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Opinion

Does Long COVID Exist in Sub-Saharan Africa?

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Abstract: Billions of people have been impacted by the SARS-CoV-2 pandemic with over 600 million infections worldwide. Researchers have turned their attention to describing the post-viral phenomenon known commonly as "Long COVID". While post-viral syndromes have been documented after other viral pandemics, the scale of the SARS-CoV-2 pandemic provides a unique opportunity to study and understand both the epidemiology and pathophysiology of the long COVID syndrome. While the pandemic impacted populations from all continents, there is a significant gap in what is known about long COVID on the sub-Saharan African continent. We review what is known about long COVID and highlight the need for further research within the African population.

Keywords: long COVID; pandemic; post-viral syndrome

1. Introduction

There are few viruses in the history of humans that have had the ability to precipitate a global crisis, create economic impact that will be felt for years or change the way we view disease in a planetary health framework. The first cases of SARS-CoV-2 (COVID-19) were reported in December 2019 and the COVID-19 pandemic was declared by the WHO in March 2020 [1,2]. In the last three years, the pandemic has had a critical impact on health and has had societal effects, including disruptions in education and the economy. The trauma and uncertainty inflicted on the global population as our understanding of this emerging infection evolved also led to the mistrust of the medical system [3]. As of March 2023, there have been more than 758 million cases and more than 6 million deaths attributed to COVID. There has been an unequal distribution of COVID cases and morbidity around the globe [4]. The European continent claims the highest number of cases (over 200 million), although the most deaths from COVID have occurred in the Americas (2.9 million) [4]. The African subcontinent has reported 9.4 million cases and approximately 175,000 deaths from COVID [4]. Globally, as cases increased, a clinical pattern consistent with post-viral syndrome began to emerge. COVID-19 cases in Africa have shown a seasonal pattern [1,4]. Peaks in the pandemic in southern Africa have occurred in January and July annually from 2020 to 2022 [4,5]. They are hypothesized to be during periods of travel (during the holidays in December/January), the colder months and during months with higher precipitation [5,6]. Studies of the seasonality of endemic coronaviruses in southern Africa have found similar patterns [7]. Furthermore, while global vaccination efforts began as early as December 2020, vaccines only became available in a part of Africa in March 2022 [8]. However, as the number of cases continued to increase globally throughout 2020, a proportion of individuals began to develop persistent symptoms after the resolution of the acute infection. First described by patient communities, these post-acute infection symptoms quickly became of interest to the medical community.

Citation: Mehta, N.; Ndhlovu, C.E.; Makadzange, T. Does Long COVID Exist in Sub-Saharan Africa? *COVID* **2023**, *3*, 1024–1030. https://doi.org/10.3390/covid3070074

Academic Editor: Giuseppe Novelli

Received: 16 May 2023
Revised: 6 July 2023
Accepted: 13 July 2023
Published: 17 July 2023

2. Review of the Current Literature

Post-viral syndromes have been documented in association with other infections, including other coronaviruses. Patients who were infected and survived COVID started reporting a cluster of persistent symptoms weeks to years after initial infection and named this syndrome "long COVID" [9]. The multi-system cluster of symptoms is broad, and, to date, there is a lack of a common consensus on the definition of long COVID or the syndrome that follows acute COVID infection. The WHO recognizes and defines this syndrome, "Post-COVID-19 condition or long COVID, as persistent symptoms at least three months post-acute infection with symptoms persistent for at least two months" [10]. Meanwhile, the Center for Disease Control and Prevention demarcates "post-COVID conditions" as occurring a month after infections and qualifies it as a disability, referred to as the post-acute sequelae of SARS-CoV-2 (PASC) or long COVID [11], while the National Health Service in the UK defines long COVID as persisting for twelve weeks post-acute infection [12]. Given the novelty of the coronavirus, the prevalence of the disease and significant impact on daily life, long COVID has become of great clinical and research interest to the global community, despite the lack of common diagnostic definition among international medical institutions and societies.

The literature reports rates of long COVID ranging between 6 and 85% [13–23]. There is currently no common diagnostic definition for long COVID, and the diagnosis is often one of exclusion [24–26]. However, the most common symptoms of long COVID are broad and include fatigue or weakness (13–87%), shortness of breath (10–71%), chest pain or tightness (12–44%), cough (17–34%) and cognitive changes (26–40%), but also includes persistent GI symptoms such as loss of appetite, IBS and abdominal pain [16,24,27–35].

Many of these symptoms have been documented after other historic respiratory viral pandemics such as the 1918 influenza pandemic, SARS and MERS. News articles and research comment on similar features of chronic fatigue and neurologic impairments such as reduced cognition and depression in survivors of the 1918 influenza pandemic [36–39]. Additionally, cohort studies from the influenza pandemic show long-term consequences on cardiopulmonary health occurring several decades later [40]. The 2003 SARS pandemic was also associated with persistent symptoms in a large proportion of survivors who had persistent chronic fatigue, shortness of breath, pulmonary disease, myopathy and a reduced quality of life [41–43]. Research suggests that patients may eventually recover from the post-infectious syndrome, although up to half of patients still had symptoms preventing their return to work within a year later [44–46]. Although limited, research around post-infection syndromes in MERS suggests similar features to long COVID [46,47]. The syndromes seen in prior pandemics have recently been compared to other documented post-viral syndromes such as chronic fatigue syndrome (CFS), myalgic encephalomyelitis (ME) or postural orthostatic tachycardia syndrome (POTS), which provides a plausible model to study the pathophysiology of long COVID [17,29].

There are currently few studies demonstrating a difference in the prevalence or phenotype of long COVID across different racial groups; however, some studies suggest that the Hispanic race is a risk factor for the development of long COVID [20,48]. One study in the US demonstrated an increase in cognitive symptoms for African American patients [49]. Other studies have attempted to characterize the different phenotypes of long COVID that are roughly grouped into respiratory, fatigue-related and neurocognitive symptoms, which do not seem to vary by country [21,50–53].

There are several proposed mechanisms for long COVID, including long-term multi-organ damage from the acute-phase inflammatory reaction and residual inflammation, autonomic dysfunction and neuronal injury, maladaptive autoimmune responses, organ dysfunction related to ACE2 receptor expression and alterations in gut microbiota [17,29,54–58].

There have been several studies aimed at characterizing long COVID and identifying risk factors. Female sex, older age, hospital and/or ICU admission, a higher BMI, existing lung disease and active smoking appear to be risk factors for developing long COVID [13,14,16,19,21,23]. In addition to host factors, viral variants may have

a differential impact on the development of long COVID. One study suggests that historic variants had a higher risk of long COVID compared to subsequent strains [18].

There are few studies assessing the impact of vaccination before acute infection on the development of long COVID. There appears to be some protective effect of vaccination against long COVID with some studies showing a dose–response pattern with a reduction in long COVID with a greater number of vaccination doses [23,59,60].

The impact on daily living for people with long COVID has been profound. Up to 80% of people with long COVID report that their activities of daily living and functional status has diminished, and up to 29% report an impairment in social functioning [9,61–63]. A recent review found that 13% of studies published on long COVID describe the employment-related effects of the syndrome leading to economic consequences, with one study reporting an unemployment rate of 22% [57,62]. In the US, estimated economic losses from COVID reached USD 16 trillion by fall of 2021 with a need to further study the impact of morbidity from the pandemic [55,64]. Recent modeling within the United States on the cost of long COVID, while taking into account the lost quality of life, wages from disability and medical costs, estimates the cost to be up to USD 3.7 trillion [65,66]. There are few data to estimate the global costs, particularly in low- and middle-income countries where the costs of long COVID may be devastating at the individual or household level.

Diagnosis and treatment remain a significant challenge. Although there is limited research on treatment options for long COVID, several studies have reported the use of multimodal treatment options for patients [67,68]. This includes but is not limited to pharmacotherapy (such as antihistamines) aimed at relieving symptoms in conjunction with physical and occupational therapy, cardiopulmonary rehabilitation, meditation and complementary-alternative medicine (CAM) and acupuncture [27,29,55,69]. Recent research is beginning to suggest that over time, these symptoms may decrease, particularly respiratory symptoms [50,61].

Long COVID will continue to affect patients significantly for the foreseeable future, although there is a gap and a lack of consensus among the global healthcare system about how to identify, diagnose, monitor and treat long COVID upon moving forward [26,70]. Furthermore, most of the research on long COVID has been conducted within high-income countries (HICs), posing a critical challenge on how to adapt these findings to an international setting. Given the phenomenon that there were less reported cases in Africa than initially expected, it is important to understand the sub-populations at risk and how long COVID may differ within this population. There have been several theories as to why the African continent saw fewer cases than anticipated at the onset of the pandemic, although limitations in data quality and reporting likely underestimate the impact of the pandemic [71]. Some researchers speculate that the younger average age of the population in combination with immunity effects from exposure to other common infectious diseases, such as malaria, contributed to the prevalence of COVID in Africa [71,72]. However, there is otherwise a relatively large gap in understanding the characteristics that led the pandemic in Africa to occur the way it did, or the sequelae of the pandemic on the population, including long COVID.

3. Discussions around Further Research

Most of the research on long COVID originates from Europe, the Americas and, less frequently, Asia and the Middle East [52,73]. There are limited COVID data from the African continent or about African populations, and the impact of vaccines on long COVID in Africa is poorly understood [71,73]. It is also crucial to study this syndrome in the context of vaccination rates, vaccine effectiveness and protection against long COVID as several studies show that vaccination may be protective against symptoms of long COVID [74]. Studying long COVID within the African continent can strengthen research and clinical monitoring systems for symptoms. Given that most research on long COVID has been conducted in high-income countries, ongoing collaboration amongst global researchers is needed to adapt these findings to the African continent. Further research will also shape how providers systematically approach diagnosis and treatment. We are conducting a

study to evaluate the vaccine effectiveness of inactivated COVID-19 vaccines in Zimbabwe and will also assess and prospectively evaluate the prevalence of symptoms of long COVID among those that are SARS-CoV-2 positive [75]. Our objective is to phenotypically characterize long COVID within this population while assessing risk factors that either contribute to or protect against long COVID, including vaccination status. We anticipate that these data may provide important insights into long COVID and its public health implications within African populations.

4. Conclusions

In conclusion, there remains significant gaps in our understanding of the pathophysiology, prevalence, risk factors and treatment options for long COVID within the global medical community. As the number of long COVID cases continues to rise across the world, it is vital that research and data collection are scaled up, particularly within Africa, to better inform the healthcare practice, optimize care for patients and improve the lives of people with long COVID now and in the future.

Author Contributions: Conceptualization, N.M., C.E.N. and T.M.; methodology, N.M. and T.M.; investigation, N.M. and T.M.; writing—original draft preparation, N.M.; writing—review and editing, N.M., C.E.N. and T.M.; supervision, C.E.N. and T.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: We would like to acknowledge the research staff at Mutala Trust.

Conflicts of Interest: The authors declare no conflict of interest.

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