

**A rapid Diagnostic Test with HRP-2 antigen as a tool  
for improving the efficacy of malaria diagnosis within  
the WHO Integrated Management of Childhood Illness Strategy  
in area of high/moderate risk of malaria transmission  
in Papua New Guinea**

by

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## ABSTRACT

A children out-patient department based study was conducted to determine if the rapid diagnostic test with HRP-2 antigen (RDT) can be used by first-line health workers to improve diagnostic efficacy of clinical algorithms of Integrated Management of Childhood Illness Strategy in area of high risk of malaria transmission in Papua New Guinea (Madang Province). Two kinds of IMCI algorithms were evaluated: *WHO IMCI Generic Check Booklet* and its country adapted version: the *PNG 10 Step Check List for ALL Sick Children*. The "gold standard" for parasitaemia was determined with microscopic examination of blood (thin and thick smears). The study group included 297 children under 5 years old admitted for initial visit (49.2% males and 50.8% females). The total number of "malaria" cases identified on clinical basis was the same (291) in both: generic and PNG adapted version of IMCI algorithms. *Plasmodium falciparum* parasitaemia (asexual stages only) was detected in 75 children (25.3%) and *Plasmodium sp.* parasitaemia (asexual stages only) was found in 100 children (33.6%). Diagnostic errors of evaluated procedures were calculated. The study proved that the Rapid Diagnostic Test *Vision Biotech Pf.* can significantly improve the specificity of *P. falciparum* malaria diagnosis based on IMCI algorithms from the value of 2.7% to 92.3% ( $\chi^2=316.91$ ,  $p<0.0001$ ) when "malaria" was defined as presence of asexual stages of *Plasmodium falciparum* parasites in blood; and from 2.5% to 86% ( $\chi^2=341.8$   $p<0.0001$ ) for "malaria" definition of "5000 or more *Plasmodium falciparum* parasites per microliter", that is more associated with "clinical malaria" in high malaria endemic region. The difference between sensitivities of "malaria" diagnosis for cut off level of 5.000 *Plasmodium falciparum* parasites per microliter for IMCI algorithms and the HRP-2 Rapid Diagnostic Test was not significant statistically ( $p=0.125$ ). For detecting *P. falciparum* parasitaemia the reduction of sensitivity from 100% (IMCI algorithm) to 89.3% (Rapid Diagnostic Test) was significant statistically (Yates' corrected  $\chi^2=6.47$ ;  $p=0.01$ ). For identifying "malaria cases" defined as parasitaemia of any malaria parasite species in specific malaria epidemiological setting of Madang Province, the HRP-2 did not reach the required level of its sensitivity (69.3%). The last finding suggests that the HRP-2 test in Madang can only be used for differentiation

between "*falciparum*" and "*non-falciparum malaria*" among patients who meet criteria of malaria case definition of IMCI algorithms. This differentiation should have its implication in anti-malarial treatment following "*falciparum malaria*" and "*non-falciparum malaria*" resistant patterns.

The results of the HRP-2 test performed by first-line health workers were also compared to the results of the same tests performed in the same children by the experienced lab technicians. The Kappa statistic for both: interpretation (0.94) and validity of the test procedure (0.92) were very high indicating "almost perfect agreement". The study showed that the health workers performed the test in much shorter time than recommended by the manufacture (mean=2'32"; SD=1'58" versus recommended 15-30 minutes), due to crowded setting of the Outpatient Department and limited time available for management of a single patient. The shorter time of the test performance did not change significantly its sensitivity ( $p=0.22$ ) and specificity ( $p=0.33$ ) when compared to the tests performed exactly as proposed in the manufacture procedure.

The test also enabled to reduce overlap of "pneumonia" and "malaria" diagnosis, excluding *Plasmodium falciparum* parasitaemia in 68.8% (when clinical diagnosis was based of *Generic IMCI Algorithm*) and in 71.4% patients (when diagnosis was made according to the *PNG 10 Step Check List for ALL Sick Children*).

HRP-2 test was also useful in identifying "*non falciparum malaria*" cases in 61.1% of children admitted with history of unsuccessful treatment with antimalarial drugs at home. It means that no *Plasmodium falciparum* parasitaemia was found in 38.9% of this group of children.

The results suggest the HRP-2 test can be used in outpatient setting and improve the diagnostic efficacy of IMCI in area of seasonal malaria or high/moderate risk or malaria transmission, like Madang city, where the prevalence of malaria parasites among children did not reach 40% among all admitted children under 5 years old.