

Post-COVID-19 condition in low-and-middle-income countries: pilot study

Summary

Study Rationale

As the COVID-19 pandemics unfold, reports of postinfectious sequelae were also cumulating. A wide number of health complaints have been described as remaining, emerging, or reemerging among COVID-19 patients. This led to the terms post-COVID condition (PCC) or long COVID. Symptoms seem very diverse, suggesting damage in different body organs, along with general fatigue and malaise, neurological and mental disorders.

Despite the widespread nature of the problem, knowledge of this condition is still limited. Most studies have included only patients discharged after COVID-related hospitalizations. Exclusion of cases with mild or no clinical disease, which account for most SARS-CoV-2 infected individuals, or lack of comparisons with non-COVID cases may overestimate the problem. Furthermore, the outcomes registered across studies have been inconsistent, making very difficult to combine and compare their findings and to generate precise estimates of the burden of this emerging public health threat.

Given the foreseeable dimension of this problem, it is necessary to reliably estimate the magnitude of this emerging condition, to understand its determinants and consequences and to find effective treatments. This will be particularly important for low-and-middle-income countries (LMICs), with more limited resources to prevent, treat, or rehabilitate from PCC.

Study aim

To conduct a pilot study on PCC in centers of LMICS:

- a) Testing the feasibility of data collection under the same protocol
- b) Generating a preliminary estimate of the burden of COVID-19
- c) Contributing to inform a full-scale study proposal
- d) Building capacity to participate in future trials of PCC treatment candidates

Study design

Centers will gather data for about two months by including different types of individuals according to their SARS-CoV-2 infection status and the severity of disease. For efficiency, we will use clinical registries, both in hospitals and diagnostic labs, to identify cases with varying clinical severity [severe/mild/asymptomatic] who were tested for SARS-CoV-2 infection with PCR [+/-].

Participant centers will identify a representative sample of *index cases* with severe/critical disease. Based on their case density, centers must choose an *index case* around the peak of admissions within 6-12 months of starting the data collection, seeking the following admissions, consecutively. Each index case will be paired with similar number of cases of different characteristics, age, sex, and disease severity, diagnosed around the same date (± 1 week), assembling the following groups:

1. Severe/critical disease

- a. COVID-19: these patients were admitted to the hospital with both clinical and laboratory diagnosis of COVID-19. May or may not be admitted to ICU or received non-invasive ventilation.
- b. Non COVID-19: these patients were admitted to the hospital with **neither** clinical suspicion **nor** laboratory test indicating COVID-19. May or may not be admitted to ICU or received non-invasive ventilation. Examples include bacterial pneumonia, surgical/wound infection, severe trauma/burns leading to ARDS, complications after non-cardiac surgery.

2. Mild disease

- a. COVID-19: these patients were seen but not admitted to the hospital or sought outpatient medical care, had clinical suspicion and laboratory diagnosis of COVID-19, but their severity did not warrant hospitalization/referral.
- b. Non COVID-19: these patients were seen at, but not admitted to, the hospital or sought outpatient medical care, may or may not had clinical suspicion of COVID-19, had a sample taken for PCR but had a **negative result**. Their clinical condition did not warrant hospitalization/referral. Examples include acute infectious diseases or underlying medical conditions.

3. Asymptomatic

These patients had, around the same time of cases 1a or 2a a sample taken for PCR, either for surveillance/research or as contact of a positive case.

- a. SARS-CoV-2 asymptomatic infection
- b. SARS-CoV-2 negative controls

Each participant center may decide to include groups 2 or 3 according to their access to PCR information for outpatients. However, all centers must collect at least 1 paired case for each participant of groups **1a and 1b**.

Exposures of interest will be socio-demographic variables including access to information related to COVID-19, vaccination status/willingness, patient's relevant medical history and medical issues around the index event (see [CRF](#)). Data will be collected retrospectively, based on patient's charts. Additional information will be gathered by remote contact (telephone/virtual interview), to include missing data on the index event and clinical status afterwards. In the meantime, participants may or may not be included in clinical trials of PCC.

The primary outcome will be a composite of hospitalization, absence from work for at least two days or getting medical care for medical reasons (excluding trauma/burns without lung injury, etc.).

Sample size

Each center will contribute with 100-150 patients, 25 per 4-6 groups. We expect to include at least 600 patients from at least 3 LMICs.

Study procedures and organization

The study will be overseen by the clinical epidemiology working group of the CRC, as steering committee. Every participating center must identify a principal site investigator (PI), responsible for conducting the study locally. The PI also holds responsibility for submission before the ethics committee/IRB when it applies. For this pilot, centers will be responsible for gathering the resources necessary to complete the expected data collection. The study coordination will provide technical support to administer the study CRFs and will be monitoring the completeness and integrity of data submitted.