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## The Long-Haul COVID-19 Phenomena

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Y ear 2020 has been, for the lack of a better word, unexpected. One virus has changed the course of our lives for the worst, in a matter of days. Everything once deemed normal, something even as simple as visiting your parents, is now dangerous. With everyone in the world being directly or indirectly affected by COVID-19, studying it in order to take steps to minimize the damage it inflicts, is top priority worldwide.

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). While early research on Covid-19 focused on its respiratory symptoms, it is now known that its impacts can be much more extensive and relentless both direct and indirectly.

The long-lasting effects of COVID on people, a phenomenon that has come to be known as 'Long COVID' or 'Long-Haul COVID' is also being focused. Although extensive studies have not been carried out due to the relative novelty of the virus, a household survey in UK has shown that around 186000 people (95% CI 153000–221000) experienced at least one symptom for weeks or months, of which some are life altering.<sup>2</sup>

Centre for Disease Control and Prevention has developed a list that encompasses cases with long term symptoms of COVID, including but not limited to brain fog, chest pain, fatigue. On December 3<sup>rd</sup> 2020, the US National Institute of Health held a seminar on Long COVID. A range of symptoms and conditions were highlighted, which may persist for weeks to months after the initial infection.

Pulmonary oedema, myopathies, myocarditis, pericarditis results from damaged endothelial cells (which is also suggested to be responsible for cytokine storm) due to COVID which in turn stimulates the production of mast cells

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and is also linked to blood clots formation. 1,5 Incidence of blood clotting have certainly increased during the pandemic. While small blood clots restrict blood flow to the lungs, larger clots can cause tissue damage, requiring amputations. Clots can also lodge in brain or heart vessels, causing strokes and heart attacks. Α study explained hypercoagulability with the presence of autoantibodies found in a significant number of COVID-19 patients, suggesting these proteins sparks a dangerous loop between clotting and hyperinflammation.<sup>6</sup> Post viral chronic fatigue syndrome, impaired cognition and dysautonomia are the neurological manifestations found in Long COVID. There is also increasing evidence that the virus may cross the blood-brain barrier, likely due to the ACE2 receptors in the Choroidal plexus of the brain. This may have serious consequences including encephalitis, seizures and may cause behavioral changes as well

COVID patients with long duration of disease have reported menstrual changes and erectile dysfunction including testicular pain, urinary problems, & menopause. Testosterone has an important role in Corona virus patients. It is reported that testis is one of the highest ACE2 expression site. ACE2 are the enzymes through which Corona virus enters cells, and significantly impact its normal functioning. Low testosterone levels have been predicted to have worse outcomes for admitted COVID patients. Similarly presence of hypogonadism and low sperm count, with evidence of relative infertility has been reported.

In order to tackle the long term symptoms in the UK, the National Health Services (NHS) has announced to launch 40 Long COVID clinics while on the other hand, it is also expected that the National Institute for Health and Clinical Excellence (NICE) will also soon release its first clinical guidelines. Meanwhile WHO is planning to update its guidance and resources for clinical management of COVID-19 to include Long COVID.

While, the world is focusing on Long COVID, there is negligible published work in Pakistan regarding persistent symptoms in our

population. Research to explore the manifestations of COVID haul is important so that based on the findings and recommendations, proper clinical and policy strategies for the management of long term symptoms can be developed. At the same time it would also help to adopt the standard guidelines in the context of Pakistan's Long COVID situation.

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