IJID Regions 8 (2023) 137–144

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

Review

Burden, causation, and particularities of Long COVID in African populations: A rapid systematic review

Peter S. Nyasulu[a,b,*], Jacques L. Tamuzi[a], Rajiv T. Erasmus[c]

[a] Division of Epidemiology & Biostatistics, Department of Global Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa
[b] Division of Epidemiology & Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Parktown, Johannesburg, South Africa
[c] Division of Chemical Pathology, Department of Pathology, Faculty of Medicine and Health Sciences, Stellenbosch University & NHLS Tygerberg Hospital, Cape Town, South Africa

ARTICLE INFO

Keywords:
Long COVID
Prevalence
Symptoms
Comorbidities
Pathophysiology
African populations

ABSTRACT

Objectives: To determine the prevalence of long COVID, its most common symptoms, comorbidities, and pathophysiological mechanisms in African populations.
Methods: A systematic review of long COVID in African populations was conducted. The random effects model was used to calculate the pooled prevalence rates (95% CI). A narrative synthesis was also performed.
Results: We included 14 studies from seven African countries, totaling 6030 previously SARS-CoV-2 infected participants and 2954 long COVID patients. Long COVID had a pooled prevalence of 41% (26-56%). Fatigue, dyspnea, and confusion or lack of concentration were the most common symptoms, with prevalence rates (95% CI) of 41% (26-56%), 25% (12-38%), and 40% (12-68%), respectively. Long COVID was mainly associated with advanced age, being female, more than three long COVID symptoms in the acute phase, initial fatigue and dyspnea, COVID-19 severity, pre-existing obesity, hypertension, diabetes mellitus, and the presence of any chronic illness ($P \leq 0.05$). High microclot and platelet-poor plasma viscosity explained the pathophysiology of long COVID.
Conclusion: Long COVID prevalence in Africa was comparable to the global prevalence. The most common symptoms were higher in Africa. Comorbidities associated with long COVID may lead to additional complications in African populations due to hypercoagulation and thrombosis.
Systematic review registration: PROSPERO CRD42023430024

Background

Post-Acute sequelae of SARS-CoV-2 (PASC), colloquially referred to as “long COVID”, is a poorly understood condition characterized by prolonged COVID-19 symptoms and/or the development of new symptoms following the resolution of acute SARS-CoV-2 infection. While there is still no formal clinical definition of long COVID, findings reported in individuals experiencing long COVID include general symptoms (tiredness or fatigue that interferes with daily life, symptoms that get worse after physical or mental effort, also known as “post-exertional malaise”), fever, respiratory and heart symptoms (difficulty in breathing or shortness of breath, cough, chest pain, fast-beating or heart palpitations), neurological symptoms (difficulty thinking or concentrating, headache, insomnia, dizziness, pins-and-needles feelings, change in smell or taste, depression or anxiety), digestive symptoms (gastroesophageal reflux disease, diarrhea, and stomach pain) and other symptoms (hyperlipidemia, thromboembolism, kidney disorders, joint or muscle pain, rash and changes in menstrual cycles) [1–4]. For example, the National Institute for Health and Care Excellence (NICE) defined the “Long COVID” as “signs and symptoms that develop during/after the COVID-19 infection persisting for more than 4 weeks and could not be explained by any other diagnosis”. In this categorization, the long COVID consists of two categories, “ongoing symptomatic COVID-19”, which indicates the symptoms last for 4-12 weeks; and “post-COVID-19 syndrome”, which means symptom persistence beyond 12 weeks [5]. Baig et al. [6] suggested using the term “Chronic COVID syndrome (CCS)” as opposed to “Long COVID” or “Long Haulers”. He also presented an organ-based staging of the illness to prioritize immediate care needs [5,6].

As of May 14, 2023, Africa recorded approximately 9.5 million confirmed COVID-19 cases accounting for just 1% over 766 millions of global COVID-19 confirmed cases [7]. In Africa, the picture of long COVID is not well described as little research has been conducted in this emerging field. However, few studies have been conducted on the burden of long COVID in Africa, long COVID prevalence has been reported to vary across and within African countries. Dryden et al. [8] reported the highest long COVID prevalence compared to other studies

* Corresponding author.
E-mail address: pnyasulu@sun.ac.za (P.S. Nyasulu).

https://doi.org/10.1016/j.ijregi.2023.08.004
Received 30 May 2023; Received in revised form 2 August 2023; Accepted 6 August 2023

Table 1
Summarizes the evidence-based studies of long COVID-19 in Africa.

Study ID/Settings	Study population	Study designs	Long COVID prevalence	Predominant symptoms	Comorbidities	Key findings
Dryden et al. [8]/South Africa	1873 enrolled hospitalized COVID-19 participants were followed up 3 months after hospital discharge. 960 (53.1%) were women and 913 (48.8%) were men, the median age was 52 years (41-62)	A prospective, observational cohort study	1249/1873(66.7%)	Fatigue (50.3%), shortness of breath (23.4%), confusion or lack of concentration (17.5%), headaches (13.8%), and problems seeing/blurred vision (10.1%)	The most common self-reported comorbidities were hypertension (n = 669; 35.7%), obesity (n = 474; 25.3%), and diabetes mellitus (n = 418; 22.3%). HIV was reported by 95 (5.1%) participants	age ≥65 years (aOR) 1.62; 95% CI 1.00-2.61]; female sex (aOR 2.00; 95% CI 1.51-2.65); requiring supplemental oxygen during admission (aOR 1.44; 95% CI 1.06-1.97); intensive care unit admission (aOR 1.87; 95% CI 1.36-2.57); pre-existing obesity (aOR 1.44; 95% CI 1.09- 1.91); and the presence of ≥4 acute symptoms (aOR 1.94; 95% CI 1.19-3.15)
Mendelsohn et al. [20]/South Africa	174 long COVID among 653 COVID-19 infected patients. The mean age of participants was 50.3 (13.6) years; 62% were female	Retrospective cross-sectional study	172/653 (35%)	Fatigue 60 (34.5%), dyspnea 35 (20.1%), loss of taste 34 (19.5%), loss of smell 32 (18.4%), headache 27 (15.5%), body aches 26 (14.9%), chest pain 19 (10.9%), gastrointestinal complaints 21 (12.1%), palpitations 18 (10.3%), rash 11 (6.3%)	Diabetes 35 (22.0%), hypertension 77 (48.4%), ischemic heart disease 7 (4.4%), chronic obstructive pulmonary disease/asthma 10 (6.3%), prior tuberculosis 1 (0.6%), HIV 1 (0.6%), other 7 (4.4%)	Sex, age, baseline severity of disease, or number of initial COVID-19 symptoms were predictive of self-reported dyspnea, fatigue, ≥ 3 long COVID symptoms, or self-reported non-recovery
Aly and Saber [1]/Egypt	A total of 115 females among them 66 had long COVID. The mean age was 73.18 ± 6.42	A retrospective cross-sectional study	66/115 (57%)	Dyspnea 20 (17.4), cough 10 (8.7), chest pain 9 (7.8), palpitations 13 (11.3), insomnia 28 (24.3), headache 14 (12.2), loss of smell and taste 14 (12.2), stress 65 (56.5), sadness 55 (47.8), fatigue 66 (57.4), cognitive dysfunction 29 (25.2), recurrent falls 29 (25.2), incontinence 21 (18.3)		The presence of post-recovery symptoms was significantly related to stress ($P = 0.005$), sadness ($P = 0.007$) and sleep disturbances ($P < 0.001$)
Crankson et al. [22]/Ghana	2334 patients, among them 50 had long COVID. 60.1% were men and 39.9% were women. The majority were aged from 30-59 years (57.5%)	A cross-sectional analysis	50/2334 (2%)	N/A	N/A	COVID-19 patients with hypertension and diabetes mellitus spent almost 2 days longer in hospital ($P = 0.00$, 95% CI = 1.42-2.33) and had four times the odds of long COVID (95% CI = 1.61-10.85, $P = 0.003$) compared to those with no comorbidities
Ogoina et al. [16]/Nigeria	51 previously hospitalized COVID-19 patients (median age, 46 years; male, 66.7%) were studied	Retrospective review	9/51 (17.65%)	Cough: 9, fatigue: 8, short of breath: 5, chest pain: 4, palpitations: 2, anxiety: 3, anorexia: 3	History of diabetes, n (%): 4; history of hypertension, n (%): 8	Mild COVID-19 ($P = 0.029$)

(*continued on next page*)

Table 1 (*continued*)

Study ID/Settings	Study population	Study designs	Long COVID prevalence	Predominant symptoms	Comorbidities	Key findings
Osikomaiya et al. [17]/Nigeria	274 patients were enrolled in the study. A majority were within the age group > 35 to ≤49 years (38.3%), and male (66.1%).	A retrospective study design	112/274 (40.9%)	Easy fatigability 35 (12.8), myalgia 24 (8.8), cough 25 (9.2), dyspnea 26 (9.5), chest pain 27 (9.8), loss of appetite 24 (8.8), palpitations 20 (7.4), headache 35 (12.8), insomnia 27 (9.8)	Comorbidities (n = 52), the most common comorbidities were hypertension (72.9%) and diabetes (15.3%)	Moderate COVID-19 (aOR): 2.03 (1.19-3.47)
Pretorius et al. [11]/South Africa	Blood was collected from healthy volunteers (N = 13; six males, seven females; mean age: 52.4 ± 4.8) to serve as controls	Case-control study	N/A	N/A	Type II diabetes mellitus	A significant difference was noted between Platelet poor plasma viscosity of controls and acute COVID-19 ($P = 0.001$) and acute COVID-19 and long COVID/PASC ($P = 0.002$)
Kruger et al. [12]/South Africa	99 long COVID patients and 29 healthy controls. Median age of 51 (40-60) median age	Case-control study	N/A	Constant fatigue: 74%; cognitive impairment ("brain fog"/forgetfulness/poor concentration): 71%; dyspnea 59%; arthralgia/myalgia: 49%; sleep disturbance: 34%; depression/anxiety: 30%; heart rate dysfunc-tion/palpitations: 30%; recurring chest pain: 29%; anosmia (loss of smell) 25%; dysgeusia: (loss of taste) 25%; low oxygen levels 13%	Hypertension 24%; hyperlipidemia 19%; type II diabetes mellitus 6%	N/A
Otmani et al. [13]/Marocco	118 healthcare workers who endured the Covid-19 infection and 118 matched controls. 71% were females. Average age-median (years) 29 (21-54)	Case-control study	56/118 (47.4%)	At least one symptom 56 (47.4%); myalgia 13.3%; anxiety 21.7%; attention disorders, memory impairment "brain fog" 14.4%; sleep disorders 12%; palpitations 10.8%; arthralgia 9.6%; asthenia 25.3%; chest pain 8.4%; anosmia/hyposmia 9.6%	N/A	Pulmonary involvement in chest computed tomography scan
Zulu et al. [19]/Zambia	27 participants. Mean participant age was 32 years (range: 1-85 years). 17 (63.0%) were females	Prospective cohort study	27/182 (37%)	Cough 10 (37.0); rhinorrhea 5 (18.5); headache 7 (25.9); chest pain 6 (22.2); arthralgia 4 (14.8)	HIV 2 (7.4%)	Those with five or more symptoms at onset had nearly ($P = 0.03$); participants with loss of appetite at symptoms onset ($P = 0.01$)
Galal et al. [21]/Egypt	430 participants. They were 156 males and 274 females, their mean age was 37.4 ± 12.6 years, and the range was 12-74 years	Cross-sectional study	268/430 (60%)	Myalgia (60.0%), arthralgia (57.2%), restriction of daily activities (57.0%), and sleeping troubles (50.9%), followed by anorexia (42.6%), chest pain (32.6%), gastritis (32.3%), cough (29.3%), and dyspnea (29.1%)	Diabetes mellitus: 10.9%; hypertension: 15.10%; cardiac disease: 1.9%; chronic pulmonary disease: 5.3%; renal disease: 2.3%; psychiatric disease: 1.6%	Need of oxygen therapy (< 0.001); hypertension (0.039); any chronic illness (0.004)

(*continued on next page*)

Table 1 (*continued*)

Study ID/Settings	Study population	Study designs	Long COVID prevalence	Predominant symptoms	Comorbidities	Key findings
Pretorius et al. [18]/South Africa	845 participants The gender balance (70% female) and the most reported long COVID/PASC symptoms. The majority (i.e., 76%) of the participants were between the ages of 31-40, 41-50, and 51-60 years.	Retrospective cohort	N/A	Fatigue, brain fog, loss of concentration and forgetfulness, shortness of breath, as well as joint and muscle pains	Hypertension, high cholesterol levels (dyslipidemia), cardiovascular disease and type II diabetes mellitus	Microclot and platelet pathologies were associated with long COVID/PASC symptoms that persisted after the recovery from acute COVID-19.
Walker et al. [14]/South Africa	30 matched healthy subjects and 30 PASC subjects	Case-control study	N/A	N/A	N/A	Significant microclot load was observed in the Platelet poor plasma of participants with PASC
Turner et al. [15]/South Africa	25 Long COVID patients. 52 (± 14) years. Females were predominant	Case-control study	N/A	N/A	Hypertension: 36%; hyperlipidemia: 40%; type II diabetes mellitus: 12%; cardiovascular disease: 8%; thrombosis (previous blood clots): 8%; cancer: 12%	Presence of microclotting, together with relatively high levels of six inflammatory molecules known to be key drivers of endothelial and clotting pathology

aOR, adjusted odds ratio; CI, confidence interval; PASC: Post-Acute Sequelae of SARS-CoV-2.

conducted worldwide. However, a single study cannot reflect the prevalence of the African continent. While Peluso et al. [9] concluded that HIV status strongly predicted the presence of long COVID. Other comorbidities associated with severe COVID-19 such as diabetes and cardiovascular disease may also be associated with long COVID. Given the high prevalence of these comorbidities on the African continent, an overall study focusing on African populations is required. We determined the burden of long COVID, prevalent symptoms, key findings, risk factors, and plausible pathophysiology in African populations in this review.

Methods

This section covers study selection strategy, study design, eligibility, inclusive and exclusive criteria, and quality of assessment and synthesis.

Study selection strategy

To ensure the reproducibility and transparency of our findings, studies were selected for systematic reviews (from January 2020 to December 2022) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10]. The studies were chosen based on the following key review research questions: How prevalent is long COVID in African populations? What are the most prevalent long COVID symptoms in African populations? What factors and comorbidities are associated with long COVID in African populations? To respond to these questions, we searched PubMed, Medline, Google Scholar, the World Health Organization COVID-19 Research Database, medRxiv, and bioRxiv for potential studies on long COVID-19 in African populations, employing the following Medical Subject Headings (MESH) terms and keywords as the search strategy: “Post-Acute COVID-19 Syndromes” OR “Long-Haul COVID-19” OR “Long COVID” OR “Post-Acute Sequelae of SARS-CoV-2 Infection” OR “Post-COVID Conditions” OR “Post-COVID Condition” OR “Long-Haul COVID” AND “Comorbidities” AND “epidemiology” [Subheading] OR “Burden of Disease” AND “African populations” OR “African people” OR “Africans”. Only English-language studies were considered. To remove duplicates, studies were imported into the Endnote online tool. The authors took a step-by-step approach, beginning with systematic reviews. The remaining abstracts were screened by one reviewer, and all excluded abstracts were screened by another. One reviewer screened all full-text papers, and a second reviewer screened those that were not. When necessary, a third reviewer was brought in. One reviewer (JLT) extracted the data, and another (PSN) double-checked it. The study ID, setting, population, long COVID prevalence, comorbidities, and statistically significant findings were all included in the data. The Newcastle-Ottawa Scale risk of bias assessment was used to evaluate the study’s quality.

Study design eligible inclusion and exclusion criteria

We only included studies that looked at long COVID prevalence, symptoms, associated comorbidities, and other important findings in African populations. This review included people of all ages. We also included African studies on COVID symptoms that persisted. Furthermore, studies on asymptomatic COVID-19 and those assessing COVID recovery time were excluded from this review.

Data extraction and synthesis

We created a data extraction table to collect information related to the research questions. However, data were extracted for the four most common long COVID symptoms. Data extraction was completed by one reviewer (JLT) and independently checked by a second reviewer (PSN), with discrepancies resolved through discussion. Only evidence directly relevant to the review question was extracted. The data included in the meta-analysis, primarily long COVID prevalence and the four most common symptoms, were extracted into an Excel spreadsheet and the effect sizes and standard errors were calculated. Long COVID prevalence was calculated for each included study by dividing the total number of SARS-CoV-2 infected patients by the total number of long COVID. The number of COVID-19 patients with symptoms divided by the total number of long COVID patients yielded the prevalence for each long COVID symptom.

A meta-analysis was performed for long COVID prevalence and the four most common symptoms. According to the Cochrane Handbook, the prevalence rates were pooled using the random effects model because we expected significant heterogeneity (I^2>50%). Subgroup analy-

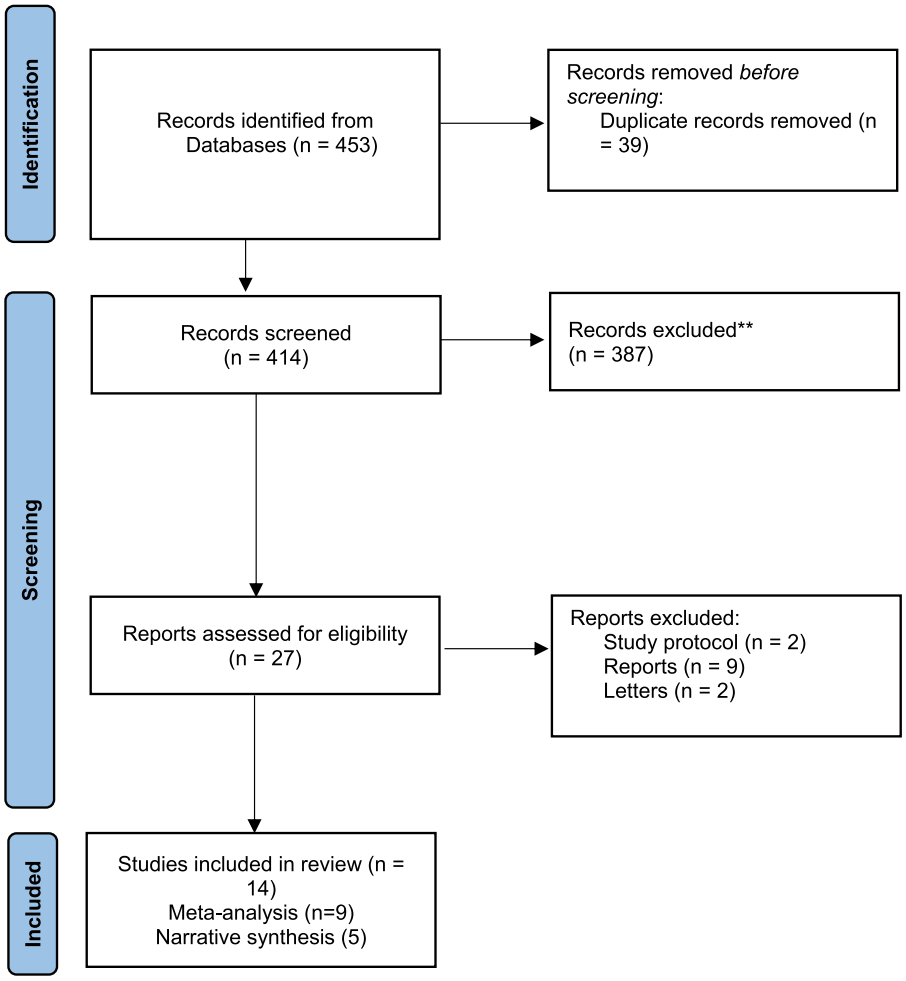

Figure 1. Flow chart of studies reviewing long COVID in African populations.

ses based on setting and long COVID were performed a priori. For small sample studies, Egger's regression and Begg's tests were used to assess publication bias. The P-value for statistical significance was set at 0.05 for all analyses. Stata (V.16, Stata Corp, College Station, Texas, USA) was used for the meta-analysis. Comorbidities and key findings were summarized in a narrative format.

Results

The databases yielded 453 articles, 39 duplicates were removed, and 414 titles and abstracts were screened for eligibility. 387 records were excluded because they were unsuitable for the review. Full texts were obtained for the 27 studies, but 13 were excluded because two were protocols, nine were reports, and two were letters to the editors. Then, 14 studies were included in our analysis, with nine included in the meta-analysis and five included in the narrative synthesis. The review flow chart is shown in Figure 1.

Study and participant characteristics

Fourteen studies were included in this review. Among them, five were case-control studies conducted in South Africa and Morocco [11–15], three retrospective cohort studies undertaken in Nigeria and South Africa [16–18], two prospective cohort studies (South Africa and Zambia) [8,19], two retrospective cross-sectional studies done in South Africa and Egypt [1,20] and two cross-Sectional studies undertaken Ghana and Egypt [21,22]. This review included a total of 6030 previously SARS-CoV-2 infected participants and 2954 long COVID patients. Seven studies reported that long COVID was prevalent among females [1,8,11,13,18–21]. In contrast, three studies have high prevalence rates among males [16,17,22]. Long COVID range of age was 1-85 years [1,8,11,12,15–17,20,21]. Methodological quality of the included studies was reported in Supplementary file 1.

Meta-analysis

The pooled results of long COVID prevalence (95% CI) in African populations revealed a 41% (26-56%) overall prevalence (Figure 2a). This prevalence, however, varied significantly across studies conducted in different African countries. Egypt had the highest prevalence, at 59% (55-64%) (Figure 2a). Nigeria had a prevalence rate of 49% (31-66%). (Figure 2). South Africa, Morocco, and Zambia had prevalence rates of 47% (7-86%), 47% (38-56%), and 15% (10-20%), respectively (Figure 2a). Ghana had the lowest prevalence of 2% (2-3%) (Figure 2a). The degree of heterogeneity between studies was high, with $I^2 = 99.5\%$.

The prevalence of the most common long COVID symptoms in African populations was assessed in Figure 2b. According to the pooled prevalence, fatigue, dyspnea, and confusion or lack of concentration were the most common and prevalent long COVID symptoms among African populations. Fatigue, dyspnea, and confusion or lack of concentration were all prevalent (95% CI) at 41% (26-56%), 25% (12-38%), and 40% (12-68%), respectively (Figure 2b). A study of 845 long COVID participants found that fatigue, brain fog, loss of concentration and forgetfulness, dyspnea, and joint and muscle pains were the most common

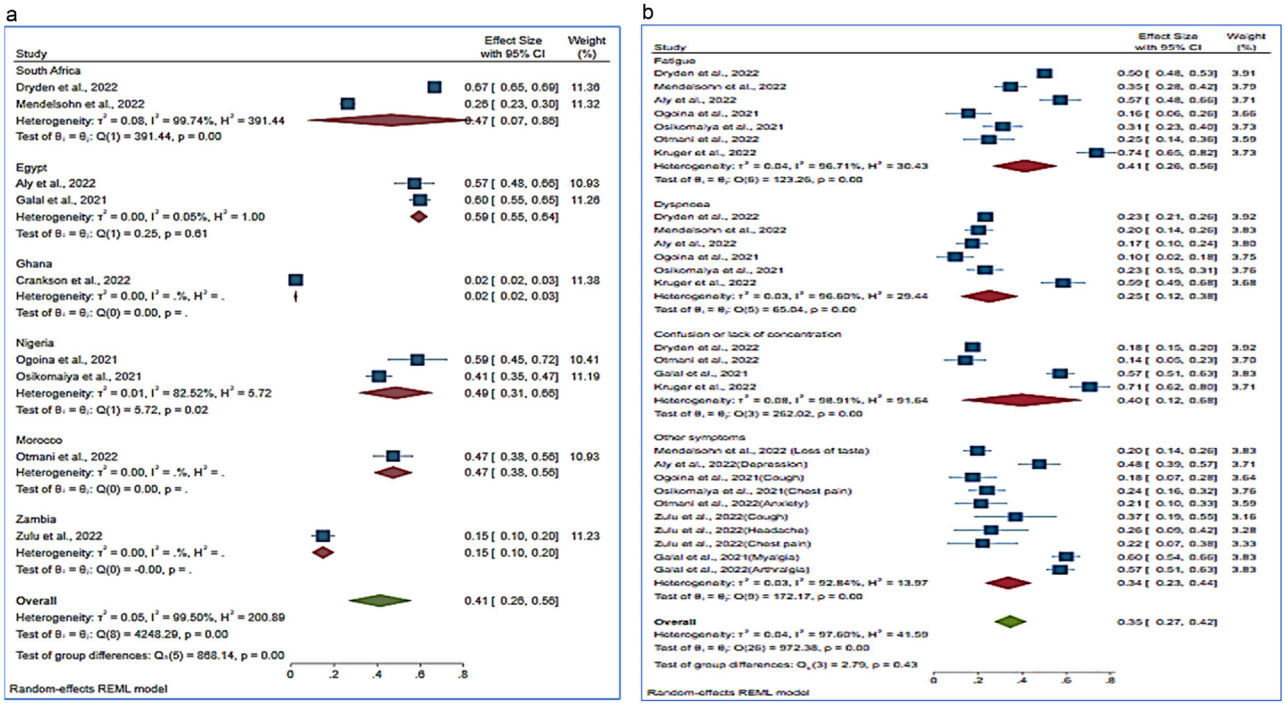

Figure 2. (a) Forest plot of long COVID prevalence in African countries (Right). (b) Forest plot of predominant symptoms of long COVID in African populations (Left). CI, confidence interval.

symptoms in African populations (Table 1). However, due to missing data, we were unable to include this in the meta-analysis.

Other common symptoms were arthralgia, myalgia, depression, chest pain, headache, anxiety, and cough (Figure 2b). Even though the test of heterogeneity between studies was high (I^2 = 97.60%), the test of group difference was not statistically significant (P = 0.43).

Using Egger's regression and Begg's tests, we assessed the publication bias of nine studies that included long COVID prevalence in African populations. With z = 1.49 (P = 0.1538) and z = -0.52 (P = 1.3978), the publication bias was less likely.

Narrative synthesis

The narrative synthesis reported all statistically significant key findings ($P \leq 0.05$) and important findings related comorbidities associated with long COVID and pathophysiology.

Long COVID was statistically associated with advanced age and female sex in African populations ($P \leq 0.05$) [11,23]. In terms of clinical symptoms, long COVID was statistically associated with more than three long COVID symptoms in the acute phase, including initial fatigue and dyspnea, post-recovery stress, sadness and sleep disturbances, and loss of appetite at symptoms onset ($P \leq 0.05$) [1,8,19,20]. Our review also found that long COVID was statistically associated with mild, moderate, and severe COVID-19 ($P \leq 0.05$) [8,16,17,20]. Long COVID was also associated with supplemental oxygen during intensive care unit (ICU) admission and pulmonary involvement in chest computed tomography scan ($P \leq 0.05$) [8,13,21]. Obesity, hypertension, diabetes mellitus, and the presence of any chronic illness were all statistically significant predictors of long COVID [8,21,22]. The most common comorbidities found in long COVID in African populations were hypertension, obesity, hyperlipidemia, diabetes mellitus, HIV, ischemic heart disease, chronic obstructive pulmonary disease/asthma, malignancies, previous tuberculosis, renal disease, thrombosis (previous blood clots), and psychiatric diseases, as shown in Table 1 and Supplemental Figure 1. In terms of pathophysiology, African studies found that long COVID patients had higher microclot and platelet-poor plasma (PPP) viscosity when compared to control groups [11,14,15,18]. Furthermore, high levels of six inflammatory molecules were detected, including serum Amyloid A (SAA), -2 antiplasmin (-2AP), platelet factor 4 (PF4), Von Willebrand Factor (VWF), endothelial-leukocyte adhesion molecule 1 (E-selectin), and platelet endothelial cell adhesion molecule-1 (PECAM-1) [15].

Discussion

We conducted a systematic review to determine the burden of long COVID, prevalent symptoms, key findings, risk factors, and plausible pathophysiology in African populations. This review included 14 studies on long COVID conducted in African populations. This study included 6030 previously SARS-CoV-2 infected participants and 2954 long COVID patients. Females outnumbered males among long COVID patients. The ages ranged from one to 85 years. The pooled prevalence (95% CI) of long COVID in the African population was 41% (26-56%). In comparison to a review of 50 included studies, 41 of which were meta-analyzed, the global estimated pooled prevalence of long COVID-19 was 43% (39-46%) [24]. Long COVID prevalence was higher in Africa than in North America (31% [21-43%]), but lower in Europe (44% [32-56%]) and Asia (51% [37-65%]) [24]. In comparison to other world regions, Africa's population is very young. Long COVID prevalence may be lower in African populations than the rest of the world based on this evidence. However, a study found a significant high frequency of undetected comorbidities associated with severe COVID-19 among hospitalized African populations, primarily HIV, active tuberculosis, diabetes mellitus, and hypertension [25]. These comorbidities were detected in 72.3% of African populations aged 18-64 years [25]. Knowing that pre-existing comorbidities such as asthma, type I diabetes, hypertension, tuberculosis, and HIV were related to long COVID-19, this could be a possible explanation for the high long COVID prevalence among African populations.

The prevalence (95% CI) of the most common symptoms were 41% (26-56%) fatigue, 40% (12-68%) confusion or lack of concentration, and 25% (12-38%) dyspnea. Our results agreed with a global review showing that fatigue was the most common symptom reported with a prevalence of 23% (17-30%) [24,25], followed by confusion or lack of

concentration 14% (10-19%) and dyspnea 13% (11-15%) [24]. Even though the African long COVID prevalence was slightly lower than the global prevalence, the Africans had higher rates of fatigue, confusion or lack of concentration, and dyspnea. Further research may be required to clarify these findings.

Our findings also revealed that long COVID was statistically associated with advanced age and being female in African populations [8,20]. Our findings were consistent with the findings of Chen et al. [24], who found that female sex was a risk factor for long COVID. Long COVID was statistically associated with more than three long COVID symptoms in the acute phase, including initial fatigue and dyspnea, post-recovery stress, sadness, sleep disturbances, and loss of appetite at the onset of symptoms [1,8,19,20]. Our findings support the results from previous systematic reviews and meta-analyses on long COVID symptoms [24,25].

Our study also found that long COVID was statistically associated with mild, moderate, and severe COVID-19 [8,16,17,20]. This could be explained by a significant increase in the rates of thrombotic events following even a mild COVID-19 infection [15,26]. Long COVID was also statistically associated with supplemental oxygen during ICU admission and pulmonary involvement in chest computed tomography scans [8,13,21]. A study that looked at the long-term outcomes of patients who needed ICU admission for severe COVID-19 found that the long-term effects of severe COVID-19 lasted more than 6 months [27]. Obesity, hypertension, diabetes mellitus, and the presence of any chronic illness were all statistically significant predictors of long COVID [8,21,22].

From the point of view pathophysiology, African studies demonstrated high microclot and PPP viscosity were statistically higher in long COVID patients compared to the control groups [11,14,15,18]. In addition, high levels of six inflammatory molecules SAA, α-2AP, PF4, VWF, E-selectin, and PECAM-1, are known to be key drivers of endothelial and clotting pathology [15]. Long COVID may generate further complications based on hypercoagulation and thrombosis associated with advanced age and pre-existing comorbidities. As an example, in African populations, a study reported that two people living with HIV developed cardiovascular complications (myocardial infarction and arrhythmia) during the 3 months of follow-up [28]. HIV status was strongly associated with long COVID, raising concerns that this condition might be common among people living with HIV recovering from COVID-19 [9]. Certainly, two main hypotheses should be considered. Firstly, it is well known how COVID-19 may cause and worsen cardiovascular events, especially in patients who are at increased risk such as people living with HIV who also are at increased risk of hypertension, diabetes mellitus, dyslipidemia, previous thrombosis, and obesity. Secondly, in patients with known pre-existing cardiovascular risk factors, SAA, α-2AP, PF4, VWF, E-selectin and PECAM-1 induced by the presence of SARS-CoV-2 may have worsened and accelerated the cardiac damage and caused stress cardiomyopathy [15,28,29]. Turner et al. [15] explained long COVID as the interaction between endothelial dysfunction, chronic inflammation, and platelet activation generating the formation of microclot, inducing the raised of the above-mentioned six inflammatory molecules and hypercoagulation and thrombosis. This is significant because diabetes type II is a risk factor for long COVID in African populations and is associated with hypercoagulation states [11]. Comorbidities associated with an increased risk of long COVID, and hypercoagulability include cardiovascular disease, renal failure, venous thrombosis, cancer, and chronic obstructive pulmonary disease [30].

Given that Africa has the lowest COVID-19 vaccination rate among continents, this could be another risk factor for long COVID in Africa. A systematic review of six studies (n = 17,256,654 individuals) investigating the impact of vaccines before acute SARS-CoV-2 infection found a low level of evidence suggesting that vaccination before SARS-CoV-2 infection could reduce the risk of subsequent long COVID infection [31]. As with most common chronic conditions, the causation is not yet well understood. However, long COVID causation should be viewed as a multifactorial interaction between individual comorbidities, past medical history, SARS-CoV-2 variants, genetic factors, and ethnicity. Supplemental Figure 1 in our study has clearly highlighted the multifactorial factors of long COVID in African populations. The reason that some individuals are more prone to develop long COVID possibly lies in their genetic profile primarily related to the immune system, such as human leukocyte antigen [5]. Long COVID may be the result of tissue/organ damage, or inflammatory and immune pathways dysfunction (including chronic inflammation, hypercoagulation, thrombosis, hyperactive immune cells, and autoimmunity because of molecular mimicry) [8,11,14,15,18]. This results in differences in long COVID prevalence rates and symptoms among populations.

To the best of our knowledge, this is the first systematic review and meta-analysis of long COVID and its most common symptoms. This review will be useful in future research on long COVID and comorbidities in African populations, particularly comorbidities associated with thrombosis risk in African populations. The review's main weaknesses were the small number of included studies, poor study design of included studies, missing data, and high heterogeneity between studies. However, publication bias was less likely because Egger's regression and Begg's tests were not statistically significant with z = 1.49 (P = 0.1538) and z = -0.52 (P = 1.3978), respectively, and the test of group difference for long COVID symptoms was not statistically significant (P = 0.43).

Conclusion

This review looked at the various characteristics of long COVID in Africa. Despite having the lowest number of COVID-19 cases, the prevalence of long COVID cases in Africa was closer to the global prevalence. Even though fatigue, dyspnea, and confusion or lack of concentration were the most common symptoms globally and in Africa, their prevalence rates were higher in Africa. Long COVID was associated with advanced age, female sex, three long COVID symptoms in the acute phase, initial fatigue and dyspnea, post-recovery stress, sadness, and sleep disturbances, and loss of appetite at symptoms onset, mild, moderate, and severe, pre-existing obesity, hypertension, diabetes mellitus, and the presence of any chronic illness in African populations. According to our review, the pathophysiology of long COVID is explained by high microclot and PPP viscosity. This may raise the risk of additional cardiovascular complications in African populations. Future research should focus on long COVID, and comorbidities associated with hypercoagulation and thrombosis in African populations.

Declarations of competing interest

The authors have no competing interests to declare.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

Not applicable.

Author contributions

PSN conceived the review. PSN and JLT searched potential peer-review manuscripts. PSN and JLT conducted the data extraction. JLT undertook the data analysis. PSN and JLT drafted the manuscript. PSN, JLT, and RTE edited the manuscript. This version was reviewed and approved by all the authors.

Informed consent statement

Not applicable.

Availability of data and materials

All data and materials are available in this manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2023.08.004.

References

[1] Aly MAEG, Saber HG. Long COVID and chronic fatigue syndrome: a survey of elderly female survivors in Egypt. *Int J Clin Pract* 2021;**75**:e14886. doi:10.1111/ijcp.14886.

[2] Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalmedicine* 2021;**38**:101019. doi:10.1016/j.eclinm.2021.101019.

[3] Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. *Nat Med* 2021;**27**:626–31. doi:10.1038/s41591-021-01292-y.

[4] Centers for Disease Control and Prevention. Long COVID or post-COVID conditions. Available on: https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html. [accessed 29 May 2023].

[5] Akbarialiabad H, Taghrir MH, Abdollahi A, Ghahramani N, Kumar M, Paydar S, et al. Long COVID, a comprehensive systematic scoping review. *Infection* 2021;**49**:1163–86. doi:10.1007/s15010-021-01666-x.

[6] Baig AM. Deleterious outcomes in Long-Hauler COVID-19: the effects of SARS-CoV-2 on the CNS in chronic COVID syndrome. *ACS Chem Neurosci* 2020;**11**:4017–20. doi:10.1021/acschemneuro.0c00725.

[7] World Health Organization. COVID-19 weekly epidemiological update. Available on: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19-18. 2023. [accessed 30 May 2023].

[8] Dryden M, Mudara C, Vika C, Blumberg L, Mayet N, Cohen C, et al. Post-COVID-19 condition 3 months after hospitalisation with SARS-CoV-2 in South Africa: a prospective cohort study. *Lancet Glob Health* 2022;**10**:e1247–56. doi:10.1016/S2214-109X.

[9] Peluso MJ, Spinelli MA, Deveau TM, Forman CA, Munter SE, Mathur S, et al. Postacute sequelae and adaptive immune responses in people with HIV recovering from SARS-COV-2 infection. *AIDS (Lond Engl)* 2022;**36**:F7–F16. doi:10.1097/QAD.0000000000003338.

[10] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *PLoS Med* 2021;**18**:e1003583. doi:10.1371/journal.pmed.1003583.

[11] Pretorius E, Vlok M, Venter C, Bezuidenhout JA, Laubscher GJ, Steenkamp J, et al. Persistent clotting protein pathology in long COVID/post-acute sequelae of COVID-19 (PASC) is accompanied by increased levels of antiplasmin. *Cardiovasc Diabetol* 2021;**20**:172. doi:10.1186/s12933-021-01359-7.

[12] Kruger A, Vlok M, Turner S, Venter C, Laubscher GJ, Kell DB, et al. Proteomics of fibrin amyloid microclots in long COVID/post-acute sequelae of COVID-19 (PASC) shows many entrapped pro-inflammatory molecules that may also contribute to a failed fibrinolytic system. *Cardiovasc Diabetol* 2022;**21**:190. doi:10.1186/s12933-022-01623-4.

[13] El Otmani H, Nabili S, Berrada M, Bellakhdar S, El Moutawakil B, Abdoh Rafai M. Prevalence, characteristics and risk factors in a Moroccan cohort of Long-Covid-19. *Neurol Sci* 2022;**43**:5175–80. doi:10.1007/s10072-022-06138-0.

[14] Walker M, Federico EM, Kell DB, Dupont C, Proal A, Pretorius E. Detection and characterization of fibrin/amyloid microclots in patients with post-acute sequelae of Covid-19. *Circulation* 2022;**146**:A15637. doi:10.1161/circ.146.suppl_1.15637.

[15] Turner S, Naidoo CA, Usher TJ, Kruger A, Venter C, Laubscher GJ, et al. Increased levels of inflammatory and endothelial biomarkers in blood of long COVID patients point to thrombotic endothelialitis. *Semin Thromb Hemost* 2023. doi:10.1055/s-0043-1769014.

[16] Ogoina D, James HI, Ogoinja SZ. Post-discharge symptoms among hospitalized COVID-19 patients in Nigeria: a single-center study. *Am J Trop Med Hyg* 2021;**105**:731–6. doi:10.4269/ajtmh.21-0509.

[17] Osikomaiya B, Erinoso O, Wright KO, Odusola AO, Thomas B, Adeyemi O, et al. 'Long COVID': persistent COVID-19 symptoms in survivors managed in Lagos State, Nigeria. *BMC Infect Dis* 2021;**21**:304. doi:10.1186/s12879-020-05716-x.

[18] Pretorius E, Venter C, Laubscher GJ, Kotze MJ, Oladejo SO, Watson LR, et al. Prevalence of symptoms, comorbidities, fibrin amyloid microclots and platelet pathology in individuals with long COVID/post-acute sequelae of COVID-19 (PASC). *Cardiovasc Diabetol* 2022;**21**:148. doi:10.1186/s12933-022-01579-5.

[19] Zulu JE, Banda D, Hines JZ, Luchembe M, Sivile S, Siwingwa M, et al. Two-month follow-up of persons with SARS-CoV-2 infection-Zambia, September 2020: a cohort study. *Pan Afr Med J* 2022;**41**:26. doi:10.11604/pamj.2022.41.26.30721.

[20] Mendelsohn AS, Nath N, De Sá A, Von Pressentin KB. Two months follow-up of patients with non-critical COVID-19 in Cape Town, South Africa. *S Afr Fam Pract (2004)* 2022;**64**:e1–6. doi:10.4102/safp.v64i1.5429.

[21] Galal I, Hussein AA, Amin MT, Saad MM, Zayan HE, Abdelsayed MZ, et al. Determinants of persistent post-COVID-19 symptoms: value of a novel COVID-19 symptom score. *Egypt J Bronchol* 2021;**15**:1–8. doi:10.1186/s43168-020-00049-4.

[22] Crankson S, Pokhrel S, Anokye NK. Determinants of COVID-19-related length of hospital stays and long COVID in Ghana: a cross-sectional analysis. *Int J Environ Res Public Health* 2022;**19**. doi:10.3390/ijerph19010527.

[23] Mazzitelli M, Trunfio M, Sasset L, Leoni D, Castelli E, Lo Menzo S, et al. Factors associated with severe COVID-19 and post-acute COVID-19 syndrome in a cohort of people living with HIV on antiretroviral treatment and with undetectable HIV RNA. *Viruses* 2022;**14**:493. doi:10.3390/v14030493.

[24] Chen C, Haupert SR, Zimmermann L, Shi X, Fritsche LG, Mukherjee B. Global prevalence of post-coronavirus disease 2019 (COVID-19) condition or long COVID: a meta-analysis and systematic review. *J Infect Dis* 2022;**226**:1593–607. doi:10.1093/infdis/jiac136.

[25] Jassat W, Blumberg L, Cohen C, Potgieter S, Black J, Parker A, et al. Undiagnosed comorbidities among individuals hospitalised with COVID-19 in South African public hospitals. *S Afr Med J* 2022;**112**:747–52. doi:10.7196/SAMJ.2022.v112i9.16417.

[26] Global Burden of Disease Long COVID CollaboratorsEstimated global proportions of individuals with persistent fatigue, cognitive, and respiratory symptom clusters following symptomatic COVID-19 in 2020 and 2021. *JAMA* 2022;**328**:1604–15. doi:10.1001/jama.2022.18931.

[27] Al-Aly Z, Bowe B, Xie Y. Long COVID after breakthrough SARS-CoV-2 infection. *Nat Med* 2022;**28**:1461–7. doi:10.1038/s41591-022-01840-0.

[28] Neville TH, Hays RD, Tseng CH, Gonzalez CA, Chen L, Hong A, et al. Survival after severe COVID-19: long-term outcomes of patients admitted to an intensive care unit. *J Intensive Care Med* 2022;**37**:1019–28. doi:10.1177/08850666221092687.

[29] Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. *Nat Rev Cardiol* 2020;**17**:543–58. doi:10.1038/s41569-020-0413-9.

[30] Rahaghi FN, Pistenmaa CL. Hypercoagulation in COPD: the clot thickens. *ERJ Open Res* 2021;**7**:00534–2021. doi:10.1183/23120541.00534-2021.

[31] Notarte KI, Catahay JA, Velasco JV, Pastrana A, Ver AT, Pangilinan FC, et al. Impact of COVID-19 vaccination on the risk of developing long-COVID and on existing long-COVID symptoms: a systematic review. *EClinicalmedicine* 2022;**53**:101624. doi:10.1016/j.eclinm.2022.101624.