No single cut-off for parasite half-life can define artemisinin-resistant malaria

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Credit: CDC

Data from southeast Asia—where artemisinin-resistant malaria strains were first detected—broadly support WHO's 'working definition' for artemisinin resistance, but the currently used definitions require important refinements, according to a study by Lisa White and colleagues, from Mahidol University in Bangkok, Thailand, published this week in *PLOS Medicine*.

The drug artemisinin rapidly clears malaria parasites from the blood of infected patients—unless the parasites have developed resistance, in which case parasite clearance after artemisinin therapy (ACT) takes longer. The best measure of parasite clearance is the parasite half-life in the blood of a patient, and a common cut-off used to denote artemisinin resistance is 5 hours. The study shows that parasite half-life predicts the likelihood of an artemisinin-resistant infection for individual patients, but is influenced by how common resistance is in the particular area. The critical half-life varied between 3.5 hours (in areas where resistance is rare) and 5.5 hours (in areas where resistance is common). This means that there is no universal cut-off value in parasite half-life that can determine whether a particular infection is "sensitive" or "resistant".

Because measuring the parasite half-life requires frequent blood sampling which is difficult to do in resource-limited settings, WHO uses the following working definition for surveillance: artemisinin resistance in a population is suspected if more than 10% of patients are still carrying parasites three days after the start of ACT. Arguing that the cut-off used in the WHO working definition is based on limited data, the researchers examined how well the definition matches actual data from patients in areas with artemisinin-resistant parasites.

Applying a model specifically developed for this purpose, they found that the current WHO 'day-3' cut-off value of 10% is useful, but would be more informative if the parasite load at the start of ACT was taken into account. The authors also conclude that the WHO definition is in general a useful tool to identify areas with suspected artemisinin resistance, but "lacks accuracy in predicting the real proportion of artemisinin-resistant parasites, and should thus be followed by a more detailed assessment".

More information: White LJ, Flegg JA, Phyo AP, Wiladpai-ngern JH, Bethell D, et al. (2015) Defining the In Vivo Phenotype of Artemisinin-

Resistant Falciparum Malaria: A Modelling Approach. *PLoS Med* 12(4): e1001823. DOI: 10.1371/journal.pmed.1001823