

Psychoemotional Disorders and Sleep Impairments in Patients with COVID-19

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Objectives. To study the prevalence of anxious-depressive disorders and sleep impairments in their structure among patients hospitalized with the new coronavirus infections (COVID-19) and to develop differential guidelines for their treatment in COVID-19 patients. **Materials and methods.** This report presents preliminary results from our own observations. We report here analysis of data from 119 patients (age 47–69 years, male and female) obtained at detailed interviews, including using telemedicine technologies, with evaluation on the following scales: the Hospital Anxiety and Depression Scale (HADS), the Multidimensional Fatigue Inventory (MFI-20) for subjective assessment of asthenia, and the Pittsburgh Sleep Quality Index (PSQI). **Results.** Results on the HADS indicated that clinically severe anxious-depressive symptomatology was seen in 33 of 119 patients (28%) hospitalized with diagnoses of COVID-19: of these, 11% of cases ($n = 13$) showed clinical signs of significant anxiety only, while five (4%) showed clinically significant depression and 13% displayed increases on both the anxiety and depression subscales ($n = 15$). Increases on the MFI-20 scale (>20 points) were seen in 87 patients (73%) and sleep impairments on the PSQI were recorded in 32 patients (27%). **Conclusions.** The results of this study showed that most patients with COVID-19 had not only depressive symptomatology, but also anxious and hypochondriac disorders, asthenic symptom complex, and sleep impairments with difficulty going to sleep and poor sleep quality. Differential guidelines were developed for the treatment of these states taking account of the side effects of the drugs prescribed, interactions between drugs, and the features of the patients' somatic condition. Drug selection must be based on the severity of the impairments found.

Keywords: COVID-19, anxious-depressive disorders, depression, asthenic syndrome, sleep impairment.

The coronavirus infection (COVID-19) pandemic creates a serious threat for physical health and life in humans. Like any large epidemic outbreak, it has adverse consequences for individual people and society in general, affecting virtually all aspects of life. One of the many negative consequences of the pandemic has been a “second epidemic” of mental disorders [1–3]. Data from foreign and Russian studies have shown that during the first wave of COVID-19, clinically complete anxious and depressive disorders have

been diagnosed in 20–40% of the population, while clinically significant symptoms of post-traumatic stress disorder and acute stress reactions are present in 20–35% of cases and sleep impairment occurs in almost 50% of the population [4].

The first year of the pandemic was marked by a significant increase in attending among the population for anxiety-phobia spectrum disorders and sleep impairment [5–8]. In relation to the group of anxiety-phobia disorders formed on the background of the pandemic, it must be noted that a previously unknown phenomenon – coronaphobia – is widely distributed in the population [9]. Coronaphobia is defined as an excessive fear of COVID-19 infection with severe hypochondriac phobias (fixation on somatic symptoms), avoidance of possible sources of infection, and significant impairments to socialization due to complete refusal to visit public

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places, fear of dying from or loss of relatives to COVID-19, and fear of decreased income and unemployment [10].

The development of coronaphobia is facilitated by a number of factors, both internal and psychosocial. In particular, there is an unprecedented potentially life-threatening situation of uncertain duration, a constant pumping of urgent information with repetition of negative factors, and an overload of contradictory information, all of which increase psychological pressure; there is the uncertain incubation period of the virus infection, the possibility of asymptomatic transmission, the lack of a uniform strategy or specificity of treatment, as well as unreliable reports of shortages of personal protective equipment and shortages of apparatus (ventilators), etc.; self-isolation and social distancing leading to social deprivation; wide-scale quarantining; degradation of the national economic situation; increases in unemployment, decreased income, etc. [10, 11].

Investigators take the view that coronaphobia is mostly not an isolated single symptom, but is associated with a whole series of psychopathological symptom complexes: adjustment disorder, post-traumatic stress disorder, generalized anxiety [12, 13], depression, and sleep impairments [14].

Thus, investigators are evaluating the role of psychiatrists who are the first to deal with coronaphobia and associated disorders [15]. Many publications have now addressed the challenges of anxiety and depressive disorders associated with COVID-19, emphasizing the importance of the problem.

The aims of the present work were to study the prevalence of anxious-depressive disorders and sleep impairments in their structure among patients hospitalized for COVID-19 and to develop differential guidelines for their treatment in patients with the new coronavirus infection.

Materials and Methods. We present the results of a questionnaire study of 119 patients receiving treatment for COVID-19. The questionnaire was presented as an anonymous electronic questionnaire with an online telemedicine consultation with patients hospitalized at the Clinical Hospital, Office of the President of the Russian Federation. The questionnaire consisted of the Hospital Anxiety and Depression Scale (HADS; subscales HADS-A and HADS-D), the Multidimensional Fatigue Inventory (MFI-20) for subjective assessment of asthenia, and the Pittsburgh Sleep Quality Index (PSQI).

The study included patients with diagnoses of COVID-19 (ICD-10 U07.1, U07.2) and Other viral pneumonia with CT 2/3 (ICD-10 J12.8). Patients with severe COVID-19 were excluded (CT 4, saturation <93%, respiratory rate >30 per min, stable elevation of body temperature to >39°C, presence of multiorgan failure), as were those with severe mental or organic pathology (schizophrenia, schizotypic and delusional disorders (ICD-10 F20–F29), organic mental disorders (ICD-10 F00–F09), mental retardation (ICD-10 F70–F79)) preventing adequate interviewing.

Anxiety and depression levels were evaluated on the HADS. The test data indicated that 72% of patients ($n = 86$)

had no clinically significant anxious-depressive disorders. Elevated scores on the anxiety scale (>8 points) were recorded in 13 patients (11%), clinically significant depression (>8 points) in five (4%), and elevated scores on the HADS-A anxiety and HADS-D depression subscales were obtained in 15 patients (13%). Increases on the MFI-20 (>20 points) were found in 87 cases (73%), sleep disorders on the PSQI were found in 32 patients (27%).

Mean age was 58.7 ± 11.1 years; 71 patients (60%) were married, 8% ($n = 10$) were single, 13% ($n = 16$) were divorced, and 18% ($n = 22$) were widowed.

Statistical analysis was run in SPSS Statistics 20. Results were processed using descriptive and comparative statistics. Descriptive methods included computation of absolute values (n) and proportions (%). Correlational relationships between values were assessed using the Spearman rank correlation coefficient. Differences were regarded as statistically significant at $p < 0.05$.

Results and Discussion. Telemedical interviews showed that patients with elevated levels of anxiety on the HADS-A subscale ($n = 13$, 11%) displayed persistent anxiety-hypochondriasis disorders with intrusive thoughts and images relating to COVID-19: pathological susceptibility to bodily sensations, increased introspection, careful recording to the slightest signs of bodily distress, excessive concern regarding the side effects of medications, fear of dying, and sleep disorders. Sleep disturbances were seen in 8 patients (7%) and consisted mainly of pre-sleep disturbances (prolongation of time to sleep onset to >30 min), which were persistent and significant, i.e., were present daily from admission to hospital. In the lying position, patients felt the need to change body position frequently, complained of incessant anxious thoughts associated with the pandemic-related situation of a threat to their own health and the health of loved ones. Complaints of marked asthenia (increased physical fatigue, difficulty concentrating, rapid onset of fatigue in mental work) were made by five patients.

Patients with elevated levels of depression on the HADS-D subscale ($n = 5$, 4%) had low background mood with oppression, melancholy (a vague, diffuse feeling, mostly in the form of intolerable sensations of pressure in the chest or epigastric area), despondency, and hopelessness. The structure of depression included an asthenic symptom complex in four cases (3%), including physical and mental weakness, rapid tiring, which sometimes started after even minor effort, emotional instability (lability) with easily provoked faintheartedness, irritation, bitterness, despair, oppression, restlessness, and panic reactions. In the framework of asthenodepressive syndrome, presleep and intrasleep disorders were noted: patients complained of difficulty going to sleep (>30 min) and interrupted sleep, onset of which stopped corresponding to time of day, an onerous and dreary state in the early morning hours, a lack of the feeling of sleep, with formation of pathological fear before the night began, and sleeplessness.

On a background of low mood, patients with clinically significant anxiety and depression ($n = 15$, 13%) showed symptoms dominated by COVID-19-related anxiety. Eight patients (7%) reported sleep impairments, consisting mainly of presleep disorders. Assessment of asthenic impairments in 10 patients showed signs of asthenization apparent mostly as increased fatigue and rapid tiring on intellectual loading.

Patients without anxiety or depression ($n = 86$, 72%) mostly formed an anosognostic or harmonic type of relationship to illness: they were committed to treatment and displayed no significant anxiety or restlessness in relation to possible poor prognoses of the course of COVID-19. Questionnaire results revealed elevated asthenia (>28 points) in 54 patients (45%) of this group, suggesting that it was of somatogenic nature, i.e., related to signs of the viral illness. Sleep impairment in this group was seen in only 12 cases (10%), with onset during the hospital period, consisted mainly of presleep disorders, and was not persistent.

Correlations were found between HADS-A and asthenia scores ($r = 0.461$, $p = 0.001$) and between HADS-D and asthenia scores ($r = 0.395$, $p = 0.006$). Assessments on the PSQI showed a positive correlation with measures of anxiety and depression: between HADS-A and PSQI ($r = 0.402$, $p = 0.005$) and between HADS-D and PSQI ($r = 0.353$, $p = 0.015$). Assessment on the PSQI showed positive correlations of measures on the anxiety and depression scales: between HADS-A and PSQI ($r = 0.402$, $p = 0.005$) and between HADS-D and PSQI ($r = 0.353$, $p = 0.015$).

Data obtained in this study lead to the conclusion that anxious-depressive disorders, sleep impairments, and asthenia are commonly diagnosed disorders in patients hospitalized for COVID-19. Detection of persistent sleep disorders in patients with clinical signs of elevated anxiety and depression scores suggests that sleep impairment is a component of anxious-depressive symptomatology while in the group of patients without anxiety or depression, insomnia is related to adjustment.

Despite the fact that these are preliminary findings, the data are consistent with results published in other countries, which have shown significant increases in anxiety disorders and sleep impairments in the populations of developed countries in the pandemic (Tables 1 and 2).

Selection of treatment is no less a problem than the differential diagnosis of neuropsychiatric disorders. It should be noted that the structure of neurological and mental disorders in COVID-19 remains to be studied systematically. Treatment in this situation is syndromal in nature and in some cases is directed to curing particular symptoms. The arsenal includes biological therapeutic methods, psychotherapeutic methods, and pharmacotherapy. The range of drugs used is wide and includes anxiolytics, antidepressants, antipsychotics, neurometabolic drugs, and normothymics.

The treatment of the patients in the present study showed that elimination of mental disorders in COVID-19 patients must be built on common approaches which can be

used for treating the mental disorders encountered in general medical practice [28, 29]: monotherapy with later-generation drugs should be used when possible, with dose titration; adequate treatment duration should be used with assessment of patients' treatment compliance throughout the treatment period; monitoring of therapeutic interactions between psychopharmacotherapy and somatotropic therapy, as well as side effects [30].

In short-term (up to a few days) anxious-phobic disorders occurring with sleep impairment, prescription of non-benzodiazepine anxiolytics is desirable. These have the advantages of rapid onset of anxiolytic effects and influence the somatic signs of anxiety, such that curing these is a significant factor in normalizing sleep. Formulations containing tetramethyltetraazabicyclooctanedione (for example, Adaptol) have the benefits of not producing mental or physical habituation or withdrawal syndrome, good safety profiles, and low risks of drug interactions, which is particularly important in polypharmacy. The mechanism of action of Adaptol is multimodal – it influences the main transmitter systems, improving their balance.

Benzodiazepine tranquilizers produce a rapid anti-anxiety action, have significant sedative and myorelaxing actions, and can be used when nonbenzodiazepine tranquilizers have inadequate effects and in severe anxiety. However, the risk of a paradoxical reaction, with exacerbation of anxiety (in about 10% of patients) and behavioral toxicity (drowsiness, cognitive impairments, decreased reaction speed) must be considered, as must the development of tolerance and dependence when used for long periods; high doses can produce marked myorelaxation, which can reach the extent of affecting the respiratory muscles (not desirable in pneumonia).

The psychopharmacotherapy of persistent anxious and anxious-depressive disorders with sleep impairments includes prescription of antidepressants, particularly selective serotonin reuptake inhibitors (SSRI), as well as antidepressants with multimodal actions (vortioxetine), melatonin receptor agonists/serotonin receptor antagonists (agomelatine), sometimes in combination with nonbenzodiazepine anxiolytics. Prescription and selection of antidepressants is needed only in relation to absolute indications; monotherapy should be used where possible; the smallest effective doses should be used; ECG and blood clotting tests should be run for monitoring.

Treatment compliance is required throughout the treatment period as the presence of anxiety and depression affects patients' compliance with treatment regimes [31]. Increasing compliance requires time to be spent with the patient, discussing the causes of illness and possible side effects, focusing attention on delayed treatment effects; long treatment periods are required.

Conclusions. The current pandemic has not only changed the world in social terms, but has also influenced the structure of diseases in the population. We are now seeing increased psychoneurological disorders of different severities. The re-

TABLE 1. Prevalence of Anxiety Disorders Before and After the Pandemic in Different Countries

Country	Anxiety disorder	Prevalence before pandemic	Prevalence during pandemic	Reference
Anxiety in the population				
Italy	Generalized anxiety	5%	31.2%	Casagrande et al. (2010) [16]
	Intermediate level of anxiety/		81.3%/	Mazza et al. (2020) [17]
	High level of anxiety/		7.2%/	
	Very high level of anxiety		11.5%	
	Undifferentiated anxiety		36%	Romito et al. (2020) [18]
China	Generalized anxiety	0.20%	35.1%	Huang and Zho (2020) [19]
	Undifferentiated anxiety	5%	37.4%/ 31.3%	Zheng et al. (2020) [20]
		–	49.5%	Li et al. (2020) [21]
Germany	Undifferentiated anxiety	15.3%	44.9%	Bäuerle et al. (2020) [22]
	Generalized anxiety	2.2%	7.2%	Hetkamp et al. (2020) [23]
Anxiety in patients				
Italy	Undifferentiated anxiety	–	42%	Gennaro Mazza et al. (2020) [24]
China	Undifferentiated anxiety	5%	22.2%/	Cai et al. (2020) [25]
			19.4%	Chen et al. (2020) [26]

TABLE 2. Prevalence of Sleep Impairments Before and After the Pandemic in China, Germany, and Italy

Country	Incidence of dyssomnic disorders in the population before pandemic (references)	Dyssomnic disorders during the pandemic		
		contingent	prevalence	reference
China	15% (W. Zheng, 2018)	Population	18.2%	Huang et al. (2020) [19]
		Working population	30.9%	Li et al. (2020) [21]
		Medical workers	30.4–38.4%	Li et al. (2020); Zhang et al. (2020) [21, 27]
Germany	5.7% (R. Schlack, 2013)	Population	13.5%	Hetkamp et al. (2020) [23]
Italy	27.6% (M. Ohayon, 2002)	Population	51.2%	Casagrande et al. (2010) [16]

sults of the present open study provide evidence that this infectious disease has significant effects on the formation of anxious-depressive symptomatology and sleep impairments.

Future studies will address a larger cohort with repeat investigation of the group of COVID-19 patients filling the questionnaire 3–6 months after illness with the aims of clarifying the prevalence and structure of psychoneurological impairments and developing guidelines for preventing anxious-depressive symptoms and sleep impairments among COVID-19 patients.

The authors declare no conflicts of interests.

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