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Evaluation of Parasite LDH Detection Strip Test (OptiMAL) for Rapid Diagnosis of Malaria in Children.

Kumar Arvind*

Department of Paediatrics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-29

ABSTRACT

Malaria is a serious protozoal disease caused by *plasmodium* parasites, affecting peoples worldwide, more prevalent and problematic in developing and underdeveloped countries with high mortality and morbidity particularly in pediatric age groups. Clinical presentation of malaria is varies from asymptomatic to severe complicated disease and in pediatric age group its presentation is not as classic as in adult. The development of rapid and specific diagnostic tests to identify individuals infected with malaria is of paramount importance in efforts to control the health impact of this disease as microscopic examination of blood film is time consuming, labour intensive, absolutely depends on good trained technician and good laboratory setup. This study evaluate the ability of a newly developed rapid malaria diagnostic test, OptiMAL (Flow Inc.-DiaMed,) in diagnosis of malaria. OptiMAL is a rapid (20-min) malaria detection test which utilizes a dipstick coated with monoclonal antibodies against the intracellular metabolic enzyme parasite lactate dehydrogenase (pLDH). Differentiation of malaria parasites is based on antigenic differences between the pLDH isoforms. Since pLDH is produced only by live *Plasmodium* parasites, this test has the ability to differentiate live from dead organisms. Results from the OptiMAL test were compared to traditional Giemsa-stained thick and thin smear blood films examination. Total 120 pediatric patient diagnosed as malaria were examined. OptiMAL test shows Sensitivity of 94% & 90.48% and specificity of 80% & 92.31% to the *p. falciparum* and *p.vivax* malaria cases respectively.

Keywords: malaria rapid diagnostic test, pLDH, OptiMAL

Corresponding author

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INTRODUCTION

Malaria is a protozoal disease caused by plasmodium parasite and transmitted to human beings by bite of female Anophelese mosquito. It is a very common cause of fever in tropical countries and the most important parasitic disease of human with transmission in more than 100 countries [6]. Despite improving health facilities, better diagnostic modalities and newer drugs, Malaria still remains the major cause of illness and even death in underdeveloped and developing countries like India. In childrens malaria having wide variability of clinical presentation. The classical paroxysm of cold stages, hot stages and sweating stages with a definite pattern of intermittent fever is invariably absent, instead irregular fever with respiratory and gastrointestinal symptoms mark onset of disease making great difficulties in clinical diagnosis and management [4,6]. Prompt and accurate diagnosis is key to effective disease control and to prevent mortality and morbidity associated with malaria. This is particularly very important in severe complicated malaria which is a medical emergency where timely and accurate diagnosis is very important to provide appropriate treatment and to prevent mortality and morbidity as most of the death is either due to delay in diagnosis or missed diagnosis [5,6,11].

Inaccurate and delay in diagnosis of malaria is contributed by many factors like nonspecific clinical presentation, high prevalence of asymptomatic infections, lack of resources and trained personels, widespread practices of self treatment and parasite sequestration (p.falciparum). Light microscopic examination of a well prepared blood film by an expert technician is the " gold standard " method for detecting and identifying malarial parasite [1,5,6]. But it has certain disadvantage like it is a labour intensive and time consuming process, absolutely depends upon good trained technician, good laboratory set up, requires considerable expertise for its interpretation particularly at low levels of parasitemia [14]. Due to these disadvantages of microscopy there is a need of another diagnostic tool of malaria which should be simple, rapid, easy to perform and reliable. In recent years, several rapid malaria tests have been developed. In addition to providing rapid diagnosis, several of these tests differentiate P. falciparum infections from non-P. falciparum infections. Here, we evaluating the use of a rapid malaria diagnostic test, Optimal (DiaMed) for the ability to increase the detection and identification of malaria parasites to the species level [11-13]. The objective of this study was to assess Optimal as an aid in rapid initial diagnosis of individuals presenting with symptoms consistent with malaria at health care facilities in rural health care setting.

METHODS

We prospectively reviewed 120 patients of malaria diagnosed and treated in our institute. Study group consist of all pediatric patients suspected of having malaria on the basis of clinical feature and history who were admitted to the pediatirc ward or consulted in outdoor.

Selection of cases

Patients with any of the following clinical feature were included in the study:

Acute febrile illness with or without chills and rigor.
Acute febrile illness with altered sensorium.
Acute febrile illness with jaundice or pallor.
Acute febrile illness with oliguria.
Acute febrile illness with seizure.
Acute febrile illness with splenomegaly or hepatomegaly or both.
Atypical presentations with suspected malaria.

Those cases were excluded from study in which malaria was ruled out by establishing an alternative diagnosis like kalaazar, meningitis, encephalitis, enteric fever, septicaemia, viral fever.

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Microscopic examination of blood smears

Thin and thick blood smears were prepared from blood samples of patients suspected of having a malaria infection. Blood smears were examined microscopically after standard Giemsa staining [3, 6, 10-12]. All slides were examined in parasitology lab with the help of expert personel.

Optimal test

The Optimal rapid malaria test (Flow Inc.-DiaMed) is basically a strip test in which dipstick method is used. The test is based on a membrane strip coated with monoclonal antibodies specific for parasite lactate dehydrogenase, an enzyme produced by intracellular metabolizing malarial parasites. Differentiation of malaria parasites is based on antigenic differences between the pLDH isoforms produced by different malarial parasites. Since pLDH is produced only by live Plasmodium parasites, this test has the ability to differentiate live from dead organisms [12,15]. After preparing patients finger, blood was collected in sample applicator pipette upto the specified mark by giving a bold prick on patient finger. The collected blood was poured in the first well containing one drop of buffer. Then the Optimal strip was placed in the well for 10 minutes. After the blood is completely wicked up, the strip was placed in the next well containing four drop of wash buffer for 10 minutes, and allowed to clear. The entire process takes approximately 20 min, and results are visually interpreted. A positive control line should always be present at the top of the strip to verify that the test strip is functional. If this is the only line that appears, then the test is considered negative for malaria. Appearance of a second line, adjacent to the positive control line, indicates the presence of a non-P. falciparum malaria parasite (P. vivax, P. ovalae, or P. malariae). When a third line is also present, this indicates a positive response for P. falciparum infection. A mixed infection is indicated when all three lines is positive [6,8,10,11]. As in our region, only P. falciparum and P. vivax species are prevalent, all non-falciparum cases diagnosed by Optimal were lebeled as P. vivax malaria cases [4,6].

RESULTS

A total of 120 patients diagnosed as malaria were tested by both microscopy and Optimal strip test. Table 1 shows Optimal in comparison to microscopy for P. Falciparum malaria.14 cases of Falciparum malaria missed by microscopy were diagnosed by Optimal, 3 cases diagnosed by microscopy who were negative by Optimal. When microscopy is considered as gold standard,, Optimal have 94% sensitivity, 80% specificity, 77.05% positive predictive value and 94.92% negative predictive value.

Table 1: Optimal in comparison to microscopy (p. Falciparum malaria)

Optimal	Microscopy		Total
	Positive	Negative	
Positive	47	14	61
Negative	3	56	59
Total	50	70	120

Table 2 show comparison of Optimal to microscopy in cases of p.vivax malaria. Optimal have 90.48% sensitivity, 92.31% specificity, 86.36% positive predictive value and 94.74% negative predictive value in comparison to gold standard microscopy.

Table 2: Optimal in comparison to microscopy (p.vivax malaria)

Optimal	Microscopy		Total
	Positive	Negative	
Positive	38	6	44
Negative	4	72	76
Total	42	78	120

Table 3 show overall efficacy of Optimal in comparison to microscopy. Out of 120 cases, Optimal were positive in 105 cases while microscopy were positive in 92 cases. When efficacy of Optimal was compared to microscopy, it was significantly better than microscopy ($p<0.05$) by CHI-SQUARE TEST.

Table 3: Efficacy of Optimal Test

	Diagnosed	Not Diagnosed
Optimal	105	15
Microscopy	92	28

DISCUSSION

Prompt and accurate diagnosis of malaria is key to effective treatment and one of the main global malaria control strategy intervention. Poor diagnosis is due to many factors like nonspecific clinical presentation, high prevalence of asymptomatic infections, lack of resources and trained personel. Microscopic examination of thick and thin film is "gold standard"[1,2,6] if performed correctly but wrong method of collection, untrained staff, poor lab facilities, sequestration of parasites and time taken in perform it, make this method difficult to timely diagnosis of malaria [4, 6]. Optimal strip test is easy, rapid and bed side test, does not need a microscope, good laboratory set up or good trained technician to perform it, has certainly advantage over microscopy. When compared to microscopy, Optimal is 94% sensitive & 80% specific in case of falciparum malaria and 90.48% sensitive & 92.31% specific in case of vivax malaria [10, 11, 15, 16]. A major benefit of using the Optimal rapid malaria test is its potential to quickly and confidently identify high parasitemia P. falciparum infections, allowing a quick decision on treatment options, including hospitalization [12]. The duration of hospitalization can thus be reduced significantly and the patient can be followed up as an outpatient. The discrepancies of results in Optimal strip test and microscopic examination may be due to many factors like, poor sensitivity of Optimal test at low level of parasitemia ,the sequestration of parasites, self medication before Optimal test to be performed as it detect pLDH which secreted by live parasite only [11,12,14-16].

CONCLUSION

Optimal strip test is effective, simple, easy to perform, and comparable to that of microscopic examination of blood film in diagnosis of malaria, especially in p.falciparum cases where urgent diagnosis is required and Waiting for microscopic demonstration of malarial parasites can be detrimental to the patients outcome. It can also be used for monitoring treatment as it only detects live parasites. This test is particularly useful in field conditions and rural area where lab facilities in not up to mark. In author view best approach for diagnosis of malaria would be both combination of optimal test and microscopic examination of blood film.

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