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Complications associated with recovered after COVID-19 in Slovenia: Epidemiological study

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Abstract

Introduction: COVID-19 is an infectious viral disease caused by Sars-cov-2, which affects various organ systems and leads the county in the field of body functions, body structure and, consequently, activity and participation. Since the virus binds to ACE 2 receptors, which are also present in myocytes, intestinal epithelium, vascular endothelium, kidneys and elsewhere, COVID-19 affects not only the respiratory system, but also other organ systems

Aim: The purpose of the study is to determine which complications arise after recovering from COVID-19.

Methods: We use a retrospective review of medical records is a research method that involves analyzing existing medical documentation to gain insights into the course of diseases, treatments, or treatment outcomes. We performed 502 reviews of medical records and identified 141 patients with post-COVID-19 complications. Statistical analysis was performed with IBM SPSS version 25.0 and show in frequency and percentage. The study was approved by the Ministry of Health, Medical Ethics Committee of the Republic of Slovenia with serial number: 0120-468/5022/6.

Results: Most complications after recovering from COVID-19 were observed in the cardiovascular system (n= 79; 56.0%) and the respiratory system (n= 59; 41.8%). Most of these are Palpitations (n= 27; 19.0%), cough (n= 23; 16.2%), Pneumonia (n= 21; 17.8%) and Infectious myocarditis (n= 17; 12.0 %). After recovering from COVID-19, arterial embolism and thromboembolism occur first (14 days), followed by pulmonary embolism (16 days), pulmonary edema (23 days), sepsis (28 days) and infectious myocarditis (29 days). In addition, we noticed complications after recovering from COVID-19 on the skin, urinary system, sensory system, endocrine system, gastrointestinal system and nervous system.

Conclusion: Our study has shown that COVID-19 is indeed a systemic disease. Post-COVID-19 complications will barely begin to show themselves, so we believe that we have laid a good foundation for further epidemiological research.

Keywords: COVID-19; Complications; Epidemiology; Systemic virus

1. Introduction

Infectious diseases are part of human history, often accompanied by major wars and human migrations. The last major pandemic to sweep the world in a matter of months was the Spanish flu, which caused tens of millions of deaths and became synonymous with pandemic disease (26). Although there were sporadic outbreaks of infectious diseases (SARS, Ebola, avian flu, etc.) after the Spanish flu pandemic, these diseases were controlled and did not cause outbreaks of

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major proportions (26). The 2019 Coronavirus Disease (COVID-19) caused an unprecedented global pandemic. Thus, on 12 March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic (8).

Coronaviruses are single-stranded RNA viruses divided into four groups (coronavirus alpha, beta, gamma and chisel). Together with the novel coronavirus, seven forms of coronavirus thus cause infection in humans. Three types of coronaviruses (SARS-CoV-1, MERS-CoV and SARS-CoV-2) can cause severe pneumonia and all three have caused major outbreaks. The incubation period of the disease is 2 - 14 days, but mainly the period between days 5 and 7 (26, 5).

During the acute phase of the course of COVID-19, patients may present with a variety of symptoms including cough, fever, nausea, diarrhoea, vomiting, muscle and joint pain, headache and fatigue (11). After about 7 days, in some cases, exacerbation occurs, which can lead to acute respiratory distress and death (14). In addition to the acute phase of the disease and the healing process, many studies report various complications after the infection is over (24). Zupanc Lejko (2020). highlights many complications in the cardiovascular system, predisposing to platelet docking and renal failure (26). While many other studies indicate that different types of complications occur in several body systems (10). Although the exact mechanisms responsible for the long-term complications of COVID-19 infection remain unknown, there are a number of viral pathophysiological mechanisms that may explain these long-term complications and sequelae. Possible pathophysiological mechanisms may include direct viral tissue damage, as the entry receptor for SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2), which is expressed at different locations in the body, allowing the virus to enter target cells through activation of its spike protein by transmembrane serine protease 2 (9, 14). These receptors are expressed in epithelial cells, nasal spindle cells, gastrointestinal epithelial cells, pancreatic β cells and renal podocytes, suggesting that direct tissue injury may be the primary mechanism of presentation of SARS-CoV-2 infection, which may also contribute to more prolonged complications (25, 21). Research at the beginning of the pandemic showed that endothelial cells have high ACE2 expression and that infection with COVID-19 caused a significant alteration of the vascular barrier integrity and promoted a procoagulant state (15). The long-term consequences of these changes were observed in follow-up studies of COVID-19 survivors, which revealed radiological abnormalities of the lung in 71% of patients and functional abnormalities in 25% of patients three months after COVID-19 infection (23).

In addition to direct cellular infection, there are several other mechanisms that may explain the pathophysiology leading to multi-organ system dysregulation after COVID-19. Other mechanisms leading to long-term complications of COVID-19 infection include endothelial damage, immune dysregulation and hypercoagulability, often leading to thrombosis (Nalbandian et al, Immune dysregulation was identified by the discovery of autoreactive T cells at autopsy in deceased individuals infected with COVID-19, likely due to mechanisms similar to those in autoimmune diseases (7).

Similar studies on the long-term complications of SARS-CoV-1, the precursor of SARS-CoV-2 (COVID-19), which emerged in 2003, have reported similar complications and consequences (20), Both virus types share the same host cell receptor in ACE2, suggesting similar mechanisms of entry into the cell, but SARS-CoV-2 has a stronger affinity for the receptor, meaning it has an additional site for division, which may allow more efficient infection and subsequently a greater chance of more serious long-term complications (27).

Despite the complications highlighted, these are not all the complications that occur in the post-COVID-19 period, but we have focused on those groups or organ systems whose complications are most pronounced. All of these complications can affect the quality of life of the individual and their families after COVID-19, as they can affect the performance of daily tasks, work and social integration.

Given the large number of people affected by COVID-19 infection worldwide, based on the limited scientific knowledge and evidence currently available, it can be expected that physiatrists and physiotherapists will be increasingly involved in the care of these patients. Of course, we need to be aware of the need to improve lung function, physical and psychological performance and to enable a good quality of life for the patient after recovery. Timely preparation and thoughtful planning can help to improve the latter.

2. Material and methods

We use an retrospective review of medical records is a research method that involves analyzing existing medical documentation to gain insights into the course of diseases, treatments, or treatment outcomes. The key feature of this method is that data are collected from past records, meaning the researcher is not involved in the primary data collection. Instead, they use documents that have been collected as part of routine medical care. This allows researchers to study large cohorts of patients without the need for long-term follow-up (28). The data collection we did in april 2024

at Health center Izola. These include demographic data, diagnosis information, treatment details, outcomes, and possible complications.

We review medical records, electronic health records (EHRs), or other documentation containing relevant information.

The study was approved by the Ministry of Health, Medical Ethics Committee of the Republic of Slovenia with serial number: 0120-468/5022/6.

2.1. Population

The sample included patients who had a sars-cov-2 infection from November 2022 to March 2022. We reviewed 502 medical records and identified 141 patients with complications from COVID-19. The youngest patient with complications from COVID-19 is 17 years old, while the oldest is 92 years old, with a mean age of 51.3 years, of

these, 65 patients (46.1%) were vaccinated against COVID-19 and 76 patient (53.9%) were not vaccinated against COVID-19. All demographic data is in Table 1.

Table 1 Demographic data

Demographic data		**N**	**%**
Gender	Male	59	41,8
	Female	82	58,2
Employment status	Employmed	92	65,3
	Unemployed	15	10,6
	Pensioner	34	24,1
Living enviroment	Countryside	55	39,0
	City	86	61,0
Vaccinated	Yes	65	46,1
	No	76	53,9

Legend: N= number, %= percentage

2.2. Statistical Analysis

Statistical analysis was performed using IBM SPSS version 25.0 and MS excel 2016. Descriptive statistics using frequencies and proportions were used to display the results. All medical diagnoses are according to the International Classification of Diseases (ICD-10).

3. Results and discussion

Post-COVID complications, commonly referred to as Long COVID or Post-COVID condition (PCC), encompass a wide range of symptoms that persist for weeks or months after recovering from the acute phase of the virus. These complications can affect multiple systems in the body and vary greatly in severity and duration.

Similar studies on the long-term complications of the SARS-CoV-1 virus, the predecessor of the SARS-CoV-2 virus (COVID-19), which emerged in 2003, reported comparable complications and consequences (20). Both types of viruses use the same host cell receptor, ACE2, suggesting similar mechanisms of cell entry. However, SARS-CoV-2 has a stronger affinity for the receptor due to the presence of an additional cleavage site, which may enable more efficient infection, potentially leading to a higher likelihood of severe long-term complications (27).

Although SARS-CoV-2 can have widespread effects on the body, COVID-19 primarily remains a respiratory disease. Numerous long-term pulmonary complications have been reported following COVID-19 infection, including dyspnea, ventilator dependency, oxygen dependency, abnormal lung function tests, and fibrotic lung disease. The most common post-COVID lung symptom is dyspnea, which persists in approximately 22.9%–53% of patients for up to two months after the onset of symptoms (2, 3, 19).

In addition to subjective symptoms, SARS-CoV-2 infection can cause long-term objective changes in lung physiology. Oxygen dependency has been reported in up to 6.6% of survivors upon hospital discharge (3). Among those with respiratory failure requiring tracheostomy, prolonged ventilator weaning is often unsuccessful. In a study of 1,890 patients who required tracheostomy in Spain, only 48% of patients were successfully weaned from mechanical ventilation after one month of follow-up (19).

Lung function abnormalities have also been documented. In a study of 55 non-critical COVID-19 patients in China, abnormalities were observed in 25% of patients over a three-month period, with the most common being a reduction in diffusing capacity for carbon monoxide (16%) (23). Similar findings were reported by Xiong idr. (2021) who observed increased rates of restrictive lung function findings compared to matched controls (24).

Radiological studies have shown persistent abnormalities in a significant number of COVID-19 survivors. In an assessment three months after hospital discharge in patients with severe COVID-19 pneumonia (defined by a respiratory rate >30, SpO2 < 90% without oxygen, or severe respiratory distress and clinical signs of pneumonia), 81% had chest CT abnormalities (4). The long-term incidence of lung fibrosis and its progression will become clearer as experience with SARS-CoV-2 continues to grow (5).

As previous studies, our research also shows that COVID-19 is a systemic virus, affecting multiple organ systems. In the Table 2, we have presented the findings of our study, highlighting the various affected systems and the corresponding complications. We also presented how long certain post-covid complications appeared.

Table 2 Postcovid complications in our study

Post covid complication	**N**	**%**	**Time of Occurrence (days)**		
			Min	**Max**	**Mean**
Urinary system					
Urinary tract infections-N39	13	9,2	4	180	61
Renal failure - N19	3	2,1	33	184	102
Cardiovascular system					
Palpitations - R00	27	19,0	5	91	32
Arterial hypertension - I10	15	10 ,6	12	365	94
Infectious myocarditis - I40	17	12,0	15	51	29
Other disorders of ven- I78	8	5,6	10	61	34
Sepsis - A41	2	1,4	17	40	28
Chest pain - R07	8	5,6	21	96	38
Arterial embolism and thrombosis - I74	2	1,4	6	22	14
Pulmonary system					
Pneumonia- J12	21	17,8	6	63	31
Pulmonary edema - j81	5	3,5	6	40	23
Pulmonary embolism- I26	4	2,8	12	21	16
Asthma - J45	4	2,8	32	63	44
Cough - R05	23	16,2	5	91	30
Difficulty breathing - R06	2	1,4	12	90	51
Skin					
Dermatitis - L30	6	4,2	8	120	50
Skin abscess - L02	2	1,4	19	21	20

Post covid complication	N	%	Time of Occurrence (days)		
			Min	Max	Mean
Herpes simplex- B00	2	1,4	6	32	19
Sensory system					
Disorders of vestibular function - H81	4	2,8	7	26	19
Disturbance of smell and taste-R43	16	11,3	6	159	44
Frequent vertigo and dizziness - R42	3	2,1	15	68	35
Gastro-intestinal system					
Gastritis and duodenitis - K52	7	4,9	7	52	30
Neurological system					
Anxiety -F41	6	4,2	31	128	72
Depression- F32	6	4,2	35	182	114
Endocrine system					
Metabolic disorder of lipids - E78	5	3,5	7	145	58
Dysfunction of the thyroid gland - E03	5	3,5	16	366	148
Diabetes type 2-E11	10	7,1	29	365	83
Iron deficiency anaemia - D50	3	2,1	15	41	24

Legend: N= number, %= percentage

Cardiovascular disease is a common complication after hospital discharge following COVID-19. Carfi, Bernabei, and Landi (2020) described chest pain in as many as 21% of patients 60 days after hospital discharge. Palpitations were also described as a common symptom at 60-day follow-up in as many as 9% of patients. In addition to the subjective symptoms of cardiovascular disease described as part of the long-term consequences of infection with COVID-19, several measurable outcomes have also been observed. An increased incidence of postural tachycardia syndrome (POTS) has been reported after infection with COVID-19 (2, 22). Some of the long-term cardiovascular effects of COVID-19 are seen as a consequence of the acute infection. In a large-scale study of young, healthy, competitive college athletes, myocarditis was found in as many as 2.3% of participants. In addition, routine cardiac magnetic resonance imaging monitoring of 100 patients discharged with COVID-19 revealed persistent inflammation in 60% of patients with persistent elevations of high-sensitivity troponin T in as many as 71% of patients (11). Finally, the acute phase of COVID-19 has been shown to be associated with high rates of abnormal cardiac ultrasound findings (6). In a prospective study of 1216 patients admitted with COVID-19, 55% of patients had an abnormal cardiac ultrasound, including abnormalities in 46% of 901 patients without prior heart disease (6). Which is consistent with our study.

Although long-term follow-up cardiac ultrasound data have not been published, complications seen in the acute setting should be considered in the long-term care of these patients. Likewise, other researches add increased heart rate, increased palpitations, increased blood pressure, chest tightness, pericardial pain, myocardial infarction, pericardial effusion, diastolic dysfunction, pulmonary hypertension, and cardiac arrhythmia (24, 4, 10).

Among the highly exposed complications, it is also worth highlighting hematological and neurological post-COVID-19 complications. The acute phase of COVID-19 was associated with an increased risk of thrombotic events, especially in critically ill patients (11, 16). The etiology of this coagulopathy is multifactorial, including microvascular dysfunction and increased expression of tissue factors in response to inflammatory cytokines, as well as the effects of hypoxia on hypoxia-induced upregulation of transcription factors (12, 17). It is for this reason that anticoagulation therapy was widely used as a method of treatment in intensive care units.

In addition to hematological complications, we also mentioned neurological complications after COVID-19. Research indicates various long-term neurological and psychiatric complications associated with infection with COVID-19. Long-term symptom data from several different studies have reported persistent neurological findings in patients two months after acute infection, including fatigue, muscle weakness, sleep problems, myalgia, and headache (2, 10). Such symptoms have become a sign of long-term COVID syndrome. Loss of smell and taste was also a feature of the COVID-

19 infection that is unique compared to other viral infections. Long-term follow-up after two months showed persistent loss of taste and smell in 11% to 13.1% of patients (10). Due to the significant burden of severe, critical illness, and acute respiratory distress syndrome (ARDS) associated with COVID-19, we might expect similar impairments in cognition to those observed in previous studies in patients with ARDS. Impairments in memory (13%), verbal communication (16%), and general functionality in the environment (49%) have been described in survivors of ARDS due to other causes after 1 year of follow-up (18). In addition, many other studies highlight post-traumatic stress disorder, depression and anxiety (13, 1)

Despite the exposed complications, these are not all the complications that occur in the period after recovering from COVID-19 (Table 3), but we focused on those groups or organ systems whose complications are the most pronounced. We also detected certain post-covid complications that are not classified by the international classification of diseases. Among the most prominent were concentration problems (n= 28; 19.9%), followed by memory problems (n= 25; 17.7%) and insomnia (n= 24; 17.0%).

Table 3 Other complication we recognize in our study

Post covid complication	**N**	**%**	**Time of Occurrence (days)**		
			Min	**Max**	**Mean**
Malaise and fatigue - R53	11	7,7	12	365	77
Fatigue syndrome after recovering from a virus - G93	2	1,4	65	69	67
Enlarged lymph nodes -R59	6	4,2	12	55	35
Tonsillitis - J03	2	1,4	33	60	46

Legend: N= number, %= percentage

4. Conclusion

This study showed that the sars-cov-2 (COVID-19) virus is a systemic virus and affected the patient where he was previously most vulnerable. Many complications can be observed, especially in the cardiovascular system and the respiratory system. The research showed the possibility of further research in this sub-region, as the complications after recovering from COVID-19 will hardly be fully apparent in the future

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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