



**ORIGINAL RESEARCH PAPER**

**General Medicine**

**RECOVERY COMPLICATION IN COVID - 19 SURVIVORSHIP: A NEW CHALLENGE**

**KEY WORDS:** pandemic, complication, COVID-19

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**ABSTRACT**

The growing population of COVID-19 survivors in second wave represents a clear challenge to clinicians and researchers to look beyond the search for a cure and to address the multifaceted needs of those living with and beyond diagnosis. Common complications that disrupt the psychosocial, physical aspects of life and multi systemic complication for adult. COVID-19 survivors after primary treatment include: fatigue, neurological, cardiovascular, hepatic impairment, ocular, dermatological manifestation, Oral manifestation, acute pancreatitis, musculoskeletal, renal and reproductive system complications.

Psychosocial interventions, particularly group-based interventions, physical activity programs, continuous monitoring and prompt treatment have shown great promise in improving these outcomes. Future research will identify even better-targeted, more efficacious, and more cost effective medication and vaccination policy to counter COVID-19 outcomes. Healthcare providers must realize that they serve as vital gatekeepers to services that will help optimize outcomes. Addressing these issues in the post-treatment period represents the new challenge to supportive care.

**INTRODUCTION**

The current coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has become a major public health crisis over the past few months.<sup>(1)</sup> Now we are in the second stage of pandemic and it is causing more widespread and potent infection resulting in multi systemic complication, prolonged hospital stay of moderate to severe type of cases and increased death rate. This growing population of COVID-19 survivors represents a clear challenge to clinicians and researchers to look beyond the search for a cure and to address the needs of and provide hope for a valued future to those after recovering from this pandemic. Although they are relieved to be ending treatment, many survivors report being unprepared to manage the long-term or chronic effects of COVID-19 and its treatment and worry about its adverse late effects, problems that may arise months or years later. Indeed, survivors are telling us that being disease-free does not mean being free of the disease—or as one survivor said, “it is not over when it’s over.”

The interrelated web of adverse medical, psychosocial, and economic issues faced by COVID-19 survivors carries great potential for physical and psychological morbidity. In this article, we review some of the more common sequelae that disrupt the psychosocial aspects of life for adult COVID-19 survivors after the conclusion of treatment. A full review of the longterm and late physical effects of COVID-19 and its treatment are beyond the scope of this article .

**COVID-19 RECOVERY COMPLICATIONS**

In the early months of the COVID-19 pandemic, doctors struggled to keep patients breathing, and focused mainly on treating damage to the lungs and circulatory system.

But even then, evidence for other systemic effects was accumulating. There are many complications in different systems of body after recovery of COVID-19.

**Fatigue**

One of the most common effects of COVID-19 is fatigue. Described as a persistent lack of energy, or weariness that impairs daily functioning and mood, COVID related fatigue is usually not alleviated by additional rest. Work by some researchers suggests that COVID related fatigue may be linked to pro-inflammatory cytokine processes and also associated with altered patterns of diurnal cortisol among affected individual. Among the most promising interventions

to address this distressing symptom are those that include some form of physical activity and positivity.

**Neurological manifestations**

Numerous neurological abnormalities have been described in patients with COVID-19. These involve the central and peripheral nervous system, range from mild to fatal, and can occur in patients with SARS CoV- 2 infection at any stage. Asymptomatic SARS CoV- 2 infection neurological symptoms are malaise, dizziness, headache, and loss of smell and taste.

Some people hospitalized with COVID-19 were experiencing delirium: they were confused, disorientated and agitated. A group in Japan published the first report of someone with COVID-19 who had swelling and inflammation in brain tissues. Another report described a patient with deterioration of myelin, a fatty coating that protects neurons and is irreversibly damaged in neurodegenerative diseases such as multiple sclerosis. The list now includes ischemic stroke, brain haemorrhage, encephalitis and memory loss. A group also analyzed clinical details for 125 people in the United Kingdom with COVID-19 who had neurological or psychiatric effects. Of these, 62% had experienced damage to the brain's blood supply, such as strokes and haemorrhages, and 31% had altered mental states, such as confusion or prolonged unconsciousness — sometimes accompanied by encephalitis, the swelling of brain tissue. Ten people who had altered mental states developed psychosis. Some of the worst-affected patients had only mild respiratory symptoms. “This was the brain being hit as their main disease,” says Zandi. SARS-CoV-2 could infect neurons in these organoids, killing some and reducing the formation of synapses between them. Alterations in mental status (confusion, disorientation, agitation, and somnolence), collectively defined as encephalopathy, have been consistently reported the neurological manifestations of COVID-19 constitute a major public health challenge not only for the acute effects on the brain, but also for the long-term harm to brain health that may ensue.<sup>(2)</sup>

**Cardiovascular Abnormality**

The manifestation of COVID-19 on the cardiovascular system include hypertension, acute myocarditis, ACS, NSTEMI, unstable angina, Arrhythmias (SVT/VT/VF), Heart failure with reduced and preserved ejection fraction, cardiogenic shock, Stress-induced cardiomyopathy, acute pericarditis with or without tamponade.

Coagulation abnormalities and thrombosis are also included

in CVS abnormalities. Thromboembolic complications: arterial thromboembolism, deep vein thrombosis, intracardiac thrombus, microvascular thrombi, pulmonary embolism, stroke.<sup>(3,4)</sup>

### Hepatic impairment

Hepatic involvement in COVID-19 could be related to the direct cytopathic effect of the virus, an uncontrolled immune reaction, sepsis or drug-induced liver injury. 2–11% of patients with COVID-19 have been reported to have underlying chronic liver disease. 14–53% of patients with COVID-19 have been reported to develop some form of hepatic dysfunction. Hepatic dysfunction was significantly more frequent in critically ill patients and was associated with poor outcome.<sup>(5,6)</sup>

### Ocular Finding

SARS-CoV-2 RNA has been found in tears of the infected patients, and reports suggest that the ocular surface could serve as a portal of entry and a reservoir for viral transmission.

Clinically, COVID-19 has been associated with mild conjunctivitis, which can be the first and only symptom of the disease. Subtle retinal changes like hyperreflective lesions in the inner layers on optical coherence tomography (OCT), cotton-wool spots, and microhemorrhages have also been reported. In addition, COVID-19 has been associated with an increased incidence of systemic diseases like diabetes mellitus and Kawasaki disease, which are particularly relevant for ophthalmologists due to their potentially severe ocular manifestations.<sup>(7)</sup>

### Dermatological Manifestation

The polymorphic nature of COVID-19-associated cutaneous manifestations include urticarial rash, confluent erythematous/maculopapular/morbilliform rash, papulovesicular exanthem, chilblain-like acral pattern, livedo reticularis/racemosa-like pattern, purpuric “vasculitic” pattern.

Urticarial rash predominantly has itching involving the trunk and limbs; angioedema may also rarely occur. Intermediate severity Confluent erythematous/ maculopapular/ morbilliform rash Generalized, symmetrical lesions starting from the trunk with centrifugal progression; purpuric lesions may coexist from the onset or develop during the course of the skin eruption.

Papulovesicular exanthem has widespread polymorphic pattern consisting of small papules, vesicles and pustules of different sizes or localized pattern consisting of papulovesicular lesions, usually involving the mid chest/ upper abdominal region or the back. Chilblain-like pattern erythematous-violaceous patches or plaques predominantly involving the feet or, to a lesser extent, hands. Pain/burning sensation as well as pruritus were commonly reported symptoms. Livedo reticularis-like lesions: mild, transient, symmetrical, lace-like, dusky patches forming complete rings surrounding a pale center. Livedo racemosa-like lesions: large, irregular and asymmetrical violaceous annular lesions frequently described in patients with severe coagulopathy. Purpuric “vasculitic” pattern may be generalized, arranged in an acral distribution or localized in the intertriginous regions. Purpuric elements may evolve into hemorrhagic blisters, possibly leading to necrotic-ulcerative lesions Several skin conditions have emerged, mainly as a result of prolonged contact with personal protective equipment and excessive personal hygiene. Pressure injury, contact dermatitis, itch, pressure urticaria, and exacerbation of preexisting skin diseases, including seborrheic dermatitis and acne, have been described.<sup>(8,9)</sup>

### Oral Manifestation

Dysgeusia is the first recognized oral symptom of novel

coronavirus disease. Oral manifestations included ulcer, erosion, bulla, vesicle, pustule, fissured or depapillated tongue, macule, papule, plaque, pigmentation, halitosis, whitish areas, hemorrhagic crust, necrosis, petechiae, swelling, erythema, and spontaneous bleeding.

The most common sites of involvement in tongue (38%), labial mucosa (26%), and palate (22%). Oral lesions were nearly equal in both genders (49% female and 51% male). Patients with older age and higher severity of COVID-19 disease had more widespread and severe oral lesions. Lack of oral hygiene, opportunistic infections, stress, immunosuppression, vasculitis, and hyper-inflammatory response secondary to COVID-19 are the most important predisposing factors for onset of oral lesions that healed between 3 and 28 days after appearance. Different types of therapies including chlorhexine mouthwash, nystatin, oral fluconazole, topical or systemic corticosteroids, systemic antibiotics, systemic acyclovir, artificial saliva, and photobiomodulation therapy (PBMT) were prescribed for oral lesions depends on the etiology.<sup>(10,11)</sup>

### Pancreas (Acute Pancreatitis)

Multiple reports have been published citing that gastrointestinal symptoms such as pancreatitis are common in patients with COVID-19 infection. It has also been found that the ACE2 receptor of SARS-CoV-2 is expressed more in the pancreas than the lungs. Despite this, little attention has been paid to the extent and details of pancreatic injury caused by COVID-19. Lack of awareness regarding the COVID-19 status of patients presenting with pancreatitis may delay interventions to manage complications of pancreatitis such as necrosis. Patients with pancreatic injury had a higher incidence of loss of appetite and diarrhea. Potential mild pancreatic injury patterns are present in patients with COVID-19 pneumonia, and these may be related to direct viral involvement of the pancreas.<sup>(12)</sup>

### Musculoskeletal Consequences

Musculoskeletal symptoms such as fatigue, myalgia and arthralgia are common COVID-19 symptoms, but their prevalence has not yet been systematically investigated. Myalgia has been frequently reported in COVID-19 patients. Several case reports have described myositis and rhabdomyolysis in COVID-19 patients, both as a late complication and presenting symptom. Myositis broadly refers to inflammation of muscles and is associated with many viral infections.

Long-term muscular sequelae of COVID-19 include sarcopenia and cachexia which have been described in COVID-19 patients with prolonged illness. Sarcopenia is typically associated with aging although other contributing factors include inactivity and poor nutrition Cachexia secondary to chronic illness. MR imaging findings of muscle atrophy, are seen in sarcopenia and cachexia, Arthralgia has been reported as a symptom of COVID-19, Various chronic rheumatologic diseases triggered by SARS-CoV-2 have been reported, including systemic lupus erythematosus, dermatomyositis, Graves' disease, rheumatoid arthritis, and psoriatic spondyloarthritis. Critical illness, corticosteroid treatment and virus-induced coagulopathy may contribute to the development of osteoporosis and osteonecrosis.<sup>(13,14)</sup>

### Renal Complications

Previously, it was thought that the kidneys are not targeted by viruses. The view has changed now. kidney infections by viruses can be caused in many ways. When trapped in glomeruli, viruses accumulate and multiply, and may cause direct damage to the host tissue. Likewise, tissue antigens can indirectly stimulate responses, and as a local stimulant, viruses can make the kidneys susceptible to bacterial invasion. Indeed, any infection in the body can activate

viruses present in the kidneys, and thus cause glomerulonephritis and pyelonephritis by a viral infection.

Recent findings have suggested that hematuria and proteinuria could result in during COVID-19 disease, whereas some patients might exert signs of Acute kidney injury. Excessive activation of these receptors is associated with many kidney diseases including ischemic kidney damage, AKI, end-stage renal failure and acute tubulointerstitial nephritis.<sup>(15,16)</sup>

### Reproductive System Complication

Numerous studies shows that COVID-19 affects male and female reproductive system.

COVID-19 could impair female fertility by binding to ACE2, which is widely expressed in ovaries, uterus, vagina and placenta. Ovarian reserve is a key determinant of female fertility. Diminished ovarian reserve could affect fecundity by reducing egg quality. A severe acute illness may alter the hypothalamic-pituitary gonadal (HPG) axis function, decreasing the endogenous production of Estrogens and Progesterone.

Decrease in sperm motility examination of the testicular and epididymal tissues of deceased COVID-19 patients revealed the presence of interstitial edema congestion, red blood cell exudation, and obvious T-lymphocytes (CD3+) infiltration around blood vessels. These are all evidence indicated an inflammatory response in testes (orchitis) and epididymides (epididymitis). These findings indicate that the male reproductive system could be vulnerable in COVID-19, as demonstrated by spermatogenic dysfunction with a significant decrease in sperm counts in COVID-19 patients. This implies to attach importance of applying further care in reproductive health in patients infected with COVID-19.<sup>(17,18)</sup>

### FUTURE DIRECTION

Despite the considerable research identifying the multifaceted effects of covid, there are many obvious gaps in our knowledge. Future work must identify the complex interplay between psychosocial and physical sequelae of covid in survivors from diverse race/ ethnic and socioeconomic backgrounds, in elderly populations. Future efforts should identify those survivors who are doing well to understand the factors that might promote positive adaptation, rehabilitation, post-traumatic growth, and continued employment. More attention to the promotion of healthy lifestyle behaviors in survivorship, including how healthy behaviors may influence COVID-19 co-morbidities and complications.

The practice of post covid care is also changing. New therapeutic agents are being developed and tested and the psychosocial impact of these new agents will need to be determined. Ongoing national efforts to widely implement screening, various SOP protocols and COVID-19 testing for populations will help bring attention to those in need of help, necessitating quick and appropriate referrals care. Clinical attention must be paid to treating the interrelated web of physical, psychological, and social covid-related symptoms in the acute term, before these symptoms develop into more severe persistent problems.

### CONCLUSION

Treating covid-19 alone is no longer enough, we now must also focus on the goal of helping those living with and beyond a covid-19 diagnosis lead full, productive, and meaningful lives.

This article reviewed number of challenges faced by covid-19 survivors in treatment as well as post-treatment period. As they transit to recovery, survivors want to know which complication to follow, which symptoms to monitor, when to

be alert to changes in health, what will be their "new normal". Addressing these issues in the post-treatment period represents the new challenge to supportive care.

### REFERENCES

1. Tondon Prakash N. COVID-19: Impact on health of people and wealth of nations. *Indian J Med Res* 151, February and March 2020:121-123.
2. Costantino Iadecola, Josef Anrather, Hooman Kamel. Effects of COVID-19 on the Nervous System. *Cell* 183, October 1, 2020:16-27.
3. Shaha KB, Manandhar DN, Cho JR, et al. COVID-19 and the heart: what we have learnt so far. *Postgrad Med J* 2020;27 Aprail 2021:1-12.
4. Masataka Nishiga et al. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nature*, volume 17; September 2020:543-558.
5. Schaefer et al. Interrelationship Between Coronavirus Infection and Liver Disease. *Clinical Liver Disease*, VOL 15, NO 5, MAY 2020:175-180.
6. Jothimani Dinesh, Venugopal Radhika et al. COVID-19 and the liver. *Journal of Hepatology*, 2020; vol. 73:1231-1240.
7. Bertoli F, Veritti D, et al. Ocular Findings in COVID-19 Patients: A Review of Direct Manifestations and Indirect Effects on the Eye. *Journal of Ophthalmology*, Volume 2020:1-9.
8. Razvigor Darienski, Nikolai Tsankov. COVID-19 pandemic and the skin: what should dermatologists know? *Clinics in Dermatology* (2020) 38, 785-787.
9. Genovese, Moltrasio, Berti, Marzano. Skin Manifestations Associated with COVID-19: Current Knowledge and Future Perspectives. *Dermatology* 2021;237:1-12.
10. Shamsoddin, E.; DeTora, L.M.; Tovani-Palone, M.R.; Bierer, B.E. Dental Care in Times of the COVID-19 Pandemic: A Review. *Med. Sci.* 2021, 9, 13. <https://doi.org/10.3390/medsci9010013>
11. Iranmanesh B Khalili M et al. Oral manifestations of COVID-19 disease: A review article. *Dermatologic Therapy*. <https://doi.org/10.1111/dth.14578>.
12. Kumaran NK, Karmakar BK, Taylor OM. *BMJ Case Rep* 2020;13:e237903. doi:10.1136/bcr-2020-237903.
13. Nathaniel P. Disser, Andrea J. De Micheli et al. Musculoskeletal Consequences of COVID-19. *The Journal Of Bone & Joint Surgery*. Jbjs. Org; Volume 102-A D Number 14 D July 15, 2020:1197-1204.
14. Cipollaro et al. Musculoskeletal symptoms in SARS-CoV-2 (COVID-19) patients. *Journal of Orthopaedic Surgery and Research* (2020) 15:178. <https://doi.org/10.1186/s13018-020-01702-w>.
15. Keivani Boroujeni E, Kellner SJ, Pezeshgi A. COVID-19 and kidney: a mini-review on current concepts and new data. *J Nephropharmacol.* 2021;10(1): e01. DOI:10.34172/npj.2021.01.
16. H. Askari et al. Kidney diseases and COVID-19 infection: causes and effect, supportive therapeutics and nutritional perspectives. *Heliyon* 7 (2021) e06008. <https://doi.org/10.1016/j.heliyon.2021.e06008>.
17. Li F, Lu H, Zhang Q, et al. Impact of COVID-19 on female fertility: a systematic review and meta-analysis protocol. *BMJ Open* 2021;11:e045524. doi:10.1136/bmjopen-2020-045524.
18. H. Li et al. Impaired spermatogenesis in COVID-19 patients. *EClinicalMedicine* 28 (2020) 100604. <https://doi.org/10.1016/j.eclinm.2020.100604>.