID-19 diagnosis and its possible adverse effects. The analysis of self-reports of these patients shows that all cases of anxiety, depressive, or combined anxiety and depressive disorders are associated with excessive psychological response to the meaning of COVID-19 diagnosis.

As early as in 1992, based on the study of psychological responses to the diagnosis of 'myocardial infarction', a specific set of 'nosogenies' – psychological responses to the significance of a dangerous diagnosis conveyed to patients (such as heart attack, cancer, etc.) was described (co-authored by O. Filts. 1992 [15]). These responses comprise a spectrum with extremes of excessive, 'exaggerated', and 'unreasonable' psychopathological reactions of anxiety, depression, or depression in combination with hypochondriasis, at one end, and the opposite behaviors of ignoring the actual danger associated with a serious diagnosis, at the other. The first type of response is called hypernosognosia (exaggerated perception of the diagnosis), and the second – hyponosognosia (ignoring the diagnosis). Hypernosognosia may include hypochondriasis but has a wider context consisting of, besides symptoms and general health condition, social, interpersonal, adjustment and other aspects related to the perception of disease by patients.

All of the examined patients with anxiety, depressive, or combined anxiety and depressive disorders reported a hypernosognostic response to the diagnosis of COVID-19 at the time of the study. In self-reports of uninfected patients, the hypernosognostic response clearly correlated with the fear of the possible fatal outcome, gradually increased in line with the information pressure, and eventually reached clinical significance, with reduced social and occupational adjustment and a need for inpatient treatment. In patients with a history of COVID-19 (N=7), we observed the *following dynamics*: anxious hy-

pernosognostic response to probable (*although virtually absent*) threats associated with COVID diagnosis caused a *disability of temporary but unpredictable duration*, triggering a subsequent development of a depressive disorder (usually with sleep disorders). Finally, in 3 out of 15 patients who previously ignored the danger of COVID-19 diagnosis, the very fact of the established diagnosis provoked an acute anxiety hypernosognostic response.

During further **clinical consultations** with psychiatrists, psychotherapists, and clinical psychologists, we found that in patients seeking consultation or treatment for encephalopathic, asthenic and mild cognitive (decreased concentration and episodes of fixation amnesia) manifestations of long COVID, hypernosognostic *anxiety* subjectively *exacerbated* the above manifestations and significantly prolonged maladaptation, which in turn exacerbated *depression* symptoms.

To sum up:

1. The concept of nosogenies, as well as hyper- and hypo-nosognostic responses to the disease, is a useful tool in evaluating mental disorders and psychological responses both in the general population and in patients who contracted COVID-19 during the SARS-CoV-2 pandemic.
2. In the general population, hypernosognostic responses, triggered primarily by information pressure regarding the immediate threats and consequences of COVID-19, including mandatory social distancing and lockdown periods, contribute to the significant increase in anxiety, depressive, stress-related, and sleep disorders in the general population during the COVID-19 pandemic; conversely, hypo-nosognostic responses result in irresponsible behavior, including the violation of quarantine requirements.
3. Symptoms of long COVID are consistent with the biopsychosocial model of clinical manifestations of mental disorders: K. Bonhoeffer's neurotoxic encephalopathic disorders and mainly – asthenic and mild cognitive disorders (*biological* factor), exacerbated by information-nosogenic anxiety (*psychological* factor), which in turn significantly reduces the adaptive capacity (*social* factor) causing depressive disorders. All three factors form a 'pathological vicious circle'.

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