

# Determining the malaria burden and long-term complications following SARS-CoV-2 infection

## Establishing the relationship between malaria and COVID-19

### Background

The continuing spread of SARS-CoV-2 remains a public health emergency. A Malaria Consortium study on COVID-19 and malaria interactions recently determined the prevalence and magnitude of the clinical overlap between SARS-CoV-2 and malaria; it also described the possible consequences of co-infection and the potential effects of previous malaria exposure on clinical profiles and outcomes of COVID-19 patients.<sup>[1]</sup> However, the potential impact of previous SARS-CoV-2 infection on the likelihood of contracting malaria among recovered patients is unknown.

We postulate that previous infection with the SARS-CoV-2 virus could potentially increase the risk of malaria infection, either through persistent inflammation post SARS-CoV-2 infection<sup>[2,3]</sup> or damage to specific tissues targeted by both pathogens,<sup>[4-6]</sup> or through ecological, epidemiological, or even sociological factors that increase the probability of exposure to both pathogens. Any possible increase in the risk of contracting malaria would be a major public health concern in sub-Saharan Africa, especially when previous gains in malaria burden reduction over the past decade have recently stalled.<sup>[7]</sup>

### Country

Ethiopia and Uganda

### Donor

Malaria Consortium U.S.

### Length of project

April 2022 – September 2023

### Partners

Ministry of Health, Ethiopia

Ministry of Health, Uganda

Mulago National Referral Hospital, Uganda

St. Paul's Hospital Addis Ababa, Ethiopia

## Project outline and objectives

This study is taking place in Ethiopia and Uganda. It uses both qualitative and quantitative approaches and a case-control study design to explore the relationship between past SARS-CoV-2 infection and malaria risk. A sample size of 2400 cases and 2400 controls (n=4800) will be enrolled from both countries. In Ethiopia, we will conduct the study in three hospitals: one in Addis Ababa and two in Hawassa. In Uganda, the study will be conducted in different COVID-19 treatment centres across the country.

The study population includes individuals across all age groups, both male and female, with previous SARS-CoV-2 infection (who were either hospitalised or not hospitalised during acute illness) as well as those without. Three overarching questions underpin this study: How do people with long term complications of COVID-19 (including those who were never hospitalised) experience the development, course and resolution of the illness over time? What services have they accessed (or tried to access), and what was their experience of those services? What are their ideas for improving the management of their condition and the design and delivery of services?

The specific objectives in both countries are to:

- compare the prevalence of, and risk factors for, malaria infection among individuals with and without previous SARS-CoV-2 infection
- compare the prevalence of fever and describe healthcare pathways for its management among individuals with and without previous SARS-CoV-2 infection
- determine the prevalence and predictors, and describe the clinical spectrum, of long-term complications of COVID-19

among individuals with previous SARS-CoV-2 infection, as well as its risk factors

- describe the association between previous malaria exposure and the development of long-term complications of COVID-19 among individuals with previous SARS-CoV-2 infection
- describe the relationship between previous malaria exposure and risk of SARS-CoV-2 infection.

## Activities

To achieve these objectives, Malaria consortium will:

- collect demographic and clinical information using standard case record forms
- compare the frequency of SARS-CoV-2-specific memory CD4+ and/or CD8+ T cell responses among the different clinical groups to determine whether previous malaria exposure and potentially important immunologic differences exist among groups with malaria versus those with no malaria, and individuals experiencing long-term complications of COVID-19 versus those who have fully recovered
- compare previous malaria exposure among individuals with past SARS-CoV-2 infection (cases) and individuals with no past SARS-CoV-2 infection (controls) to establish whether previous malaria exposure is protective against SARS-CoV-2 infection
- conduct at least 200 individual interviews and four focus group discussions in each country with individuals who report a previous episode of fever post-acute COVID-19 illness, and/or those with other long-term complications of COVID-19.

## References

1. Achan J, Serwanga A, Wanzira H, Kyagulanyi T, Nuwa A, Magumba G, et al. Current malaria infection, previous malaria exposure and clinical profiles and outcomes of COVID-19 in a setting of high malaria transmission: An exploratory cohort study in Uganda. *The Lancet Microbe*, 2022; 3(1):e62-e71. doi.org/10.1016/S2666-5247(21)00240-8.
2. Rahmani-Kukia N, Abbasi A. Physiological and immunological causes of the susceptibility of chronic inflammatory patients to COVID-19 infection: Focus on diabetes. *Frontiers in Endocrinology*, 2021; doi.org/10.3389/fendo.2021.576412.
3. Merad M, Subramanian A, Wang TT. An aberrant inflammatory response in severe COVID-19. *Cell Host & Microbe*, 2021; 29(7): 1043–47.
4. Peiris S, Mesa H, Aysola A, Manivel J, Toledo J, Borges-Sa M, et al. Pathological findings in organs and tissues of patients with COVID-19: A systematic review. *PLOS ONE*, 2021; <https://doi.org/10.1371/journal.pone.0250708>.
5. Mokhtari T, Hassani F, Ghaffari N, Ebrahimi B, Yarahmadi A, Hassanzadeh G. COVID-19 and multiorgan failure: A narrative review on potential mechanisms. *Journal of Molecular Histology*, 2020, 51: 613–28. doi: 10.1007/s10735-020-09915-3.
6. Knackstedt SL, Georgiadou A, Apel F, Abu-Abed U, Moxon CA, Cunnington AJ, et al. Neutrophil extracellular traps drive inflammatory pathogenesis in malaria. *Science Immunology*, 2019; 4(40): eaaw0336 DOI: 10.1126/sciimmunol.aaw0336.
7. World Health Organization. World malaria report 2020. Geneva: World Health Organization; 2020. Available from: <https://www.who.int/publications/i/item/978924001579>.

## © Malaria Consortium / July 2022

Unless indicated otherwise, this publication may be reproduced in whole or in part for non-profit or educational purposes without permission from the copyright holder. Please clearly acknowledge the source and send a copy or link of the reprinted material to Malaria Consortium. No images from this publication may be used without prior permission from Malaria Consortium.

UK Registered Charity No: 1099776

Contact: [info@malariaconsortium.org](mailto:info@malariaconsortium.org)

Cover image: COVID-19 virus visualisation

 **FightingMalaria**  
 **MalariaConsortium**  
[www.malariaconsortium.org](http://www.malariaconsortium.org)



**malaria  
consortium**  
disease control, better health