

TGHN Workshop Report – COVID-19 Hub

What Impact Could COVID-19 Have on Malaria?

Introduction

On the 14th of April The Global Health Network ([TGHN](#)) supported the virtual workshop “[What impact could COVID-19 have on malaria?](#)”. This workshop contributed to the [workshop series](#) on the COVID-19 response from various regions across the globe, organized by TGHN at the University of Oxford, UK in partnership with the [Malaria Consortium](#).

The [Malaria Consortium](#), established in 2003, is one of the world’s leading non-profit organisations specialising in the prevention, control and treatment of malaria and other communicable diseases among vulnerable populations. Having found that their work on malaria can be effectively integrated with similar public health interventions for greater impact they have expanded their remit to include child health and neglected tropical disease interventions. Their areas of expertise include:

- disease prevention, diagnosis and treatment
- disease control and elimination
- health systems strengthening
- research, monitoring and evaluation leading to best practice
- behaviour change communication
- national and international advocacy, and policy development

The Workshop aimed to identify and discuss the potential clinical interactions between malaria and COVID-19, the effects of the responses to the pandemic on health systems in the context of malaria control and research priorities regarding malaria in the context of the COVID-19 pandemic. The workshop featured a panel of 3 experts – Dr Prudence Hamade, Dr James Tibenderana and Dr Jane Achan – who are Senior Technical Advisor, Global Technical Director and Senior Research Advisor at the Malaria Consortium.

A total of almost 1000 people registered for the webinar and so the registration system was closed, as this number far exceeded the capacity of the teleconferencing software’s license purchased at that time. We then invited the maximum number of participants that could be accommodated (200). As a result, 190 participants, spanning 48 countries attended the workshop.



Figure 1 Location of attendees. Participants attended the workshop from the 48 countries shaded in dark blue.

Summary of Panellist Presentations:

Potential clinical interactions between COVID-19 and malaria in different at-risk populations

Dr Prudence Hamade,

Senior Technical Advisor, Malaria Consortium

Demography of the populations at risk from both malaria and COVID-19:

COVID-19	Malaria
Older adults in upper and middle-income countries have been most affected by COVID-19 as associated risk factors for severe disease and mortality have been non-communicable disease and age.	In high transmission areas children and pregnant women have been most affected by malaria due to lack of acquired immunity.
ACE ₂ receptors play a major role in hypertension and diabetes, and these have been identified as major contributors to excess mortality in COVID-19.	In low transmission/pre-elimination settings all age groups can be infected. In Asia young men going into forested areas can be most affected due to the nature of the vectors and the behaviors of the population.

Then Prudence described the case fatality rate by age range of COVID-19 using as examples the populations in South Korea and Italy. The risk of mortality increases with age, and the age distribution of a country may affect the mortality rate.

Pathophysiology and symptoms of both malaria and COVID-19 was explored.

COVID-19

- Coronavirus attaches to ACE₂ receptors in epithelial cells mainly of nose, pharynx and lungs but also of the gastrointestinal tract replicate and travels to other organs such as heart liver and kidneys.
- Destruction of the alveolar cells can lead to less oxygen transfer leading to ARDS
- COVID-19 pneumonia can also produce anaemia due to pro-inflammatory response which shortens the RBC life and suppresses progenitors of RBCs response to erythropoietin
- Exaggerated pro-inflammatory response leads to exudation of fluids into alveolar space reducing oxygen transfer and leading to ANDS, tissue hypoxia and septic shock
- Virus can attack epithelial cells throughout the body damaging kidneys heart and blood vessels
- ACE 2 receptors play a major role in hypertension and diabetes and these have been identified as major contributors to excess mortality in COVID-19 patients so adults mainly affected

Malaria

- Malaria parasites enter liver cells, multiply and burst into the circulation, entering the RBCs
- Vivax malaria can recur due to stored parasites in liver leading to debilitation and increased risk of chronic anaemia
- Malaria parasites can sequester in major organs blocking circulation leading to tissue hypoxia and organ failure, increase in lactic acid and acute respiratory distress syndrome (ARDS) and septic shock
- Increased metabolic demand can lead to hypoglycaemia
- Breakdown of RBC can lead to acute severe anaemia contributing to reduced capacity to transport oxygen and adding to risk of tissue hypoxia and septic shock
- Overreaction of pro-inflammatory response due to sequestration of parasite in vital organs can lead to organ failure and septic shock

Symptoms, diagnosis, treatment and associated challenges for asymptomatic/mild/severe Malaria and COVID-19

	Symptoms	Diagnosis and Treatment	Challenges
uncomplicated malaria Simple P. vivax infection Asymptomatic malaria	Fever: headache, malaise, weakness, body aches	Can be treated in the community Biological test plus ACT Home Visit after three days to determine status of patient Chloroquine plus primaquine Refer if no improvement PCR hsRDT Sleep under LLIN	Can be infectious
Asymptomatic COVID-19	None	Self-isolation for 7 days	Can be infectious
Mild COVID	Fever cough: fast breathing headache malaise, sore throat, weakness fatigue diarrhoea, anosmia	Seek urgent help if condition deteriorates	Difficult in LMIC settings How will patient be taken to hospital to avoid contaminating others
Malaria/ mild COVID-19	Fever cough fast breathing malaise weakness sore throat diarrhoea	Test and treat for malaria Refer for COVID test	Malaria diagnostic and follow up challenges Role of antimalarial drugs ACTS Chloroquine and primaquine/tafenoquine not known
Severe Malaria	Can progress very rapidly after first symptoms Is a multi-organ disease (kidney, liver) Hypoglycaemia and cerebral signs, convulsions, loss of consciousness ARDS, lactic acidosis, septic shock	Injectable artesunate followed by ACT Supportive treatment O2 Blood transfusion for severe anaemia Glucose for hypoglycaemia	High mortality if untreated Health workers not at risk
Severe COVID-19	Long delay between onset of Symptoms and onset of severe disease Low lymphocyte count and low platelets associated with poor prognosis Can affect kidney liver, and especially heart and circulatory systems	Would interventions during this period such as glucocorticoids prevent over reaction of the inflammatory system Supportive treatment O2/ventilation Experimental drugs	Risk Of infection in A&E and triage areas Patients should be treated in isolation or COVID only wards. Will specific interventions for malaria coinfection be in place such as LLINs, antimalarials Need protection for health workers
Severe coinfection	High risk of ARDS and Shock	Rapid treatment with injectable AS plus antibiotics Supportive treatment Blood transfusion Y/N Risks of Intubation/ventilation in patients with cerebral malaria Role Of glucose for hypoglycaemia	What effect will blood transfusion have on outcomes Role of glucose; and anticoagulants-not a good idea in malaria Experimental treatment drug interactions

Comparison of malaria and COVID-19 regarding referral and management at the health facility level:

Malaria:

- If severe symptoms immediate transfer to a hospital with facilities to care for severely ill patients. ICU ideal but not always needed

- No special requirements for protection of patient or caregivers needed to prevent infection during transfer
- Diagnosis with both RDT and microscopy should be done
- Can be treated on any ward no special isolation needed (LLINS should be used)
- Triage needed to ensure rapid case management
- In areas with proven COVID-19 community transmission should follow COVID-19 protocols
- If patient has any respiratory symptoms should test for COVID-19 and give antibiotics

COVID-19:

- If severe symptoms immediate transfer to a hospital with facilities to care for severely ill patients ICU often needed
- Special protection and IPC needed for transfer (no public transport should be used), patient and care giver should wear mask and care giver gloves. Transport means should be disinfected after transfer where possible
- If COVID-19 is suspected should be placed in separate room immediately with as much ventilation as possible and sample taken for testing. Nasal and pharyngeal swabs
- Staff should wear PPE, patient should be tested for malaria HIV and possibly TB (at least take history)
- Staff conducting triage should have access to PPE if community transmission is taking place

Comparison of malaria and COVID-19 regarding diagnostic issues and challenges:

	Malaria	COVID-19
Diagnostic tests	RDT Microscopy PCR LAMP Serology	rtPCR: sensitivity at different stages of the disease may vary. In China sometimes needed to repeat test up to five time to determine positivity. Some patients have seemed to get better and then tested positive again after a negative test: reason unknown (reinfection, resurgence of old infection, unreliable test) Rapid point of care molecular tests are under development but test validity may be questionable LAMP Serology
Diagnostic challenges	Asymptomatic infection Quality assurance of tests What does serology actually mean in terms of surveillance	Asymptomatic infection Quality assurance of tests Reliability and validity of tests What does serology actually mean in terms of surveillance?

Comparison of malaria and COVID-19 regarding therapeutic options:

	Malaria	COVID-19
Drug Therapies	ACT's Injectable artesunate Gametocytocidals (primaquine) Hypnocytoicidals (primaquine/tafenoquine)	Non-proven [Chloroquine/hydroxychloroquine Remdesivir (nucleotide analogue) Protease inhibitors Statins and ACE2 inhibitors Immunotherapy
Chemoprevention	SP (IPTi, IPTp) SPAQ (SMC)	Possibly Chloroquine

Non drug therapies	Oxygen, glucose, blood transfusion, Vitamin A Kidney dialysis Anticonvulsants Fluids with care	Oxygen, ventilation, supportive therapies, fluids with care
Non pharmaceutical prevention activities	LLINs IRS IVCN SBC Vaccine (one in advanced human testing after 30 years)	PPE, social distancing, self-isolation for suspected cases SBC Vaccine not available at present

How and why the COVID-19 pandemic could affect LMICs differently:

- High levels of malnutrition and vitamin/mineral deficiencies leading to poor immune status in general
- Possibility of large numbers of people/children with underlying conditions such as other infectious diseases, malaria, bacterial and viral pneumonias, TB, HIV
- High levels of inflammation due to infectious diseases
- High levels of anaemia contributing to greater risk of acute respiratory distress and tissue hypoxia
- Low immunisation uptake
- Role Of helminth infections in damping down pro-inflammatory responses
- Overcrowding making social distancing impossible: will this result in acquisition of herd immunity more rapid?
- Less death due to younger population with less chronic disease more infectious disease higher induced immunity to infectious agents
- Poor access to testing and care for both malaria, bacterial pneumonia, TB, dengue lead to increased risks of death from these diseases as well as COVID-19

Research gaps:

- Why are children not so severely infected?
- How will pregnant women be affected?
- Why is there a risk difference in men compared to women

Effects of the pandemic or responses to the pandemic on health systems in the context of malaria control and elimination

Dr James Tibenderana,

Global Technical Director, Malaria Consortium

The key points covered in this presentation were supply and demand side issues of the 6 WHO health system building blocks:

Health Workforce: facility- and community-based; public and private health sectors:

- Supply side issues
 - Availability of PPE, work overload, task shifting, movement restrictions, closures of health facilities, fear of infection, training & supervision, mental & psychosocial support needs. remuneration, limited telemedicine capabilities
- Demand side issues
 - Fear of being infected by health workforce, confidence in health workforce in public and private sectors

Information

- Supply side issues

- Routine reporting, paper-based reporting and transmission of routine health management information, case definitions for COVID-19, Syndromic surveillance, reliable information for micro- and macro-planning, infodemic, risk perceptions
- Demand side issues
 - Infodemic, reliable sources of information, rumours, risk perceptions

Medical products: vaccines and technologies in both public and private sectors

- Supply side issues
 - Transportation, stock-outs, reprioritisation of commodities, reallocation of resources, off-label use of medicines
- Demand side issues
 - Erratic demand, use of technologies with physical distancing, increased cost in the private sector, off-label use of medicines

Financing

- Supply side issues
 - Reallocation of resources, reduced government expenditure, reprioritisation
- Demand side issues
 - Increased out-of-pocket expenditure vis-à-vis reduced household incomes

Leadership and governance

- Supply side issues
 - Attention diverted to COVID-19, policies to suppress transmission of COVID-19, national technical guidance on malaria prevention and case management in the context of COVID-19, definition of core services, prioritisation of delivery platforms to respond to COVID.19
- Demand side issues
 - Community engagement, community participation/compliance, community fatigue

Service delivery: public and private health care sectors

- Supply side issues
 - Availability and use of PPE, handwashing facilities, work space for physical distancing, triage, continuation-interruption of core services such as ANC & RMNCH; OPD & IP admissions, outreaches, campaigns such as LLIN distribution, SMC, IRS
- Demand side issues
 - Overlapping symptomatology, occurrence of febrile illnesses, movement restrictions, cost of care, stigmatisation, myths & fears, switch from confirmatory diagnosis to presumptive diagnosis

Research Gaps relating to the interaction between malaria and COVID-19

Dr Jane Achan

Senior Research Advisor, Malaria Consortium

Dr Achan listed the following key questions/research gaps relating to:

Surveillance

- What is the age-pattern of COVID-19 disease in different malaria-endemic areas?
- What are the clinical features of mild, moderate and severe COVID-19 disease in malaria-endemic countries?
- Is there seasonal variation in the incidence of COVID-19 in malaria-endemic countries?
- Does co-infection with the COVID-19 virus and *p. falciparum* or *p. vivax* influence the presentation or prognosis of the illness episode in different age groups?

Clinical Management

- How should patients presenting with fever in malaria endemic countries be managed in the context of the COVID-19 pandemic?
- What is the role of anaemia in the severity of malaria and COVID-19 coinfections?
- What is the optimal treatment of a patient with COVID-19 and *P. falciparum* or *P. vivax* co-infection?
- What is the role of ACTS and antibiotics given by community health workers on the course of COVID-19 infections in children?
- How should the case management algorithm change at different levels of malaria and COVID-19 disease, to optimise health outcomes?
- In coinfections with malaria and COVID-19 What is the role Of blood transfusion in managing anaemia and septic shock?
- Does the national health infrastructure in these countries have the capacity to effectively respond to outbreaks of significant magnitude without significantly impacting the ability to maintain existing health programmes?
 - What are the key bottlenecks and short-comings?
- Implementation and evaluation of mass antimalarial drug administration may be needed to manage malaria in populations where COVID-19 is spreading.
 - The impact on malaria and COVID-19 Of such efforts should be carefully evaluated

Epidemiology

- What are the early warning signs for malaria outbreak as a result of activity interruptions due to COVID-19?
- Does infection with either COVID-19, malaria, or dengue, reduce immune protection against infection by any of the others?
- Will developing fever algorithms/symptom checkers be useful to screen out patients with fever - for early detection/response strategies for COVID-19 in the community?
- Does a child's immunisation status affect the severity of COVID-19?
 - BCG, Measles, Hep B and influenza vaccines
- Helminth infections have been shown to mediate adverse inflammatory responses. What is the association between COVID-19 and helminths infections?

IPC

- What is the level of knowledge for frontline health care providers (including malaria volunteers) for infection control at the sites where they provide services to the community?
- What should be considered the minimum PPE requirements for community health workers/volunteers in the context of COVID-19?
- What are the perceptions Of community health workers/volunteers with minimal PPE supply, to serving febrile patients presenting to them in the context Of COVID-19?

Community mobilisation

- What is the most effective method of providing information to communities about COVID-19 especially the need for early treatment seeking for patients with fever and the safe uptake of continuing preventive and curative approaches to ongoing diseases such as malaria, pneumonia, diarrhoea and dengue?
- Does the methodology have to be rapidly adapted to the stage of transmission present in the country?
- What are the most effective ways to address the underlying drivers of fear, anxieties, rumours, stigma, and how to improve public knowledge, awareness, and trust during the response?

Mental and psychosocial support

- What are the relevant, acceptable and feasible approaches for supporting the physical health/psychosocial needs of care providers?

- How can malaria volunteers help to deliver positive messaging, following up for people who are in home/community quarantine/isolation advice?

Social Sciences and Ethics

- How will social distancing messaging impact on utilisation of malaria control and prevention measures like bed nets?
- Can inter-personal communication/social network theory used in malaria prevention campaigns be useful for populations adoption of social distancing advice?
- What are the enablers for people to adopt social distancing advice?
- Ethics considerations for research: what ethical insights should be routinely integrated into emergency research and response?

Summary of Q&A, open discussion and comments

The workshop was recorded, and comments and questions captured. The following chart shows the themes that emerged.

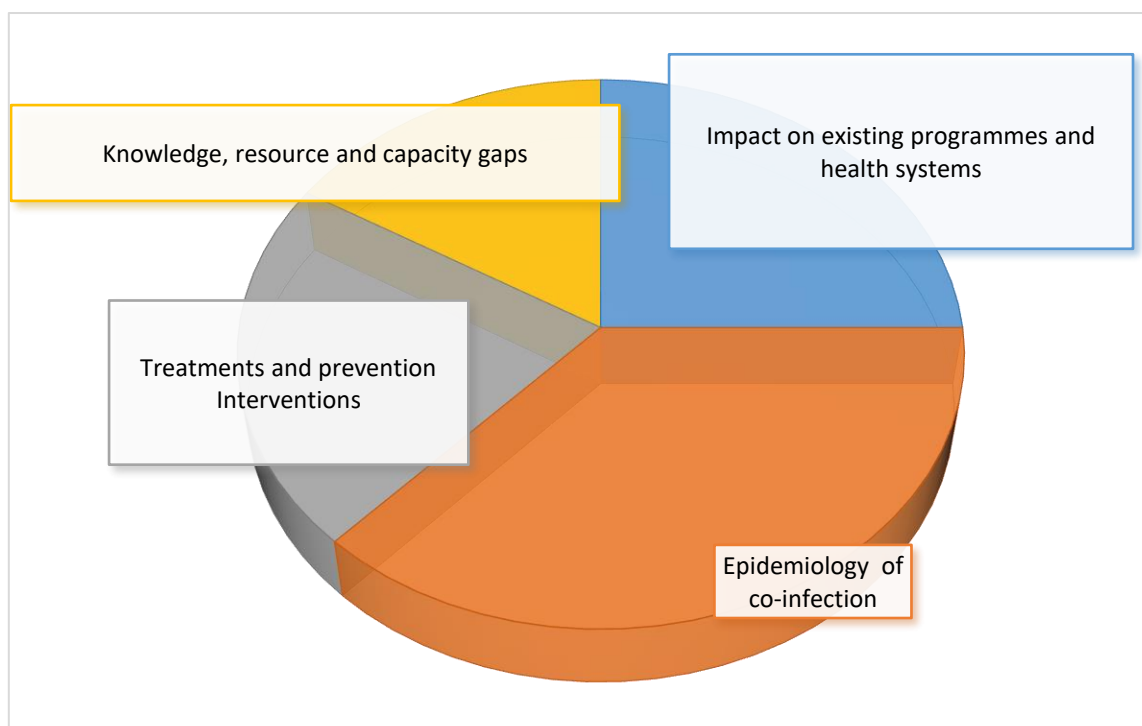


Fig 2. Main themes for research priority within COVID-19 epidemic from workshop feedback review.

Within these four themes it was then possible to categorise the questions, comments and discussions into these further sub-specific areas:

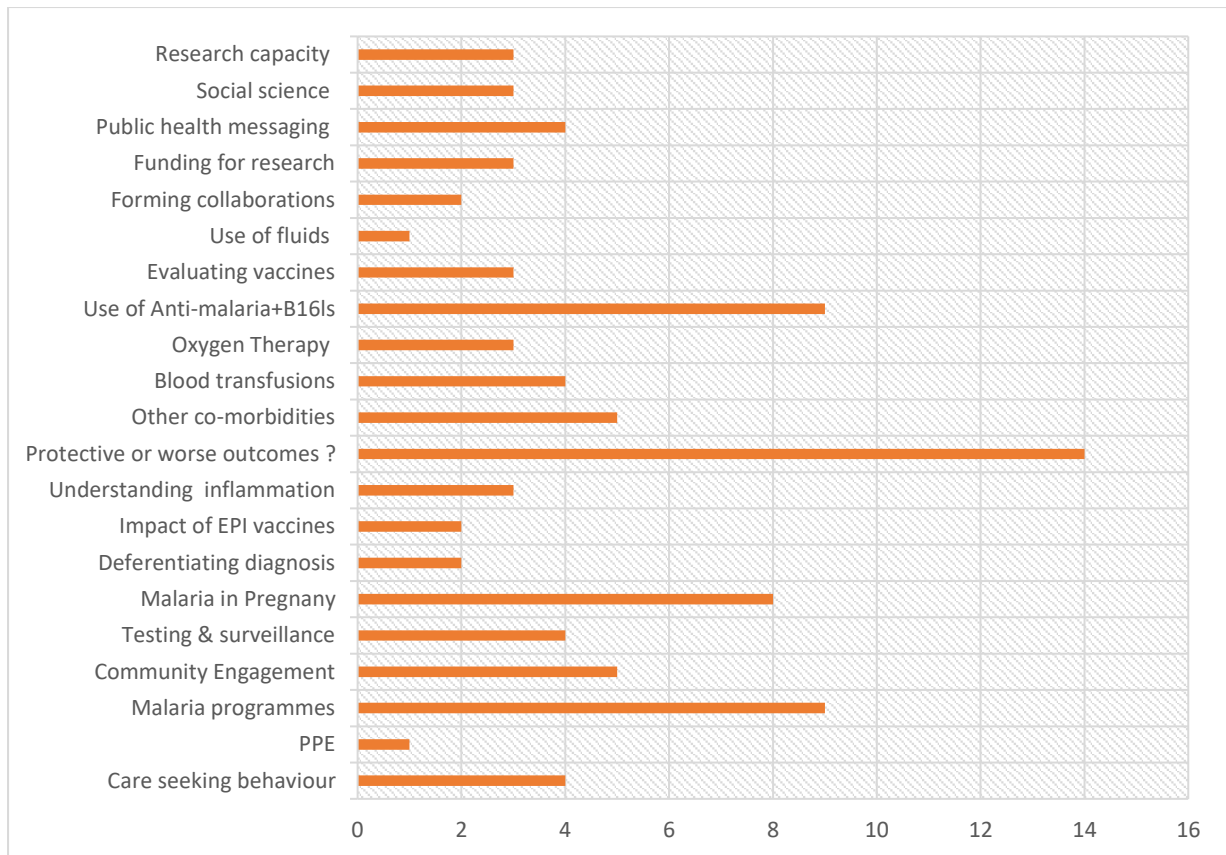


Fig. 3. Categorisation of questions, comments and discussions to sub-specific areas.

Summary of Workshop

Consolidating feedback from the panellists and the questions and comments, we can conclude that this workshop particularly emphasised the need for studies evaluating:

- *Is co-infection with malaria protective, or does it worsen COVID-19 outcomes?*
- *What are the implications for managing malaria and COVID-19 co-infection in pregnancy and in children?*
- *What is the impact of COVID-19 on malaria control and eradication programmes?*
- *Case detection: How can malaria and COVID-19 infection be differentiated in a community setting?*
- *How should severe disease be managed in cases of co-infection?*
- *Possible use of anti-malaria therapies as treatment for COVID-19*

Call to action and next steps

If you are involved in research studying any of the above topics, please get in touch and share any relevant protocols, experiences or advice.

Further virtual workshops are planned, which will be topic-specific and based on demand. If you would like us to conduct an open workshop related to a specific area of COVID-19 research, please let us know what aspects would be most helpful. We will also be running Working Groups on several different topics related to the COVID-19 pandemic for those with experience in research in the relevant areas. You can get in touch here: info@theglobalhealthnetwork.org.