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## Malaria Rapid Diagnostic Test (RDTs)

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### Abstract

Malaria is a disease of the tropics and sub-tropics which is transmitted by infected female Anopheles mosquito. Malaria is one of the major infections challenging this part of the world. This leads to loss of lives every year especially children and mothers. The use of laboratory methods has become necessary because health workers cannot identify malaria cases reliably using clinical signs and symptoms alone. Conventionally, light microscopy of a blood smear is the reference gold standard for the detection of malaria parasites and the established method for the laboratory confirmation of malaria. It can detect malaria parasites even at low densities of 5-10 parasites/ $\mu$ l of blood when used by skilled and careful scientist. However, malaria diagnosis based on microscopy is labour intensive and time-consuming. Rapid diagnostic tests (RDTs) are recommended by WHO to enhance diagnosis and management of case prevention of complications of declared treatment, prolonging survival and monitoring of treatment especially in children. More research should be done in RDTs for higher sensitivity and specificity. Health workers especially medical laboratory scientist and clinicians should not neglect microscopy which is the gold standard for the diagnosis of malaria. Life is precious and should be carefully handled.

**Keywords:** Malaria; Infected female anopheles mosquito; Laboratory methods

## Introduction

### Malaria Rapid Diagnostic Test (RDTs)

Malaria Rapid Diagnostic Tests (RDTs), sometimes called dipsticks or Malaria Rapid Diagnostic Devices (MRDDS) are simple immunochromatographic tests that identify specific antigens of malaria parasites in whole or peripheral blood [1]. Rapid diagnostic tests are available as simple dipsticks, cassettes, or in card formats. Simplicity of formats may be crucial to overall sensitivity.

**Target antigens:** Malaria antigens currently targeted by RDT are Histidine-rich protein II of *Plasmodium falciparum* (PfHRP II), *plasmodium aldolase* and *parasite lactate dehydrogenase* (pLDH). Histidine-rich protein II of *P. falciparum* (PfHRP II) is a water-soluble protein that is produced by the sexual stages and gametocytes of *P. falciparum* and shown to remain in the blood for at antimalaria therapy. It has been reported that several RDTs targeting PfHRP II have been *plasmodium aldolase* is an enzyme of the parasite stage of *P. falciparum* as well as the non-falciparum malaria parasites. Monoclonal antibodies against *Plasmodium aldolase* are pan-specific in their reaction and have been used in a combined P.f/P.v immunochromatographic test that targets the pan malarial antigen (PMA) along with PfHRP II Parasite lactate dehydrogenase (pLDH) is a soluble glycolytic enzyme produced by the sexual and asexual stages of the live parasites and it is present in and released from the parasite infected erythrocytes. It has been found in all 4 human malaria species, and different isomers of pLDH for each of the 4 species exist. With pLDH as the target a quantitative immunocapture assay, a qualitative immunochromatographic dipstick assay using monoclonal antibodies, an immune-dot assay, and a dipstick assay using polyclonal antibodies have been developed.

### Test Performance of RDTs

**Dipstick RDTs:** Dipsticks are commonly used forms of RDTs. This may be due to the fact that they are readily available in the market at a cheap price [2]. They are easy and quick to use and thus require very little training and a shorter turn-around time. Dipsticks do not offer enough protection against blood contamination, but if protective gloves are used during testing procedures this problem can be solved or minimized. Most formats detect only the HRP II antigen which is specific for *P. falciparum* and therefore areas where non-falciparum malaria is predominant may not find this type of RDT formats very useful [2].

**Cassette and cards RDTs:** These RDT formats are much safer to use. This is because they prevent blood contamination. They are also readily available but at a 40% price higher than the dipsticks [3]. These tests are not as simple as the dipsticks and thus require much time for results to be ready unlike the dipsticks most of these RDT formats target 2 antigens

(HRPII/Pan pLDH, HRPII/Pan aldolase or HRPII/pLDH) making it possible to detect all the plasmodium species.

#### Sensitivity and specificity of malaria rapid diagnostic tests:

Rapid Diagnostic Test works based on immunochromatographic principle, with the formation of antigen-antibody complexes with the specific malaria antigen released from lysed blood. The specific malaria antigen is identified as a prodedural line on the test strip. The intracellular strip is coated with specific antibody wells. Histidine-rich protein II (HRPII) is a water-soluble protein produced by trophozoites and young gametocytes of *P. falciparum* while parasite lactate dehydrogenase (pLDH) is produced by asexual and sexual stages of all malaria parasites. HRPII base RDT detects HRP of *P. falciparum* and the pLDH RDT detects all 4 species in humans. The choice of the RDT by each country/geographical area depends on level of endemicity, prevalence and type of drug resistance, geographical accessibility social and economic characteristics and underlying health infrastructure [3].

WHO recommends a sensitivity of  $\geq 95\%$  at  $\geq 100$  parasites/ $\mu\text{l}$  for *P. falciparum*. This depends on RDT product in use as well as its mechanism of action, endemicity, prevalence and type of drug resistance geographical accessibility, social and economic characteristics and underlying health infrastructure [3].

WHO recommends a sensitive of  $\geq 95\%$  at  $\geq 100$  parasites/ $\mu\text{l}$  for *P. falciparum*. This depends on RDT product in use as well as its mechanism of action. This could vary whether it is used in clinical or field settings. Using SD Bio line malaria antigen test kits which detect all plasmodium species, in a study of 98 and specificity 94.9% using microscopy as gold standard were found. There was disparity in the rate of detection of malaria by the rapid test respectively. in a study done in 3 government hospitals in Tanzania at peak malaria season of January to March (low transmission areas) and June-August (high transmission areas) used *paracheck a P. faciparium* HRP-2 specific RDT revealed a sensitive of 95.4% and specificity of 95.9%. Similarly, in a study conducted in rural Madagascar, a sensitive and specificity of 93.5% and 98.9% respectively for SD Bio line Ag Pf test and 92.9% and 98.9% for SD Bioline malaria Ag of Pf/pan test were found. A sensitivity of 93.5% was found for pervasight F dipstick for *P. faciparium*, used in screening patients at a primary health care centre in Thailand [4].

In a study carried out at the hospital tropical diseases, London, Using PLDH specific RDT for *P. faciparum* and *P. vivax*, a sensitivity and specificity of 95.3% and 96% for *P. faciparum* and 96% and 100% for *P. vivax* were reported. In a study conducted in a similar setting (non-endemic) reported a sensitivity of 91.6% for *P. faciparum* (*P. faciparum* specific HRP-2 RDT) and 75.8% for *P. vivax* (*P. vivax* specific PLDH RDT). However, a sensitivity of 42.3% for a P.f RDT in a study conducted among 83 febrile children at the paediatrics clinic, University of Nigeria teaching hospital, Enugu, Nigeria was found. Field settings, a sensitivity of 47.5% has been found using parascreen RST [5].

**Factors influencing sensitivity, specificity and predictive value of a RDT for *P. falciparum*:** Several factors could affect the diagnostic accuracy of RDT. These can be broadly categorized into test device related factors (quality control/assurance, storage, transportation, handling environmental conditions). Preparation and interpretation issues (volume of blood and buffer, age and storage of blood sample, visual activity of scientist) and antigen, density and species). Others include host related factors such as the treatment history and effectiveness of treatment. Interpretation of RDT results should take into account of clinical history of antimalarial treatment because of delayed parasite clearance ( $>1$  month) for HRP-2 antigen. In this case, malaria diagnosis should be reached only in the absence of other infectious diseases. studies have shown decreasing sensitivity at low parasitaemia in a study conducted in food (non-endemic area) with symptoms suggestive of malaria, recorded 100% sensitivity for  $\geq 500$  *P. faciparium* parasites/ $\mu\text{l}$  which decreased to  $\leq 73\%$  at lower parasite density ( $<500$  parasite/ $\mu\text{l}$ ). This agrees with a study conducted in Port-Harcourt, Nigeria Madagascar nd on mount Cameroon Region [6]. In that study a PLDH detecting Pan-specific optimal was used. The sensitivity was also found to be specific related, because in that study, 95.3% was recorded for *plasmodium faciparium*, *plasmodium vivax* (96%) *plasmodium ovale* (57%) and *plasmodium vivax* (96%) *plasmodium ovale* (57%) and *plasmodium vivax* (96%), *plasmodium ovale* (57%) and *plasmodium malaria* (47%). The last two were found to be quite low. This variation has been reported in mixed infections. The dependence of sensitivity on parasite species was clearly elucidated in previous works [7]. This could be due to defective RDT kits and or change in predominant plasmodium specie studies in Enugu and Ethiopia showed low sensitivity of a P.f. RDT and parascreen RDT irrespective of parasite density or species variability [8].

## Discussion

### Advantage of RTDS

- RTDs are simpler to perform and to interpret. They do not require electricity, special equipment or training as in microscopy. Peripheral health workers (and other health providers as well as community volunteer) can be taught the procedure in a matter of hours, with good retention of skills over one year period.
- RDTs are no labour intensive.
- Since RDTs detect circulating antigen, they may detect *P. faciparium* infection even when the parasite are suggested in the deep vascular compartment and this understandable by microscopic examination of a peripheral blood smear.
- RDTs are faster than microscopy.

### Disadvantages

- Some commercially available RDTs are targeted for HRP-11 which can detect only a *P. faciparium* necessarily the most prevalent species.

- The current RDTs are more expensive than microscopy and possibly depending on the marketing area.
- RDTs are not quantitative. They then fail to provide information of possible important and are not suitable for detailed investigations in the therapeutic efficacy of antimalarial drugs.
- Earlier version of the test kits targeting HRP-II of a *P. falciparum* have given false positive results in patients with rheumatoid factor, all though this problem has been corrected.
- Kits that detect, both *p. falciparum* and non-falciparum species cannot differentiate between *P. vivax*, *P. ovale* and malaria, nor can they distinguish pure *P. falciparum* from mixed infections that include *P. falciparum* [8].

## Conclusion

Malaria Rapid Diagnostic Kits (RDTs) are immunochromatographic test kits made simple that can appear as dipstick or cassettes (formats) used in the rapid diagnosis of malaria infection especially in areas of high endemicity. Malaria infection is a major public health challenge in this part of the world. Many persons die each year especially the children and mothers as a result of malaria. Malaria rapid diagnostic kits were developed for fast and timely diagnosis to save life. It can be used in low resource laboratory and can be utilized in the rural areas. It has stable storage temperature of room temperatures. RDTs are developed to improve lives through timely and accurate diagnosis when the parasite density is high. Microscopy should be a reference method of malaria diagnosis which will help in the identification of stage of malaria parasite for better prognosis in the treatment for malaria patients. Health workers should be well trained to ensure proper reporting and interpretation of results.

## Conflicts of Interest

The authors declare no conflict of interest.

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