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Review Article

RELEVANCE OF RAPID IMMUNODIAGNOSTIC TEST KITS IN MALARIA DIAGNOSIS

SAHEED A. AYOOLA[1]*, SEGUN S. ADEWUMI[1], JULIUS O. OYEDELE[1], ADAMU B. SAIDU[1], KHAFAYAT O. MUSTAPHA[1], OLUWAKEMI B. ADETORO[1], RAM P. TIWARI[2]

[1]Bioresourses Development Centre, National Biotechnology Development Agency (NABDA), Ogbomosho, Oyo State, Nigeria, [2]Department of Biotechnology, Immunodiagnostic division, Van Guard Diagnostics Pvt. Ltd., Delhi-110019, India.
Email: profsaheed4u@yahoo.com

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ABSTRACT

Over the past few decades, rapid immunodiagnostic test kits (RIDTK) have been used to compliment microscopy in parasitemia detection. In order to reduce malaria mortality in Sub-Saharan Africa where malaria is endemic, the most important characteristics required for a diagnostic method are high sensitivity for detecting *Plasmodium falciparum* and rapid availability of test results. However, in environments where malaria incidence is low, high specificity and high sensitivity for detection of non-*P. falciparum* species is very important; a repeat testing paradigm is also highly necessary. The requirements of a malaria rapid immunodiagnostic test differ with respect to regional malaria epidemiology and the goals of a malaria control program. Prompt and accurate diagnosis is very important for proper management and prevention of malaria and also to prevent morbidity, mortality and indiscriminate use of anti malaria agents. There has been a great progress in the development of many rapid and specific immunodiagnostic tests for diagnosing patients suffering from malaria. In this regard, the development is done with respect to the antigen(s) the antibodies are meant to detect. The three categories of rapid immunodiagnostic test kits that have so far been developed comprise Histidine-Rich Protein 2 (HRP-2), Parasite specific plasmodium lactate dehydrogenase (pLDH) and aldolase. Despite the fact that microscopy is still used as the reference test for malaria detection and having the ability to detect lower parasite densities, there abound a lot of shortcomings with it. However, the advent and development of rapid immunodiagnostic test kits has brought lasting solutions to some of these problems In order to reduce morbidity, mortality and transmission of malaria, prompt diagnosis and adequate treatment is highly essential and these can be achieved if an only when malaria rapid immunodiagnostic tests are used.

Keywords: Malaria, Rapid immunodiagnostic test kits (RIDTK), Sensitivity, Specificity, Microscopy.

INTRODUCTION

In 2006, The World Health Organizations (WHO) estimated that about 3.3 billion people were at risk of contacting malaria. Out of these, 247 million people developed clinical malaria; majority of them are in Africa. Also, about 1million which mostly comprise of African children are dying from malaria. Despite the fact that this disease is still endemic in 109 countries and parasite-based diagnosis is increasing, many cases of malaria are not well diagnosed and therefore poorly monitored [1].

Prompt and accurate diagnosis is very important for proper management of malaria [2]. Accurate diagnosis is also very important in order to prevent morbidity and mortality; avoiding indiscriminate use of anti malaria agents [3]. There has been a great progress in the development of many rapid and specific immunodiagnostics tests for diagnosing patients suffering from malaria [4-6].

The requirements of a malaria rapid immunodiagnostic test differ with respect to regional malaria epidemiology and the goals of a malaria control program [7]. For instance, in order to reduce malaria mortality in Sub-Saharan Africa, the most important characteristics required for a diagnostic method are high sensitivity for detecting *Plasmodium falciparum* and rapid availability of test results. Conversely, in environments where the incidence of malaria is low, high specificity and high sensitivity for detection of non-*P. falciparum* species is very important; a repeat testing paradigm is necessary [3].

Morbidity, mortality and transmission of malaria can be reduced if there is prompt diagnosis and adequate treatment [8]. To achieve this, malaria rapid immunodiagnostic tests are very useful.

Sensitivity and specificity

Sensitivity and specificity are the most widely employed methods in accessing the accuracy of rapid diagnostic tests. Sensitivity is the ability of a test to correctly identify individuals with a given disease or disorder [8]. This implies that if any test claims to be 95% sensitive, it accurately detects 95 out of 100 patients presented with a particular disease condition. The remaining 5 patients will definitely be carrying the disease but the test will fail to pick them. This means the remaining 5 patients carrying the disease, the test pronounces them as negative and hence not having it. Those 5 results are termed false negative results and false-negativity is a big problem in rapid immunodiagnostic tests. If a particular test is 95% sensitive and there is another of 90% sensitivity, the former is more sensitive than the latter. Likewise a 100% sensitive test is more sensitive than a 95% sensitive one. In other words, the more accurately a test is able to detect positive results, the more sensitive it is and hence the fewer false-negative results it produces.

Specificity on the other hand is the ability of a test result to correctly exclude individuals who do not have a particular disease or disorder [8]. The implication of this is that, for a test that is 95% specific, it specifically detects 95 out of 100 normal people that are not having a certain disease as truly negative. The remaining 5 people will be pronounced by the test as having the disease whereas they don't. These 5 results are termed false-positive results. False positivity can lead to abnormal use of antimicrobials. A test is said to be more specific when it correctly excludes many people that do not have a particular disease as truly negative. This means that the lesser numbers of false results a test gives the more specific the test is.

Available malaria rapid diagnostic tests (MRDTs)

Malaria RDTs are devices that detect antigens that are produced by malaria parasites secreted into the blood of an infected individual. RDTs can be in various forms. It could be in form of a strip, the strip can in turn be inserted into a card or a cassette.

Also, MRDT can be categorized into three groups based on the type of antigen(s) the antibodies are meant to detect [8].

Histidine-Rich Protein 2 (HRP-2) which is a water soluble protein that is only found in *P. falciparum.* HRP-2 is present in the parasite's cytoplasm and on the membrane of an infected individual's erythrocyte [9, 10]. HRP-2 is a heat stable antigen [8], it spreads into the plasma and its concentration increases as the parasite develops in the host [9, 11]. Histidine-rich protein 2 (HRP-2) can be detected

even if the parasite density is very low [12, 13]. Monoclonal antibodies specific to *P. falciparum* has been developed for Histidine-rich protein 2 [8].

Parasite specific plasmodium lactate dehydrogenase (pLDH) is a terminal enzyme in the glycolytic pathway of plasmodium. It also determines the sexual or asexual nature of malaria parasites [3]. pLDH is available as *P. falciparum*-specific, pan-specific (detecting all the four types of plasmodia that affect human) and *P. vivax*-specific pLDH antibodies [8].

Another antigen that has antibodies developed to detect is aldolase which is also a very important enzyme in the glycolytic pathway of malaria parasites. Aldolase is well conserved across all the four human-specific *Plasmodium* species and therefore is a target antigen for pan malaria [14, 15].

Importance of malaria rapid immunodiagnostic tests

Although, microscopy still remains the reference test for the detection of parasitemia, having the ability to detect lower parasite densities of between 5 and 10 parasites/µl of blood [16]. Despite the many advantages of microscopy, it is confronted with many limitations [17-19]. Among the many limitations of microscopy are that of differences in staining and techniques used [7, 20]; also, proper microscopic diagnosis requires experience and extensive training [3].

The last few decades have witnessed the development of new techniques to solve some of the problems associated with the use of microscopy. Among these new developed techniques are malaria rapid immunodiagnostic tests [16]. Lateral-flow techniques malaria rapid immunodiagnostic tests that work based on the principle of immuno chromatography were also introduced and remains the basis for all MRDTs till date [3].

CONCLUSION

There has been a considerable improvement in malarial diagnosis as a large number of rapid immunodiagnostic test kits are now available which can be used to accurately detect malaria parasite. Due to the problems and limitations associated with microscopy which still remains the reference test for malaria detection, the use of rapid immunodiagnostic test kits proffer solutions to some of those problems. These immunodiagnostic test kits are relatively easy to use, save time and can detect all the *Plasmodium* species. In order to reduce morbidity, mortality and transmission of malaria, prompt diagnosis and adequate treatment is highly essential and these can be achieved if an only when malaria rapid immuno diagnostic tests are used.

CONFLICT OF INTERESTS

Declared None

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