Evaluation of the sensitivity of a pLDH-based and an aldolase-based Rapid Diagnostic Test for the diagnosis of uncomplicated and severe malaria caused by PCR-confirmed Plasmodium knowlesi, Plasmodium falciparum and Plasmodium vivax

Bridget E Barber1,2, Timothy William2,3, Matthew J Grigg1,2, Kim Piera1, Tsin W Yeo1,4 and Nicholas M Anstey1,4,+ Author Affiliations

1Global Health Division, Menzies School of Health Research and Charles Darwin University, Darwin, Northern Territory 0810, Australia
2Infectious Diseases Unit, Queen Elizabeth Hospital, Kota Kinabalu, Sabah 88560, Malaysia
3Sabah Department of Health, Kota Kinabalu, Sabah 88814, Malaysia
4Royal Darwin Hospital, Darwin, Northern Territory 0810, Australia

ABSTRACT

Background: Plasmodium knowlesi can cause severe and fatal human malaria in South-East Asia. Rapid diagnosis of all Plasmodium species is essential for initiation of effective treatment. Rapid Diagnostic Tests (RDTs) are sensitive for detection of uncomplicated and severe falciparum malaria, but have not been systematically evaluated in knowlesi malaria.

Methods: At a tertiary-referral hospital in Sabah, we prospectively evaluated the sensitivity of two combination RDTs for the diagnosis of uncomplicated and severe malaria from all three potentially-fatal Plasmodium species, using a pan-Plasmodium lactate dehydrogenase (pLDH)-P. falciparum histidine-rich-protein2 (PfHRP2) RDT (First Response™) and a pan-Plasmodium aldolase-PfHRP2 RDT (ParaHIT™).

Results: Among 293 hospitalized adults with PCR-confirmed Plasmodium monoinfection, the sensitivity of the pLDH component of the pLDH-PfHRP2 RDT was 74% (95/129; 95% CI 65 – 80%), 91% (110/121; 95% CI 84 – 95%) and 95% (41/43; 95% CI 85 – 99%) for PCR-confirmed P. knowlesi, P. falciparum and P. vivax respectively, and 88% (30/34; 73 – 95%), 90% (38/42; 95% CI 78 – 96%) and 100% (12/12; 95% CI 76 – 100%) among patients tested before commencing antimalarial treatment. Sensitivity in severe malaria was 95% (36/38; 95% CI 83 - 99), 100% (13/13; 95% CI 77 - 100) and 100% (7/7; 95% CI 65 – 100%) respectively. The aldolase component of the aldolase-PfHRP2 RDT performed poorly in all Plasmodium species.

Conclusions: The pLDH-based RDT was highly sensitive for the diagnosis of severe malaria from all species; however, neither the pLDH- or aldolase-based RDT demonstrated sufficiently high overall sensitivity for P. knowlesi. More sensitive RDTs are needed in knowlesi-endemic regions.