

Screening strategies and laboratory assays to support *Plasmodium falciparum* histidine-rich protein deletion surveillance: where we are and what is needed

Rapid diagnostic tests (RDTs) detecting *Plasmodium falciparum* histidine-rich protein 2 (HRP2) have been an important tool for malaria diagnosis, especially in resource-limited settings lacking quality microscopy....

Khalid B. Beshir, Jonathan B. Parr, Jane Cunningham, Qin Cheng and Eric Rogier

Malaria Journal 2022 21:201

ReviewPublished on: 24 June 2022

The [Correction to this article](#) has been published in *Malaria Journal* 2022 21:266

[Full Text](#) [PDF](#)

Implementation and acceptance of government-sponsored malaria control interventions in Meghalaya, India

India has made considerable progress in malaria reduction over the past two decades, with government-sponsored indoor residual spraying (IRS) and insecticide-treated bed net (ITN) or long-lasting insecticidal ...

Mattimi Passah, Carinthia Balabet Nengnong, Mark L. Wilson, Jane M. Carlton, Larry Kharbamon and Sandra Albert

Malaria Journal 2022 21:200

ResearchPublished on: 23 June 2022

[Full Text](#) [PDF](#)

Prolonged fever and exaggerated hypercoagulopathy in malaria vivax relapse and COVID-19 co-infection: a case report

Coronavirus disease 2019 (COVID-19) often causes atypical clinical manifestations similar to other infectious diseases. In malaria-endemic areas, the pandemic situation will very likely result in co-infection ...

Tri Pudy Asmarawati, Okla Sekar Martani, Bramantono Bramantono and **Muhammad Vitanata Arfijanto**

Malaria Journal 2022 21:199

Case reportPublished on: 23 June 2022

[Full Text](#) [PDF](#)

Quinine plus clindamycin vs artemether-lumefantrine for treatment of uncomplicated falciparum malaria in western Kenya

Charles O. Obonyo and Bernhards R. Ogutu

Malaria Journal 2022 21:198

ResponsePublished on: 21 June 2022

[Full Text](#) [PDF](#)

Gaps in knowledge and practices of malaria prevention in Francophone African immigrants in Metropolitan Edmonton

Important knowledge gaps exist in the understanding of the management of the risks of imported malaria in Canada among Francophone immigrants from sub-Saharan Africa (FISSA). The aim of this cross-sectional st...

Taylor A. Hanna, Ali Ahmed, Rémi Vincent, Kongnon Sangué Coulibaly, Youssef Ahmed, Ryland Petrick, Etienne Vincent, Mélanie El Hafid, Michel T. Hawkes, Srilata Ravi and Sedami Gnidehou

Malaria Journal 2022 21:197

ResearchPublished on: 21 June 2022

[Full Text](#) [PDF](#)

Mechanisms of Transcranial Doppler Ultrasound phenotypes in paediatric cerebral malaria remain elusive

Cerebral malaria (CM) results in significant paediatric death and neurodisability in sub-Saharan Africa. Several different alterations to typical Transcranial Doppler Ultrasound (TCD) flow velocities and wavef...

Nicole F. O'Brien, Yudy Fonseca, Hunter C. Johnson, Douglas Postels, Gretchen L. Birbeck, Yamikani Chimalizeni, Karl B. Seydel, Montfort Bernard Gushu, Tusekile Phiri, Sylvester June, Karen Chetcuti, Lorena Vidal, Manu S. Goyal and Terrie E. Taylor

Malaria Journal 2022 21:196

ResearchPublished on: 21 June 2022

[Full Text](#) [PDF](#)

A cluster randomized trial of delivery of intermittent preventive treatment of malaria in pregnancy at the community level in Malawi

Malaria in pregnancy doubles the risk of low birthweight; up to 11% of all neonatal deaths in sub-Saharan Africa are associated with malaria in pregnancy. To prevent these and other adverse health consequences...

Beth L. Rubenstein, Jobiba Chinkhumba, Ethel Chilima, Collins Kwizombe, Ashley Malpass, Shelby Cash, Katherine Wright, Peter Troell, Humphrey Nsona, Fannie Kachale, Doreen Ali, Evans Kaunda, Sosten Lankhulani, Michael Kayange, Don P. Mathanga, John Munthali...

Malaria Journal 2022 21:195

ResearchPublished on: 21 June 2022

[Full Text](#) [PDF](#)

Need for optimized dosages in the design of comparative clinical trials of anti-malarial drugs

We read with interest the publication on malaria treatment by Obonyo et al. (*Malaria J* 21:30, 2022). This commentary questions the methodology, especially the chosen time points of treatment outcome measures.

Sanjeev Krishna and Peter G. Kremsner

Malaria Journal 2022 21:194

CommentPublished on: 20 June 2022

[Full Text](#) [PDF](#)

Malaria-associated risk factors among adolescents living in areas with persistent transmission in Senegal: a case-control study

In Senegal, malaria morbidity has sharply decreased over these past years. However, malaria epidemiology remains heterogeneous with persistent transmission in the southeastern part of the country and many case...

Fassiatou Tairou, Abdoulaye Diallo, Ousmane Sy, Aminatou Kone, Isaac Akhenaton Manga, Khadim Sylla, Souleye Lelo, Cheikh Binetou Fall, Doudou Sow, Magatte Ndiaye, Babacar Faye and Roger C. K. Tine

Malaria Journal 2022 21:193

ResearchPublished on: 20 June 2022

[Full Text](#) [PDF](#)

Maintenance of high temporal *Plasmodium falciparum* genetic diversity and complexity of infection in asymptomatic and symptomatic infections in Kilifi, Kenya from 2007 to 2018

High levels of genetic diversity are common characteristics of *Plasmodium falciparum* parasite populations in high malaria transmission regions. There has been a decline in malaria transmission intensity over 12 y...

Kelvin M. Kimenyi, Kevin Wamae, Joyce M. Ngoi, Zaydah R. de Laurent, Leonard Ndwiga, Victor Osoi, George Obiero, Abdurahman I. Abdi, Philip Bejon and Lynette Isabella Ochola-Oyier

Malaria Journal 2022 21:192

ResearchPublished on: 20 June 2022

[Full Text](#) [PDF](#)

Cellular and antibody response in GMZ2-vaccinated Gabonese volunteers in a controlled human malaria infection trial

Antibody and cellular memory responses following vaccination are important measures of immunogenicity. These immune markers were quantified in the framework of a vaccine trial investigating the malaria vaccine...

Odilon Nouatin, Javier Ibáñez, Rolf Fendel, Ulysse A. Ngoa, Freia-Raphaella Lorenz, Jean-Claude Dejon-Agobé, Jean Ronald Edoa, Judith Flügge, Sina Brückner, Meral Esen, Michael Theisen, Stephen L. Hoffman, Kabirou Moutairou, Adrian J. F. Luty, Bertrand Lell, Peter G. Kremsner...

Malaria Journal 2022 21:191

ResearchPublished on: 17 June 2022

[Full Text](#) [PDF](#)

The private sector market for malaria rapid diagnostic tests in Nigeria: results of the 2018 market survey

To avoid misuse of anti-malarials, correct diagnosis of fever prior to drug prescription is essential. Presumptive treatment in the private healthcare sector is a concern in Nigeria, where availability of affo...

Hannah M. Edwards, Rubaiyath Sarwar, Parvez Mahmud, Shekarau Emmanuel, Kolawole Maxwell and James K. Tibenderana

Malaria Journal 2022 21:190

ResearchPublished on: 16 June 2022

[Full Text](#) [PDF](#)

A reverse vaccinology approach on transmembrane carbonic anhydrases from *Plasmodium* species as vaccine candidates for malaria prevention

Malaria is a significant parasitic infection, and human infection is mediated by mosquito (*Anopheles*) biting and subsequent transmission of protozoa (*Plasmodium*) to the blood. Carbonic anhydrases (CAs) are known ...

Reza Zolfaghari Emameh, Harlan R. Barker, Hannu Turpeinen, Seppo Parkkila and Vesa P. Hytönen

Malaria Journal 2022 21:189

ResearchPublished on: 15 June 2022

[Full Text](#) [PDF](#)

Entomological indicators of malaria transmission prior to a cluster-randomized controlled trial of a 'lethal house lure' intervention in central Côte d'Ivoire

A study was conducted prior to implementing a cluster-randomized controlled trial (CRT) of a lethal house lure strategy in central Côte d'Ivoire to provide baseline information on malaria indicators in 40 vill...

Rosine Z. Wolie, Alphonsine A. Koffi, Leslie Ayuk-Taylor, Ludovic P. Ahoua Alou, Eleanore D. Sternberg, Oulo N'Nan-Alla, Yao N'Guessan, Amal Dahounto, Welbeck A. Oumbouke, Innocent Z. Tia, Simon-Pierre A. N'Guetta, Jackie Cook, Matthew B. Thomas and Raphael N'Guessan

Malaria Journal 2022 21:188

ResearchPublished on: 15 June 2022

[Full Text](#) [PDF](#)

STARTER checklist for antimalarial therapeutic efficacy reporting

Mateusz M. Plucinski, Elizabeth A. Ashley, Quique Bassat, Meera Venkatesan, Philip J. Rosenthal and Eric S. Halsey

Malaria Journal 2022 21:187

EditorialPublished on: 13 June 2022

[Full Text](#) [PDF](#)

How has mass drug administration with dihydroartemisinin-piperazine impacted molecular markers of drug resistance? A systematic review

The World Health Organization (WHO) recommends surveillance of molecular markers of resistance to anti-malarial drugs. This is particularly important in the case of mass drug administration (MDA), which is end...

Sophie Moss, Emilia Mañko, Sanjeev Krishna, Susana Campino, Taane G. Clark and Anna Last

Malaria Journal 2022 21:186

ReviewPublished on: 11 June 2022

[Full Text](#) [PDF](#)

Incremental cost and cost-effectiveness of the addition of indoor residual spraying with pirimiphos-methyl in sub-Saharan Africa versus standard malaria control: results of data collection and analysis in the Next Generation Indoor Residual Sprays (NgenIRS) project, an economic-evaluation

Malaria is a major cause of morbidity and mortality globally, especially in sub-Saharan Africa. Widespread resistance to pyrethroids threatens the gains achieved by vector control. To counter resistance to pyr...

Joshua Yukich, Peder Digre, Sara Scates, Luc Boydens, Emmanuel Obi, Nicky Moran, Allison Belemvire, Mariandrea Chamorro, Benjamin Johns, Keziah L. Malm, Lena Kolyada, Ignatius Williams, Samuel Asiedu, Seydou Fomba, Jules Mihigo, Desire Boko...

Malaria Journal 2022 21:185

ResearchPublished on: 11 June 2022

[Full Text](#) [PDF](#)

High asymptomatic malaria among seasonal migrant workers departing to home from malaria endemic areas in northwest Ethiopia

In Ethiopia, thousands of seasonal migrant workers travel from non-malaria or mild malaria transmission areas to malaria-endemic areas for seasonal farm activities. Most of these migrants stay in the farm area...

Tesfaye Tilaye, Belay Tessema and Kassahun Alemu

Malaria Journal 2022 21:184

ResearchPublished on: 11 June 2022

[Full Text](#) [PDF](#)

Implementing OECD GLP principles for the evaluation of novel vector control tools: a case study with two novel LLINs, SafeNet® and SafeNet NF®

To sustain high universal Long-Lasting Insecticidal Nets (LLINs) coverage, affordable nets that provide equivalent or better protection than standard LLINs, are required. Test facilities evaluating new LLINs r...

Salum Azizi, Janneke Snetelaar, Robert Kaaya, Johnson Matowo, Hudson Onen, Magreth Shayo, Ezekia Kisengwa, Evod Tilya, Baltazari Manunda, Benson Mawa, Franklin Mosha and Matthew Kirby

Malaria Journal 2022 21:183

ResearchPublished on: 11 June 2022

[Full Text](#) [PDF](#)

Treatment-seeking behaviour, awareness and preventive practice toward malaria in Abu Ushar, Gezira state, Sudan: a household survey experience from a rural area

Usage of mosquito bed nets and the practice of other prevention methods are essential for the prevention of malaria in endemic areas. Proper community knowledge about malaria and prompt treatment-seeking behav...

Elfatih A. Hasabo, Rawan I. Khalid, Ghassan E. Mustafa, Ruaa E. Taha, Riham S. Abdalla, Reham A. Mohammed, Mazin S. Haroun, Rawaa Adil, Riham A. Khalil, Rawaa M. Mansour, Reham K. Mohamed and Heitham Awadalla

Malaria Journal 2022 21:182

ResearchPublished on: 11 June 2022

[Full Text](#) [PDF](#)

The Centres for Disease Control light trap (CDC-LT) and the human decoy trap (HDT) compared to the human landing catch (HLC) for measuring *Anopheles* biting in rural Tanzania

Vector mosquito biting intensity is an important measure to understand malaria transmission. Human landing catch (HLC) is an effective but labour-intensive, expensive, and potentially hazardous entomological s...

Isaac Haggai Namango, Carly Marshall, Adam Saddler, Amanda Ross, David Kaftan, Frank Tenywa, Noely Makungwa, Olukayode G. Odufuwa, Godfrey Ligema, Hassan Ngonyani, Isaya Matanila, Jameel Bharmal, Jason Moore, Sarah J. Moore and Manuel W. Hetzel

Malaria Journal 2022 21:181

ResearchPublished on: 11 June 2022

[Full Text](#) [PDF](#)

Malaria mosquitoes acquire and allocate cattle urine to enhance life history traits

Nutrient acquisition and allocation integrate foraging and life-history traits in insects. To compensate for the lack of a particular nutrient at different life stages, insects may acquire these through supple...

Mengistu Dawit, Sharon R. Hill, Göran Birgersson, Habte Tekie and Rickard Ignell

Malaria Journal 2022 21:180

ResearchPublished on: 11 June 2022

[Full Text](#) [PDF](#)

Cattle-related risk factors for malaria in southwest Ethiopia: a cross-sectional study

Despite the low to moderate intensity of malaria transmission present in Ethiopia, malaria is still a leading public health problem. Current vector control interventions, principally long-lasting insecticidal ...

Kallista Chan, Jorge Cano, Fekadu Massebo and Louisa A. Messenger

Malaria Journal 2022 21:179

ResearchPublished on: 10 June 2022

[Full Text](#) [PDF](#)

Global water quality changes posing threat of increasing infectious diseases, a case study on malaria vector *Anopheles stephensi* coping with the water pollutants using age-stage, two-sex life table method

Water pollution due to uncontrolled release of chemical pollutants is an important global problem. Its effect on medically important insects, especially mosquitoes, is a critical issue in the epidemiology of m...

Mahmoud Fazeli-Dinan, Mostafa Azarnoosh, Mehmet Salih Özgökçe, Hsin Chi, Nasibeh Hosseini-Vasoukolaei, Farzad Motevalli Haghi, Mohamad Ali Zazouli, Seyed Hassan Nikookar, Reza Dehbandi, Ahmadali Enayati, Morteza Zaim and Janet Hemingway

Malaria Journal 2022 21:178

ResearchPublished on: 8 June 2022

[Full Text](#) [PDF](#)

Systems biology of malaria explored with nonhuman primates

"The Primate Malaria" book has been a uniquely important resource for multiple generations of scientists, since its debut in 1971, and remains pertinent to the present day. Indeed, nonhuman primates (NHPs) ha...

Mary R. Galinski

Malaria Journal 2022 21:177

ReviewPublished on: 7 June 2022

[Full Text](#) [PDF](#)

Comparison of two malaria multiplex immunoassays that enable quantification of malaria antigens

Immunoassay platforms that simultaneously detect malaria antigens including histidine-rich protein 2 (HRP2)/HRP3 and *Plasmodium* lactate dehydrogenase (pLDH), are useful epidemiological tools for rapid diagnostic ...

Ihn Kyung Jang, Alfons Jiménez, Andrew Rashid, Rebecca Barney, Allison Golden, Xavier C. Ding, Gonzalo J. Domingo and Alfredo Mayor

Malaria Journal 2022 21:176

ResearchPublished on: 7 June 2022

[Full Text](#) [PDF](#)

Surveillance to achieve malaria elimination in eastern Myanmar: a 7-year observational study

The collection and utilization of surveillance data is essential in monitoring progress towards achieving malaria elimination, in the timely response to increases in malaria case numbers and in the assessment ...

Jade D. Rae, Suphak Nosten, Ladda Kajechiwa, Jacher Wiladphaingern, Daniel M. Parker, Jordi Landier, Aung Myint Thu, Hsa Dah, Aye Be, Win Cho Cho, K'Nyaw Paw, Eh Shee Paw, Paw Bway Shee, Christ Poe, Chit Nu, Baw Nyaw...

Malaria Journal 2022 21:175

ResearchPublished on: 7 June 2022

[Full Text](#) [PDF](#)

A microfluidic paper analytical device using capture aptamers for the detection of pLDH in blood matrices

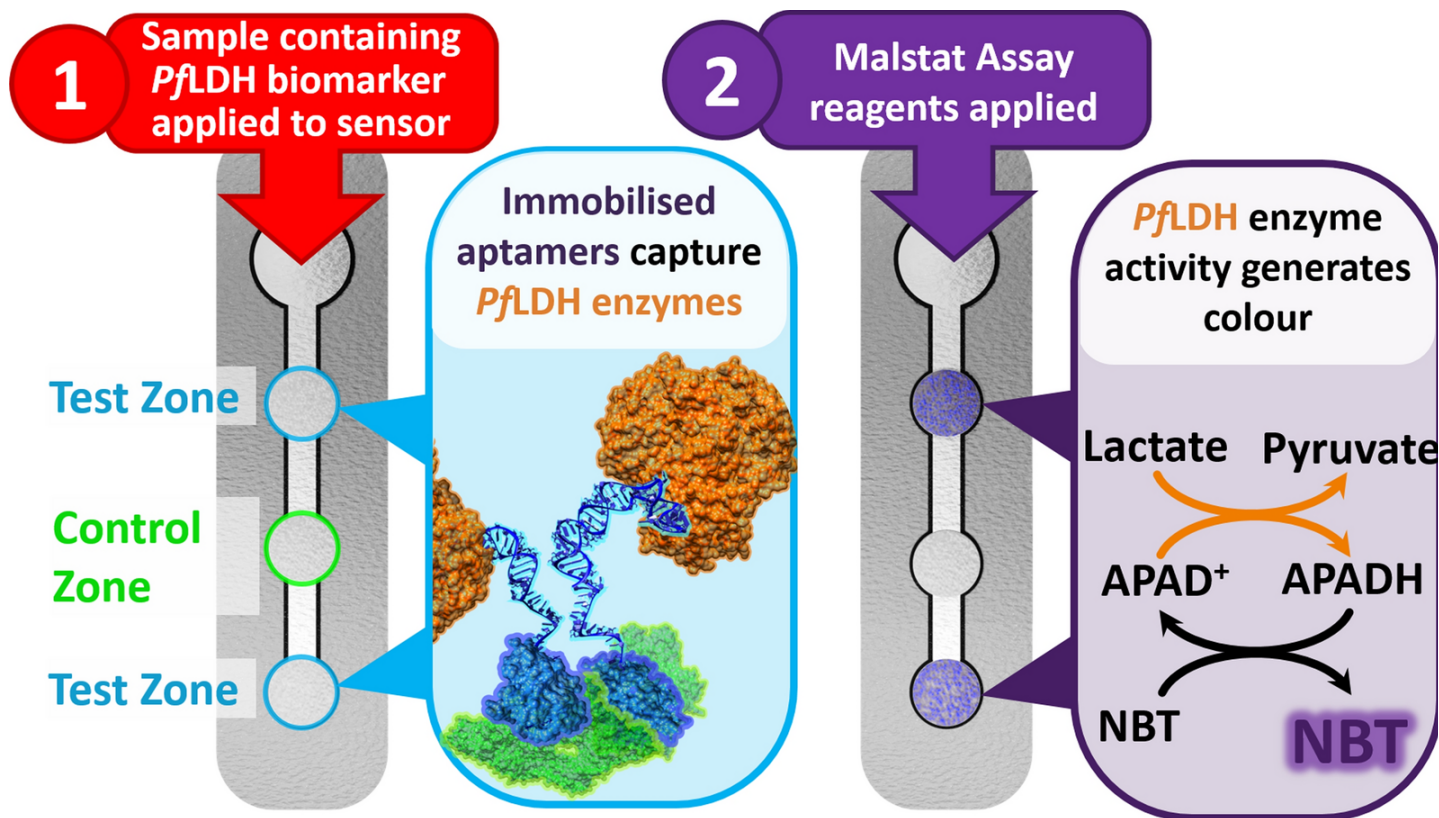
The prevalence and death rate arising from malaria infection, and emergence of other diseases showing similar symptoms to malaria require the development of malaria-specific and sensitive devices for its diagn...

Adewoyin Martin Ogunmolasuyi, Ronen Fogel, Heinrich Hoppe, Dean Goldring and Janice Limson

Malaria Journal 2022 21:174

ResearchPublished on: 7 June 2022

[Full Text](#) [PDF](#)



Expression and copper binding characteristics of *Plasmodium falciparum* cytochrome c oxidase assembly factor 11, Cox11

Copper is an essential metal for living organisms as a catalytic co-factor for important enzymes, like cytochrome c oxidase the final enzyme in the electron transport chain. *Plasmodium falciparum* parasites in inf...

Abdulmalik Abdullahi Salman and J. P. Dean Goldring

Malaria Journal 2022 21:173

ResearchPublished on: 7 June 2022

[Full Text](#) [PDF](#)

Outdoor biting and pyrethroid resistance as potential drivers of persistent malaria transmission in Zanzibar

Low-level of malaria transmission persist in Zanzibar despite high coverage of core vector control interventions. This study was carried out in hot-spot sites to better understand entomological factors that ma...

Revocatus M. Musiba, Brian B. Tarimo, April Monroe, Dickson Msaky, Halfan Ngowo, Kimberly Mihayo, Alex Limwagu, Godlove T. Chilla, Gasper K. Shubis, Ahmada Ibrahim, George Greer, Juma H. Mcha, Khamis A. Haji, Faiza B. Abbas, Abdullah Ali, Fredros O. Okumu...

Malaria Journal 2022 21:172

ResearchPublished on: 7 June 2022

[Full Text](#) [PDF](#)

Dry season prevalence of *Plasmodium falciparum* in asymptomatic Gambian children, with a comparative evaluation of diagnostic methods

Subclinical infection with *Plasmodium falciparum* remains highly prevalent, yet diagnosing these often low-density infections remains a challenge. Infections can be subpatent, falling below the limit of detection ...

Jason P. Mooney, Sophia M. DonVito, Maimuna Jahateh, Haddy Bittaye, Christian Bottomley, Umberto D'Alessandro and Eleanor M. Riley

Malaria Journal 2022 21:171

ResearchPublished on: 7 June 2022

[Full Text](#) [PDF](#)

Motivators and demotivators to accessing malaria in pregnancy interventions in sub-Saharan Africa: a meta-ethnographic review

Despite the introduction of efficacious interventions for malaria control, sub-Saharan Africa continues to bear the highest burden of malaria and its associated effects on vulnerable populations, such as pregn...

Matilda Aberese-Ako, Phidelia Doegah, Evelyn Acquah, Pascal Magnussen, Evelyn Anseh, Gifty Ampofo, Dominic Dankwah Agyei, Desmond Klu, Elsie Mottey, Julie Balen, Safiatou Doumbo, Wilfred Mbacham, Ouma Gaye, Margaret Gyapong, Seth Owusu-Agyei and Harry Tagbor

Malaria Journal 2022 21:170

ResearchPublished on: 3 June 2022

[Full Text](#) [PDF](#)

Simultaneous and enantiospecific quantification of primaquine and carboxyprimaquine in human plasma using liquid chromatography-tandem mass spectrometry

The enantiomers of the 8-aminoquinoline anti-malarial primaquine have different pharmacological properties. Development of an analytical method for simultaneous quantification of the enantiomers of primaquine ...

Warunee Hanpithakpong, Nicholas P. J. Day, Nicholas J. White and Joel Tarning

[Full Text](#) [PDF](#)

Regional heterogeneity of malaria prevalence and associated risk factors among children under five in Togo: evidence from a national malaria indicators survey

Malaria remains a major cause of morbidity and death among children less than 5 years of age. In Togo, despite intensification of malaria control interventions, malaria remained highly prevalent, with significant...

Gountante Kombate, Wakpaouyare Gmakouba, Susana Scott, Komi Ameko Azianu, Didier Koumavi Ekouevi and Marianne A. B. van der Sande

Malaria Journal 2022 21:168

Research Published on: 3 June 2022

[Full Text](#) [PDF](#)

The prevalence of symptomatic and asymptomatic malaria and its associated factors in Debre Elias district communities, Northwest Ethiopia

Malaria is a major cause of morbidity and mortality worldwide. According to the World Health Organization 2021 malaria report, it is considered to be endemic in 85 countries and territories. Malaria elimination...

Abtie Abebaw, Yibeltal Aschale, Tadesse Kebede and Asrat Hailu

Malaria Journal 2022 21:167

Research Published on: 3 June 2022

[Full Text](#) [PDF](#)

Impact of a spatial repellent product on *Anopheles* and non-*Anopheles* mosquitoes in Sumba, Indonesia

The East Nusa Tenggara province, Indonesia, contributed to 5% of malaria cases nationally in 2020, with other mosquito-borne diseases, such as dengue and filariasis also being endemic. Monitoring of spatial an...

Dendi H. Permana, Siti Zubaidah, Lepa Syahrani, Puji B. S. Asih, Din Syafruddin, Ismail E. Rozi, Anggi P. N. Hidayati, Sully Kosasih, Farahana K. Dewayanti, Nia Rachmawati, Rifqi Risandi, Michael J. Bangs, Claus Bagh, Jenna R. Davidson, Allison L. Hendershot, Timothy A. Burton...

Malaria Journal 2022 21:166

Research Published on: 3 June 2022

[Full Text](#) [PDF](#)

Trends in malaria indicators after scale-up of community-based malaria management in Afghanistan

The Community-Based Malaria Management (CBMM) strategy, introduced in 2013 and expanded to all health facilities and health posts in Afghanistan by 2016, aimed to deliver rapid diagnostic testing and more time...

Sayed Daoud Mahmoodi, Abdul Alim Atarud, Ahmad Walid Sediqi, Sarah Gallalee, Willi McFarland, Temesgen Birara Aynie, Mohmmad Sami Nahzat, Hamida Hamid, Ghulam Qader Qader, Mohammad Shoaib Tamim and Ali Mirzazadeh

Malaria Journal 2022 21:165

Research Published on: 3 June 2022

[Full Text](#) [PDF](#)

Adherence to national malaria clinical management and testing guidelines in selected private clinics of Gambela Town, Gambela Region, Ethiopia: a mixed method study

The World Health Organization World Malaria Report of 2019 indicated an estimated 228 million cases of malaria occurred worldwide in 2018. More than 75% of the total area of Ethiopia is malarious, making malar...

Yamlak Gindola, Desalegn Getahun, David Sugerman, Eric Tongren, Ryan Tokarz, Mesfin Wossen, Kassahun Demissie, Etsehiwot Zemelak, Akuma Okugn, Jimmawork Wendimu, Girmay Hailu, Mesfin Tegistu and Dumesa Begna

Malaria Journal 2022 21:164

Research Published on: 3 June 2022

[Full Text](#) [PDF](#)

Evaluation of sustainable susceptibility to *Plasmodium vivax* infection among colonized *Anopheles darlingi* and *Anopheles deaneorum*

The colonization of mosquitoes susceptible to *Plasmodium vivax* via direct membrane feeding assay (DMFA) has the potential to significantly advance our knowledge of *P. vivax* biology, vector-parasite interaction an...

Najara A. C. Santos, Alice O. Andrade, Thais C. Santos, Leandro N. Martinez, Amália S. Ferreira, Alessandra S. Bastos, Mirilene M. Martins, José D. C. Pontual, Carolina B. G. Teles, Jansen F. Medeiros and Maisa S. Araújo

Malaria Journal 2022 21:163

Research Published on: 3 June 2022

[Full Text](#) [PDF](#)

A comparison of malaria prevention behaviours, care-seeking practices and barriers between malaria at-risk worksite migrant workers and villagers in Northern Shan State, Myanmar—a mixed method study

Migrant populations are at an increased risk of exposure to malaria due to their nature of work and seasonal migration. This study aimed to compare malaria prevention behaviours and care-seeking practices amon...

Ye Kyaw Aung, Su Su Zin, Kemi Tesfazghi, Mahesh Paudel, May Me Thet and Si Thu Thein

Malaria Journal 2022 21:162

Research Published on: 3 June 2022

[Full Text](#) [PDF](#)

Using Bayesian state-space models to understand the population dynamics of the dominant malaria vector, *Anopheles funestus* in rural Tanzania

It is often assumed that the population dynamics of the malaria vector *Anopheles funestus*, its role in malaria transmission and the way it responds to interventions are similar to the more elaborately characterized...

Halfan S. Ngowo, Fredros O. Okumu, Emmanuel E. Hape, Issa H. Mshani, Heather M. Ferguson and Jason Matthiopoulos

Malaria Journal 2022 21:161

ResearchPublished on: 3 June 2022

[Full Text](#) [PDF](#)

Multiple *Plasmodium falciparum* drug resistance polymorphisms identified in a pregnant woman with severe malaria and a concomitant spontaneous abortion in Cross River, Nigeria, West Africa

The development of resistance by *Plasmodium falciparum* to anti-malarial drugs impedes any benefits of the drug. In addition, absence or delayed availability of current anti-malarial drugs in remote areas has the ...

Mary Aigbiremo Oboh, Fatou Faal, Oluwagbemisola Elizabeth Adeniji, Simon Correa, Anthony Uyimulam Amawu, Ekon Ogban, Eva Heinz, Grant Hughes, Martin M. Meremikwu and Alfred Amambua-Ngwa

Malaria Journal 2022 21:160

Case reportPublished on: 3 June 2022

[Full Text](#) [PDF](#)

Evaluation of the Pfs25-IMX313/Matrix-M malaria transmission-blocking candidate vaccine in endemic settings

Malaria control relies heavily on the use of anti-malarial drugs and insecticides against malaria parasites and mosquito vectors. Drug and insecticide resistance threatens the effectiveness of conventional mal...

Charles Mulamba, Chris Williams, Katharina Kreppel, Jean Bosco Ouedraogo and Ally I. Olotu

Malaria Journal 2022 21:159

ReviewPublished on: 2 June 2022

[Full Text](#) [PDF](#)

Using ecological observations to improve malaria control in areas where *Anopheles funestus* is the dominant vector

The most important malaria vectors in sub-Saharan Africa are *Anopheles gambiae*, *Anopheles arabiensis*, *Anopheles funestus*, and *Anopheles coluzzii*. Of these, *An. funestus* presently dominates in many settings in eas...

Najat F. Kahamba, Marceline Finda, Halfan S. Ngowo, Betwel J. Msugupakulya, Francesco Baldini, Lizette L. Koekemoer, Heather M. Ferguson and Fredros O. Okumu

Malaria Journal 2022 21:158

ReviewPublished on: 2 June 2022

[Full Text](#) [PDF](#)

Malaria time series in the extra-Amazon region of Brazil: epidemiological scenario and a two-year prediction model

In Brazil, malaria is caused mainly by the *Plasmodium vivax* and *Plasmodium falciparum* species. Its transmission occurs in endemic and non-endemic areas. Malaria geography in Brazil has retracted and is now concen...

Klauss Kleydmann Sabino Garcia, Amanda Amaral Abrahão, Ana Flávia de Moraes Oliveira, Karina Medeiros de Deus Henriques, Anielle de Pina-Costa, André Machado Siqueira and Walter Massa Ramalho

Malaria Journal 2022 21:157

ResearchPublished on: 31 May 2022

[Full Text](#) [PDF](#)

***Anopheles stephensi* in Africa requires a more integrated response**

There are increasing reports of the Asian malaria mosquito, *Anopheles stephensi* invading and spreading in Eastern Africa. We discuss the importance of these invasions in the context of broader challenges facing m...

Abraham Mnzava, April C. Monroe and Fredros Okumu

Malaria Journal 2022 21:156

ReviewPublished on: 31 May 2022

[Full Text](#) [PDF](#)

Attitudes, practices, and determinants of community care-seeking behaviours for fever/malaria episodes in the context of the implementation of multiple first-line therapies for uncomplicated malaria in the health district of Kaya, Burkina Faso

Malaria case management relies on World Health Organization (WHO)-recommended artemisinin-based combination therapy (ACT), and a continuous understanding of local community knowledge, attitudes, and practices ...

Jean Moise Tanga Kaboré, Mohamadou Siribié, Denise Hien, Issiaka Soulama, Nouhoun Barry, Yacouba Nombéré, Frederic Dianda, Adama Baguïya, Alfred Bewendtaoré Tiono, Christian Burri, André-Marie Tchouatieu and Sodiomon Bienvenu Sirima

Malaria Journal 2022 21:155

ResearchPublished on: 30 May 2022

[Full Text](#) [PDF](#)

Reflections on the 2021 World Malaria Report and the future of malaria control

The World Malaria Report, released in December 2021, reflects the unique challenges currently facing the global malaria community. The report showed the devastating toll of malaria, with an estimated 627,000 p...

April Monroe, Nana Aba Williams, Sheila Ogoma, Corine Karema and Fredros Okumu

Malaria Journal 2022 21:154

Meeting reportPublished on: 27 May 2022

[Full Text](#) [PDF](#)

Associations of maternal iron deficiency with malaria infection in a cohort of pregnant Papua New Guinean women

Iron deficiency (ID) is common in malaria-endemic settings. Intermittent preventative treatment of malaria in pregnancy (IPTp) and iron supplementation are core components of antenatal care in endemic regions ...

Holger W. Unger, Andie Bleicher, Maria Ome-Kaius, Elizabeth H. Aitken and Stephen J. Rogerson

Malaria Journal 2022 21:153

ResearchPublished on: 26 May 2022

[Full Text](#) [PDF](#)

Recommendations for environmental risk assessment of gene drive applications for malaria vector control

Building on an exercise that identified potential harms from simulated investigational releases of a population suppression gene drive for malaria vector control, a series of online workshops identified nine r...

John B. Connolly, John D. Mumford, Debora C. M. Glandorf, Sarah Hartley, Owen T. Lewis, Sam Weiss Evans, Geoff Turner, Camilla Beech, Naima Sykes, Mamadou B. Coulibaly, Jörg Romeis, John L. Teem, Willy Tonui, Brian Lovett, Aditi Mankad, Abraham Mnzava...

Malaria Journal 2022 21:152

Meeting ReportPublished on: 25 May 2022

[Full Text](#) [PDF](#)

Editorial Board

Editor-in-Chief

Marcel Hommel



Emeritus Professor of Tropical Medicine, University of Liverpool, United Kingdom

[Research website](#)

Specialisms: **Malaria, Leishmaniasis**

Associate Editors

Elizabeth Ashley



Lao-Oxford-Mahosot Hospital, Laos

[Research website](#)

[ORCID profile](#)

Specialisms: **Malaria, Treatment, Antimicrobial resistance**

Quique Bassat



ISGlobal, Spain

[Research website](#)

[ORCID profile](#)

Specialisms: **Malaria, Cause of death, Severe Malaria, Drugs**

Hans-Peter Fuehrer



University of Veterinary Medicine, Austria

[Research website](#)

[ORCID profile](#)

Specialisms: **Plasmodium Ovale spp, Plasmodium malariae, Mosquitoes, Vector-borne diseases**

Louisa Messenger



The London School of Hygiene & Tropical Medicine, United Kingdom

[Research website](#)

[ORCID profile](#)

Specialisms: **Entomology; Parasitology, Molecular Biology, Disease Control**

Tanya Russell



James Cook University, Australia

[Research website](#)

[ORCID profile](#)

Twitter: [@dr_tanyarussell](#)

Specialisms: **Vector control, Anopheles, Aedes, Malaria, Dengue**

Neena Valecha



Public Health Foundation of India, India
Research website
[ORCID profile](#)
Specialisms: **Malaria, Clinical research, Pharmacovigilance**

Dr Sara Canavati, Save the Children US, USA
Dr Chris Drakeley, London School of Hygiene and Tropical Medicine, UK
Prof Ananias Escalante, Inst for Genomics and Evolutionary Medicine, Temple University, USA
Prof Michelle Gatton, Queensland University of Technology, Australia
Dr John E Gimnig, Centers for Disease Control, USA
Prof Michael Good, Griffith University, Australia
Dr Mateusz Plucinski, CDC, USA
Dr Bruno Pradines, IHU Méditerranée Infection, France
Dr Tanya Russell, James Cook University, Australia
Dr Larry Slutsker, Path, USA
Prof Marcel Tanner, Swiss Tropical Institute, Switzerland
Prof Maxine Whittaker, James Cook University, Australia

Editorial Board

Dr Mohammad Shafiu Alam, International Centre for Diarrhoeal Disease Research, Bangladesh
Dr Nicholas Anstey, Menzies School of Health Research, Australia
Dr Anupkumar Anvikar, National Institute of Biologicals, Ministry of Health and Family Welfare, India
Dr Sarah Auburn, Menzies School of Health Research, Australia
Dr Leonardo Basco, Institut de Recherche pour le Développement, France
Prof M. Asim Beg, Aga Khan University, Pakistan
Prof Ron Behrens, London School of Hygiene and Tropical Medicine, UK
Dr Peter Billingsley, Sanaria Inc, USA
Prof Zbynek Bozdech, Nanyang Technological University, Singapore
Dr Teun Bousema, London School of Hygiene & Tropical Medicine, UK
Dr Cindy S Chu, University of Oxford, UK
Prof A. P. Dash, Asian Institute of Public Health University, India
Prof. Cristiana Ferreira de Brito, Laboratory of Malaria, Institute Rene Rachou/Fiocruz, Brazil
Dr J. Brian de Souza, London School of Hygiene and Tropical Medicine, UK
Prof Delmiro Fernandez-Reyes, University College London, UK
Dr Michal Fried, NIH, USA
Dr Friedrich Frischknecht, University of Heidelberg, Germany
Dr Sophie Githinji, Kenya National Malaria Control Program, Kenya
Dr Iveth J González, Terre des Hommes, Switzerland
Dr Matthew Grigg, Menzies School of Health Research and Charles Darwin University, Australia
Dr Steven A. Harvey, Johns Hopkins University Bloomberg School of Public Health, USA
Dr Manuel Hetzel, Swiss Tropical and Public Health Institute, Switzerland
Dr Deus Ishengoma, National Institute for Medical Research, Tanzania
Dr Simon Kariuki, Kenya Medical Research Institute/Centre for Global Health Research, Kenya
Dr Catherine Lavazec, Université Paris Descartes, France
Prof Sylvie Manguin, Institute of Research for Development, France
Dr Rose McGready, Shoklo Malaria Research Unit, Thailand
Prof Wuelton Marcelo Monteiro, Universidade do Estado do Amazonas, Brazil
Prof Olaf Mueller, University of Heidelberg, Germany
Prof Manuel Alfonso Patarroyo, Universidad del Rosario, Colombia
Prof Wendy Prudhomme O'Meara, Duke University School of Medicine, USA
Prof Michael Ramharter, Medical University of Vienna, Gabon
Dr Julian C Rayner, Wellcome Trust Sanger Institute, UK
Prof Sarah Reece, University of Edinburgh, UK
Dr Adam Richards, George Washington University, USA
Prof Philip Rosenthal, University of California, San Francisco, USA
Prof Dennis Shanks, Australian Army Malaria Institute, Australia
Prof Carol Sibley, University of Washington, USA
Dr André Siqueira, FIOCRUZ, Brazil
Dr Ole Skovmand, Intelligent Insect Control, France
Dr Danielle Stanistic, Institute for Glycomics, Griffith University, Australia
Dr David Sullivan, Johns Hopkins Malaria Research Institute, USA
Dr Gote Swedberg, University of Uppsala, Sweden
Prof Din Syafruddin, Hasanuddin University, Indonesia

Dr Ambrose Talisuna, University of Oxford-KEMRI-Wellcome Trust Program, Kenya
Dr Julie Thwing, Centers for Disease Control and Prevention, USA
Prof Takafumi Tsuboi, Ehime University, Japan
Dr Lorenz von Seidlein, MORU Mahidol University, Thailand
Prof Diane Wallace Taylor, University of Hawaii, USA
Dr Marian Warsame, University of Gothenburg, Sweden
Dr Sam Wassmer, London School of Hygiene & Tropical Medicine, UK
Dr Michael White, Institut Pasteur, France
Dr Danny Wilson, The University of Adelaide, Australia
Dr Colin Wright, University of Bradford, UK
Dr Dejan Zurovac, KEMRI/Wellcome Trust Collaborative Programme, Kenya

CASE REPORT

Open Access



Prolonged fever and exaggerated hypercoagulopathy in malaria vivax relapse and COVID-19 co-infection: a case report

Tri Pudy Asmarawati^{1,2,3*} , Okla Sekar Martani⁴, Bramantono Bramantono^{1,3} and Muhammad Vitanata Arfijanto^{1,3}

Abstract

Background: Coronavirus disease 2019 (COVID-19) often causes atypical clinical manifestations similar to other infectious diseases. In malaria-endemic areas, the pandemic situation will very likely result in co-infection of COVID-19 and malaria, although reports to date are still few. Meanwhile, this disease will be challenging to diagnose in areas with low malaria prevalence because the symptoms closely resemble COVID-19.

Case presentation: A 23-year-old male patient presented to the hospital with fever, anosmia, headache, and nausea 1 week before. He was diagnosed with COVID-19 and treated for approximately 10 days, then discharged to continue self-quarantine at home. 2 weeks later, he returned to the hospital with a fever raised intermittently every 2 days and marked by a chilling-fever-sweating cycle. A laboratory test for malaria and a nasopharyngeal swab for SARS CoV-2 PCR were conducted, confirming both diagnoses. The laboratory examination showed markedly elevated D-dimer. He was treated with dihydroartemisinin-piperazine (DHP) 4 tablets per day for 3 days and primaquine 2 tablets per day for 14 days according to Indonesian National Anti-malarial Treatment Guidelines. After 6 days of treatment, the patient had no complaints, and the results of laboratory tests had improved. This report describes the key points in considering the differential diagnosis and prompt treatment of malaria infection during the pandemic of COVID-19 in an endemic country to prevent the worse clinical outcomes. COVID-19 and malaria may also cause a hypercoagulable state, so a co-infection of those diseases may impact the prognosis of the disease.

Conclusion: This case report shows that considering the possibility of a co-infection in a COVID-19 patient who presents with fever can prevent delayed treatment that can worsen the disease outcome. Paying more attention to a history of travel to malaria-endemic areas, a history of previous malaria infection, and exploring anamnesis regarding the fever patterns in patients are important points in making a differential diagnosis of malaria infection during the COVID-19 pandemic.

Keywords: COVID-19, malaria, *Plasmodium vivax*, Infectious diseases

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new strain of coronavirus that started to emerge in December 2019 in Wuhan, China, and spread rapidly throughout the world, causing a coronavirus disease (COVID-19) pandemic [1]. The Indonesian government reported that the number of confirmed cases of COVID-19 on August 1, 2021, was 3,409,658, with a

*Correspondence: tpasmarawati@fk.unair.ac.id

¹ Tropical and Infectious Diseases Division, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java 60115, Indonesia
Full list of author information is available at the end of the article



© The Author(s) 2022. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

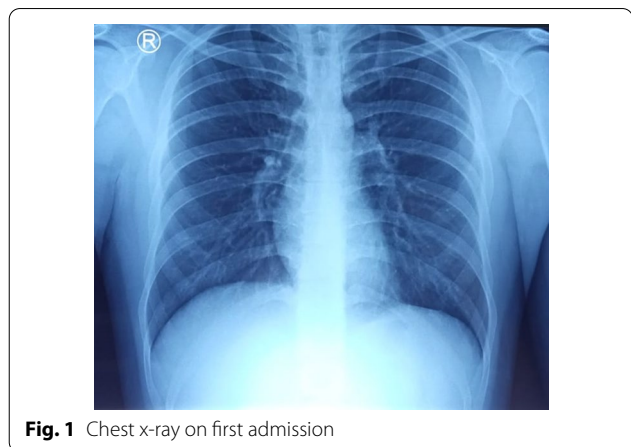
total number of 94,119 deaths or a case fatality rate of 2.76% [2]. The SARS-CoV-2 infection causes various clinical manifestations ranging from asymptomatic to a broad spectrum of symptoms, such as mild symptoms of upper respiratory tract disorders and life-threatening sepsis. Recent studies have also reported that COVID-19 patients frequently develop hypercoagulopathy and a high prevalence of thromboembolic events [3]. The most common feature in hospitalized COVID-19 patients is fever (70–90%), impaired sense of smell and taste (64–80%), dry cough (60–86%), shortness of breath (53–80%), fatigue (38%), nausea/vomiting or diarrhoea (15–39%), and myalgia (15–44%) [4]. Coagulopathy with abnormally elevated D-dimer levels has been reported in 260 of 560 cases of COVID-19 (46.4%), with the prevalence of 43% in non-severe patients compared with 60% in critically ill ICU patients.

Malaria is an infectious disease caused by protozoa of the genus *Plasmodium*, which is transmitted through the bite of an *Anopheles* mosquito. Malaria infections can cause severe clinical manifestations and death if not promptly diagnosed and treated. There are five species of *Plasmodium* that cause malaria in humans, with the most deaths caused by *Plasmodium falciparum*. *Plasmodium vivax* predominates as a cause of morbidity, while *Plasmodium ovale* and *Plasmodium malariae* rarely cause severe malaria. *Plasmodium knowlesi* primarily infects macaques in Southeast Asia, but humans living around these animals can become infected [5].

Malaria remains a serious global health problem, especially in endemic countries. In 2019, an estimated 229 million malaria cases occurred worldwide, with 3% of all cases caused by *Plasmodium vivax*, which is the predominant parasite responsible for 51.7% of malaria cases in Southeast Asia, including Indonesia [6]. Patients with malaria will usually experience paroxysmal fever, fatigue, malaise, and myalgia [7]. A co-infection between COVID-19 and malaria is rarely reported, and the mechanism is unclear. It is suggested that a co-infection leads to excess proinflammatory responses and pro-coagulant states that might result in more severe manifestations and poor prognosis. Heightened clinical suspicion is needed to diagnose other infections during the COVID-19 pandemic, especially for patients with a travelling history of malaria-endemic areas. In this case report, we found a confirmed COVID-19 patient diagnosed with malaria.

Case presentation

A 23-year-old male patient came to the emergency department at Universitas Airlangga Hospital presenting fever, anosmia, headache, and nausea 5 days before. He was diagnosed with COVID-19, confirmed by the RT-PCR amplification of SARS-CoV-2 virus nucleic



acid on a nasopharyngeal swab. The patient had abnormal laboratory findings, such as lymphopenia, neutrophilia, thrombocytopenia, and high CRP, with a normal chest X-ray (Fig. 1). The patient was treated with Favipiravir at 1600 mg per 12 h on day 1, then 600 mg per 12 h on day 2–day 5, intravenous drip of paracetamol 1000 mg every 8 h, oral vitamin C 500 mg per 8 h, and oral vitamin D 1000 IU per day according to Indonesian national COVID-19 treatment guidelines. After 10 days of treatment, the patient was still PCR positive despite no complaints. He was then discharged to continue self-quarantine at home.

He returned to the hospital two weeks later with general weakness and fever. The fever did not resolve during his self-quarantine, was raised intermittently every 2 days, and was marked by a chilling–fever–sweating cycle. The fever temperature measured was around 39.7°–40 °C. The fever improved when the patient took paracetamol, but the fever returned 6 h later. The fever was accompanied by malaise and muscle pain. The next day the patient was fever-free and able to carry out his daily activities. The physical examination revealed a body temperature of 38 °C, a blood pressure of 112/72 mmHg, a heart rate of 93 bpm, a respiratory rate of 20 breaths/minute, and oxygen saturation of 98% under ambient air. The patient weighs 65 kg with a height of 170 cm (BMI 22.5 kg/m²). Other physical examinations were normal.

The laboratory results reflected a white blood cell count of 8750/μL with 76.3% neutrophils, 13.5% lymphocytes, and 0.6% eosinophils. Haemoglobin level and platelet counts were 12.2 g/dL and 231,000/μL, respectively. CRP and D-dimer levels were 41.51 mg/L and 9.52 mg/L, respectively. Serum electrolytes and renal function tests were normal, with urea and creatinine serum 6 mg/dL and 0.4 mg/dL, respectively. The liver enzymes test was normal, with ALT being 14 IU/L and AST being 25 IU/L. Electrocardiography showed normal sinus rhythm and

axis. The chest X-ray was unremarkable (Fig. 2). The RT-PCR amplification of the SARS-CoV-2 virus nucleic acid test from the nasopharyngeal swab was still positive.

From the previous history, he said that he traveled to Timika District, Papua, for office work for the last 2 years. In May 2021, the patient was infected with *P vivax*, with initial symptoms including fever, dizziness, nausea, and muscle pain. The patient was treated until declared fully cured. A laboratory test for malaria was performed. The rapid malaria test was positive for PAN antigen, and microscopic diagnosis on blood smear revealed *Plasmodium vivax* on ring form, trophozoite, and gametocyte stage (Figs. 3, 4, 5). Based on anamnesis, physical examination, and laboratory results, the patient was diagnosed with confirmed COVID-19 with hypercoagulopathy



Fig. 2 Chest x-ray on second admission

and malaria vivax relapse (Fig. 6). According to Indonesian National Guidelines for Antimalarial Treatment [8], he was treated with dihydroartemisinin-piperaquine (DHP) 4 tablets per day for 3 days and primaquine 2 tablets per day for 14 days. The G6PD status was not tested. The patient was given an intravenous drip of paracetamol 1000 mg every 8 h and a subcutaneous injection of heparin 5000 IU every 12 h during treatment. After six days of treatment, the patient had no complaints, and the results of laboratory tests had improved. The patient was discharged from the hospital, continued self-isolation at home, and followed up with the internal medicine outpatient clinic two weeks later. Furthermore, the patient was called later and reported feeling healthy with no complaints.

Discussion

Indonesia is one of the tropical countries in the world still facing a high risk of malaria. Approximately 80% of cities or districts in Indonesia are endemic to malaria, one of

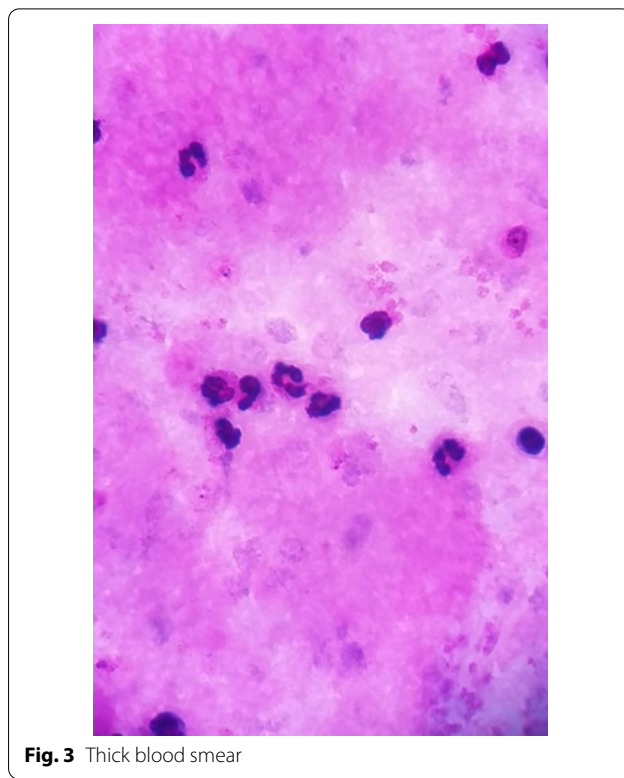


Fig. 3 Thick blood smear

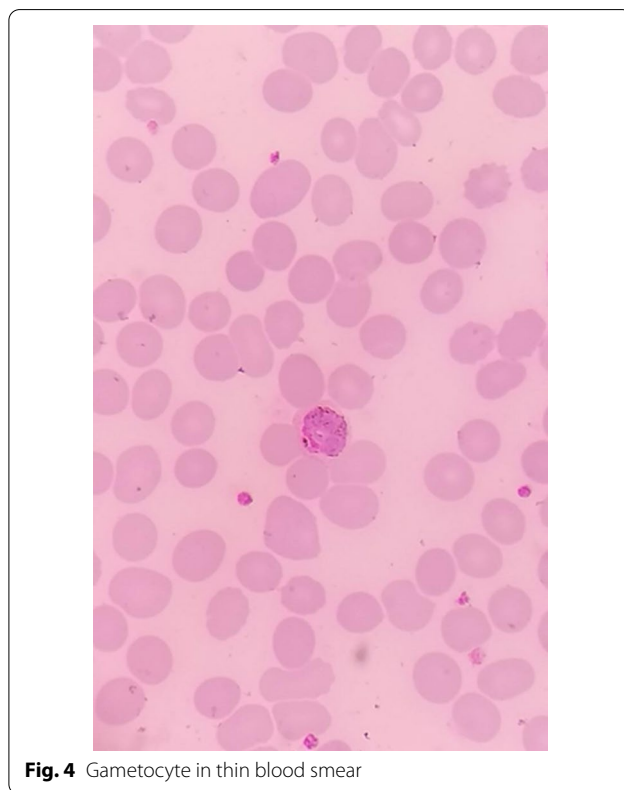


Fig. 4 Gametocyte in thin blood smear

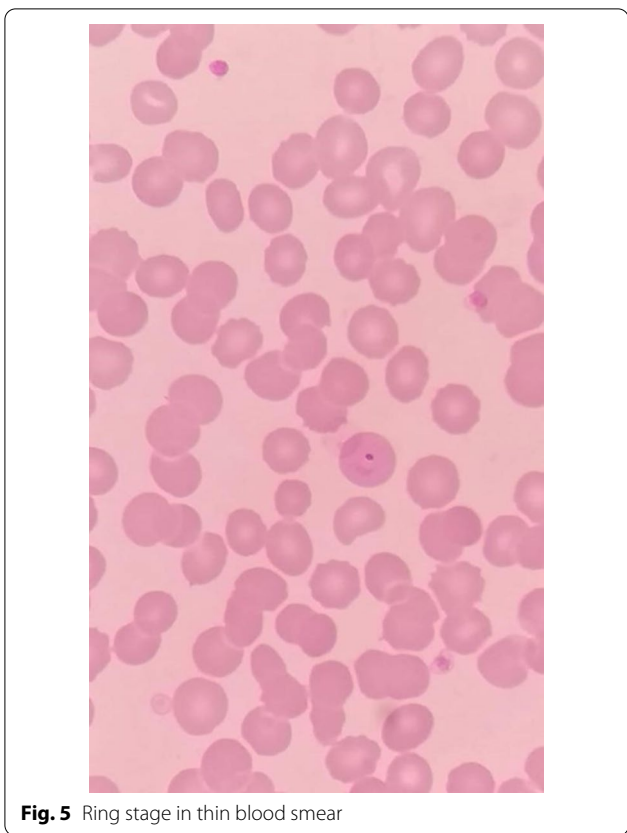
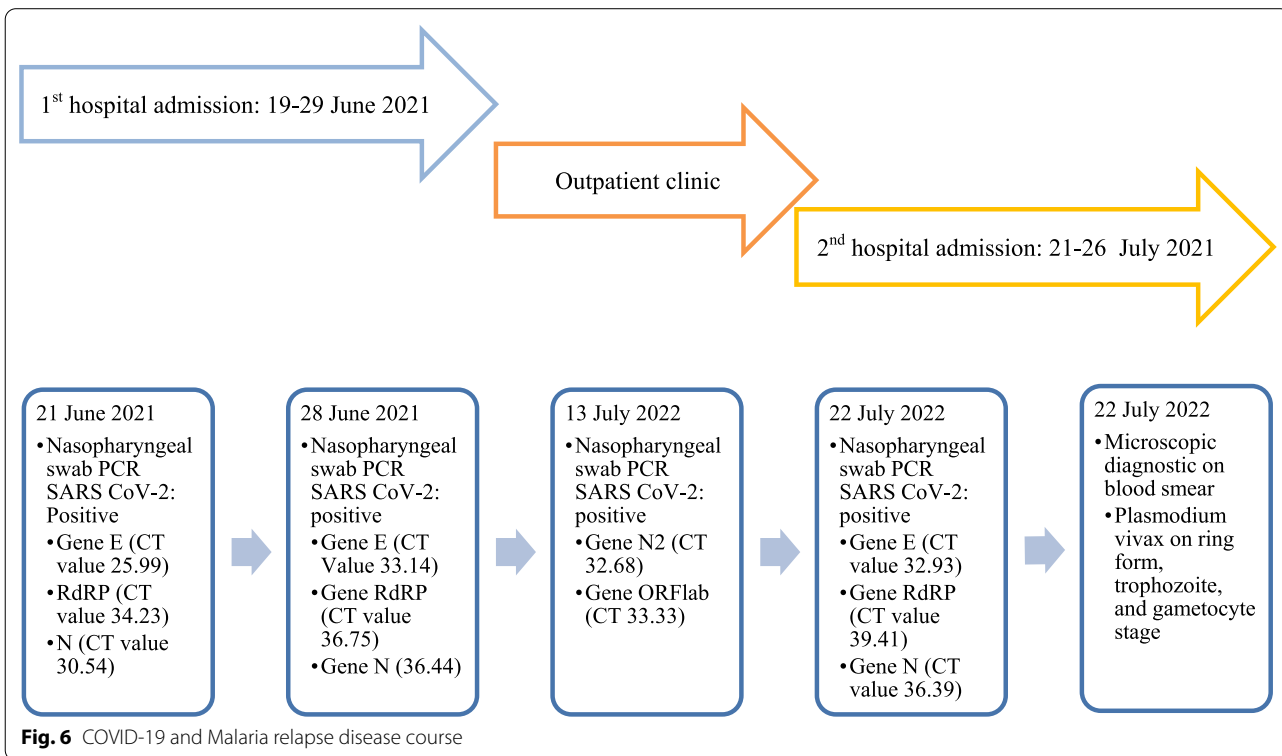


Fig. 5 Ring stage in thin blood smear

which is Papua. Based on the data from Annual Parasite Incidence (API) in 2019, the number of positive cases of malaria in Papua is 64.03% per 1000 population [9]. *Plasmodium vivax* malaria still causes significant morbidity in endemic areas. Reactivation of the dormant stage of hypnozoite can cause *P. vivax* relapse [10]. A single inoculation by a female *Anopheles* mosquito can be followed by multiple relapses [11].

Plasmodium vivax is capable of undergoing early and frequent relapses. In addition to blood-stage parasite replication, *P. vivax* has a dormant stage of hypozoites that can persist in the liver and reactivate to cause relapses weeks or even years later [12]. This reactivation may be triggered by the host’s inflammatory response to systemic illnesses or parasitic and bacterial infections, but not viral infections [13]. The estimated ratio of *P. vivax* relapses to total infections is 76–90% in the Papua New Guinea cohort study and 79% in the Thailand cohort study [12]. Based on the study conducted by Chu et al. *P. vivax* parasitaemia recurrences, mainly relapses, occurred in 377 from 644 (59%) patients treated with artesunate, chloroquine, or chloroquine-primaquine. A history of the previous malaria was more common in patients with recurrences (61%) than without recurrence (39%). About 90% of all *P. vivax* recurrences occurred by week 16 following treatment. Primaquine, as the radical cure with an estimated efficacy of 92%, would reduce the risk of



relapses and lessen the significant burden of morbidity caused by *P. vivax* [14].

The pathophysiology behind the co-infection of COVID-19 with *P. vivax* malaria remains unclear. It is unknown whether SARS-CoV-2 infection reduces the immunity that leads to malaria reactivation or if complications from malaria increase the susceptibility to get COVID-19 [15]. Based on the disease course, this patient was suspected of having reactivation of *P. vivax* infection due to COVID-19 infection. The mechanism that caused the reactivation is still unclear and may be attributed to the cytokine response to COVID-19. There is still a possibility of natural reactivation or reinfection not related to COVID-19 infection that cannot be completely ruled out [16]. The excessive proinflammatory cytokine response generated in co-infection of COVID-19 and Malaria can worsen the prognosis [17].

The patient was also suspected of having prolonged viral shedding of SARS-CoV-2; the PCR was still positive on day 38 after symptom onset. This phenomenon may be attributable to several risk factors, including male sex, disease severity, delayed hospital admission, underlying comorbidities, and a higher pro-inflammatory cytokine level [18–20]. In a large Italian cohort study, Mondini et al. stated that pro-inflammatory marker changes, especially lymphopenia, and elevated D-dimer, were strongly associated with prolonged viral shedding [19]. A higher neutrophil count and CRP were also mentioned in a report by Gao et al. as independent risk factors of prolonged viral shedding found in COVID-19 patients with bacterial co-infection [20]. Rather than bacterial infection, the abnormal proinflammatory cytokine and infection markers related to prolonged SARS-CoV-2 RNA shedding in this case were exaggerated by malaria vivax relapse.

Early symptoms of SARS-CoV-2 infection, such as fever, fatigue, and myalgia, similar to those of malaria, can lead to delayed diagnosis, especially in malaria-endemic areas [16]. In contrast to severe malaria, which is often caused by *P. falciparum*, where neurological symptoms are predominant and more severe symptoms such as loss of consciousness, signs of focal neurological abnormalities, and severe anaemia can further narrow the diagnosis of malaria. The results of blood tests can also be confusing. Therefore, a diagnostic test for both malaria and COVID-19 is crucial. The principal diagnosis of malaria to date is the microscopic examination to detect the presence of *Plasmodium* at all stages. However, the sensitivity and specificity of this examination are highly dependent on the examiner's subjectivity. If a microscopy test is not available, malaria rapid diagnostic test (RDT) can be an alternative to confirm the diagnosis. Another method using a PCR is more sensitive than microscopy, but the results take too long, so it is rarely

used [21]. *Plasmodium* spp and COVID-19 have incubation periods that are not much different. For COVID-19, the incubation period reaches 14 days from exposure with a median value of 4–5 days, while for malaria, the incubation period varies from 7 to 30 days [21]. Hence, it is essential to gain a thorough anamnesis in differentiating these two diagnoses.

Hypercoagulopathy is common in COVID-19 patients, especially in those with severe disease [22]. SARS-CoV-2 induces tissue factor expression, a primary initiator of the coagulation cascade, by cytokines produced by inflammatory cells. Moreover, SARS-CoV-2 causes endothelial dysfunction through an angiotensin-converting enzyme-2 (ACE-2) receptor expressed on the surface of vascular endothelial cells and induces neutrophil extracellular traps (NETs) release, which activates the coagulation pathways and platelet [23]. Abnormal coagulation parameters such as elevated D-dimer and fibrin degradation product levels and prolonged prothrombin time are related to a poor outcome. The most common manifestations of COVID-19 hypercoagulopathy are venous thromboembolism and arterial thrombotic complications, including pulmonary embolism and stroke [3]. COVID-19 patients are at risk for developing disseminated intravascular coagulation (DIC), pulmonary haemorrhage, and thrombosis. Thrombocytopenia associated with a higher risk of severe COVID-19 is suspected to be caused by platelet consumption in the lungs and infected haematopoietic stem cells and megakaryocytes [24].

Malaria is also strongly associated with a hypercoagulopathy condition through activation of the coagulation cascade triggered by proinflammatory cytokines [e.g., tumour necrosis factor (TNF) and interleukin (IL)-6] [25]. The most common coagulopathy condition is microthrombotic complications, besides thrombosis of large vessels, including cerebral venous thrombosis and pulmonary embolism. Thrombocytopenia is a common finding (60–80%) that may be due to impaired coagulation, splenomegaly, bone marrow disorders, antibody-mediated platelet destruction, oxidative stress, and platelet aggregation. DIC and bleeding are related to high mortality, occurring only in severe malaria. Tissue factors released from damaged vascular endothelial cells and the lysis of activated platelets contribute to the development of a pro-coagulant state similar to the underlying mechanism in COVID-19 [26]. Therefore, *Plasmodium* spp. and SARS-CoV-2 co-infection could lead to severe coagulopathy and worse outcomes than with either infection alone. In this case, the patient had a high risk of mortality due to hypercoagulopathy, characterized by markedly increased D-dimer levels which was also aggravated by malaria vivax relapse. Regarding this condition,

Table 1 A Literature review of COVID-19 and *Plasmodium vivax* Co-infection

No	Author	Country	Year of Publication	Age	Clinical symptoms	History of <i>P. vivax</i> infection
1	Shahid et al. [11]	Qatar	2021	55	Dry cough, high-grade fever, chills, rigors, profuse sweating, lethargy	Documented (1 year before)
2	Ray et al. [27]	India	2020	67	Fever, shortness of breath	Not documented
3	Kishore et al. [16]	India	2020	10	High-grade fever, chills, rigors, headache, cold, cough, abdominal pain	Documented (6 months before)
4	Sardar et al. [17]	Qatar	2020	34	Fever, myalgia, vomiting, right upper quadrant abdominal pain	Not documented (but there was a travel history to Pakistan 3 months before)

thromboprophylaxis has a crucial role in reducing the risk of thrombotic events.

There was also some similar report regarding malaria and COVID-19 co-infection, as shown in Table 1. The first case report was described by Sardar et al. [17] in Qatar as a possible *P. vivax* reactivation secondary to COVID-19, similar to the case reports presented by Kishore et al. [16] in India and Shahid et al. [11] in Qatar. Ray et al. reported a concomitant infection between malaria vivax and COVID-19 in India without suggesting the possibility of *P. vivax* re-activation [27]. However, this report is the first case of malaria vivax and COVID-19 co-infection in Indonesia that discussed the possibility of *P. vivax* relapse related to COVID-19 with symptoms of prolonged fever and exaggerated hypercoagulopathy.

Based on World Health Organization recommendations, in terms of facing challenges caused by the COVID-19 pandemic, such as the disruption of the malaria rapid test kits supply, the shortage of health workers and personal protective equipment, as well as the limited facilities of the Intensive Care Unit (ICU), the diagnosis of malaria must always be considered in all cases of fever in malaria-endemic countries [21]. Considering the differential diagnosis of malaria infection other than SARS-CoV-2 infection can reduce the risk of morbidity and mortality due to delayed and inappropriate treatment.

Various clinical trials to determine the appropriate COVID-19 therapeutic regimen are still ongoing. The massive use of hydroxychloroquine to treat COVID-19 in Malaria endemic areas will further increase the risk of anti-malarial drug resistance [17]. In this case report, the patient was treated with Favipiravir, a nucleoside analogue antiviral efficacious in various clinical trials for treating mild-to-moderate COVID-19 [28]. In a 2021 review study, Zenchenko et al. concluded that nucleoside analogue antivirals could treat a parasitic infection, such as malaria caused by *P. falciparum*. Meanwhile, studies on the nucleoside analogue

antiparasitic effect in vivax malaria are limited [29]. Artemisinin is a very potent anti-malarial drug and can overcome the problem of resistance to quinolones. Artemisinin is also able to inhibit endocytosis more strongly than chloroquine. Artesunate, a semisynthetic derivative of artemisinin, has lately attracted much attention to be tested as a COVID-19 therapy because of its anti-viral and anti-inflammatory effects through inhibition of Nuclear Factor kappa B (NF- κ B) downregulation and protein synthesis in the early stages of viral replication [30]. Further research is required to study the role of artemisinin in treating COVID-19 and the prognosis of COVID-19 co-infection with malaria.

Conclusion

This case report shows that considering the possibility of a secondary infection diagnosis other than COVID-19 in a patient who presents with fever can prevent delayed treatment that can worsen the disease outcome. Paying more attention to a history of travel to malaria-endemic areas, a history of previous malaria infection, and exploring anamnesis regarding the fever patterns in patients are important points in making a differential diagnosis of malaria infection during the COVID-19 pandemic. Hypercoagulopathy is another phenomenon that needs further analysis in Malaria and COVID-19 co-infection. Further research is required to study the role of artemisinin in treating COVID-19 and the prognosis of COVID-19 co-infection with malaria.

Abbreviations

ACE-2: Angiotensin-converting enzyme-2; ALT: Alanine transferase; API: Annual parasite incidence; AST: Aspartate transaminase; COVID-19: Coronavirus disease 2019; CRP: C-reactive protein; DHP: Dihydroartemisinin-piperazine; DIC: Disseminated intravascular coagulation; ICU: Intensive care unit; IL-6: Interleukin-6; IU: International unit; LDH: Lactate dehydrogenase; NETs: Neutrophil extracellular traps; NF- κ B: Nuclear factor kappa B; RDT: Rapid diagnostic test; RT-PCR: Real-time polymerase chain reaction; SARS CoV-2: Severe acute respiratory syndrome coronavirus-2; TNF: Tumour necrosis factor.

Acknowledgements

Not applicable.

Author contributions

TP and OS contributed to the conception and manuscript preparation. BB and MV contributed to the literature search. All authors have read and approved the submitted version. All authors read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

Not applicable.

Declarations**Ethics approval and consent to participate**

Not applicable.

Consent for publication

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

Author details

¹Tropical and Infectious Diseases Division, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, East Java 60115, Indonesia. ²Universitas Airlangga Hospital, Surabaya, East Java 60115, Indonesia. ³Dr. Soetomo General Teaching Hospital, Surabaya, East Java 60286, Indonesia. ⁴Faculty of Medicine, Universitas Airlangga, Surabaya, East Java 60115, Indonesia.

Received: 14 September 2021 Accepted: 9 June 2022

Published online: 23 June 2022

References

- Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA*. 2020;324:782–93.
- Gugus Tugas Percepatan Penanganan COVID-19 : Peta Sebaran COVID-19 Indonesia 2021 [cited 2021 2 August 2021]. Available from: URL.
- Iba T, Levy JH, Levi M, Connors JM, Thachil J. Coagulopathy of coronavirus disease 2019. *Crit Care Med*. 2020;48:1358–64.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–20.
- Moxon CA, Gibbins MP, McGuinness D, Milner DA Jr, Marti M. New insights into malaria pathogenesis. *Annu Rev Pathol*. 2020;15:315–43.
- WHO. World Malaria Report. 20 years of global progress and challenges. Geneva: World Health Organization; 2020. p. 2020.
- Cowman AF, Healer J, Marapana D, Marsh K. Malaria: biology and disease. *Cell*. 2016;167:610–24.
- Kemendes. Kementerian Kesehatan RI. Buku Saku Tatalaksana Kasus Malaria. Jakarta: Kementerian Kesehatan RI; 2019. <https://www.malaria.id/en/report>.
- Kemendes. Kementerian Kesehatan RI. Profil Kesehatan Indonesia Tahun 2019. Jakarta: Kementerian Kesehatan RI; 2020. <https://pusdatin.kemkes.go.id/resources/download/pusdatin/profil-kesehatan-indonesia/Profil-Kesehatan-indonesia-2019.pdf>.
- Dayananda KK, Achur RN, Gowda DC. Epidemiology, drug resistance, and pathophysiology of *Plasmodium vivax* malaria. *J Vector Borne Dis*. 2018;55:1–8.
- Shahid Z, Karim N, Shahid F, Yousaf Z. COVID-19 associated imported *Plasmodium vivax* malaria relapse: first reported case and literature review. *Res Rep Trop Med*. 2021;12:77–80.
- White MT, Karl S, Koepfli C, Longley RJ, Hofmann NE, Wampfler R, et al. *Plasmodium vivax* and *Plasmodium falciparum* infection dynamics: re-infections, recrudescences and relapses. *Malar J*. 2018;17:170.
- Shanks GD, White NJ. The activation of vivax malaria hypnozoites by infectious diseases. *Lancet Infect Dis*. 2013;13:900–6.
- Chu CS, Phyo AP, Lwin KM, Win HH, San T, Aung AA, et al. Comparison of the cumulative efficacy and safety of chloroquine, artesunate, and chloroquine-primaquine in *Plasmodium vivax* malaria. *Clin Infect Dis*. 2018;67:1543–9.
- Eid MM. Co-infection with COVID-19 and malaria in a young man. *Dubai Med J*. 2021;4:1–3.
- Kishore R, Dhakad S, Arif N, Dar L, Mirdha BR, Aggarwal R, et al. COVID-19: possible cause of induction of relapse of *Plasmodium vivax* Infection. *Indian J Pediatr*. 2020;87:751–2.
- Sardar S, Sharma R, Alyamani TYM, Aboukamar M. COVID-19 and *Plasmodium vivax* malaria co-infection. *IDCases*. 2020;21: e00879.
- Xu K, Chen Y, Yuan J, Yi P, Ding C, Wu W, et al. Factors associated with prolonged viral RNA shedding in patients with coronavirus disease 2019 (COVID-19). *Clin Infect Dis*. 2020;71:799–806.
- Mondi A, Lorenzini P, Castilletti C, Gagliardini R, Lalle E, Corpolongo A, et al. Risk and predictive factors of prolonged viral RNA shedding in upper respiratory specimens in a large cohort of COVID-19 patients admitted to an Italian reference hospital. *Int J Infect Dis*. 2021;105:532–9.
- Gao C, Zhu L, Jin CC, Tong YX, Xiao AT, Zhang S. Proinflammatory cytokines are associated with prolonged viral RNA shedding in COVID-19 patients. *Clin Immunol (Orlando, Fla)*. 2020;221: 108611. <https://doi.org/10.1016/j.clim.2020.108611>.
- Gao C, Zhu L, Jin CC, Tong YX, Xiao AT, Zhang S. Proinflammatory cytokines are associated with prolonged viral RNA shedding in COVID-19 patients. *Clin Immunol*. 2020;221: 108611.
- Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. *Am J Hematol*. 2020;95:834–47.
- Mori H, Ohkawara H, Togawa R, Rikimaru M, Shibata Y, Ikezoe T. Diagnosis and treatment of disseminated intravascular coagulation in COVID-19 patients: a scoping review. *Int J Hematol*. 2021;113:320–9.
- Lin J, Yan H, Chen H, He C, Lin C, He H, et al. COVID-19 and coagulation dysfunction in adults: a systematic review and meta-analysis. *J Med Virol*. 2021;93:934–44.
- Francischetti IM, Seydel KB, Monteiro RQ. Blood coagulation, inflammation, and malaria. *Microcirculation*. 2008;15:81–107.
- Autino B, Corbett Y, Castelli F, Taramelli D. Pathogenesis of malaria in tissues and blood. *Mediterr J Hematol Infect Dis*. 2012;4: e2012061.
- Ray M, Vazifdar A, Shivaprakash S. Co-infection with malaria and coronavirus disease-2019. *J Glob Infect Dis*. 2020;12:162–3.
- Manabe T, Kambayashi D, Akatsu H, Kudo K. Favipiravir for the treatment of patients with COVID-19: a systematic review and meta-analysis. *BMC Infect Dis*. 2021;21:489.
- Zenchenko AA, Drenichev MS, Il'icheva IA, Mikhailov SN. Antiviral and antimicrobial nucleoside derivatives: structural features and mechanisms of action. *Mol Biol*. 2021;55:786–812.
- Uzun T, Toptas O. Artesunate: could be an alternative drug to chloroquine in COVID-19 treatment? *Chin Med*. 2020;15:54.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.