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Mental Disorders in Patients during the Recovery Period after Viral Pneumonia Caused by COVID-19

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Abstract: The SARS-CoV-2 virus can penetrate and infect the brain, but the mechanisms of the disease are not fully understood. It is unclear to what extent the severe neurological and psychiatric complications are due to a catastrophic overreaction of the immune system to the virus, known as hypercytokinemia; in what cases these complications may be due to a disproportionate thrombotic reaction; and whether concerns that some complications may be a consequence of massive empirical drug therapy are justified. It is unclear whether this damage is caused by an overreaction of the immune system, by medications, or by the virus itself. Understanding this is critical because these scenarios require very different therapeutic approaches and treatment regimens.

Keywords: COVID-19, mental disorders, mental health, anxiety, depression, cognitive impairment.

Among the mental disorders that were noted during the previous SARS and MERS epidemics, syndromes of confusion (27.9%), depression (32.6%), memory impairment (34.1%), insomnia (41.9%) and, less frequently, mania and psychosis (0.7%) were described. Studies have also shown long-term mental health effects in survivors of infections caused by various viruses of the Coronaviridae family, including depression, insomnia, anxiety, irritability, chronic asthenic conditions and post-traumatic stress disorder (PTSD) [1–3].

Patients with severe mental disorders (SMD) and pneumonia often present to the doctor at a late stage of pneumonia and are hospitalized in the intensive care unit. Mortality from pneumonia in this group of patients is comparatively higher. For example, in schizophrenia, the probability of dying from pneumonia or influenza increases sevenfold compared to the general population. The group of patients with SMD is characterized by smoking, psychoactive substance use, and obesity - all of which aggravate the course of pneumonia.

In addition, such patients may have reduced respiratory reserve due to malnutrition and poor control of comorbid conditions such as asthma or chronic obstructive pulmonary disease. Patients with SMD are relatively more likely to be diagnosed with HIV infection, which negatively affects the severity and incidence of community-acquired pneumonia.

Patients with SMI have a disproportionately high proportion of homeless people, people with a history of incarceration, and people with vitamin D deficiency. All of the above are risk factors for tuberculosis.

Overall, in the population, those with the highest risk of severe COVID-19 and the highest risk of dying from COVID-19 include those with the following risk factors: smoking, obesity, hypertension, diabetes, cardiovascular disease, chronic respiratory disease, and cancer. Given the level of multimorbidity and the prevalence of smoking among people with SMD, it can be said

that belonging to the group of people with SMD increases the risk of developing severe COVID-19 infection.

The risk of respiratory complications, including aspiration pneumonia, is increased by psychotropic drugs. In particular, the risk of pneumonia is increased by clozapine, which may be related not only to the risk of aspiration of saliva, but also to its immunosuppressive effects.

There are currently no specific guidelines for the treatment of psychiatric hospital-acquired pneumonia (PHAP). This type of pneumonia is known to be associated with increased mortality – 21.3%. There is evidence that PHAP is the cause of 9.5-18% of deaths in psychiatric hospitals. Predictors of fatal outcome from PHAP include age over 65, body mass index less than 18.5, and bilateral pulmonary infiltrates.

It was found that of the mental disorders that were noted during the previous SARS and MERS epidemics, the following were described: confusion syndromes (27.9%), depression (32.6%), memory impairment (34.1%), insomnia (41.9%), and less frequently mania and psychosis (0.7%). Studies have also shown long-term mental health effects in survivors of infections caused by various viruses of the Coronaviridae family, including depression, insomnia, anxiety, irritability, chronic asthenic conditions and post-traumatic stress disorder (PTSD) [1–3].

The aim of the study is to study the presence and prevalence of mental disorders among patients who have had proven COVID-19-associated pneumonia.

Material and methods

The study included 40 patients (women) and 40 patients (men) aged 18 to 65 years (mean age 46.6 ± 15.8 years) who had proven COVID-19-associated pneumonia, 3 months ± 2 weeks after discharge from the hospital.

The study complies with Good Clinical Practice standards and the provisions of the Declaration of Helsinki. The study protocol was approved by the local ethics committee (protocol No. 159 dated 23.07.20).

Inclusion criteria for the study: documented diagnosis of COVID-19-associated pneumonia and the patient's desire to participate in observation.

Exclusion criteria: pregnancy, refusal to participate, chronic diseases in the acute stage, history of oncological diseases no more than 5 years before the start of the study, tuberculosis and other diseases accompanied by pulmonary fibrosis, surgical interventions on the lungs, HIV, heart defects, chronic hepatitis.

The presence of stress was assessed using the Perceived Stress Scale 10 (PSS-10). PSS-10 is a reliable questionnaire consisting of 10 questions that allows one to assess the level of subjectively perceived stress [9]. To assess the signs of anxiety and depression, the Generalized Anxiety Disorder Scale (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9) were used, respectively.

The statistical significance of differences between the sample proportions of the population was assessed using contingency table analysis using Fisher's exact test and Pearson's $\chi 2$. To compare quantitative values in two groups with a normal distribution, the Student t-test was used; with a distribution different from normal, the nonparametric Mann-Whitney test was used.

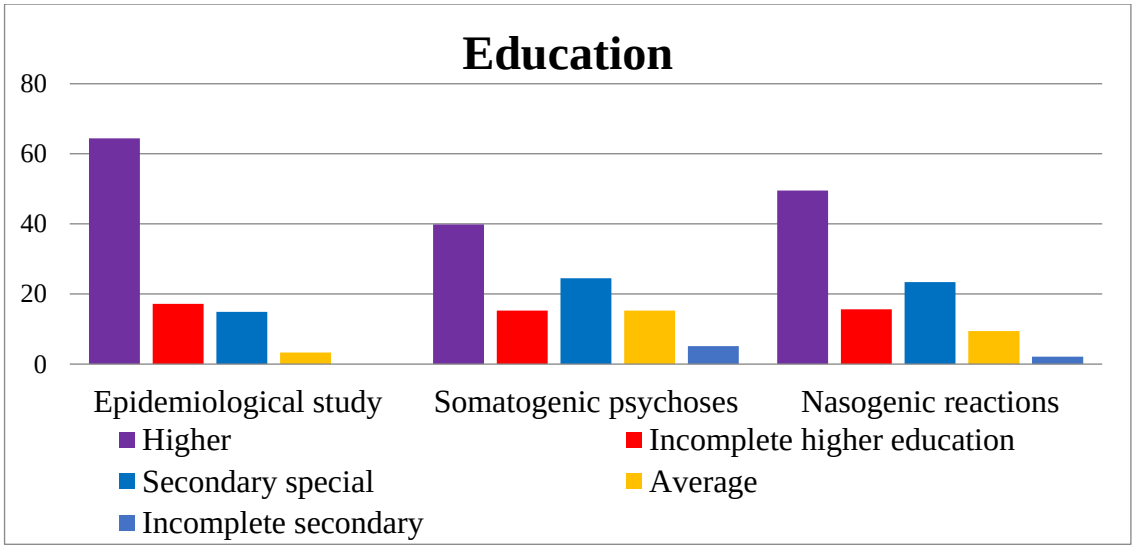
In the examined sample, signs of anxiety and depression were recorded in approximately patients (29.1%), a combination of signs of anxiety and depression - in 18.4% of patients. Stress was detected in 8.7% of patients.

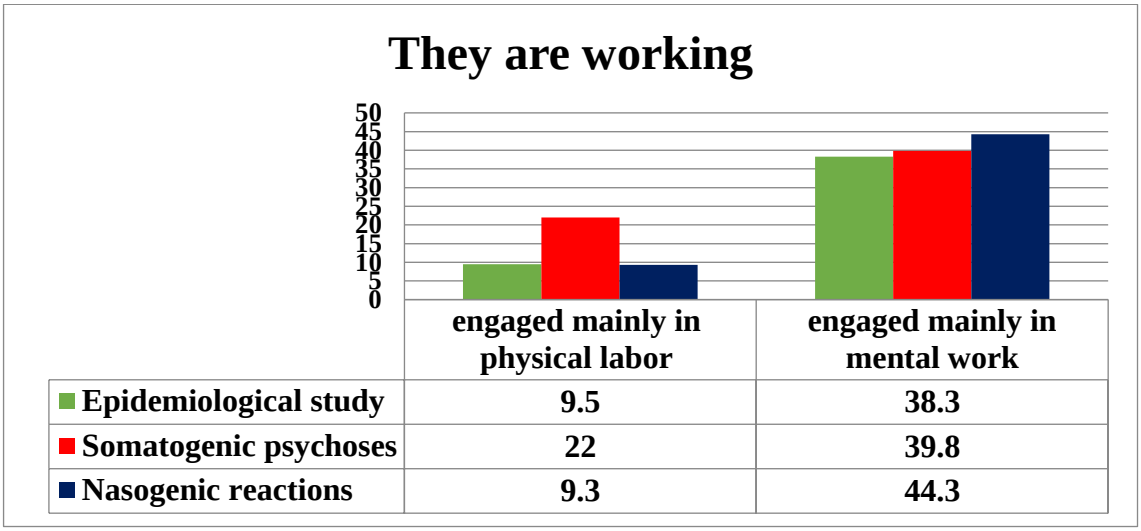
The prevalence of signs of depression differed significantly depending on gender: they were detected more often in women ($p=0.023$). The median score of the PHQ-9 questionnaire, reflecting signs of depression, was also significantly higher in the group of women than in the group of men (3.00 [1.00; 8.00] and 1.00 [0; 3.75], respectively; $p=0.006$). Logistic regression

analysis showed that female gender increases the likelihood of developing depression by 2.83 times (95% CI 1.35-7.08). Despite the fact that no differences by gender were found in assessing the prevalence of anxiety symptoms (18.4% and 10.7%; p=0.072), when comparing the median scores of the GAD-7 questionnaire in the groups of men and women, the difference was statistically significant (1.00 [0; 4.00] and 3.00 [2.00; 7.00], respectively; p=0.001). There were no differences between women and men in the frequency of the combination of anxiety and depression symptoms, as well as in manifestations of stress. However, manifestations of stress were detected significantly less frequently among married people compared to unmarried people (2.9% versus 5.8%; p=0.037).

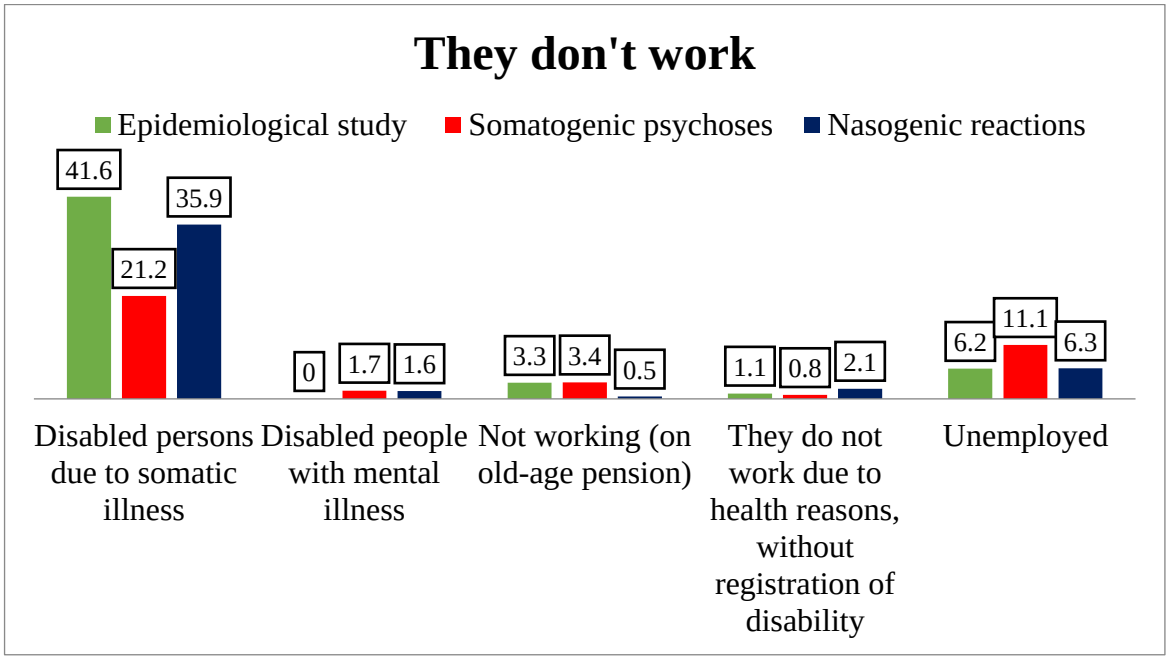
Table 1. Socio-demographic indicators of the studied patients with viral pneumonia caused by COVID-19

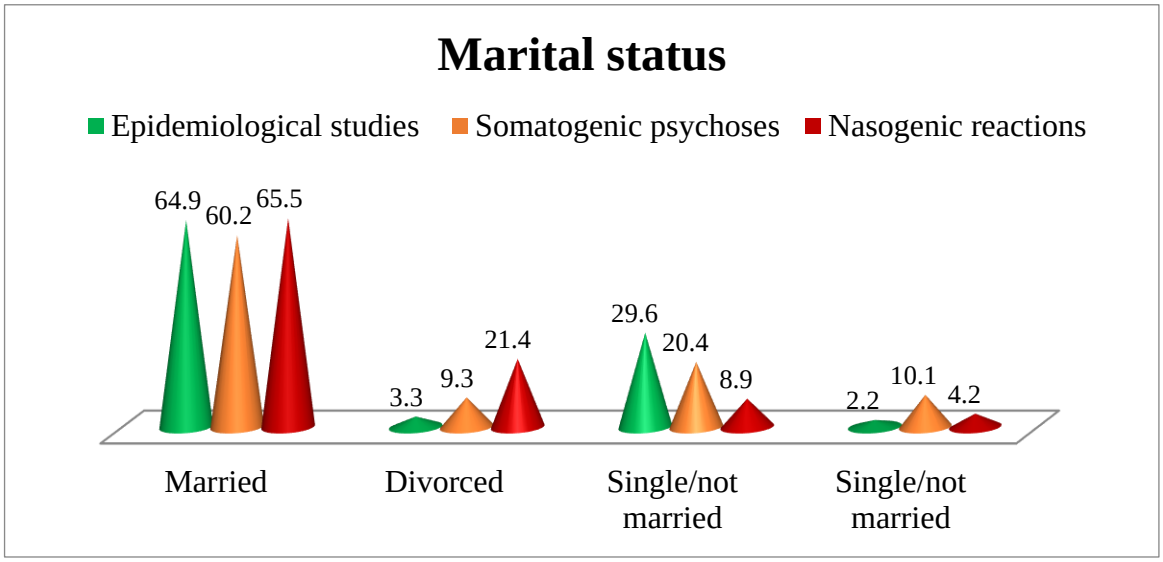
Socio-demographic indicators	Epidemiological study		Somatogenic psychoses		Nasogenic reactions	
	Abs.	**%**	**Abs.**	**%**	**Abs.**	**%**
Average age (in years)	39,21=16,88		49,27=18,18		36,63=13,07	
Men	125	45,6	75	63,6	99	51,6
Women	149	54,4	43	36,4	93	48,4
Total	**274**	**100,0**	**118**	**100,0**	**192**	**100,0**

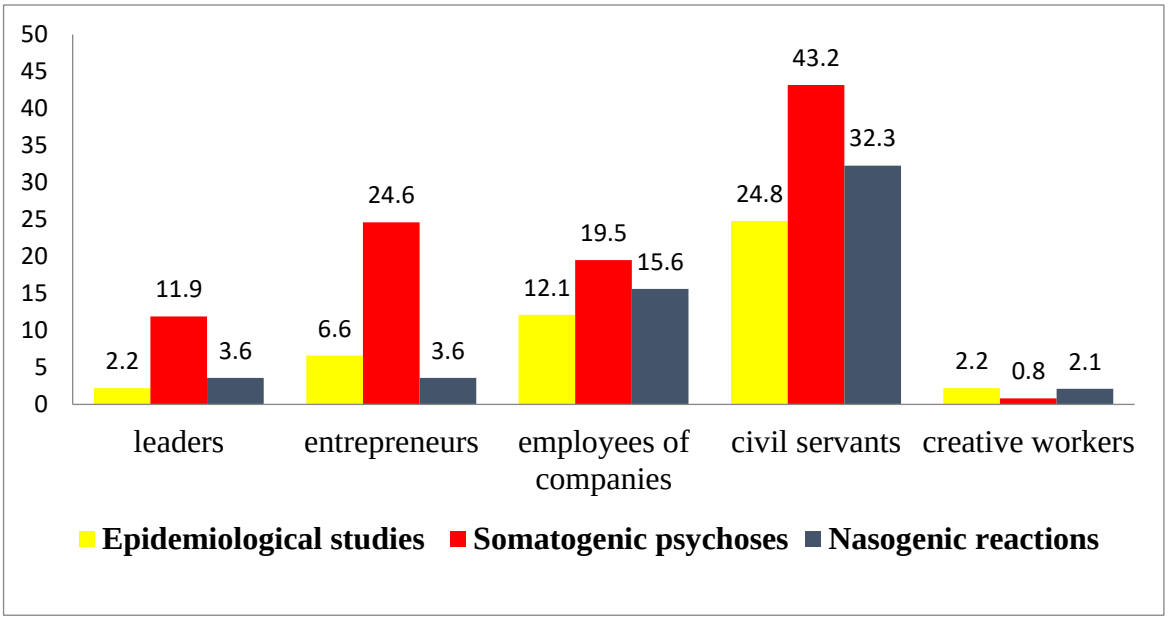




	engaged mainly in physical labor	engaged mainly in mental work
Epidemiological study	**9.5**	**38.3**
Somatogenic psychoses	**22**	**39.8**
Nasogenic reactions	**9.3**	**44.3**





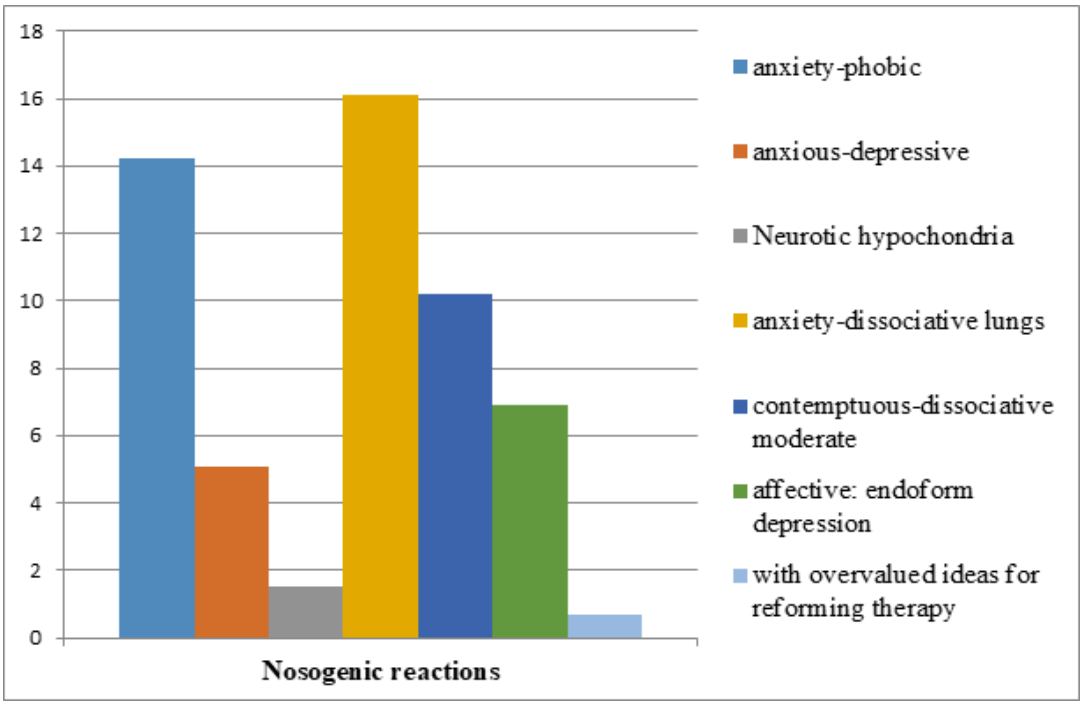


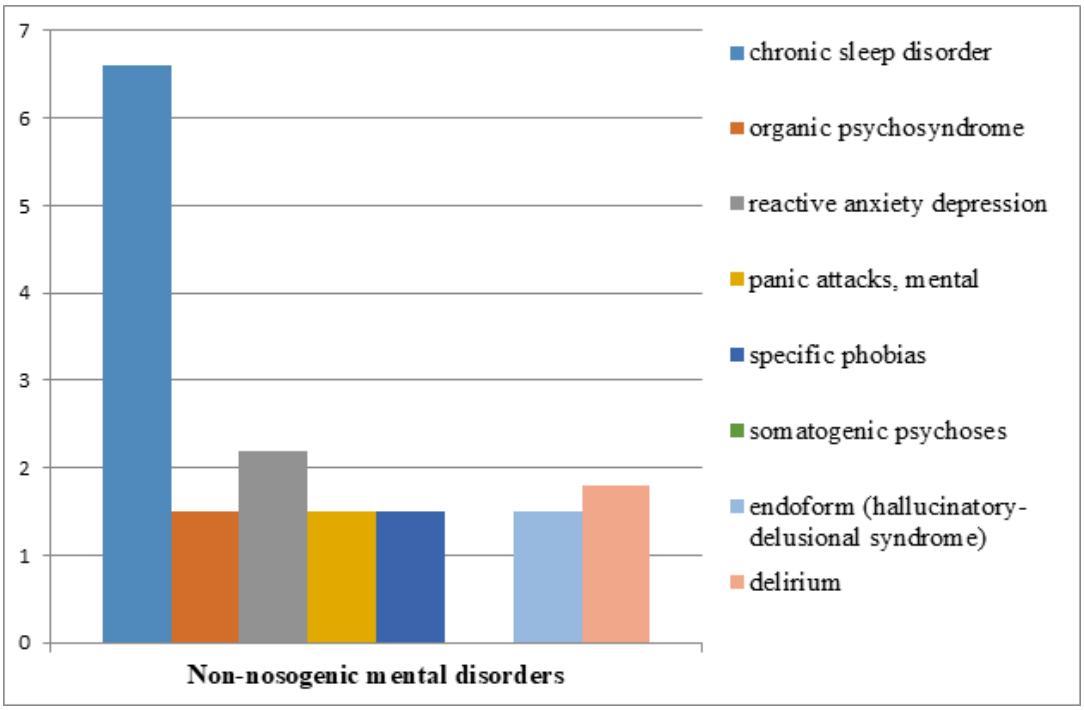
*** Of these, 30 patients had 2 or more higher educations.**

Among the individual nosologies and psychopathological syndromes identified in the studied patients, nosogenic reactions (54.8%), chronic sleep disorders (6.6%) and somatogenic psychoses (3.3%) predominate (Table 2). As already indicated, the prevalence of nosogenies significantly exceeds the figures presented in the literature, which can be explained by the difference in the diagnostic approach used in this work and in the works of other authors. At the same time, the prevalence of somatogenic psychoses corresponds to the average figures reflected in literary sources. However, no data on the prevalence of chronic sleep disorders were found in the available literature.

Table 2. Mental disorders in the studied patients with viral pneumonia caused by COVID-19.

(n=80)





The personality structure of the examined patients was studied. Personality disorders were detected in ¼ of the patients, among which personality anomalies of the schizoid circle,

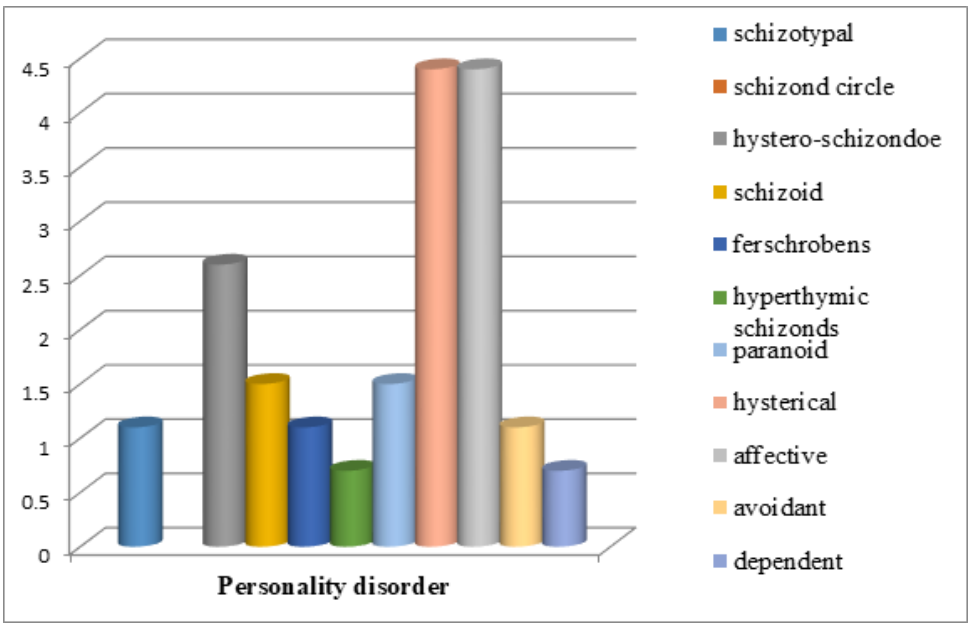
hysterical and affective personality disorder predominated. The same ratio was preserved in the personality structure of patients who did not reach the level of personality disorders (Table 3).

During the epidemiological survey, in addition to personality disorders, personality developments were recorded, and a conclusion was made about the existing somatopsychic accentuation (Table 4).

The clinical examination included an analysis of the mental state, subjective and objective anamnestic data, medical documentation (medical history, including archival, outpatient cards), specialist opinions on the hematological and neurological status, taking into account paraclinical data (studies of peripheral blood parameters, bone marrow, ultrasound, electrocardiography, computed tomography, radiography, electroencephalography, etc.).

The analysis of the somatic condition used the results of a clinical examination performed by the staff of the clinical departments of the State Clinical Hospital.

Table 3. Personality structure of the studied patients with viral pneumonia caused by COVID-19 (n=80)



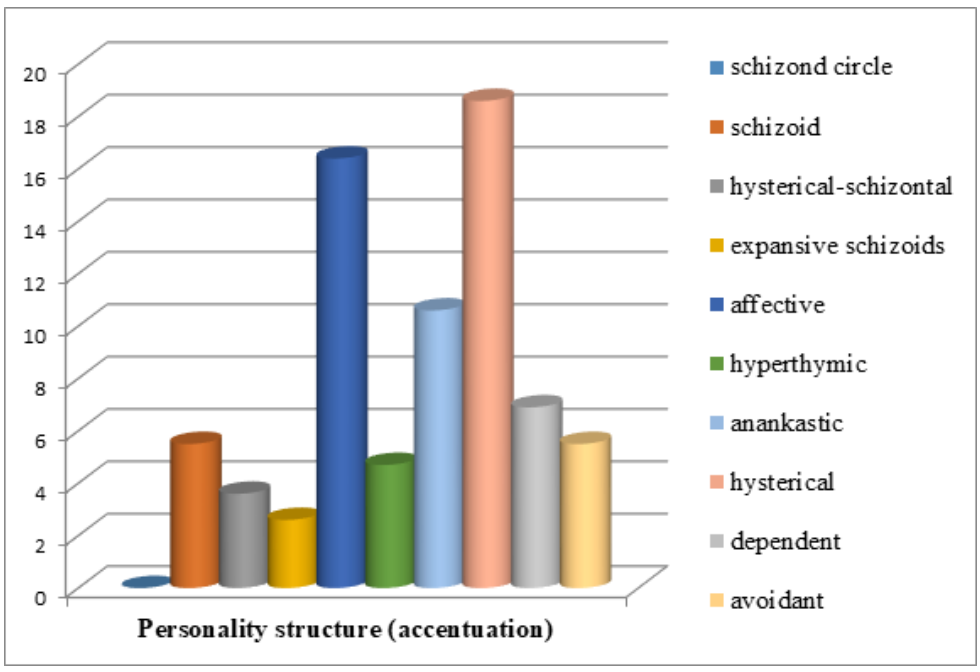


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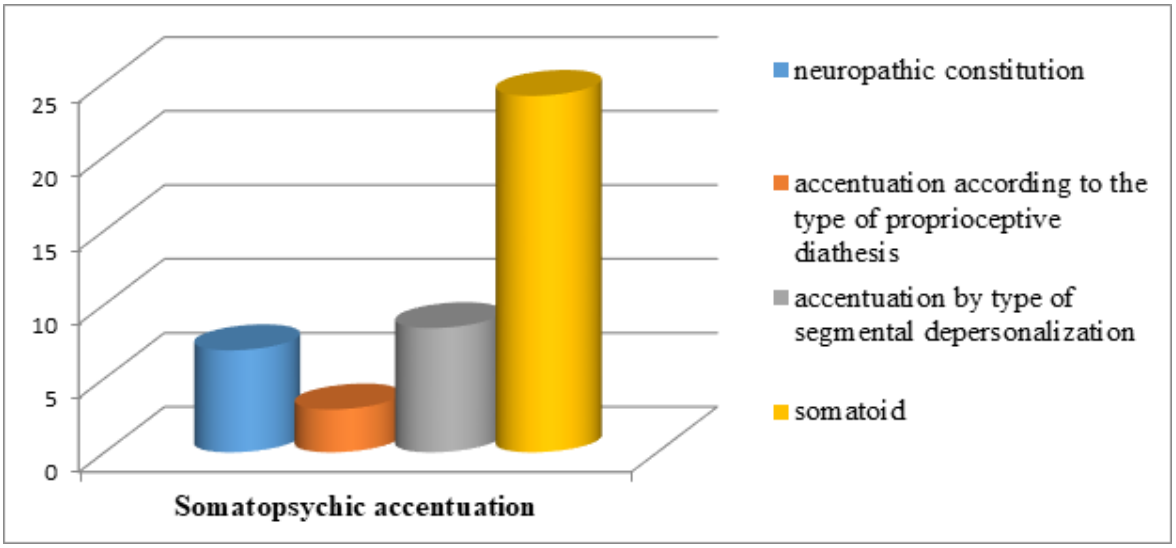
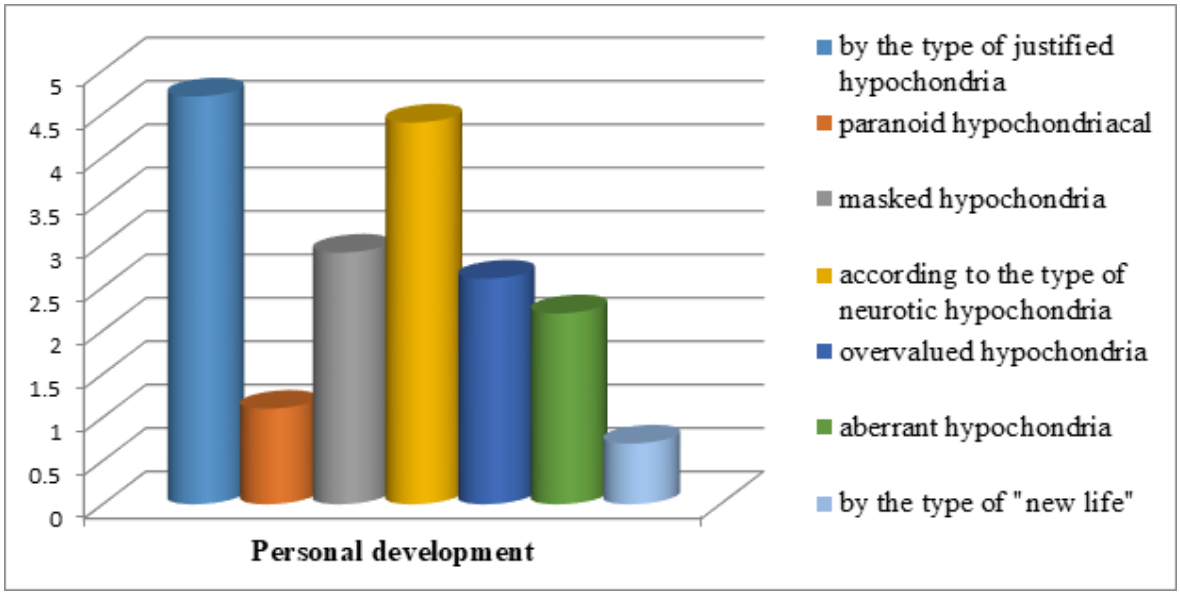
Table 4. Somatopsychic accentuation and personality development in the studied patients with viral pneumonia caused by COVID-19. (n=80)



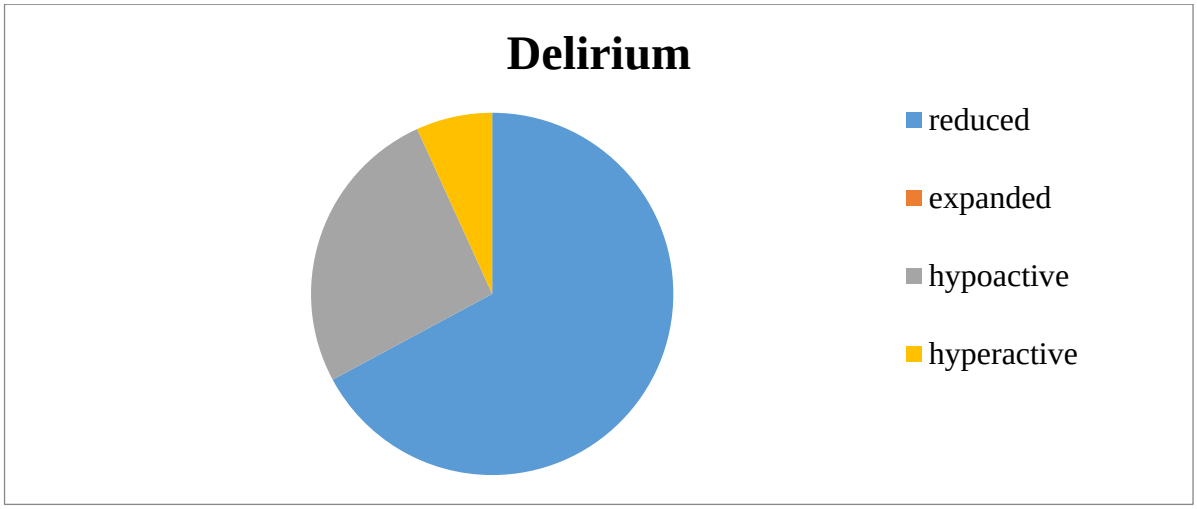


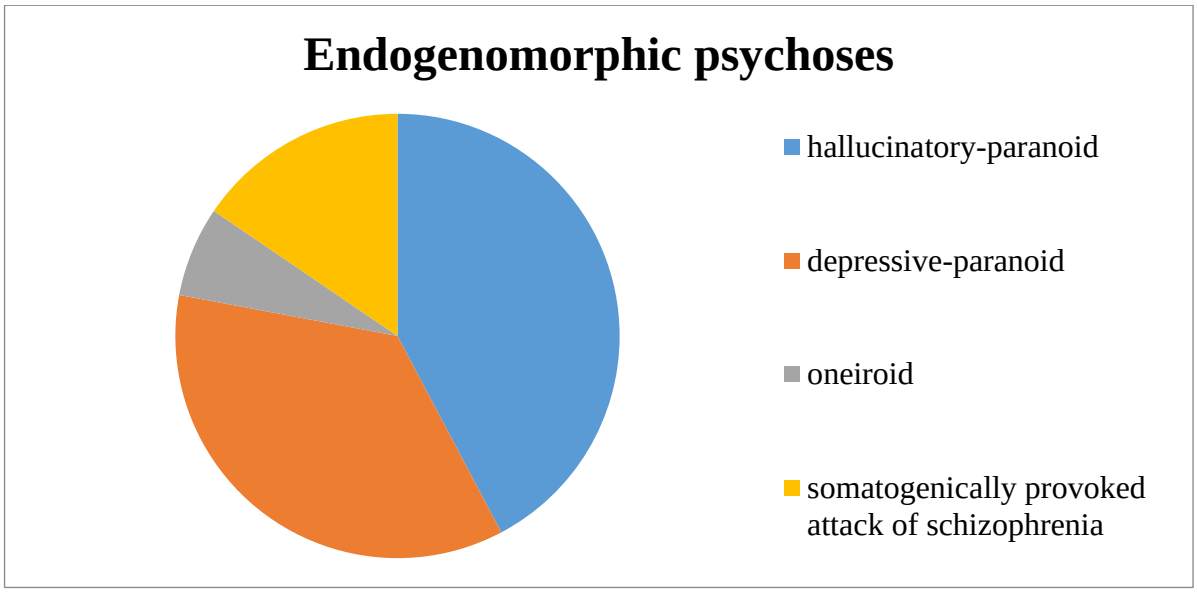
A clinical study (using somatic examination data) was conducted on 46 patients with somatogenic psychoses that manifested against the background of severe pneumonia (the majority (64.7%) were men, median age was 53 years (from 16 to 84 years). In addition, 52 patients were studied who developed nosogenic reactions against the background of pneumonia (a slight predominance of men (51.6%), average age 36.63±13.07 years (from 19 to 68 years).

Typological heterogeneity of mental disorders in patients with viral pneumonia caused by COVID-19 has been established.

Three types of somatogenic psychoses were identified: 1) delirium, 2) endogenomorphic psychoses (hallucinatory-delusional, depressive-delusional, oneiroid symptom complexes) and 3) somatogenically provoked exacerbations of schizophrenia (Table 5).

Table 5. Typology of somatogenic psychoses in patients with viral pneumonia caused by COVID-19.





Type 1, delirium (73 (61.9%) observations). In this group, the clinical picture was generally comparable to delirious states in other severe somatic diseases [Burlakov A.V., 2005] and included disturbances of consciousness, influxes of visual hallucinations, acute sensory (hallucinatory) delirium, and pronounced motor agitation. Phenomena of clouding of consciousness were represented by complete or partial disorientation in the surroundings. In a series of affective disorders, the feeling of anxiety, fear with symptoms of confusion prevailed. In some cases (5 (6.8%) observations), episodes of anxious-angry arousal with aggressive actions towards medical personnel were noted.

At the end of psychosis (psychopathological disorders were reduced as the somatic condition improved), signs of retrograde amnesia (complete loss of memories associated with the symptoms of delirium) were revealed.

For 5-7 days after the reduction of psychopathological symptoms, mood instability with a tendency to depression, asthenia with increased fatigue, rapid exhaustion with minimal physical or mental exertion, capriciousness and resentment persisted.

It should be emphasized that in the studied sample, delirious disorders were predominantly of a latent nature, with clouding of consciousness occurring with pronounced asthenic and apathetic disorders. This rudimentary form of delirious clouding of consciousness, in which psychomotor agitation is either absent or not expressed, was detected in the majority – 49 out of 73 patients (67.1%).

The clinical picture was dominated by irritable weakness, short-term episodes of increased excitability, followed by long periods of exhaustion. Affective lability with a predominance of hypothymia was revealed; at the same time, depression with increased tearfulness alternated with apathy or elements of dysphoria. In some cases, phenomena of asthenic mentism with a flow of figurative representations were noted. The attention function was sharply upset, and then disturbances of orientation in time and space manifested.

Full-blown delirium (with a predominance of perceptual deceptions and psychomotor agitation) was diagnosed in 24 of 73 (32.9%) patients. Within such delirious states, two variants were identified, designated in accordance with the terminology of modern researchers [Liptzin B., 1999; O'Keeffe S.T., 1999] as hypoactive (19 of 73 observations (79.2%) and hyperactive (5 of 73 observations (20.8%).

The hypoactive variant of advanced delirium was characterized by the addition of deceptions of perception (true - visual, auditory or tactile hallucinations) to the phenomena of confusion, often of an ordinary nature. Hallucinatory disorders were fragmentary in nature or (less often) had a more complex plot structure and intensified in the evening. Such disorders were often accompanied by psychomotor agitation, usually limited to the bed.

The hyperactive variant of full-blown delirium most often acquired a mumbling character, in which there was no reaction to external stimuli, and motor excitation was limited to stereotypically repeated movements with inarticulate, incoherent muttering. At the height of such reduced excitation, a symptom of picking (carphology) developed in the form of pulling the blanket or shaking off imaginary specks of dust, senseless grasping movements or movements of the fingers, smoothing or gathering into folds the sheet or linen.

In our study, the duration of delirium averaged 4.5?0.8 days. In 7 (29.2%) cases of advanced delirium, despite the therapy, patients developed an amentive disorder of consciousness with chaotic disordered agitation, which accompanied the development of septic shock and ended in death in 6 (25%) patients. In another 3 (12.5%) cases of advanced delirium, the development of non-alcoholic Korsakoff syndrome with massive polyneuropathy was observed.

Type 2, endogenomorphic psychoses (38 (32.2%) observations). Along with a longer course than with delirium (7–11 days) and comparability of clinical manifestations (changes in consciousness, deceptions of perception) in the first day, significant differences from the picture of delirium were gradually revealed in the picture of such psychoses.

Endogenomorphic psychoses in the studied sample were represented by the following forms: hallucinatory-paranoid and depressive-delusional psychoses, as well as states of oneiroid clouding of consciousness.

In hallucinatory-paranoid states (19 (50%) observations), from the very first days of psychosis, verbal illusions, manifested at the onset as acoasms (hissing, creaking) or elementary functional hallucinations (individual words or phrases addressed to the patient, arising against the background of real sounds of medical equipment or the speech of personnel), gradually became more complex. Verbal pseudohallucinations and phenomena of mental automatism (ideas of influence with the help of medical equipment) were formed. At the same time, delusional ideas of persecution corresponding to the content of deceptions of perception were manifested. The

plot of the delusion was limited to poorly systematized ideas of relationship. Patients attached special importance to any actions of medical personnel, "noticed" that doctors looked at each other in a special way in their presence or did not tell them something, probably to avoid communicating "fatal" information. The idea of "bias" of medical personnel was dominant, but the plot of the "conspiracy" was not developed.

In 16 observations (42.1%), the manifestation of depressive-delusional states was accompanied by pronounced hypothymia with a distinct anxious affect, reaching its maximum expression in the evening hours. In 8 of 16 (50%) patients, the development of deceptions of perception in the form of true hypnagogic visual hallucinations of an elementary nature was noted at night. In 6 out of 16 (37.5%) observations, depressive disorders acquired a vital character with a feeling of melancholy, helplessness, ideas of self-accusation and even suicidal thoughts. As the anxious and melancholy affect increased, paranoid disorders were added, represented by phenomena of persecutory delusions (ideas of reference, persecution). The latter were distinguished by a monothematic plot, without showing a tendency towards systematization and were limited to ideas of prejudice and condemnation from those around them (medical staff, patients) or ideas of persecution by judicial authorities for “past misdeeds”.

In most cases, the duration of hallucinatory-paranoid and depressive-delusional states was less than 2 weeks. In the process of reverse dynamics of psychosis, delusional ideas, hallucinations, and then depressive manifestations and asthenic disorders were subject to successive reduction.

The clinical features of endogenomorphic psychoses require differentiation from an attack of schizophrenia. The conditions classified in the present study within the framework of endogenomorphic psychoses exhibit a number of differential diagnostic differences from similar disorders characteristic of schizophrenia. These include the foreground phenomena of asthenia with tearfulness and exhaustion of affect, rather than the detachment and indifference inherent in patients with schizophrenia. Other distinctive features are the variability of behavior and affect that are not monotonous, and the somatogenic nature of the dominant asthenic disorders that are not displaced by hallucinatory-delusional or depressive-delusional symptoms. In addition, the psychopathological characteristics of delusional disorders, which do not tend to systematize, complicate, expand the plot, or become chronic, are different. The final diagnostic judgment is based on the absence of personality changes, emotional or cognitive deficits after the psychosis has ended.

In individual observations (3 (7.9%) patients (out of 118) against the background of a severe somatic condition requiring observation in the intensive care unit, disturbances of consciousness acquired signs characteristic of oneiroid [Tiganov A.S., 1999] with phenomena of dual orientation. Patients simultaneously acted as patients of the clinic and outside observers. The scene-like hallucinatory disorders that developed in this case were characterized (in contrast to the fantastic-illusory pictures characteristic of "classical" oneiroid psychoses) by their everyday content. The picture of psychosis was supplemented by signs of catatonia with episodes of stupor and mutism. Along with oneiroid-catatonic manifestations, fragmentary ideas of persecution were revealed.

Type 3 somatogenic psychoses - somatogenically provoked attacks within the framework of paroxysmal schizophrenia (7 observations (5.9%)). In 6 patients, the attacks occurred with hallucinatory-paranoid syndrome, and in 1 - with manic-delusional syndrome.

The psychopathological structure of psychosis was determined by a combination of process-related and somatogenic pathology. Along with the signs characteristic of somatogenic psychoses (clouding of consciousness with disorientation in place and time, psychomotor agitation, daily fluctuations with an increase in the evening and night time), already at the onset of psychosis, psychopathological disorders inherent in endogenous-processual disease were revealed. Subsequently, as the patient’s somatic state normalized with the reverse development of disturbances of consciousness and other somatogenic disorders, the manifestations of

psychosis did not decrease, but acquired the syndromic character of a psychotic attack within the framework of paroxysmal schizophrenia. In psychoses with leading hallucinatory-paranoid symptoms, the restoration of the somatic state was accompanied by the crystallization of delirium (influence on thoughts and actions by personnel or special services, including with the help of medical equipment), the replacement of frightening visual hallucinations with verbal pseudo-hallucinations. The manifestation of hallucinatory-delusional symptoms was accompanied by aggression with attempts at physical violence against the "persecutors" - medical workers and patients.

In cases of somatogenically provoked attacks of schizophrenia, endogenous psychosis acquired a protracted course; remission formed only after 2.5-3 months, even under conditions of adequate therapy.

It should be emphasized that the psychoses we classified as somatogenically provoked attacks of schizophrenia are comparable in their manifestations to psychotic attacks that were identified in the patients' anamnesis and required inpatient treatment in a psychiatric clinic in 3 observations. The duration of the endogenous process averaged 9.2±3.5 years.

The risk factors for the development of somatogenic psychoses in patients with pneumonia were studied. It was found that in all the studied cases, somatogenic psychoses were formed against the background of a severe course of pneumonia, accompanied by the development of multiple organ pathology (acute renal, hepatic, cardiovascular failure), massive intoxication, severe electrolyte disturbances (hypercalcemia, hyponatremia or hypernatremia), and suppression of hematopoiesis (agranulocytosis, thrombocytopenia, anemia).

As for the risk factors associated with premorbid characteristics of patients, such characteristics in patients with endogenomorphic psychoses are represented by personality disorders of the schizoid (17 patients) or paranoid (7 patients) circle. In 3 observations, personality anomalies were classified within the framework of schizotypal personality disorder (positive, negative, cognitive, affective disorders of the schizophrenic spectrum, without signs of the current process). In another 3 observations, patients met the criteria of sluggish psychopathic-like schizophrenia. Psychopathological personality disorders in three patients who developed oneiroid clouding of consciousness were classified within the framework of schizotypal personality disorder. Somatogenically provoked endogenous psychoses developed in patients suffering from paroxysmal schizophrenia (5 observations).

In turn, patients who have experienced delirium have a higher incidence of alcoholism in their anamnesis - 26.1% among patients with delirium versus less than 2% in other types of somatogenic psychoses.

CONCLUSIONS

1. Mental disorders in viral pneumonia caused by COVID-19 are characterized by a high frequency of occurrence, which in our material was 71.3%. This means that the risk of developing mental disorders in such patients is at least 0.7. The most frequently detected are nosogenic reactions (54.7% of the total number of patients with mental disorders), less frequently – chronic sleep disorder (6.6%), somatogenic psychoses (3.3%), reactive anxiety depression (2.2%), organic psychosyndrome (1.5%), panic attacks (1.5%) and specific phobias (1.5%).

2. Psychogenic (nosogenic - semantics of diagnosis, events associated with somatic pathology), somatogenic, iatrogenic and premorbid (mental, drug pathology, personality disorders) factors are involved in the formation of mental disorders in viral pneumonia caused by COVID-19.

3. Somatogenic psychoses in viral pneumonia caused by COVID-19 are clinically heterogeneous and are differentiated into three types: delirious clouding of consciousness (61.9%), endogenomorphic psychoses (32.2%) (of which hallucinatory-paranoid - 50%, depressive-

delusional - 42.1%, oneiroid - 7.9%) and somatogenically provoked attacks of schizophrenia (5.9%).

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