Malaria parasite evades rapid test detection in children

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Jonathan Parr, M.D., M.P.H., a researcher at UNC, stands on the banks of the Congo River in the Democratic Republic of the Congo. Credit: Jonathan Parr

The Democratic Republic of the Congo (DRC) has one of the highest rates of people living with malaria. Rapid diagnostic tests (RDTs) account for more than 70 percent of diagnostic testing for malaria in Africa. Most rapid test diagnostics rely on the detection of histidine-rich protein 2 (HRP2), an antigen specific to Plasmodium falciparum malaria. However, one of every 15 children infected with Plasmodium falciparum malaria parasites in the DRC is infected by a pfhrp2-deleted mutant, producing a false-negative result when an RDT is used, investigators from the University of North Carolina at Chapel Hill

found. Their results were published in the *Journal of Infectious Diseases* and discussed during a recent World Health Organization meeting during the American Society of Tropical Medicine and Hygiene's annual conference in Atlanta.

"This is the first nationwide study to demonstrate the presence and estimate the prevalence of malaria caused by pfhrp2-deleted P. falciparum in asymptomatic children," said Jonathan Parr, M.D., M.P.H., the study's lead author and a researcher within UNC's Infectious Disease Epidemiology and Ecology Lab. "Because most rapid diagnostic tests in the DRC are HRP2-based, they will fail to detect these parasites. Their spread would represent a serious threat to malaria elimination efforts."

Samples were collected from children under the age of 5 during the 2013-2014 Demographic and Health Survey in the DRC. The UNC team focused on 783 samples with opposing rapid test diagnostic test and polymerase chain reaction (PCR) results. PCR testing showed positive results for malaria where rapid diagnostic testing did not.

"We identified 149 P. falciparum isolates with a deletion of the pfhrp2 gene, representing a country-wide prevalence of 6.4 percent," Parr said. "This proved that pfhrp2-deleted P. falciparum is a common cause of rapid diagnostic test negative, but PCR positive malaria test results among asymptomatic children in the Democratic Republic of the Congo. Surveillance for these deletions is needed and alternatives to HRP2-specific rapid diagnostic tests may be necessary."

The WHO and UNC coordinated a meeting Tuesday morning in Atlanta to address these parasites. The meeting brought together leading researchers, policy makers, commercial diagnostic developers, and representatives from diverse national malaria control programs to review what's known and to formulate a response. Alternate rapid diagnostic

tests will be deployed in settings where they are found to be common, and further research into their clinical impact and distribution throughout Africa will be undertaken.

The DRC project resulted from an NIH-funded study of malaria transmission led by Steven Meshnick, M.D., Ph.D., professor and associate chair of epidemiology at the UNC Gillings School of Global Public Health. Meshnick emphasized the need for a measured response.

"It is important to note that these mutated parasites have only been found in a small number of places in the world," Meshnick said. "HRP2-based rapid tests continue to play a key role in malaria control and elimination efforts."

The team is actively investigating these parasites through applied genomics studies recently funded by the Thrasher Research Fund and the ASTMH/Burroughs Wellcome Fund and ongoing NIH-funded epidemiological studies in Kinshasa Province, DRC.

More information: Jonathan B. Parr et al. -deletedparasites in the Democratic Republic of Congo: A national cross-sectional survey, *Journal of Infectious Diseases* (2016). DOI: 10.1093/infdis/jiw538

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