

Received: 2021.06.03
Accepted: 2021.06.04
Available online: 2021.06.07
Published: 2021.06.07

Editorial: Long COVID, or Post-COVID Syndrome, and the Global Impact on Health Care

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Abstract During 2020, increasing numbers of case reports, case series, and small observational studies reported long-term complications of coronavirus disease 2019 (COVID-19) in patients who had recovered from acute infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Long COVID has a prevalence of between 10-30% in patients with a recent history of SARS-CoV-2 infection. Pulmonary, hematologic, cardiovascular, neuropsychiatric, renal, endocrine, gastrointestinal and hepatobiliary, and dermatologic involvement, and chronic multisystem inflammatory syndrome in children (MIS-C) highlights the requirement for a multidisciplinary approach to the management of patients with long COVID. This Editorial aims to present the current status of long COVID, or post-COVID syndrome, and its global impact on health and the provision of health care.

Keywords: Editorial • COVID-19 • Severe Acute Respiratory Syndrome Coronavirus 2

During 2020, increasing numbers of case reports, case series, and small observational studies reported long-term complications of coronavirus disease 2019 (COVID-19) [1]. Long COVID, or post-COVID syndrome, was described in patients who had recovered from acute infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. There have been recent hypotheses regarding the cause of cognitive impairment associated with long COVID [2,3]. However, the prevalence of the systemic effects of long COVID are now emerging from the analysis of global patient electronic records and registries, including in the USA and the UK [4,5].

As recently as April 2021, clinical guidelines have been proposed by public health and primary care physicians for the definition, diagnosis, and management of long COVID [6]. Long COVID occurs in patients who continue to have signs and symptoms of illness four weeks after the initial diagnosis of SARS-CoV-2 infection, which are not explained by other causes [6]. Observational studies and data from studies using patient health records have shown that the prevalence of long COVID following acute SARS-CoV-2 infection is between 10-30%, with signs and symptoms that may last for several months [4-6].

Preliminary data have recently been published from the community-based COVERSCAN clinical trial (NCT04369807) [4]. This study included 201 individuals with a mean age of 45 years (range, 21-71 years) and was conducted between April to September 2020 [4]. The COVERSCAN trial aimed to assess medium-term organ impairment in individuals ≥ 18 years with persistent symptoms after initial recovery from acute SARS-CoV-2 infection compared with age-matched healthy controls [4]. This

study population was at low risk of mortality from COVID-19, and only 19% were hospitalized [4]. However, four months after initial SARS-CoV-2 infection, 42% of individuals had ten or more long COVID symptoms, and 60% had severe long COVID symptoms, which included breathlessness (88%), headache (83%), fatigue (98%), and myalgia (87%) [4]. Mild cardiac impairment was present in 26%, impaired lung function in 11%, and impaired liver function tests were present in 28%, renal failure in 4%, single-organ impairment in 70%, and multiorgan impairment in 29% [4]. The preliminary analysis of data from this trial showed that in individuals at low risk of mortality from COVID-19 mortality but with long COVID symptoms, 70% had impairment in one or more organs four months later [4].

In May 2021, Daugherty and colleagues published the findings from a retrospective analysis of three US patient databases to evaluate the prevalence of persistent symptoms after the acute phase of SARS-CoV-2 infection in 193,113 adults between 18-65 years of age [5]. The study included an outpatient laboratory testing database, an extensive US national administrative claims database, and a database of hospital admissions, with clinical sequelae identified by ICD-10 codes and defined as being present from 21 days after the date of first SARS-CoV-2 diagnosis [5]. This study identified more than 50 clinical sequelae, or types of long COVID, in patients who had recovered from the acute phase of SARS-CoV-2 infection [5]. Importantly, 14% of adults aged ≤ 65 years had at least one new type of clinical condition that required medical management [5]. In this study, long COVID included chronic respiratory failure, hypercoagulation states, cardiac arrhythmia, myocarditis, peripheral neuropathy, encephalopathy, cognitive

impairment, hyperglycemia, abnormal liver function tests, fatigue, and anxiety [5]. Long COVID was more common in older individuals, patients with pre-existing conditions, and patients who had required hospital admission for acute SARS-CoV-2 infection [5]. Also, all ages and previously healthy individuals who were not initially hospitalized also developed long COVID [5].

Multisystem inflammatory syndrome in children (MIS-C) can present acutely following SARS-CoV-2 infection but is also a form of long COVID in children and adolescents [7]. A recently reported cross-sectional study from Italy included 129 children ≤ 18 years old diagnosed with SARS-CoV-2 infection and COVID-19 between March to October 2020, who were assessed 30 days later [8]. The mean age of the study population was 11 ± 4.4 years, and 48.1% were female [8]. During acute COVID-19, 25.6% were asymptomatic, and 4.7% were hospitalized, with 2.3% requiring admission to the pediatric intensive care unit (PICU) [8]. Following acute infection with SARS-CoV-2, 2.3% developed MIS-C, and 1.6% developed myocarditis, 35.7% had one or two symptoms, 22.5% had three or more symptoms of long COVID, and 41.8% completely recovered [8].

In the past 18 months, the global pandemic of acute cases of COVID-19, early mortality, and the vaccine development program have detracted from the lasting health, social, and economic burden of long COVID. A recent US population study reported that 1 in 10 people hospitalized with COVID-19 had a new and disabling clinical condition following hospital discharge and 12 weeks after a positive test for SARS-CoV-2 [9]. A recent review by Nalbandian and colleagues has summarized the effects of long COVID, which they have termed 'post-acute COVID-19,' by organ system and presentation [10]. Pulmonary, hematologic, cardiovascular, neuropsychiatric, renal, endocrine,

gastrointestinal and hepatobiliary, dermatologic, and MIS-C groups with distinct presentations highlights the requirement for a multidisciplinary approach to managing patients with long COVID [10].

Long-term health resource planning for the consequences of long COVID is starting to affect healthcare delivery services. Health economics using both disability-adjusted life years (DALYs) and quality-adjusted life-years (QALYs) may best capture the impact of long COVID, as up to 30% of the associated health burden may be due to long COVID-induced disability and not to mortality [11]. The health burden due to COVID-induced disability across all age groups might be as high as 30% [11]. Longitudinal studies should be implemented to assess the health effects and long-term economic impacts of living with chronic diseases of long COVID [12]. The pathogenesis, risk factors, and treatment of the many clinical components of the long COVID syndrome should be studied in parallel with their effects on society and health economics [10,11,13].

Conclusions

The clinical manifestations of long COVID and its prevalence in all age groups who initially appear to have recovered from acute SARS-CoV-2 infection are now recognized. However, the effects on society, the economy, and healthcare provision have yet to be realized. There is also concern that in older adults, the symptoms of long COVID are under-reported and may be assumed to be due to age-related comorbidities. Now that SARS-CoV-2 infection and its variants are endemic, and vaccination programs may not be completely effective the diagnosis and management of long COVID is expected to become a global public health priority.

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