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REVIEW

Long-term side effects and lingering symptoms post COVID-19 recovery

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Summary

Since the Coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), our understanding regarding the pathophysiology and clinical manifestations of this disease have been improving. However, we still have limited data on long-term effects and lingering symptoms of post COVID-19 recovery. Despite predilection of COVID-19 for lungs, multiple extra-pulmonary manifestations appear in multiple organs and biological systems and with continued infection and recovery worldwide. It is necessary that clinicians provide patients with previous SARS-CoV-2 infection with expectations of long-term effects during or after recovery from COVID-19. Herein, we review the long-term impact of COVID-19 on different organ systems reported from different clinical studies. Understanding risk factors and signs and symptoms of long-term consequences after recovery from COVID-19 will allow for proper follow-up and management of the disease post recovery.

KEYWORDS
clinical, manifestations, coronavirus disease 2019, long term adverse effects, severe acute respiratory syndrome coronavirus 2

Abbreviations: 6MWD, 6 min walking distance; AKI, acute kidney injury; ALT, alanine aminotransferase; AST, aspartate aminotransferases; CMR, cardiovascular magnetic resonance; COVID-19, coronavirus disease 2019; DLCO, diffusing capacity of the lung for carbon monoxide; ECG, electrocardiogram; ESKD, end stage kidney disease; GGO, ground-glass opacity; ICU, intensive care unit; IL, interleukin; PIRP, prevention of progressive renal insufficiency; PNS, peripheral nervous system; SARS-CoV-2, syndrome coronavirus 2; TMPRSS2, transmembrane serine protease 2; TNF, tumor necrosis factor; TSH, thyroid-stimulating hormone.

Mohammad Zarei and Deepanwita Bose contributed equally to this work.

1 | INTRODUCTION

The Coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was reported in December 2019 after an outbreak of pneumonia in Wuhan, China. It belongs to the genus Betacoronavirus (subgenus Sarbecovirus).[1]

COVID-19 has spread globally, according to WHO[2] updates by end of July 2021 there were over 200 million confirmed patients infected and 4.2 million deaths with developing countries like India that underwent a massive second wave of infection, and other Southeast Asian countries being ravaged by the Delta strain, there will be many more recovered COVID-19 patients facing the long-term sequelae of infection. Thus, it is important to detail the long-term effects of COVID-19 infection following recovery to appropriately analyse, evaluate and manage any persistent or emerging health consequences.

This review will detail each COVID-19 affected organ and analyse the effects on it post-COVID-19 recovery with a major focus on long-term effects that patients might experience.

1.1 | COVID-19 recovery: long-term side effects and lingering symptoms

1.1.1 | Long-term effects on the pulmonary system during the path to recovery

ACE2 receptor is expressed in bronchial epithelium and type II pneumocytes. These cells are the major alveolar surfactant producer with immunoregulatory functions besides their function as stem cell progenitors of type I pneumocytes. The most clinically manifested complication is acute hypoxaemia, requiring ventilators.[3] The comparison to non-intensive care unit (ICU) and ICU admitted patients had higher levels of interleukin (IL-7), IL-10, GCSF, IP10 (CXCL10), MCP1 (CCL2), MIP1A (CCL3) and tumor necrosis factor (TNF)-α.[3]

A recent retrospective study on 57 patients, the impact of COVID-19 on pulmonary function in the early convalescence phase was investigated.[4] It collected the data 30 days after discharge and they reported that 54.3% had abnormal CT findings and 75.4% had an abnormal pulmonary function. Compared to the non-severe cases, severe infection cases showed diffusing capacity of the lung for carbon monoxide (DLCO) impairment (75.6% vs. 42.5%). They reported that in more than half of the COVID-19 patients there was an impaired diffusion capacity, lower muscle strength and lung imaging abnormalities.[4]

A 3-month post-discharge study on critical COVID-19 patients who were admitted to ICU showed 55% of patients had impaired lung function, exhibiting restrictive patterns, altered DLCO, 65% of patients reported 6 min walking distance (6MWD) below 80%. The study also reported obstructive sleep apnoea as a predictor of fibrosis on a 3-month chest computed tomography (CT) scan.[5]

Weerahandi et al.[6] studied a post-discharge health status and symptoms in patients with severe COVID-19, their study was conducted 30–40 days post-discharge on 152 participants. About 74% of participants reported shortness of breath. Physical and mental health deterioration was also reported in the post-COVID-19 participants.

In a study done on 55 COVID-19 survivors 3 months after recovery, it was reported that there were radiological (ground-glass opacity [GGO], consolidation and interstitial thickening) and physiological abnormalities in 70% of the patients. The measurements of D-dimers can be a potential marker for the prediction of impaired diffusion defect.[7] For the patients with higher D-dimer, pulmonary rehabilitation as a management strategy with necessary follow-ups are recommended.

A comprehensive multicentre clinical follow-up (clinical examination, laboratory testing, lung function analysis, electrocardiogram [ECG] and CT scans) evaluated 145 COVID-19 patients, 60 and 100 days after diagnosis. The group reported that 36% of patients reported dyspnoea, 21% reported reduced diffusion capacity and 41% of patients had symptoms 100 days after COVID-19 infection. Lung pathologies in 63% of patients were confirmed by CT scans, the majority of the patients had bilateral GGO and reticulation in the lower lung lobes. The study also concluded significant improvements in symptoms and cardiopulmonary conditions over time.[8]

Most recent reviews address that the pulmonary fibrosis[9,10] is the novel sequelae of the current pandemic and a follow-up treatment to be considered for pulmonary long COVID.[11]

1.1.2 | Long-term effects on the cardiovascular system during the path to recovery

Vascular injury or myocardial injury can occur by a direct viral infection and/or indirectly from immune responses to viral infection.

Acute clinical cardiovascular manifestations among hospitalised patients with COVID-19 are ventricular dysfunction, cardiogenic shock, myocardial ischaemia/infarction, acute heart failure, cardiac shock, stress cardiomyopathy, arrhythmias, venous thromboembolism and arterial thrombosis.[12] Indirect myocardial injury corresponds to the hypoxia-induced due to hypoxic respiratory failure causing small vessel ischaemia microvascular injury and thrombosis. Cardiac injury can be also caused due to the dysfunctional immune response reviewed in detail by Chung et al.[13]

The study by Lindner et al. evaluated the presence of SARS-CoV-2 in the myocardial tissues of 39 autopsy cases. SARS-CoV-2 was found in 24 of 39 patients, with a viral load above 1000 copies per microgram RNA in 16 patients. The expression of pro-inflammatory genes was increased in the 16 patients with high viral load.[14]

In a German cohort of 100 COVID-19 recovered patients, 78 patients were detected with cardiac involvement, of which 60 had

myocardial inflammation. They report that the recently recovered patients had lower left ventricular ejection fraction, higher left ventricular volumes, higher left ventricular mass and raised levels of T1 and T2. Highly sensitive troponin T was also detected (3 pg/mL or greater) in 71 patients which was significantly elevated in 5 patients (13.9 pg/mL). COVID-19 has evidence of Troponin being elevated which is an indicator of cardiac damage. Lymphatic inflammation was revealed by the endomyocardial biopsies from patients with the most abnormal cardiovascular magnetic resonance (CMR). The overall findings suggested that 25% have evidence of ongoing myocardial inflammation 3 months after diagnosis.[15] Huang et al.[16] evaluated cardiac involvement in 26 patients recovering from COVID-19, they conducted CMR examination. They reported 15 patients (58%) had abnormal CMR findings with myocardial oedema and late gadolinium enhancement and significantly elevated T1,T2 and extracellular volume.

In another study, 139 healthcare workers recovered from SARS-CoV-2 infection underwent a complete cardiac clinical assessment including ECG, CMR 10.4 (9.3-11) weeks after infection-like symptoms. The prevalence of pericarditis or myocarditis was found in up to 40% of patients. In 11% of patients, myocardial inflammation co-existed with pericarditis. ECG abnormalities were found in 50% of participants and CMR abnormalities in 75% of participants. Chest pain, dyspnoea or palpitations were observed in 42% of participants and Troponin was elevated in 1 participant.[17]

Long-term side effects of the SARS-CoV-2 infection on cardiovascular symptoms are still not completely known but as from the above studies, there are recent reviews on cardiovascular involvement during COVID-19 and its sequelae[18–20] suggesting the patients who recovered from the infection need follow-up and management strategies. More details are included in Table 1.

1.1.3 | Long-term effects on kidney during the path to recovery

Acute kidney injury (AKI) risks are associated with COVID-19. The virus could enter the kidney by invading podocytes first, then through tubular fluids accessing proximal tubules binding to ACE2. Distal nephron expresses transmembrane serine protease 2 (TMPRSS2) which primes the SARS-CoV-2 S protein.[30–34] Nugent et al. who studied the longitudinal kidney function post-hospital discharge and compared it in patients with and without SARS-CoV-2 infection. This retrospective study was conducted on 182 patients with COVID-19-associated AKI and 1430 AKI patients without COVID-19. COVID-19-associated AKI had a greater rate of eGFR decrease, develop more severe AKI, have greater dialysis requirement after discharge.[22]

In these studies, a sizable percentage did not recover to baseline serum creatinine at discharge it brings the importance of management and monitoring patients post-AKI to reduce any reoccurrence and mitigate long-term adverse consequences. Stockman et al.[23] followed 74 hospitalised patients and found a high rate of long-term recovery in survivors of COVID-19-associated AKI requiring kidney replacement therapy. Whilst another study with 115 ICU patients requiring AKI renal replacement therapy. By the end of follow-up, 51% of patients died whilst 41% had recovery. Stevens et al.[24] concluded that a high rate of renal recovery survivors of COVID-19 is associated with AKI requiring replacement therapy. Recent reviews described in detail the viral neuropathy[31] and pathophysiology of COVID-19 associated AKI.[32,35] Study conducted by Prevention of Progressive Renal Insufficiency (PIRP) project, concluded that COVID-19 infection and mortality in chronic non dialysis patients were higher than the general population.[33] Another study on patients with end stage kidney disease (ESKD) shows that death was 17% higher among patients with dialysis and 30% higher with patients with kidney transplant.[34]

1.1.4 | Long-term effects on the liver during the path to recovery

Elevated liver function tests have been reported with abnormal levels of aspartate aminotransferases (AST) and alanine aminotransferase (ALT).[36] Liver injury can also be related to drugs. Most patients with COVID-19 show mild liver damage and return to normal, targetted hepatoprotective therapy is necessary in patients with severe liver injury.[37]

Zhan et al. followed 192 SARS-CoV-2 hospitalised patients. Liver injury was detected in 39% at admission and 69.2% had a liver injury during hospitalisation. In case of severe COVID-19 hospitalisations, liver injury was observed in 86% of patients.[38] An et al.[25] did 2 months follow-up study of COVID-19 patients with liver recovery they studied 253 discharged patients in which 20.2% had chronic liver diseases before being infected with SARS-CoV-2. The study demonstrates that patients with the severe condition during hospitalisation with chronic liver conditions, such as hepatitis B, fatty liver, hepatic cyst and cholecystopathy had significantly higher probabilities to be diagnosed with liver injury compared to the non-severe cases. They also compared the serological hepatic condition of 163 COVID-19 patients at 14 days post-discharge with the healthy people. The level of total protein, albumin, albumin to globulin ratio (A/G) and AST/ALT in patients was significantly lower than in the control group. And the levels of ALT, gamma-glutamyl transferase and alkaline phosphatase levels were significantly higher. A total of 46 patients did the serologic tests at 40 days after discharge, the outlier ratio of total protein, albumin and globulin remain extremely low. The outlier ratio of ALT/AST and gamma-glutamyl transferase continues to decline and was less than 10%.[25] Multivariant metabotyping study by Holmes et al.[39] indicated that several parameters like taurine were elevated whilst glutamine/glutamate ration reduced in post COVID-19 infected patients compared to healthy controls. Emphasising the fact that for COVID-19 patients' appropriate interventions and liver function repair is necessary. The chronic liver conditions also carry greater risk and adverse risk and needs special interventions.[40]

TABLE 1 Summary of long-term side effects and lingering symptoms in different tissues and organs post COVID-19 recovery

Organ/Tissue	Study	Issues observed in recently recovered patients	References
Cardiovascular system	A German cohort of 100 COVID-19 recovered patients	Myocardial inflammation. Left ventricular ejection fraction was lower, higher left ventricular volumes, higher left ventricular mass and raised T1 and T2. High sensitive troponin T was also detected (3 pg/mL or greater) in 71 patients which were significantly elevated in five patients (13.9 pg/mL).	[15]
	Cohort of 139 healthcare workers recovered from SARS-CoV-2 infection	The prevalence of pericarditis or myocarditis was found in up to 40% of patients. In 11% of patients, myocardial inflammation co-existed with pericarditis. ECG abnormalities were found in 50% of participants, CMR abnormalities in 75% of participants. Chest pain, dyspnoea or palpitations were observed in 42% of participants. And troponin was elevated in 1 participant	[17]
Pulmonary system	Retrospective study with 57 patients the impact of COVID-19 on pulmonary function in the early convalescence phase	A 54.3% had abnormal CT findings, 75.4% had an abnormal pulmonary function. Compared to the non-severe cases, severe infection cases showed DLCO impairment (75.6% vs. 42.5%). Impaired diffusion capacity, lower muscle strength and lung imaging abnormalities	[4]
	Three-month post-discharge study on critical COVID-19 patients who were admitted to ICU	A 55% of patients had impaired lung function, exhibiting restrictive patterns, altered DLCO, 65% of patients reported 6MWDT below 80%. Obstructive sleep apnoea as a predictor of fibrosis on 3-month chest CT scan	[5]
	About 30 to 40 days post-discharge health status and symptoms in 152 patients with severe COVID-19	A 74% of participants reported shortness of breath	[6]
	Follow-up study of 55 COVID-19 survivors 3 months after recovery	Radiological and physiological abnormalities in 70% of the patients. The measurements of D-dimers can be a potential marker for the prediction of impaired diffusion defect	[7]
	Comprehensive multicentre clinical follow-up. Evaluated 145 COVID-19 patients 60 and 100 days after diagnosis	A 36% of patients reported dyspnoea, 21% reported reduced diffusion capacity and 41% of patients had symptoms 100 days after COVID-19 infection. Lung pathologies in 63% of patients were confirmed by CT scans, the majority of the patients had bilateral GGO, reticulation in the lower lung lobes	[8]
Renal system	Cohort of 5216 US veterans	32% had acute kidney injury (AKI), 12% of whom received kidney replacement therapy (KRT) and 47% did not recover to the baseline serum creatinine at discharge	[21]
	Longitudinal kidney function post-hospital discharge: Retrospective study was conducted on 182 patients with COVID-19-associated AKI	COVID-19-associated AKI had a greater rate of eGFR decrease, develop more severe AKI, have greater dialysis requirement after discharge	[22]
	Study on 74 hospitalised patients	Survivors of COVID-19-associated AKI requiring kidney replacement therapy	[23]
	Follow-up study of 115 ICU patients requiring AKI renal replacement therapy	High rate of renal recovery survivors of COVID-19 is associated with AKI requiring replacement therapy	[24]
Liver	Two months follow-up study of 253 COVID-19 discharged patients	Serological hepatic condition of 163 COVID-19 patients at day 14: The level of total protein, albumin, albumin to globulin ratio (A/G) and AST/ALT in patients were significantly lower than the control group. And the levels of ALT, gamma-glutamyl transferase and alkaline phosphatase levels were significantly higher. About 46 patients did the serologic tests at 40 days after discharge,	[25]

TABLE 1 (Continued)

Organ/Tissue	Study	Issues observed in recently recovered patients	References
		the outlier ratio of total protein, A/G remain extremely low. The outlier ratio of ALT/AST and gamma-glutamyl transferase continues to decline and was less than 10%	
Hormone: estrogen	Study with 237 patients: Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age	A 20% of the women reported decreased volume whilst 19% had a prolonged cycle. The average sex hormone concentration of women of childbearing age with COVID-19 was not different with age-matched controls	26
Hormone: testicular function	Effects of SARS-CoV-2 infection on male sex-related hormones in 39 recovering patients	Testosterone, follicle-stimulating hormone and luteinising hormone levels were normal in patients recovered from COVID-19	27
Endocrine system	Retrospective study of thyroid function analysis with 50 COVID-19 infected patients has been done in comparison to healthy control.	The severity of the COVID-19 infection lowers the thyroid hormone and thyroid-stimulating hormone (TSH) and total triiodothyronine levels. A 53% of the patients had lower TSH. After recovery: thyroid hormones and thyroid function was similar to healthy controls	28
Neurological systems	Retrospective cohort study had 236,379 COVID-19 survivors: 6-months neurological and psychiatric outcome	A 33.62% had a neurological or psychiatric diagnosis. The patients requiring intensive therapy unit treatment, the neurological or psychiatric diagnosis was 46.2%.	29

1.1.5 | Fertility and COVID-19

COVID-19 was not just age bias but also sex bias towards severe disease.[41] A meta-analysis on more than 3 million reported global cases conformed that male COVID-19 infected patients had 3 times the odds of requiring the intensive treatment unit admission and higher odds of death compared to women.[42]

In a recent in vitro study, it was shown that 17β-estradiol can reduce SARS-CoV-2 infection, the group also showed that TMPRSS2 gene expression can be reduced by estrogen after SARS-Cov-2 infection, TMPRSS2 is involved in COVID-19 infectiveness capacity.[43]

In a meta-data study with 68,466 global cases, it was observed that there was a higher fatalities rate in males compared to aged-matched females. They also observed that premenopausal women are disproportionately more infected than men, but they do not become seriously ill as shown with a low fatality rate.[44]

A randomised interventional clinical trial with 110 participants is currently in phase II clinical trial of estradiol to reduce the severity of COVID-19 infection in patients with positive infection or presumptive positive infection (ClinicalTrials.gov Identifier: NCT04359329). The trial hypothesises that a short 7-day transdermal patch applied to the infected patients will be safe and reduce severe symptoms in men and older women, the patients will be followed for a time course and disease outcome.

A study by Li et al. analysed sex hormone and menstruation in 237 COVID-19 women.[26] About 20% of women reported decreased volume, whereas 19% had a prolonged cycle. To access the effects of sex-related testicular function in COVID-19 recovering patients Xu et al.[27] followed 39 infected patients and concluded (testosterone, follicle-stimulating hormone and luteinising hormone levels) were normal in patients recovered from COVID-19.

1.1.6 | COVID-19 effects on the endocrine system

A retrospective study of thyroid function analysis with 50 COVID-19 infected patients has been done in comparison to healthy control. The severity of the COVID-19 infection lowers the thyroid hormone and thyroid-stimulating hormone (TSH) and total triiodothyronine levels. About 53% of the patients had lower TSH. After recovery, there were no significant differences were observed in the thyroid functions TSH, total triiodothyronine, total thyroxin, free triiodothyronine and free thyroxin.[28]

COVID-19 induced new onset of diabetes mellitus,[45,46] thus, enhancing the need for proactive monitoring of endocrine functions in COVID-19 patients. Detailed review of evolution of knowledge and care for patients with endocrine dysfunction, or new onset of endocrine diseases suggests follow-up and strategies to implement better solutions to address the sequelae of COVID-19.[47,48]

1.1.7 | Effects on nervous system during the path to recovery

Peripheral nervous system (PNS) manifestations have also been reported including neuropathic pain, skeletal muscle injury and hyperCKaemia, Guillain-Barré syndrome, cranial polyneuritis,

neuromuscular junction disorders, neuro-ophthalmological disorders, neurosensory hearing loss and dysautonomia.[49] Most recent reviews give more detailed mechanisms and complications of the Neuro COVID.[49–52]

A retrospective cohort study of 6-month neurological and psychiatric outcome in 236,379 COVID-19 survivors along with 2 control cohort of 105,579 patients diagnosed with influenza and 236,038 patients diagnosed with respiratory tract infection has been recently published.[29] The COVID-19 cohort was further divided into 46,302 hospitalised and 190,977 non-hospitalised patients. Among hospitalised patients, 8945 subjects received intensive therapy unit treatment and 6229 patients were diagnosed with encephalopathy. In this cohort, overall 33.62% of patients had a neurological or psychiatric manifestation; and patients requiring intensive therapy unit treatment for the neurological or psychiatric diagnosis were 46.2%.

The severity of the COVID-19 had a clear effect on the subsequent neurological diagnosis. The risk of cerebrovascular events (ischaemic stroke and intracranial haemorrhage) was elevated after COVID-19. The study also found an association between COVID-19 and dementia within 6 months of infection with 2.66% in the COVID-19 cohort and 4.72% who had encephalopathy. The study presented significant rates of neurological and psychiatric diagnosis over the subsequent 6 months. These findings highlight the follow-up of patients who were admitted to ICU or had encephalopathy.[29]

1.1.8 | Long-term effects on mental health during the path to recovery

Concerns have been raised regarding mental health disorders following COVID-19. In a study by Garrigues et al.[53] after a mean of 110.9 days, loss of memory (34%), concentration disorder (30.8%), sleep disorder (28%) and attention disorder (26.7%) were the most frequent mental health disorders.

In a large sample size study in USA, COVID-19 were associated with increased rate of psychiatric disease onset in 14 to 90 days follow-up especially for anxiety disorders, insomnia and dementia.[54] The incidence of first mood anxiety or psychotic disorder in a 6-month following a COVID-19 diagnosis was 8.63% followed by anxiety disorder (7.11%), mood disorder (4.22%) and psychotic disorder (0.42%).[29]

1.1.9 | COVID-19 recovery of cancer patients

A prospective study by Lee et al. with 800 cancer patients with COVID-19 infection reported that 52% of patients had mild COVID-19, whereas 28% of patients died. The risk factors associated with risk of death were significantly associated with old age, males, co-morbidity factors like hypertension and cardiovascular disease. There was no change in the effect of mortality on patients who received cytotoxic chemotherapy, immunotherapy, hormonal therapy, targetted therapy or radiotherapy.[55] Moreover, Yang et al.[56] found that patients with hematological malignancies had faster disease progression, more frequent hospital admission for chemotherapy and increased susceptibility to bacterial infection compared to patients with solid tumors. Also, patients who had received recent anti-tumor treatment may experience higher risk of severe condition of COVID-19[57] and this pandemic have adverse impact on cancer survivors and their family.[58]

1.1.10 | COVID-19 and mucormycosis

Initially, it was debated whether a person taking immunosuppressants, such as corticosteroids and monoclonal antibodies, will be at higher risk for COVID-19 or whether the immunosuppressive state would cause a more severe COVID-19 disease. However, immunosuppressants are currently continued unless the patients are at greater risk of severe COVID-19 infection or are on high-dose corticosteroid therapy.[59]

Moorthy et al. found that on 18 COVID-19 patients, 16 patients received steroids for COVID-19 treatment and 16 patients were diabetic (of whom 15 patients who were diabetics received steroids for COVID-19 treatment). Loss of vision was noted in 12 of the 18 patients and 7 of them underwent orbital exenteration. The fungi noted were mucormycosis in 16 patients, aspergillosis in 1 patient and mixed fungal infection in 1 patient. About 11 of the patients survived, 6 died and 1 was lost to follow-up. There was a significantly higher incidence of diabetes ($p = 0.03$) amongst these cohorts of patients who were COVID-19 positive with mucormycosis. A significantly higher number of patients were administered steroids at some point during the treatment.[60]

In a study by Szarpak et al. it was demonstrated that opportunistic infections are especially common in patients, who apart from the current COVID-19 disease, have other comorbidities, such as diabetes or chronic obstructive pulmonary disease (COPD). An additional factor contributing to exposure to co-infections is treatment with mechanical ventilation, antibiotic therapy, monoclonal antibodies and the use of corticosteroids. Especially corticosteroids are commonly used to treat a serious form of COVID-19 disease and reduce the damage caused by the own body's immune system during SARS-CoV-2 infection. Unfortunately, corticosteroids are also immunosuppressive and increase blood sugar levels in both diabetic and non-diabetic patients. Both of these effects are now believed to contribute to mucormycosis. The signs of mucormycosis are sinus pain, nasal obstruction on 1 side of the face, 1-sided headache, swelling or numbness, toothache and loosening of the teeth and must be carefully considered in all COVID-19 patients. Mucormycosis usually leads to discolouration or reddening of the nose, blurred or double vision, chest pain, coughing up blood and difficulty breathing which is an additional very heavy burden for COVID-19 patients. Diabetes, being closely related to mucormycosis infection and a much higher risk of SARS-CoV-2 infection, may have tragic consequences for the local community.[61]

2 | POST-COVID-19 SYNDROME CONSIDERATION

Post COVID-19 syndrome signs and symptoms that develop during or after the SARS-CoV-2 infection present for more than 12 weeks and not attributable to alternative diagnosis.[62]

Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations and are the main target population for the intervention of long-term recovery.[63]

The clusters of symptoms that persist longest include a combination of neurological/cognitive and systemic symptoms. The reduced work capacity because of cognitive dysfunction, in addition to other debilitating symptoms, translated into the loss of hours, jobs and ability to work relative to pre-illness levels.[64]

Sequelae in the respiratory system, as well as several other sequelae that include nervous system and neurocognitive disorders, mental health disorders, metabolic disorders, cardiovascular disorders, gastrointestinal disorders, malaise, fatigue, musculoskeletal pain and anaemia.[65]

The absolute risk of severe post-acute complications after SARS-CoV-2 infection not requiring hospital admission is low. However, increases in visits to general practitioners and outpatient hospital visits could indicate COVID-19 sequelae.[66]

3 | CONCLUDING REMARKS AND FUTURE PERSPECTIVES

SARS-CoV-2 has been a pan-systemic disease affecting multi-organ beyond the acute phase of infection and it is yet to be understood. Approaching to a COVID-19 patient with general considerations, some organs are needed to be closely and immediately assessed when the diagnosis of infection is made, such as kidneys for AKI and cardiac system for myocarditis as well as other systems for later and more persistent effects, such as hormonal imbalances, neuropsychological complications and respiratory insufficiencies. Whilst considering persistent symptoms and effects of the post-COVID-19 syndrome (or as called 'long-COVID') special attention must be paid to patients with underlying co-morbidities. Furthermore, future studies are needed to provide an accurate guideline for approaching this issue as well as a detailed understanding of its pathophysiology.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Mohammad Zarei and Mehdi Ghasemi conceptualised, edited and supervised the study. Mohammad Zarei, Deepanwita Bose, Masoud Nouri-Vaskeh, Vida Tajiknia, Ramin Zand and Mehdi Ghasemi wrote the first draft and revised the manuscript. Mohammad Zarei, Deepanwita Bose, Masoud Nouri-Vaskeh and Vida Tajiknia involved in investigation. All authors reviewed and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in the cited reference.

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