

Long COVID: A brief introduction

Amity Eliaz and Mike Reid give an overview of what is known so far on Long COVID.

Introduction

Since the onset of the coronavirus disease 2019 (COVID-19) pandemic, patients' clinical presentations have varied widely both in terms of symptoms and time course. While many patients fully recover to their baseline health following Severe Acute Respiratory Syndrome Coronavirus² (SARS-CoV-2) infection, others experience ongoing sequelae. The persistent sequelae have important implications for patient health and quality of life, and are therefore of great importance for patients and providers.¹

The constellation of persistent COVID-19 symptoms several weeks after infection is referred to by several terms including "Long haul COVID," "Long COVID," or "post COVID-19 condition." Many medical professionals refer to it as 'Post-Acute Coronavirus Disease Syndrome' (PACS). According to the World Health Organization (WHO) 'Post COVID-19 condition occurs in individuals with a probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least two months and cannot be explained by an alternative diagnosis.'² In contrast the US Center for Disease Control and Prevention (CDC) and the UK defines Long COVID as persistent, returning, or new symptoms at least four weeks following SARS-CoV-2 infection.^{3,4}

Epidemiology

Given the variable definitions of Long COVID, the true burden of disease remains unknown. However, current estimates of the prevalence of Long COVID range from 20% percent to 75%. Among over 500,000 patients in the United Kingdom (UK), 37.7% reported one or more symptoms at least 12 weeks after COVID-19.⁵ Similarly, in a prospective cohort study in the United States (US), Logue et al. found that approximately 30% of patients in the outpatient setting reported ongoing symptoms at three to nine months following an episode of COVID-19.⁶

Comparatively, among a cohort of 968 adult patients in France, 10% experienced Long COVID following severe SARS-CoV-2 infection.³ Eighty five percent of the patients who were symptomatic at two months following infection remained symptomatic at one year.³ Similarly, in another study in the UK, 13.3% of patients with COVID-19 reported symptoms lasting at least four weeks.⁷ In addition, the authors reported an association between Long COVID and the occurrence of over five symptoms during the initial week of infection.⁷

Nasserie et al. conducted a systematic review evaluating persistence of COVID-19 symptoms following SARS-CoV-2 infection among patients in China, the UK, Spain, Italy, France, the US, Germany, Canada, the Netherlands, Austria, Ireland, Norway, Turkey, Belgium, England, and Bangladesh.⁸ The authors found that 72.5% of patients experienced at least one symptom at 30 days following infection.⁸ Commonly reported symptoms included dyspnea (36%), fatigue or exhaustion (40%), and insomnia (29.4%).⁸ Comparatively, in a systematic review of 41 studies by Chen et al., the pooled global prevalence of Long COVID was 43%.⁹

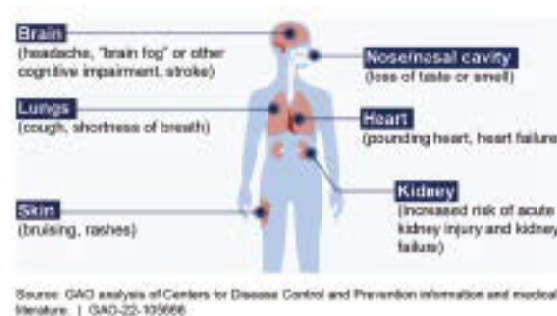
Unfortunately, little data exists currently describing the burden of Long COVID in Africa; although several research studies are underway in South Africa to characterize the disease burden in that country.

Pathophysiology

A variety of mechanisms are speculated to underlie the

development of Long COVID (Figure 1).^{10,11} Data supports the hypothesis that some people may harbor virus in their tissue after the resolution of the initial infection and this lingering virus can both cause direct damage to cells and leak viral particles into the blood, where they can cause microclots, activate inflammation and ultimately cause more damage. Other research suggests that SARS-CoV-2 may dysregulate gene expression, metabolism, and immunity, which may in turn contribute to the occurrence of Long-term sequelae following infection.¹² Even prior to the COVID-19 pandemic, studies demonstrated persistent sequelae following other coronavirus infections.¹² In the case of Long COVID, it may be that both immune dysregulation and tissue injury from lingering virus contribute to ongoing symptoms.¹² Vijayakumar et al. report ongoing immunological abnormalities in patients experiencing Long COVID characterized by pulmonary symptoms.¹³ Patients with Long COVID were found to have significantly increased CD8+ and CD4+ T cells on evaluation of bronchoalveolar lavage (BAL) compared to healthy controls, as well as proteomic abnormalities suggestive of persistent epithelial injury, apoptosis, and tissue repair.¹³

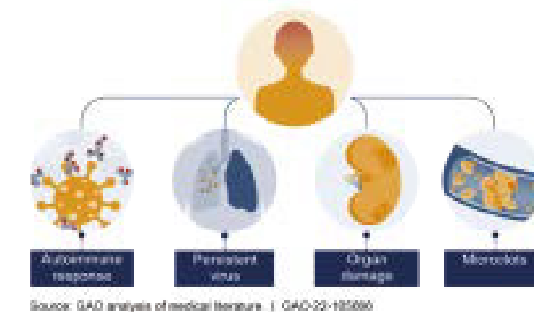
Figure 1.



Signs and Symptoms

Long COVID symptoms vary widely in terms of character, severity, and time course. As illustrated in Figure 2, Long COVID can present with a range of symptoms affecting many different organ systems. Persistent symptoms range from general malaise to shortness of breath to chest pain. In addition, while some patients may experience persistence of their acute COVID-19 symptoms, other patients report entirely new symptoms.

Figure 2.



In their living systematic review and meta-analysis, Michelen et al. reported the most common Long COVID symptoms were weakness (41%), general malaise (33%), fatigue (31%), impaired concentration

(26%), and breathlessness (25%).¹⁴ Importantly, the authors noted that 37% of patients reported decreased quality of life compared to their baseline.¹⁴ Additionally, 26% of studies in the review reported decreased pulmonary function among patients with Long COVID.¹⁴

What is clear across all these studies is that the symptoms can range from mild to debilitating. In the US it is estimated that Long COVID has resulted in 1.1 million Americans not working at any given time and another 2.1 million workers reducing their hours rather than taking time off.

Diagnosis

Researchers are working to develop methods to reliably diagnose and treat Long COVID. Healthcare providers may use COVID-19 antibody tests in an attempt to confirm previous infection, then rule out other conditions that may cause other symptoms. Blood tests should be ordered selectively and for specific indications after care history and examination; the patient may not need any. Anemia should be excluded in the breathless patient. Elevated biomarkers including C reactive protein, white cell count and ferritin may be useful in highlighting evidence of infection or inflammatory response.

Clinical Management

Every Long COVID patient is different, as such, every patient will need treatments specific to their symptoms. Clinical evaluation and management of patients with Long COVID should be driven by their signs and symptoms following

careful history and physical examination.¹⁵ For example, patients with significant ongoing respiratory illness may undergo follow-up chest x-ray and a referral to pulmonary rehabilitation.¹⁵ By contrast, patients with Long COVID chest pain should be carefully evaluated for cardiovascular disease risk factors and may require urgent referral to cardiology for further assessment.¹⁶

The UK's National Institute for Health and Care Excellence recommends a holistic, person-centered approach to assessment of patients with persistent symptoms following COVID-19.¹⁷ After ruling out urgent conditions, patients should be referred for multidisciplinary assessment and rehabilitation services as local resources permit.¹⁷ For patients not admitted to intensive care, the British Thoracic Society guidance on follow up on COVID-19 patients who have had significant respiratory illness proposes follow up with a chest X-ray at 12 months. For those with evidence of lung damage (such as persistent abnormal chest X-ray) referral to pulmonary specialist and pulmonary rehabilitation probably aids recovery.¹⁵

There are no drugs to prevent or treat Long COVID. However, for mild symptoms presumed to be related to Long COVID, treatments include over the counter medication, advice on self-treatment strategies, caregiver support and education, support groups, stress management, and lifestyle changes (including a healthy diet, graded exercise and return to normal activity over an adequate period of time).

When possible, continuity of care should be optimized for patients experiencing Long COVID.¹⁶ Most patients can expect a gradual, if sometimes protracted, improvement in energy levels and breathlessness. They should be supported by careful pacing, prioritization and modest goal setting. Post-COVID-19 symptoms in the elderly tend to be more severe than in younger patients and support for older patients should be personalized with input from the multidisciplinary team.

Vaccines

Current evidence supports vaccination as a means of protection against Long COVID to varying degrees. A recent study by Al-Aly et al. suggests that vaccination prior to SARS-CoV-2 infection confers partial protection against persistent symptoms.¹⁸ The authors evaluated patients in the US Department of Veterans Affairs and found that patients with breakthrough infections following vaccination had lower risk of ongoing COVID-19 sequelae compared to unvaccinated patients.¹⁸

Antonelli et al. conducted a prospective, community-based, nested case-control study of adults in the UK with confirmed infection with

SARS-CoV-2 following vaccination.¹⁹ Participants who had received two doses of vaccination prior to COVID-19 had approximately half the odds of persistent symptoms lasting four weeks or longer compared to participants who received only one dose.¹⁹ A recent study in Israel also found that COVID-19 vaccination was associated with reduced risk of Long COVID.²⁰ Among 951 patients following SARS-CoV-2 infection, vaccinated patients reported significantly decreased risk of COVID-19 symptoms.²⁰

Summary

Long COVID is common and broad in its impact on the body, making it incredibly difficult to diagnose and challenging to manage. What is clear though is that this is a major global public health problem and will continue to have impacts for years to come, even if cases of acute SARS-CoV-2 dwindle in the coming months. Given the prevalence of persistent symptoms following COVID-19, Long COVID carries important implications for healthcare providers across Africa. From the limited current evidence, it appears that many patients with Long COVID recover through a holistic and paced approach. Nonetheless, the long-lasting effects of the syndrome require an interprofessional, community-facing, holistic approach to management. In turn, this places new burden on healthcare systems and health workforce capacity.²¹ As the understanding and management of Long COVID evolve, accessible primary care will likely play a critical role in the care of patients with persistent COVID-19 sequelae.²²

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Article written by:

- Amity Eliaz -Department of Medicine, Stanford University, Palo Alto, California, USA,
- Mike Reid- Institute for Global Health Sciences, University of California, San Francisco, California, USA., Email: Michael.reid@ucsf.edu