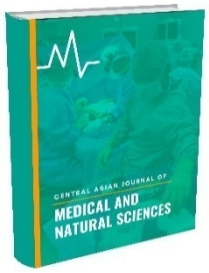
CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES



Volume: 04 Issue: 06 | Nov-Dec 2023 ISSN:2660-4159

www.cajmns.centralasianstudies.org/index.php

Clinical Manifesttations of Post – Covid Syndrome

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Received 20th Sep 2023,
Accepted 24th Oct 2023,
Online 13th Nov 2023

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Abstract. Studying the frequency of various clinical manifestations in patients who have had COVID-19, depending on the period of time elapsed after the disease, the severity of the course and the presence of multimorbid pathology is written in the article.

Key words: coronavirus infection, COVID-19, post-Covid syndrome, comorbid pathology, rhinogenic complications.

Introduction. As the number of patients infected with the new coronavirus infection, COVID-19, increases, so does the number of people who have recovered from it. At the same time, patients who have had COVID-19 of any severity have symptoms that reduce the quality of life [1]. It is possible that patients in this group make up the bulk of patients with post-Covid syndrome. Despite the large number of studies devoted to post-Covid syndrome [4–9], many questions remain regarding the factors influencing its development (age, gender differences, multimorbid pathology, etc.). The significant variation in the frequency of detected symptoms may be due to both the difference in the time elapsed since COVID-19 and the study of the frequency of clinical manifestations without taking into account the severity of the course, the presence of comorbid pathology and the intensity of treatment in the acute period.

Purpose of the research is to study the frequency of various clinical manifestations in patients who have had COVID-19, depending on the period elapsed after the disease, the severity of the course and the presence of multimorbid pathology.

Material and methods. Using a random sampling method, 253 patients (187 women, 66 men) aged 18 to 85 years were selected among patients who had suffered COVID-19. All patients signed informed consent to participate in the study. Approval from the local ethics committee was obtained (protocol No. 9 of 04/05/2021). The diagnosis of the disease was confirmed by identification of RNA of the SARS-COV-2 virus by PCR / detection of IgM class antibodies to the virus in 190 (75%) patients

during the acute period or identification of IgG class antibodies in 45 (17.8%) during the convalescence period. In 18 (7.1%) patients, the diagnosis of COVID-19 was not confirmed, but the development of a typical clinical picture of the disease after close contact with patients in whom SARS-CoV-2 was detected suggests the development of COVID-19. Depending on the severity of the disease during the acute period, patients were divided into 2 groups: Group 1 consisted of patients who had mild COVID-19 (n=133), in whom the disease proceeded as an acute respiratory viral infection and in most cases did not require hospitalization; The 2nd group consisted of patients who had moderate to severe COVID-19 (n=120), in whom the disease occurred in the form of pneumonia (according to CT data, 25–80% of lung damage) and in most cases required hospitalization. Patients in each group were divided into 2 subgroups depending on the time elapsed after the acute period of COVID-19: in subgroup A, patients were examined for up to 3 months. (12 weeks) after the acute period of the disease, in subgroups B - after 3 months. (12 weeks) after the disease, i.e., from 3 months. up to a year after COVID-19. The characteristics of the patients are presented in Table 1.

Table 1. Characteristics of patients with post-COVID-19 syndrome

Patient characteristics	Group 1 (n=133)	Group 2 (n=120)
Age , years	51,1±13,2	55,4±14,6 *
Gender, n (%): **Males** **Females**	 40(30,1) 93(69,9)	 26(21,7) 94(78,3)
Identification of SARS-CoV-2 virus RNA and/or IgM antibodies to S-protein during the acute phase, n (%)	101(75,9)	89(74,2)
Identification of IgG antibodies during the convalescence period, n (%)	23(17,3)	22(18,3)
Comorbidities, %	95(71,4)	105(87,5) *

Note. * - p <0,01.

Dysfunction of cellular immunity was also considered as a sign of post-Covid syndrome. The survey was conducted at various times after the illness, but the duration of certain clinical manifestations was specified. Statistical analysis of the study results was carried out using the Statistica 10.0 program (StatSoft Inc., USA) using standard statistical methods. Differences between groups were considered statistically significant at $p<0.05$.

Results and discussion. Patients with clinical manifestations in whom symptoms lasted up to 3 months. (12 weeks), were assigned to the group with the so-called post-acute COVID-19 syndrome (post-Covid syndrome with clinical signs up to 3 months). Duration of symptoms more than 3 months. (12 weeks) was regarded as the presence of post-Covid syndrome in patients. Symptoms were detected both in patients from subgroup 1A (45/52 (86.5%)) and in patients from subgroup 2A (42/45 (93.3%)), i.e. they had no symptoms 7 (13, 5%) and 3 (6.7%) patients, respectively. At follow-up after 3 months.

after COVID-19, 34 (42%) patients from subgroup 1B and 13 (17.3%) patients from subgroup 2B were asymptomatic ($p<0.001$), while at least 1 symptom persisted in 47/81 (58%) patients from subgroup 1B and in 62/75 (82%) patients from subgroup 2B. A. Carfi et al. [10] noted that 87% of patients had some symptoms upon discharge from hospital. Thus, the results of our study are consistent with the literature. The frequency of clinical manifestations after recovery from coronavirus infection, depending on the observation periods presented in the literature, differs slightly from the indicators of this study, with rare exceptions [3, 11, 12]. Most often in patients who have had mild COVID-19 within 3 months. and more after the acute period, general weakness, shortness of breath, and cough were encountered. They were also often found in patients who had moderate and severe COVID-19, but after pneumonia, consequences of damage to the central nervous system are often found: cognitive disorders, headache, insomnia; cardiovascular system: arterial hypertension, tachycardia; other systems: arthralgia. The cause of the damage to the circulatory system remains unclear. The direct cardiotoxic effect of coronavirus, plaque rupture and coronary thrombosis, the effect of pro-inflammatory cytokines, coagulopathy are discussed, and the cardiotoxic effect of drugs used in the treatment of the disease cannot be excluded. The causes of damage to the nervous system could presumably be the neurotoxic effect of SARS-CoV-2 on the central and peripheral nervous system, the action of pro-inflammatory cytokines, autoimmune factors, and hypoxemia [13–18]. Damage to the gastrointestinal tract and urinary system after recovery from COVID-19 is rare. As the time elapsed after the acute period of COVID-19 increases, the frequency of symptoms decreases, but a statistically significant difference was found only in relation to cognitive impairment. After 8–12 months after the illness, most symptoms disappear completely or the intensity of their manifestation decreases. With very rare exceptions, anosmia/dysgeusia does not always disappear, even after 12 months after the disease. A comparative analysis of clinical manifestations after ARVI (mild COVID-19) and pneumonia (moderate and severe COVID-19) indicates that after pneumonia during the first 3 months after the acute period, certain symptoms were statistically significantly more common than after ARVI : general weakness, cognitive impairment, headache, shortness of breath and tachycardia. In patients who were observed 3 months after acute COVID-19 and later, the differences were less pronounced. It is possible that a more severe course of residual effects in the first 3 months after pneumonia may be due not only to severe forms of damage to organs and systems by coronavirus, but also to the active use of medications that affect the patient's body. Among the rare consequences in patients with post-Covid syndrome included in this study are weight loss/gain and the development of autoimmune hepatitis after 6 months. after the acute period, intrauterine fetal death. If dysfunction of cellular immunity is included in the list of signs of post-Covid syndrome, its development does not depend on the severity of COVID-19 in the acute period and can be observed in both mild and severe cases, however, the number of symptoms in the latter case is more numerous. Gender differences in post-Covid syndrome are as follows: general weakness after a mild form of COVID-19 occurs 2 times more often in women in the first 3 months of observation, but then the difference is leveled out. After moderate and severe forms of the disease, shortness of breath is more common in men (72.8% vs. 44.1%, $p<0.05$) in the first 3 months. observations, then the frequency of shortness of breath decreases in both men and women. The distribution of patients by age made it possible to establish that the frequency of general weakness and shortness of breath increases with age. Perhaps this is determined not only by damage to the bronchopulmonary and nervous systems, but also by damage to the cardiovascular system. Comorbid pathology was detected in 33/52 (63.5%) patients who had mild COVID-19 during follow-up for up to 3 months. after the acute period, and in 62/81 (76.6%) - after observation for more than 3

months; in the group of patients who had moderate and severe COVID-19, comorbid pathology was identified in 41/45 (91.1%) and 64/75 (85.3%) patients during follow-up for up to 3 months. after the acute period and at follow-up after 3 months. after the acute period, respectively. Comorbid pathology may determine the severity of the course, as it was more often observed in patients from group 2 ($p<0.01$) (see Table 1). Most often, patients were diagnosed with cardiovascular diseases, diabetes mellitus, obesity, and chronic obstructive pulmonary disease. Most researchers also note that comorbid pathology worsens the prognosis.

Conclusions. The development of post-Covid syndrome does not depend on the severity of the coronavirus infection in the acute period and can be observed in both mild and severe cases, however, the number of symptoms in the latter case is more numerous. After recovery from COVID-19, with the development of post-Covid syndrome, the central nervous system, bronchopulmonary and cardiovascular systems are most often affected, which manifests itself in the development of general weakness, cognitive disorders, headache, shortness of breath and tachycardia. As you move away from the acute period of the disease, the frequency of symptoms decreases, and the further you go, the better patients feel: both the frequency of symptoms and the severity of their manifestation decrease. Among the rare consequences in patients with post-Covid syndrome are weight loss/gain and the development of autoimmune hepatitis after 6 months. after the acute period, intrauterine fetal death. Comorbid pathology determines the severity of coronavirus infection in the acute period, as it is more often observed in patients with the development of pneumonia. Patients who have had coronavirus infection, as in the first 3 months. after an acute period, they continue to need observation from specialists in various fields to fully restore health and improve the quality of life.

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