BALNEO and PRM Research Journal

Vol 13, No. 1, March 2022

Asociatia Romana de Balneologie

I.S.M.H.

SOCIETATEA ROMANA
DE MEDICINA
FIZICA
DE RECUPERARE
SI BALNEOCLIMATOLOGIE

BALNEO RESEARCH

Balneo and PRM Research Journal

English Edition

e ISSN 2734 - 8458 p ISSN 2734 - 844X

ROMANIAN ASSOCIATION OF BALNEOLOGY

Website http://bioclima.ro/Journal.htm

E-mail: office@bioclima.ro

Balneo and PRM Research Journal is part of the international data bases (BDI) as follow:
EBSCOhost, CrossRef, DOAJ, Electronic Journals Library (GIGA), USA National Library of Medicine - NLM, Emerging Sources Citation Index — ESCI (Thomson Reuters)

Publisher: Romanian Association of Balneology (Bucharest)

Asociatia Romana de Balneologie / Romanian Association of Balneology

Editura Balneara

Balneo and PRM Reserch Journal

Table of Contents:

BALNEO RESEARCH Balneo and PRM Research Journal
English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Rehabilitation of post-COVID patients with chronic fatigue and cognitive disorders syndromes

Liudmila Babliuk [1], Svitlana Fediaeva [2], Iryna Babova [3], Vita Mesoedova [1], Sergii Tamazlykar [4]

1. Ivano-Frankivsk national medical university, Ivano-Frankivsk, Ukraine
2. Danylo Halytsky Lviv National Medical University, Lviv, Ukraine
3. South Ukrainian National Pedagogical University named after K.D.Ushynsky, Odessa, Ukraine
4. Central City Clinical Hospital of Ivano-Frankivsk City Council, Ivano-Frankivsk, Ukraine

Correspondence: Liudmila Babliuk E-mail: ohdyrya@ukr.net

ABSTRACT: Introduction. Almost all patients, who have experienced acute manifestations of COVID-19, regardless of the severity of the acute phase of the disease, are only at the beginning of a long way to recovery. According to experts, SARS-CoV-2 infection should affect almost 80% of the world's population, so all these patients to a greater or lesser extent will need a rehabilitation of certain manifestations of postcovid syndrome.
Purpose: to study the effectiveness of rehabilitation program and the dynamics of cognitive impairment and manifestations of chronic fatigue syndrome in patients after coronavirus disease.
Methods: The study design included 60 patients after SARS-Cov-2 infection. Among the examined patients there were 26 (43,3%) women and 34 (56,7%) men. An average age of the patients was 43,9±1,08 years. Patients were referred to the Department of Physical Rehabilitation after coronavirus disease with chronic fatigue and cognitive disorders syndromes. Accordingly, all patients, who participated in the study, were divided into two groups: group I - 28 patients with a general condition of moderate severity at the hospital stage and 32 patients - group II, with severe course of the disease and oxygen demand at the hospital stage. Depending on the duration of rehabilitation, two observation periods were used - on the 7th and 14th day of rehabilitation program.
Results: It has been proven, that patients, who didn't need oxygen, were complaining about anosmia, cephalgia, cognitive impairment, increased anxiety and fatigue. Dysgeusia, dyssomnia, and depression were more common in patients, requiring oxygen therapy at the hospital stage. Rehabilitation program eliminated cognitive dysfunction, depression, cephalgia, drowsiness and dyssomnia on the 7th day in patients, who did not require oxygen therapy (p>0,05), and in patients, who needed oxygen therapy - on the 14th day of the rehabilitation program (p>0,05). However, 2 (6,3%) and 3 (9,4%) patients, who needed oxygen therapy, even after 14 days of rehabilitation had manifestations of minor recurrent headache and drowsiness.
Conclusion: Thus, patients after coronavirus disease, who needed oxygen therapy at the hospital stage, need long-term rehabilitation program.

Keywords: *postcovid syndrome, anxiety, depression, drowsiness, rehabilitation*

Citation: Babliuk et al. Rehabilitation of post-COVID patients with chronic fatigue and cognitive disorders syndromes, *Balneo and PRM Research Journal* **2022**, *13*(1): 497.

Academic Editor(s):
Constantin Munteanu

Reviewers:
Gabriela Dogaru
Mariana Rotariu

Received: date
Accepted: date
Published: 20.03.2022

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1. INTRODUCTION

The pandemic, caused by COVID-19, has changed not only the lifestyle of each of us, but also the stereotype of our thinking. Stepping confidently for more than a year, SARS-Cov-2 infection has absorbed the world's medicine with its scale and created new conditions for the development of virology, immunology and medicine in general.
The COVID-19 pandemic, caused by the new coronavirus SARS-CoV-2, or 2019-nCoV, is an infectious disease, first detected in humans in Wuhan, Central China, in December 2019. The disease began as an outbreak, that developed in a pandemic. SARS-CoV-2 coronavirus, the circulation of which in the human population was unknown until December

2019, has become a cause of the disease (1). Due to data of Johns Hopkins University of Medicine Coronavirus Resource Center on February 22, 2022 there were registered 427 005 566 total cases of this disease; the largest epicenters of the disease remain USA, with 78 583 084 cases, India with 42 851 929 cases, and Brazil with 28 258 458 cases (2). The SARS-Cov-2 epidemic monitoring system records new cases of disease, mortality and recovery from SARS-Cov-2 infection on a daily basis. According to the statistical data of Public Health Center of Ministry of Health of Ukraine 4 758 773 cases of this disease were diagnosed in Ukraine, which is approximately 10 % of the total population, with 104932 deaths and 3 985 601 people recovered (on February 22, 2022) (3).

On the early stages of pandemic development the efforts of world medicine were aimed at the treatment of acute life-threatening consequences of COVID 19. But more and more often people after SARS-Cov-2 infection seek medical help with certain symptoms of postcovid syndrome and need immediate rehabilitation (4).

SARS-Cov2 virus can cause pathological changes in the central and peripheral nervous system due to both direct infection of neurons and indirectly, through immune and inflammatory mechanisms.

Disorders of smell and taste in COVID-19 occur due to infection of epithelial cells in mucous membranes. Angiotensin-converting enzyme 2 (ACE2) is present in significant amounts on the sensory cells of the nasopharynx and oral cavity. By binding to ACE2, the SARS-Cov2 virus can inhibit sensory cell function by penetrating the cribriform plate and infecting olfactory bulb neurons. Similarly, the retrograde spread of the virus from receptor cells on the tongue to neurons of the solitary nucleus of the medulla oblongata may explain the loss of sense of taste in individuals with SARS-Cov2 infection (5). However, data from some studies have shown, that taste dysfunction is more common in patients with COVID-19, than olfactory disturbances, and that 10,2-22,5 % of COVID-19 cases are accompanied by loss of taste perception without olfactory disturbance (6,7).

There is a high probability, that cytokine storm, large and small strokes, damage to the blood-encephalic barrier, high level of inflammation in the brain substance, cause long-term neurocognitive disorders (8). Neurons contain a large number of ACE-2, so SARS-Cov2 is able to penetrate them and disrupt important intracellular processes, such as energy production in mitochondria and conformation of SARS-Cov2 proteins (9). Impaired conformation and aggregation of proteins in patients, who survived and recovered from acute infection, could theoretically lead to brain degeneration in the following decades (10). Health systems around the world in the coming years may be loaded by the influx of people with depression, post-traumatic stress disorder, anxiety, insomnia (11), psychosis, cognitive impairment (1).

According to the WHO, the time from onset to clinical recovery in mild cases of coronavirus disease is about 2 weeks, while in severe or critical cases – 3-6 weeks (12).

Currently there is no clear agreed definition of postcoronavirus syndrome. The clinical guidelines of the National Institutes of Health and the Improvement of Health Care of Great Britain (NICE) "Treatment of long-term consequences of COVID-19" (NG188) use the following clinical definitions for primary disease and long-term coronavirus disease 2019, depending on when they occurred and during which time they persist: acute coronavirus disease 2019-signs and symptoms of the disease persist for up to 4 weeks; long-term coronavirus disease 2019 with symptoms – signs and manifestations persist for 4-12 weeks; post-COVID-syndrome – signs and manifestations develop during or after coronavirus disease 2019, persist for more than 12 weeks and are not explained by alternative diagnoses (4).

Taking into account the obvious need for the guidance on the rehabilitation of those, who have undergone COVID-19, a team of experts from the rehabilitation center of Ministry of Defense in Stanford Hall (United Kingdom) developed a document – The "Stanford Hall" Consensus (13), which contains the following general recommendations after

COVID: the rehabilitation treatment plan should be individualized, according to the patient's needs, taking into account the concomitant diseases; for patients with COVID-19 rehabilitation should be aimed at relieving symptoms (shortness of breath), improving the psychological state (14), physical shape and quality of life; patients should be periodically examined during rehabilitation; patients should receive information about their condition and recovery strategies after COVID-19 (15, 16).

Purpose: to study the effectiveness of rehabilitation program and the dynamics of cognitive impairment and manifestations of chronic fatigue syndrome in patients after coronavirus disease.

Methods. The study involved 60 patients who had SARS-Cov-2 infection approximately 12 weeks ago which was confirmed by polymerase chain reaction of nasopharyngeal swab and enzyme-linked immunosorbent method. Among the examined patients there were 26 (43,3%) women and 34 (56,7%) men. An average age of patients was 43,9 ± 1,08 years. Patients were referred to the physical rehabilitation department of Central City Clinical Hospital of Ivano-Frankivsk City Council under the direction of a family doctor or physician, in the presence of symptoms of postcovid syndrome. Symptoms of neurological-cognitive nature and chronic fatigue syndrome were frequent complaints of such patients. By retrospective analysis of medical records of inpatients and case history, it was found, that all patients were hospitalized in specialized departments. However, 32 (53,3%) patients in the inpatient stage of treatment required oxygen therapy and had a severe course of disease, which corresponded to class 3, according to the systemic classification of patients of the American Association of Anesthesiologists (ASA), and 28 (46,7%) patients with moderate condition, class 2 according to ASA, did not require oxygen therapy.

All patients, who participated in the study and were included in the rehabilitation program, were divided according to the severity of the condition and the need for oxygen therapy in the inpatient phase of treatment into two groups: group I – 28 patients with condition of moderate severity and 32 patients – II group with severe course of disease. Depending on the frequency of rehabilitation measures, two observation periods were used with evaluation of chronic fatigue syndrome and cognitive impairment: after the use of 7- and 14-week rehabilitation programs. As a control group served 12 healthy persons, 7 women (58.3%) and 5 men (41.7%) of 44,2 ± 0,98 years old. The evaluation criteria were a reduction in the manifestations of chronic fatigue syndrome, or complete leveling of certain symptoms. The clinical trial was conducted in accordance with the principles and norms of the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with human participation as the object of study", participants were giving a written informed consent to participate in the study. The trial was approved by the bioethics committee of the Ivano-Frankivsk national medical university.

The rehabilitation program included the following measures. The first week of the rehabilitation program included massage of the neck area, galvanization with the application of the 1st electrode of the shawl collar type on the neck area, and the 2nd on the lumbar area, connecting to the anode and cathode of the device. The first procedure was performed at the amperage of 6 mA, lasting 6 minutes. Then, after two procedures, the amperage was increased by 2 mA and the duration by 2 min, 5 procedures per course of treatment, every other day. Galvanization was carried out using the device galvanizer “Potok-1”. We also used low-frequency magnetic therapy of 25-30 MT for up to 20 min, 5 procedures per course, every other day (“DIMAP” device). On the second week of rehabilitation the massage procedures of the neck area proceed, amplipulse in the projections of the cervical sympathetic ganglia, paravertebral and interscapular area with an average frequency of modulation (30-50 Hz), 5 procedures per course, every other day (“Amplipulse-5” device); darsonval of the scalp region of the head, capacity of 4-6 divisions, lasting 10 minutes, 5 procedures per course, every other day (“ISKRA-1” device)

were prescribed. Throughout the rehabilitation program, electrosleep procedure was used, according to the ocular-occipital technique, using a pulsed current of rectangular shape with a frequency of 15-20 Hz, a pulse duration of 0,2-2 ms, a current of up to 10 mA, the duration of the procedure was 40-60 min, 5 procedures per course, every 3rd day (device "Electroson-4T").

For the evaluation of clinical effectiveness of the rehabilitation program, testing of patients before rehabilitation and on the 7th and 14th days of rehabilitation was used. To evaluate cognitive functions, a modified online Stroop Test was used (17); to determine the signs of depression – depression scale of Beck (Beck Depression Inventory) (18), to determine anxiety – Spielberger-Khanin test (STAI) (19); to detect the severity of headache – a modified facial pain scale, The Faces Pain Scale-Revised (FPS-R) (20); to determine the signs of dyssomnia and drowsiness – sleepiness scale of Epworth (Epworth Sleepiness Scale) (21, 22) and the Pittsburgh Sleep Quality Questionnaire (PSQI) (23, 24, 25).

Statistical analysis was performed depending on the distribution of the statistical sample using Student's parametric criteria and Fisher's exact criterion. To represent the obtained data, we used the method of descriptive statistics (mean, standard deviation, minimum and maximum value, scope, number of valid cases for quantitative changes); number, fraction and distribution for qualitative parameters. The results were considered significant at $p < 0,05$.

Results and discussion. Patients sought rehabilitation care with the following manifestations of postcovid syndrome. Anosmia persisted in 6 (10,0%) patients, dysgeusia - in 18 patients (30.0%), cephalgia - in 58 (96,7%), impaired concentration of attention and memory were observed (mild cognitive impairment) - in 59 people (93,7%) , dyssomnia - in 48 (80,0%), increased anxiety - in 59 (98,3%), depression - in 46 (76,7%), drowsiness - 57 (95,0%), rapid fatigue was observed in all patients (100,0%).

Analyzing the manifestations of postcovid syndrome, in patients of both study groups (table 1), according to the distribution of Fisher's exact criterion, it is seen, that symptoms, such as anosmia, cephalgia, impaired concentration and memory, increased anxiety, rapid fatigue, were observed for a long time in patients of both groups to the same extent, dysgeusia (ageusia), dyssomnia, drowsiness, depression - more often observed in patients of group II.

In order to detect cognitive impairment, a modified online Stroop test was used in the examined patients. Based on testing, it was found, that patients, who did not require oxygen therapy during inpatient treatment of SARS-Cov-2 infection, answered questions for an average of 6,18±0,39 s, which was 1,3 times faster, than in patients, who required oxygen therapy during inpatient treatment – 7,78±072 s (table 2). In addition, patients of group I needed 46,8% more of the average time to respond to the test, and patients of group II – 84,8% more, compared to the group of healthy individuals ($p < 0,001$).

However, after the application of the rehabilitation program on the 7th day in patients of group I, the average response time was 4,54±0,16 s, which almost did not differ from the same indicator in healthy individuals ($p > 0,05$) and the average time of passing the test decreased by 36,1%, in comparison to the indicator before rehabilitation ($p < 0,001$). In patients of group II on the 7th day of rehabilitation, the dynamics was not significant, so the average response time was 6,16±0,36 s and decreased by 26,3% ($p < 0,05$), which was significantly higher than in healthy individuals ($p < 0,001$).

On the 14th day of rehabilitation program the average response time in patients of group I did not decrease significantly compared to the previous observation period and was 4,11±0,08 s ($p < 0,05$), but decreased by 50,4% compared to the same indicator before treatment. Accordingly, patients of group I in the second stage of observation required the same time for response, as healthy individuals ($p > 0,05$). In patients of group II, after a 14-day course of rehabilitation measures, the average response time decreased to

4,15±0,08 s, which was 88,3% less, than before rehabilitation and 48,4% compared to the previous observation period (7 day), p <0,001. Patients of II group at the end of the rehabilitation program spent the same average time for responding to the test (4,15±0,08 s) as healthy individuals (p>0,05). The total test time in patients of group I was 1,2 times shorter compared to patients of group II. Patients of group I were spending 14,5% more time on the test compared to healthy individuals, and group II patients – by 25,3% (p<0,001). On the 7th day of rehabilitation program the total test time decreased to 45,75±0,55 s in patients of group I, which was 13,02% less, than before treatment (p<0,01) and was almost the same as in healthy individuals (p>0,05). In patients of group II the total test time decreased to 51,47±1,91 s compared to the beginning of rehabilitation (p<0,05), and by 14,08% compared to healthy people (p<0,001). Continuation of rehabilitation program helped to reduce the total test time to 44,25±0,25 s in patients of group I, which did not differ significantly from the previous observation period by 3,4% (p<0,05) and healthy individuals (p>005). However, significant dynamics of this indicator was observed in patients of group II on the 14th day of rehabilitation program, which was manifested by a decrease in the total test time to 45,03±0,55 s, which was 31,5% lower compared to the beginning of rehabilitation (p<0,001) and by 14,3% in comparison with the previous period of rehabilitation program (p<0,01). In patients of group II on the 14th day of treatment the total test time was almost the same as in healthy individuals (p> 0,05).

The dynamics was similar with the following test parameters - the total number of correct answers and the percentage of correct answers. Thus, in patients of group I, these two indicators were 1,2 times higher than in patients of group II. Group I patients were answering 36,9% less questions before rehabilitation, and the percentage of their answers was 36,5% lower in relation to healthy individuals, compared to group II patients - by 47,6% and 44,6% (p<0,001). On the 7th day of rehabilitation program, the number of correct answers in patients of group I increased to 9,29±0,21, and the percentage - to 92,5±2,12, which was 32,7% and 30,0% more, than before rehabilitation (p<0,001), and practically did not differ from healthy individuals (p>0,05). In patients of group II after 7 days of the rehabilitation program, the number of correct answers increased to 6,69±0,53, and the percentage - to 69,38±5,25, which was 22,4% and 21,6% more, than before rehabilitation (p<0,05), but differed significantly from healthy individuals (p<0,001). On the 14th day of rehabilitation in patients of group I the number of correct answers increased to 9,71±0,17, and the percentage - to 97,14±1,74, which was 35,6% and 34,64% higher, than before rehabilitation (p<0,001) and by 4,3% and 4,64% compared to the previous period (p<0,05). In group II patients, this difference was 45,7% and 41,07%, respectively, in comparison with rehabilitation (p<0,001) and 29,9% and 26,07% compared to the previous observation period (p<0,001).

In both groups at the end of the rehabilitation program, the total number of correct answers and the percentage of correct answers were the same as in healthy individuals (p>0,05).

The following scales were used and analyzed to evaluate chronic fatigue syndrome. According to the Beck depression scale, 15 (53,6%) patients of group I were diagnosed with mild depression, and 5 (17,9%) - with moderate depression. However, in patients of group II, the distribution on the Beck depression scale was as follows: mild depression was diagnosed in 4 (12,5%) patients, moderate - in 18 (56,3%), severe - in 4 (12,5%) patients. Evaluating the data of the Beck depression scale, it is seen, that patients of group I, taking the questionnaire, scored 1,5 times less points, than patients of group II (table 3).

Prior to rehabilitation program, patients of group I scored 42,3% more points than healthy individuals, and patients of group II - by 62,2%, respectively (p<0,001). On the 7th day of rehabilitation, the number of points in patients of group I in the survey decreased

from 19,96±0,93 points to 12,32±0,91 points, which was 38,3% less, than before the rehabilitation program (p<0,001), and coincided with the data of the survey of healthy individuals – 11,51±0,49 points (p>0,05). Group II patients also had a positive dynamics of reduction of signs of depression - from 30,41±2,53 points to 20,88±3,11 points, which was 31,3% less, than at the beginning of rehabilitation (p<0,001) and 44,8 % more in comparison with healthy individuals (p<0,01). The last observation period, 14 days, showed, that in patients of group I the manifestations of depression were significantly reduced to 11,29±89 points, by 76,8% compared with the beginning of rehabilitation (p<0,001) and by 9,1% relative to the 7th day of rehabilitation (p>0,05), and in patients of group II - by 97,2% relative to the beginning of rehabilitation (p<0,001) and by 38,8% relative to the 7th day of rehabilitation program (p<0,05). At the last stage of observation, patients in both groups underwent a questionnaire, which was evaluated in the same number of points as in healthy individuals (p>0,05).

The distribution according to the situational anxiety test was as follows: 23 (82,1%) and 24 (75,0%) patients of I and II groups showed moderate anxiety, and 4 (14,3%) and 8 (25,0%) had high anxiety. Mathematical analysis of the level of situational anxiety showed, that in patients of group I the rate of anxiety was higher in comparison with healthy individuals by 38,4%, and in patients of group II - by 41,5% (p<0,001). Situational anxiety had a significant tendency to decrease from 41,89±0,94 points to 29,11±1,56 points on the 7th day in patients of group I (p<0,001), and the survey data almost did not differ from healthy individuals (p>0,05). In patients of group II, after 7 days of rehabilitation program the signs of situational anxiety were not significantly reduced, which was reflected in the decrease of the survey data from 44,09±1,34 points to 36,03±2,06 points and by 22,4% (p<0,01) in relation to treatment and by 28,4% in relation to healthy individuals (p<0,001). On the 14th day of rehabilitation, the rate of situational anxiety was significantly reduced in patients of group I to 26,11±0,91 points and by 60,4% as before rehabilitation (p<0,001) and by 10,3% relative to the 7th day of rehabilitation (p>0,05), and in patients of the second group - by 54,4% (p<0,001) relative to the indicator before rehabilitation and by 22,9% compared to the previous period of the rehabilitation program (p<0,01). According to the Spielberger-Khanin questionnaire, patients in both groups had almost the same number of points after a 14-week rehabilitation program as healthy individuals (p> 0,05).

The study of the modified facial pain scale showed, that 20 (71,4%) and 20 (62,5%) patients of groups I and II were diagnosed with mild headache, 7 (25,0%) and 6 (18,8%) patients of both groups - moderate cephalgia, and 5 (15,6%) patients of group II, complained of severe headache. Statistical analysis of the modified facial pain scale The Faces Pain Scale-Revised (FPS-R) showed, that patients, who required inpatient oxygen therapy during treatment of SARS-Cov-2 infection, were 1,3 times more likely to complain of headache. Prior to rehabilitation, patients of group I during the test on the pain scale scored 2,96±0,28 points, and after the rehabilitation - 1,11±0,11, which was 62,5% less, than before treatment (p<0,001), and patients of the II group from 3,84±0,46 points to 2,75±0,33 points, which was 28,4% less, than the indicator before rehabilitation (p>0,05). After 14 days of rehabilitation program, patients of group I did not complain of headache, but 2 patients of group II complained of minor recurrent headache, which on the pain scale corresponded to 0,97±0,03 points, which was 74,7% lower, as before treatment and 64,7% lower in comparison with the 7th day of rehabilitation (p<0,001).

Evaluation of such a complaint as drowsiness, according to the Epworth drowsiness scale, showed, that 25 (89,3%) patients in group I had moderate drowsiness, and 1 (3,6%) - severe drowsiness. Moderate drowsiness was observed in 26 (81,3%) patients of the group II, and 5 (15,6%) - complained of severe drowsiness. Testing on the Epworth Sleepiness Scale and a summary assessment of sleep quality according to the Pittsburgh questionnaire showed, that patients in group I scored 43,3% and 68,3% more in comparison

with group of healthy people before rehabilitation, and patients in group II – 47,7% and 72,8% ($p<0,001$) more scores. In patients of group I, on the 7th and 14th day, the dynamics of drowsiness and sleep quality according to the respective questionnaires was the same, as when using the scales described above, thus the number of points was progressively decreasing ($p<0,001$) and was approaching the norm ($p>0,05$) after 7 days of rehabilitation program. In patients of group II on the 7th day of rehabilitation the manifestations of drowsiness in the questionnaire decreased to 7,09±0,26 points and by 21,7% in comparison with the indicator before rehabilitation (8,63±0,67 points), $p<0,05$ and was 36,4% different from the same indicator of healthy people ($p<0,001$). On the 14th day of rehabilitation in patients of group II, the manifestations of drowsiness decreased by 41,0% in comparison with the beginning of rehabilitation ($p<0,001$) and by 15,8% relative to the 7th day of rehabilitation ($p<0,05$). However, in patients of group II, the manifestations of drowsiness were not completely leveled and were observed on the 14th day of rehabilitation in 3 study participants ($p<0,05$). The total quality of sleep according to the Pittsburgh questionnaire in patients of group II on the 7th day of rehabilitation decreased by 31,4% ($p<0,001$), but still exceeded the value of healthy individuals by 2,5 times ($p<0,001$), but on the 14th day of rehabilitation program, the indicator decreased by 3,4 times relative to the beginning of rehabilitation and practically did not differ from the indicator of healthy individuals ($p>0,05$).

Conclusions

Thus, SARS-Cov-2 infection, in addition to high mortality, significantly reduces the quality of life of patients with this disease. According to the study, the manifestations of postcovid syndrome after 12 weeks of acute illness depended on the severity of the general condition of the patient in the hospital stage of medical care and the need for oxygen therapy. Thus, in patients, who did not need oxygen in the inpatient stage, anosmia, cephalgia, cognitive impairment, increased anxiety and fatigue were frequent manifestations of the postcovid syndrome in the future. Patients, who required oxygen therapy in the hospital, in addition to the above manifestations of postcovid syndrome, were more likely to experience taste disturbances and loss of taste, sleep disturbances, increased drowsiness and severe depression.

The rehabilitation program (26-28), which was used for all patients to the same extent, has led to the leveling of cognitive dysfunctions on the 7th day in people, who did not require oxygen therapy at the hospital stage. However, patients, who required oxygen therapy at the hospital stage, noted an improvement in memory and attention, based on the performance of the modified online Stroop Test, only on the 14th day of the rehabilitation program.

Positive dynamics in relation to depression due to BDI scale, anxiety according to the STAI test, cephalgia according to FPS-R parameters, drowsiness and sleep disturbances (ESS and PSQI) were observed in patients, who did not require oxygen therapy at the hospital stage, before the 7th day of use of the rehabilitation program. In patients, who required oxygen therapy during inpatient treatment in the acute period, the manifestations of depression and anxiety were disappearing after 14 days of rehabilitation program, and manifestations of minor recurrent headache and drowsiness were observed in 2 (6,3%) and 3 (9,4%) patients after another 14 days of rehabilitation.

Thus, this study proves, that patients, who needed oxygen therapy at hospital stage of treatment, and severe course of disease require longer rehabilitation measures for the manifestations of postcovid syndrome of chronic fatigue and cognitive disorders nature, than patients, who did not require oxygen at inhospital stage of treatment of acute SARS-Cov-2 infection.

Table 1. Characteristics of postcovid syndrome symptoms (in absolute numbers and %)

Symptoms	General number of patients (n=60), 100%	Group I (n=28),%	Group II (n=32),%	Fisher's exact criterion, p
Anosmia	9 (15.0)	3 (10.7)	5 (15.6)	=0.43
Dysgeusia (ageusia)	18 (30.0)	5 (17.9)	13 (40.6)	=0.49
Cephalgia	58 (96.7)	27 (96.4)	31 (96.9)	=0.72
Impaired concentration of attention and memory	59 (98.3)	27 (96.4)	32(100.0)	=0.02
Dyssomnia	48 (80.0)	21 (75.0)	27 (84.4)	=0.28
Increased anxiety	59 (98.3)	27 (96.4)	32 (100.0)	=0.47
Depressed condition	46 (76.7)	20 (71.4)	26 (81.3)	=0.7
Drowsiness	57 (95.0)	26 (92.9)	31 (96.9)	=0.71
Rapid fatigue	60 (100.0)	28 (100.0)	32(100.0)	=0.99

Table 2. Dynamics in the process of using the rehabilitation measures, modified online Stroop Test, for the determination of cognitive functions of patients after SARS-Cov-2, M±m

Indicators	Healthy	Before rehabilitation		7th day		14th day	
		Group I (n=28)	Group II (n=32)	Group I (n=28)	Group II (n=32)	Group I (n=28)	Group II (n=32)
	1	2	3	4	5	6	7
Average response time, sec	4,21±0,13	6,18±0,39 p1-2<0,001	7,78±0,72 p1-3<0,001	4,54±0,16 p2-4<0,001 p1-4>0,05	6,16±0,36 p3-5<0,05 p1-5<0,001	4,11±0,08 p4-6<0,05 p1-6>0,05	4,15±0,08 p7-3<0,001 p7-5<0,001 p1-7>0,05
Total test time, sec	44,22±0,13	51,71±1,86 p1-2<0,001	59,22±2,91 p1-3<0,001	45,75±0,55 p2-4<0,01 p1-4>0,05	51,47±1,91 p3-5<0,05 p1-5<0,001	44,25±0,25 p4-6<0,05 p1-6>0,05	45,03±0,55 p7-3<0,001 p7-5<0,01 p1-7>0,05
Total number of correct answers	9,9±0,09	6,25±0,61 p1-2<0,001	5,19±0,52 p1-3<0,001	9,29±0,21 p2-4<0,001 p1-4>0,05	6,69±0,53 p3-5<0,05 p1-5<0,001	9,71±0,17 p4-6<0,05 p1-6>0,05	9,55±0,19 p7-3<0,001 p7-5<0,001 p1-7>0,05
% of correct answers	99,0±0,95	62,5±6,13 p1-2<0,001	54,38±5,28 p1-3<0,001	92,5±2,12 p2-4<0,001 p1-4>0,05	69,38±5,25 p3-5<0,05 p1-5<0,001	97,14±1,74 p4-6<0,05 p1-6>0,05	95,45±1,92 p7-3<0,001 p7-5<0,001 p1-7>0,05

Notes: n- number of patients; p - reliability of the indicator.

Table 3. Dynamics of antenovegetative syndrome in the process of using the rehabilitation measures in patients after SARS-Cov-2 infection, M±m

Psychological tests	Healthy	Before rehabilitation		7th day		14th day	
		Group I (n=28)	Group II (n=32)	Group I (n=28)	Group II (n=32)	Group I (n=28)	Group II (n=32)
	1	2	3	4	5	6	7
Beck Depression Inventory, scores	11,51±0,49	19,96±0,93 p1-2<0,001	30,41±2,53 p1-3<0,001	12,32±0,91 p2-4<0,001 p1-4>0,05	20,88±3,11 p3-5<0,05 p1-5<0,01	11,29±,89 p2-6<0,001 p4-6>0,05 p1-6>0,05	12,78±2,06 p3-7<0,001 p5-7<0,05 p1-7>0,05
Determine of anxiety (Spielberger-Hanin test), STAI, scores	25,81±1,09	41,89±0,94 p1-2<0,001	44,09±1,34 p1-3<0,001	29,11±1,56 p2-4<0,001 p1-4>0,05	36,03±2,06 p3-5<0,01 p1-5<0,001	26,11±0,91 p2-6<0,001 p6-4>0,05 p1-6>0,05	29,31±1,33 p3-7<0,001 p5-7<0,01 p1-7>0,05
Modified facial pain scale The Faces Pain Scale-Revised (FPS-R) , scores	-	2,96±0,28	3,84±0,46	1,11±0,11 p2-4<0,001	2,75±0,33 p3-5>0,05	-	0,97±0,03 p3-7<0,001 p5-7<0,001
Epworth Sleepiness Scale, scores	4,51±0,29	7,96±0,52 p1-2<0,001	8,63±0,67 p1-3<0,001	5,07±0,24 p2-4<0,001 p1-4>0,05	7,09±0,26 p3-5<0,05 p1-5<0,001	4,89±0,25 p2-6<0,001 p4-6>0,05 p1-6>0,05	6,12±0,29 p3-7<0,001 p5-7<0,05 p1-7<0,05
Pittsburgh Sleep Quality Questionnaire (PSQI), scores	2,71±0,34	8,54±0,53 p1-2<0,001	9,97±,87 p1-3<0,001	3,04±0,22 p2-4<0,001 p1-4>0,05	6,84±0,31 p3-5<0,001 p1-5<0,001	2,86±0,21 p2-6<0,001 p4-6>0,05 p1-6>0,05	3,06±0,32 p3-7<0,001 p5-7<0,001 p1-7>0,05

Notes: n- number of patients; p - reliability of the indicator.

References

1. COVID-19 rapid guideline: managing the long-term effects of COVID-19. NICE guideline. Published: 18 December 2020. Available at: www.nice.org.uk/guidance/ng188.
2. Johns Hopkins University of Medicine. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). (Internet). (cited 2022 Feb 22). Available from:https://corona-virus.jhu.edu/map.html
3. Public Health Center of the Ministry of Health of Ukraine (Internet). (cited 2022 Feb 22). Available from: https://phc.org.ua/kontrol-zakhvoryuvan/inshi-infekciyni-zakhvoryuvannya/koronavirusna-infekciya-covid-19 (In Ukrainian).
4. Ivanova GE, Shmonin AA, Maltseva MN et al. Rehabilitation care in the epidemic period of new COVID-19 infection on first, second and third stage of medical rehabilitation. Physical and rehabilitation medicine, medical rehabilitation. 2020;2(2):98-117. (In Russian).
5. Romaniuk S. Neurological manifestations of COVID-19. Neurology, Psychiatry, Psychotherapy. 2020;3(54):11-3. (in Ukrainian).
6. Almeria M, Cejudo J, Sotoca J, Deus J, Krupinski J. Cognitive profile following COVID-19 infection: clinical predictors leading to neuropsychological impairment. Brain Behav. Immun. Health. 2020 Dec; 9:100163.
7. Levison ME. Commentary: what we know so far about post-COVID syndrome. Available from: https://www.msdmanuals.com/professional/news/editorial/2020/09/23/20/17/post-covid-syndrome.
8. Fortier-Brochu É. Cognitive impairment in individuals with insomnia: clinical significance and correlates. Sleep. 2014;37(11):1787-98.
9. Najjar S, Najjar A, Chong D, et al. Central nervous system complications associated with SARS-CoV-2 infection: integrative concepts of pathophysiology and case reports. Journal of Neuroinflammation. 2020;17:231.
10. Wijeratne T, et al. Post-COVID 19 Neurological Syndrome (PCNS); a novel syndrome with challenges for the global neurology community. Journal of the Neurological Sciences. 2020;419:117-179.
11. Gobin C, Banks J, Fins A, et. al. Poor sleep quality is associated with a negative cognitive bias and decreased sustained attention. Journal of Sleep Research. 2015;24:1-8.
12. Golubovska OA. Post-COVID syndrome: pathogenesis and main ways of rehabilitation. Health of Ukraine. 2021;2(495):24-6. (in Ukrainian).
13. Ivanova GE, Balandina IN, Bakhtina IS et al. Medical rehabilitation in new COVID-19 infection. Physical and rehabilitation medicine, medical rehabilitation. 2020;2(2):140-89. (In Russian).
14. Carvalho-Schneider C, et al. Follow-up of adults with noncritical COVID-19 two months after symptom onset. Clin. Microbiol. Infect. 2020;5(10):1016.
15. Barker-Davies R, O'Sullivan O, Senaratne K, et al. The Stanford Hall consensus statement for post-COVID-19 rehabilitation. Br. J. Sports Med. 2020;54:949-59.
16. Gemelli Against COVID-19 Post-Acute Care Study Group. Post-COVID-19 global health strategies: the need for an interdisciplinary approach. Aging Clinical and Experimental Research. Available from: https://doi.org/10.1007/s40520-020-01616-x.
17. Preobrazhenskaya IS. Cognitive and sleep disorders. Effective pharmacotherapy. 2015;23:20-9. (In Russian).
18. Khaustova OO, Bezsheyko VG. Neuroimmunoendocrin aspects of depressive disorders in chronic somatic diseases. The Universe of social psychiatry, medical psychology and psychosomatic medicine. 2010;T.1;3(3):112–19. (in Ukrainian).
19. Mironova EE. Collection of psychological tests. Part I: manual: Women's Institute of ENVIL; 2005. pp. 16-8. (In Russian).
20. Meredith P, Ownsworth T, Strong J. Areview of the evidence linking adult attachment theory and chronic pain: Presenting a conceptual model Clin. Psychol. Rev. 2008;28: 407-29.
21. American Academy of Sleep Medicine. *ICSD-2* – International Classification of Sleep Disorders, 3d edition, pocket version: Diagnosticand coding manual. Westchester, IL: American Academy of Sleep Medicine; 2014. doi:10.3109/9781616310059-3.
22. Hon K, Suen L, Tam W. Association of sleep hygiene – related factors and sleep quality among university students in Hong Kong. Hong Kong Med. 2010;16:180-5.
23. Barger LK, Rajaratnam SM, Wang W, et. al. Common Sleep Disorders Increase Risk of Motor Vehicle Crashes and Adverse Health Outcomes in Firefighters. Journal of Clinical Sleep Medicine. 2015;11(3):233-40.
24. Fernandez-Mendoza J, Vgontzas AN, Kritikou I, Calhoun SL, Liao D, Bixler EO. Natural history of excessive daytime sleepiness: role of obesity, weight loss, depression, and sleep propensity. SLEEP. 2015;38(3):351-60.
25. Lichstein KL, Kryger MH, Roth T. Insomnia: epidemiology and risk factors Principles and Practice of Sleep Medicine. 6th ed. – Philadelphia: Elsevier. 2016:761-8.
26. Ionițe C., Arotăriței D, Turnea M., Ilea M., Rotariu M., Applications of fitness function in Pubalgia affliction, Balneo and PRM Research Journal. 2021;12(1):77–81 Full Text DOI 10.12680/balneo.2021.423
27. Condurache I., Turnea M., Rotariu M., Improving functional and motor capacity through means/resources and methods specific to acvatic activities, Balneo and PRM Research Journal. 2021;12(1):27–30 Full Text DOI 10.12680/balneo.2021.414
28. Iordan D.A., Mocanu G.-D., Mocanu M.-D., Munteanu C., Constantin G.B., Onu I., Nechifor A., Age-Related, Sport-Specific Dysfunctions of the Shoulder and Pelvic Girdle in Athletes Table Tennis Players. Observational Study, Balneo and PRM Research Journal. 2021;12(4):337–344 Full Text DOI 10.12680/balneo.2021.461

Article Publication Charges: 200 Euro per admitted for publication article - see LINK

- **For submitting articles for Balneo Research Journal, authors must use the following template: Balneo Template**

For submitting systematic review articles based on the PRISMA methodology, authors must provide: PRISMA Abstract checklist, PRISMA checklist and PRISMA registration

· **The Peer Review process is a double - blind process.**
· **Published Conflict-of-Interest Statement: Link**

· **Published Statement of Informed Consent: Link**

· **Published Statement of Human and Animal Rights: Link**

· **Assignment of copyright and authorship responsibilities: Link -**

NEXT issue: Vol 13 No. 2 is planned to be published on the 1st of June, 2022

For publication in this issue, the deadline for submitting your articles is: 20th of April, 2022

All the articles must be submitted on the platform: https://bioclima.ro/Journal/index.php/BRJ/login

Editing regulations / (peer-review protocol) – Instructions for authors

· **Balneo and PRM Research Journal provides a platform for authors to publish their articles as peer-reviewed original papers, systematic reviews, meta-analyses, short communications and letters to the editor in the following fields: Balneology, Physical and Rehabilitation Medicine (PRM), Healthy Ageing, Climatology and Hydrothermotherapy.**

· **We consider as general rules those included in the document: Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication - updated February 2006 by International Committee of Medical Journal Editors.**
· **The manuscripts will be submitted via the online submission system at http://bioclima.ro/ojs or by email as an attachment in Word format to articleonbrj@bioclima.ro.**
· **For submitting articles for Balneo Research Journal, authors must use the following template: Balneo Template.**
· **The manuscripts must be accompanied by Published Conflict-of-Interest Statement (see Form), Published Statement of Informed Consent (see Form), and Published Statement of Human and Animal Rights (see Form), signed by the main author, in the name of all authors, scanned and attached to the email.**
· **Authors retain unrestricted copyright and all publishing rights when publishing under any license permitted by the journal.**
· **The language of papers is English.**
· **After manuscript receipt, the corresponding author will receive a short e-mail confirming the receipt which will contain the registration number, the date the manuscript was received, and the fact that the manuscript was sent for peer-review. The Journal Peer-review Board Secretary chooses aleatory 2 peer-reviewers (from the Peer-review Board) and sends them by e-mail the manuscript.**
· **The reviewer's decision (approval with no changes, approval with major/minor changes, rejection), taken on the responsibility of the peer-reviewers, will be immediately communicated by e-mail to the corresponding author by the editor.**
· **If the manuscript gets approval with changes, the corresponding author shall send the improved manuscript within 4 weeks. The editor will convey the corresponding author's answer to the peer reviewers. If they are satisfied with the corresponding author's answer, they will send the executive editor the decision of approval for publication of the improved manuscript.**
· **If the peer reviewers consider that the corresponding author did not meet/or met poorly the revision requests, they will deny the approval for publication, which will be communicated to the editor. The approval for publication once taken by the reviewers, the decision will be communicated in the editorial meeting.**
· **The author who has the quality of editor-in-chief or editor does not participate in any way in the decision-making process of selection and publication of the respective article.**

BALNEO RESEARCH

Balneo and PRM Research Journal

English Edition

e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

· **International title: Balneo and PRM Research Journal / Index name: BALNEO, Publisher: Romanian Association of Balneology / Asociația Română de Balneologie, Website http://bioclima.ro/Journal.htm**

· **Aims and scope: The Journal publishes peer-reviewed original papers, systematic reviews, meta-analyses, short communications and letters to the editor in the following fields:**

Balneology, Physical and Rehabilitation Medicine (PRM), Physio / Kinesiotherapy, Lifestyle and Healthy Ageing, Climatology and Hydrothermal / Aquatic Therapy.

· **Publication Ethics and Malpractice Statement Document: Link**

· **ISSN-L: 2734-844X / p ISSN: 2734-844X / e ISSN: 2734-8458, Frequency: 4 issues per year, The language of publication: English, License:** **see: https://creativecommons.org/licenses/by-nc-nd/4.0/**

· **Published Conflict-of-Interest Statement: Link, Published Statement of Informed Consent: Link, Published Statement of Human and Animal Rights: Link, Assignment of copyright and authorship responsibilities: Link**

· **Online submission link:** Submit **, Offline submission by email: articleonbrj@bioclima.ro**

· **Balneo and PRM Research Journal was recognized by the Romanian College of Physicians for 10**

· **Article Publication Charges 200 Euro per admitted for publication article - it covers indexing and editing. See submit page: Submit**

· **For submitting articles for Balneo and PRM Research Journal, authors must use the following template: Balneo Template**

· **Peer reviewers details: Peer review process.**

· **The journal's presence in various indexing services, directories and listings: At the present moment, Balneo and PRM Research Journal is part of the International Databases (BDI) as follow:**

EBSCOhost, CrossRef, DOAJ, Electronic Journals Library (GIGA), National Library of Medicine - NLM, ISI: Emerging Sources Citation Index (ESCI)

Supporting organizations: