

Review Article

Potential long term adverse health outcomes of COVID-19

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Abstract:

The coronavirus disease 2019(COVID-19) pandemic poses an extraordinary challenges to patients, communities and overall health care systems. It has resulted in millions of people infected worldwide and has indirectly devastated even more individuals with prolonged post-infectious symptoms. The burden of survivors having post-COVID symptoms is likely to be huge. Multidisciplinary post-COVID-19 clinics are now playing a pivotal role addressing both persistent symptoms and potential long term sequelae. In this review, we tried to summarize the adverse health outcomes based on current evidences, assess the potential risk of long-term complications and make certain recommendations.

Key Words: COVID-19, post-COVID symptoms, health outcomes.

Introduction:

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has affected more than 215 countries and territories, with over 10 crore cases and 24 lac deaths worldwide as of February 2021¹. The virus was confirmed to have spread to Bangladesh in March 2020 and since then more than 5 lac cases have been detected so far with near about 8 thousand deaths¹. The global community is now concerned about COVID-19 vaccines and acute treatment which is very much reasonable, but at the same time it is equally important to assess and evaluate the long-term health outcomes of COVID-19 survivors. Despite the fact that there is increasing number of recovered cases, concern is rising regarding the post-COVID sequelae. Until now, a lot of information could be collected about the acute infective process of SARS-CoV-2. However, there has been growing concern regarding long term health outcomes particularly on immunological and respiratory systems. Although the greatest effort must be made on managing the ongoing pandemic, but effective multidisciplinary collaboration must address persistent symptoms to minimize long-term pulmonary and also non-pulmonary complications. In this review, we tried to figure out the features of acute disease that may have an impact on post-COVID-19 period, and explore the potential post-COVID sequelae.

Brief literature review:

Approximately 10% of patients with COVID-19 experience different symptoms which persist beyond the acute illness (4weeks)². We call it "Long COVID". In December 2020, the

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National Institute for Health and Care Excellence (NICE) in collaboration with the Scottish Intercollegiate Guidelines Network (SIGN) and the Royal College of General Practitioners (RCGP) published a guideline for clinicians to make recommendations about the long-term effects of COVID-19³. In this guideline, following definitions are used:

- **Acute COVID-19:** signs and symptoms of COVID-19 for up to 4 weeks.
- **Ongoing symptomatic COVID-19:** signs and symptoms of COVID-19 from 4 to 12 weeks.
- **Post-COVID-19 syndrome:** signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis.

People with long COVID seems to fall into three categories : a) history of previous hospital admission with COVID-19 including those who required critical care support at that time, b) individuals not hospitalized before but experience persistent respiratory symptoms following COVID-19, and c) patients with preexisting lung disease complicated by COVID-19.

Current Centers for Disease Control and Prevention (CDC) guidelines have identified several possible risk factors responsible for severe disease and complications: old age, obesity, COPD,CKD, malignancy, type 2 DM, serious heart disease, immunocompromised cases⁴.

Potential Post-COVID-19 Outcomes

Patients with long COVID experience a confusing array of fluctuating and persistent symptoms(Figure1) the cause of which is still not fully explained but probably involves different mechanisms of inflammatory and vasculitic nature. The clinical trajectory is based on emerging data in COVID survivors, evidence from prior established coronavirus outbreaks, complications of other respiratory and zoonotic coronavirus outbreaks.

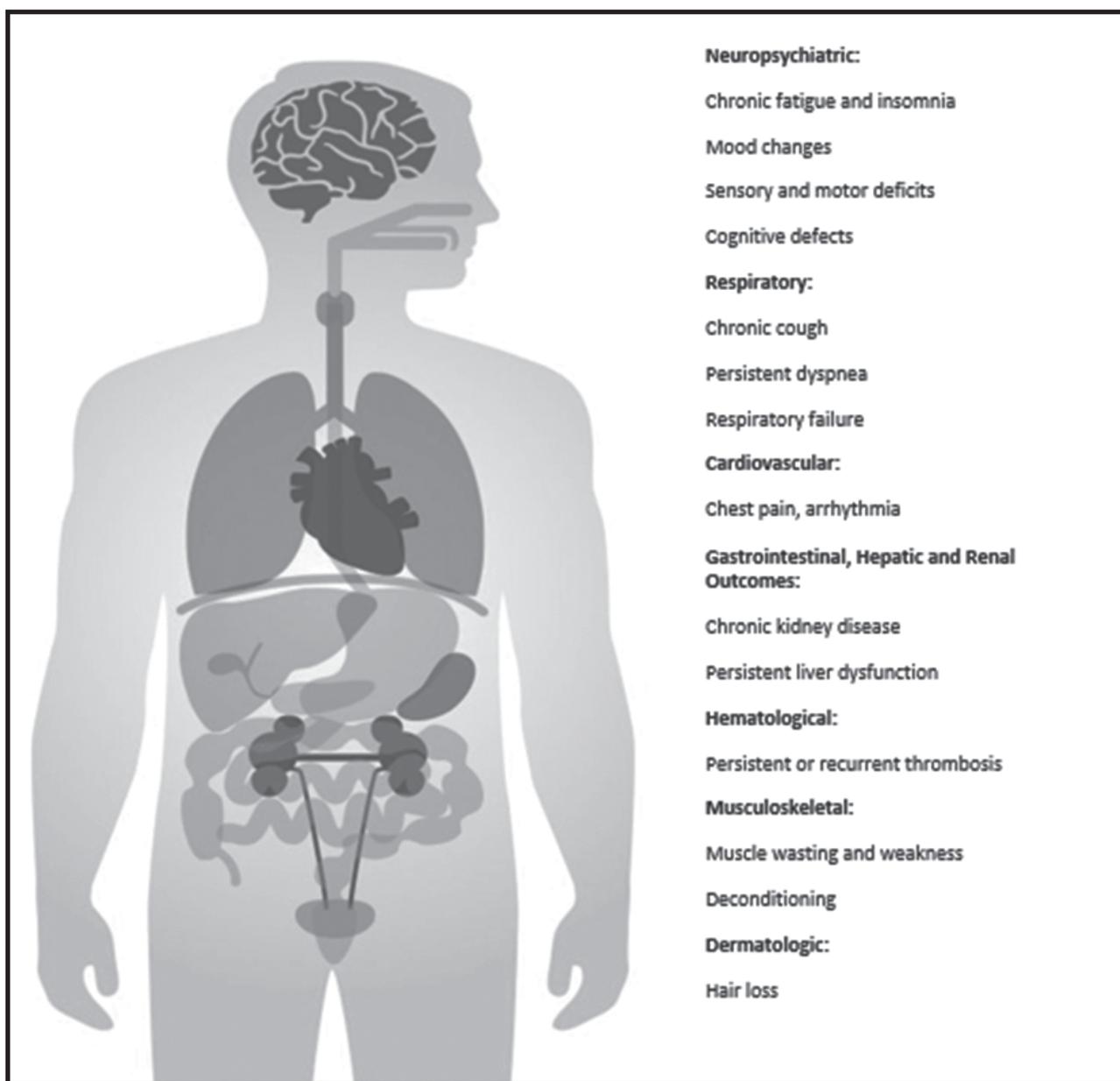


Figure 1: Pulmonary and Extra-pulmonary post-COVID symptoms and end-organ sequelae. (Adapted from Lutchmansingh et al⁴)

The lungs being considered as the most common organ of serious outcome and major cause of mortality. People who survive the acute phase remain at risk of chronic respiratory complications, like- post-viral lung fibrosis, pulmonary thromboembolism, and functional impairment. Available studies have shown that, residual chest CT abnormalities and impairment of carbon monoxide diffusing capacity persist even 4-6 weeks after the onset of disease^{5,6}. Researchers have stated that a subset of people may develop permanent lung fibrosis and another subset may develop secondary organizing pneumonia⁷⁻¹⁰. Limited autopsy studies have revealed diffuse alveolar damage, fibrosis, and evidence of widespread microthrombi which in the long run may increase the risk of

chronic thromboembolic pulmonary hypertension¹¹⁻¹³. Further studies are required to monitor the progression of residual lung damage already observed on imaging and most importantly to quantify the impact on health related quality of life, exercise capacity and lung function. Moreover, the survivors with persistent respiratory impairments are needed to be further explored to determine the factors, particularly the use of anti-inflammatory and immunomodulatory agents, antivirals, advanced life support.

The heightened pro-inflammatory and pro-coagulant activity can be persistent even after recovery that may lead to adverse cerebrovascular and cardiovascular outcomes. Myocardial injury is a frequently reported cardiovascular complications of COVID-19. Longitudinal follow-up of COVID-19 survivors is very much required in this regard.

Lastly, COVID-19 survivors requiring intensive care are likely to develop post-intensive care syndrome (PICS). PICS includes physical, mental and cognitive impairment after any illness of critical nature¹⁴. Worldwide COVID-19 pandemic is undoubtedly having a profound impact on mental health of the survivors. This is possibly directly related to hypoxic brain damage due to viral infection or indirectly due to immunological response¹⁵. A meta-analysis of SARS, MERS and COVID-19 survivors demonstrated increased prevalence of PTSD (post-traumatic stress disorder), anxiety, depression and poor health related quality of life¹⁶.

Discussion and conclusion

The majority of people surviving COVID-19 have not more than six months of follow-up after recovery; hence there is limited data on long term outcomes in different systems in the body. Most of the available data gathered till now are collected from limited cohort study of relatively short period, case reports. So statistically significant conclusion cannot be drawn. But one thing which can be assumed clearly that most of the adverse outcomes were mediated by the activated immune response on exposure to the virus or due to the direct attack of the virus itself. Adverse respiratory health outcomes are of great concern because lung fibrosis and impaired pulmonary function have been found to persist beyond recovery in some cases. Experience with SARS and MERS in terms of long term follow-up is not satisfactory in this regard. The same thing is applicable for cardiovascular and cerebrovascular cases, as elevated risk of adverse health outcomes persist beyond decades after pneumonia. Elevated risk of adverse mental health outcomes is a matter of great concern chronic fatigue, insomnia, PTSD, anxiety, depressive disorder can impair quality of life. For gastrointestinal, hepatic and renal outcomes, majority of adverse reports were found during acute phase of the infection.

This short review was attempted to address the potential long-term health outcomes of COVID-19. It was evident that multiple organ systems are affected as well as the mental health. Post-infection care of the survivors is the new challenge to the health care system as it is likely to add an extra burden. Comprehensive monitoring of the survivors will definitely help us in understanding the course and progression of the disease process. So, a comprehensive approach is needed to fix strategies and gather resources to address both pulmonary and extra-pulmonary complications. So, work is needed in parallel to address the need for those surviving and recovering from the disease. Post-COVID -19 programs are likely to play an important role in this regard for many years to come.

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