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Efficacy of Parasight F Test in Diagnosis of Falciparum Malaria

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Abstract- A rural hospital based study was conducted on children with clinical suspicion of malaria to evaluate the efficacy of the rapid diagnostic immunochromatographic test, Parasight F test in diagnosis of falciparum malaria compared to the gold standard, the peripheral blood smear. Blood samples from 105 children who presented with clinical suspicion of malaria(fever with splenomegaly) were investigated at the time of admission by both peripheral blood smear and the Parasight F test to detect the plasmodium falciparum species. Of the 63 confirmed cases of malaria, 23 children showed a positive result in the Parasight F test. The Parasight F test showed 100% sensitivity and 100% specificity for the diagnosis of falciparum malaria.

Index Terms- falciparum malaria in children, Peripheral blood smear, Parasight F test

I. INTRODUCTION

Despite more than 100 years since Laveran described the Plasmodium species and Ross confirmed its transmission by the female anopheles mosquito, malaria remains to be one of the leading causes of morbidity and mortality worldwide.[1]As per the WHO fact sheet 2012, in the South East Asia, the second most affected region in the world, India has the highest malaria burden with an estimated 24 million cases per year.[2] Worldwide, about 219 million cases of malaria are estimated to occur every year with 6.6million malaria deaths each year whose main victims were children less than 5 years old.[2]Majority of them were due to cerebral malaria and anemia. Among the children referred to hospitals with severe malaria, fatality rate of 10-30% is reported[1,3,4] Severe malaria is caused by the deadly plasmodium falciparum. Rapid detection of the species is hence necessary. Microscopic detection of the parasite is the gold standard for diagnosis of malaria[5]. However, it is time consuming, labor intensive, requires skilled technician and adequate instrumentation and methodology including staining procedures particularly at low parasitemia levels, an energy source to power the microscope and is rather impractical in remote areas. In many areas, malaria patients are treated outside of the formal health services, e.g. in the community, in the home or by private providers where microscopy is generally not feasible in many such circumstances. In these conditions , empirical treatment of malaria becomes a norm which may lead to emergence of resistence.[5,6,7,8,9] Alternatives to this have long been sought and have spurred the development of many nonmicroscopic diagnostic devices based on the antigen detection in the whole blood. Parasight F test is one such immunochromatic test which detects the histidine rich protein 2 antigen of the deadly plasmodium falciparum.[7,8] This aids in the detection of the malaria including in remote areas where health facility coverage is low.[10] Also it allows for a rapid institution of antimalarial treatment.[5]

Though there are many studies conducted on the RDT, not many studies are done exclusively on the children. Hence this study aims at detection of the falciparum malaria in the pediatric age group.

II. MATERIALS AND METHOD

Study was conducted at a rural hospital, Sri Adichunchanagiri Institute of Medical Sciences, Belur. After taking ethical committee clearance and informed consent from the respective parents, children between the ages of 6months to 18 years presenting with fever with splenomegaly were enrolled in the study. Children who received antimalarials in the past 14 days, rheumatoid arthritis, teenage pregnancy were excluded from the study as they may show false positivity.

Details of history and clinical examination of the suspected malaria cases were recorded. Following investigations were sent simultaneously on the day of admission- hemoglobin, total and differential count, platelet count, urine microscopy, peripheral blood smear(PBS), parasight F(PF) test. Depending on the condition of the children, additional tests like blood sugars, liver function test, renal function tests, widal test, CT scan head, lumbar puncture were planned.

Peripheral blood smear: 2ml of venous blood was drawn with aseptic precautions and collected in a sterile EDTA test tube. Two slides, one for thick smear and one for thin smear examination were prepared. Slide for thick smear was dehemoglobinised using distilled water before staining. Slide for thin smear was fixed by dipping it into methanol for 5 seconds. Both the slides were stained with Leishmann stain and allowed to stand for 30 seconds and was then diluted with double volume of distilled water. It was allowed to dry for 15minutes.The slide was then read at 1000X magnification. The duration of examination of the thick and thin smear was 10 minutes and 15-20 minutes which included visualization of 100 fields in each smear. The species and the stage of parasite were reported after examining the thin smear. The patient was considered not to have malaria after 3 negative samples.

Parasight F test: This immunochromatographic assay was done to detect the histidine-rich protein 2 antigen produced and

released by plasmodium falciparum. The commercial kit ParaHIT^{TM} f (manufactured by Span diagnostics Limited developed by PATH, Seattle, Washington, USA).

The test strip composed of chromatographic layer with two invisible transverse parallel lines, are labeled with patient identification number. After puncturing the tip of a finger with a sterile lancet given in the kit, the blood was aspirated into the heparinized glass capillary up to the mark, was transferred immediately to the test strip and placed in 200µl or 4 drops of reaction buffer was added to the test tube. At the end of 15 minutes, the test was interpreted. The test was interpreted as positive if both the test and control band appeared. The test was negative if band appears only in control region. The test was interpreted as invalid if no band appeared in either test or control region. In such a case, the test was repeated on a fresh strip.

III. Statistical Methods

The statistical software namely SPSS 15.0, Stata 8.0, MedCale 9.0.1 and Systat 11.0 were used for the analysis of the data and Microsoft word and Excel to generate graphs, tables etc. To find significance of association of findings of Parasight F test with peripheral smear findings for falciparum malaria. Diagnostic statistics viz., sensitivity, specificity, PPV, NPV were computed..

IV. Results

During the study, 105 children clinically suspected as malaria were included who fulfilled inclusion criteria(fever with splenomegaly). Of the 105 children, 63 were confirmed positive for malaria (90% CI:malaria 50.44-68.89) by either gold standard test, the peripheral smear and the rapid immunochromatographic assay, the Parasight F test. Rest of the cases were 17% of viral fever, 11.4% of urinary tract infections, 8.6% enteric fever and3.9% of septicemia with meningitis. Of the 63 confirmed cases of malaria, 3 children had both Plasmodium vivax and plasmodium falciparum malaria positive. Details of the PBS is given in Table 1

Table 1

Peripheral smear findings	Number(n=105)	Percentage	90%CI
Positive for falciparum only	20	19.1	12.7-27.6
Positive for vivax only	40	38	29.4-47.7
Positive for falciparum and vivax	3	2.9	0.9-8.1
Negative for malaria	42	40	31.1-49.6

Of the 63 confirmed malaria cases, only 23 were falciparum positive cases. 2 children whose blood culture confirmed enteric fever also showed Pl. vivax species on PBS. Parasight F test was positive in all the falciparum positive cases. In these, 56.5% were male children and 43.5% were female children. Most of the falciparum cases(56.5%) were in the age group of 10-14 years followed by 5-9 years(30.4%) and 2-4 years(13.1%). Presenting symptoms were fever with splenomegaly. Other features included chills and rigors, sweating, headache. Of the 23 falciparum malaria positive children, all of them had splenomegaly. 5 children had hepatomegaly too and 21 had pallor. Investigations showed anemia in 21 out of 23 falciparum positive children. Diagnosis based on PBS and PF test is given in Table 2

Table 2:

Diagnosis	Number(n=105)	Parasight F test		Peripheral blood smear	
		Number	%	Number	%
Falciparum malaria	20	20	100	20	100
Falciparum + Vivax malaria	3	3	100	3	100
Vivax malaria	38	0	0	38	100
Vivax malaria+enteric fever	2	0	0	2	100

V. Discussion

105 children enrolled in the study conducted at the rural hospital in malaria endemic area. PBS and Parasight F test(which detects pl.falciparum species only) done at the time of admission showed 63 confirmed malaria cases. Of these, 23 cases showed positivity to falciparum malaria both on PBS and PF test. The PF test band of 3 children with mixed malaria showed positive results though the band was weakly positive. None of other cases showed any positivity for the Parasight F test. Thus the test was 100% sensitive and 100% specific in comparison to the PBS.

The average time to get the PBS result was 2hours. The preparation of the PBS required to be done by a skilled laboratory technician and the preparation time was about 30minutes and additional few minutes was required to examine the slides either by the microbiologist or atleast by the skilled technician which was reconfirmed by the microbiologist while the PF test was done and results interpreted in 15 minutes and the treatment was started immediately. A similar result was seen in the study of RDTs in travellers.[11]

Though PBS is the gold standard, studies have shown that not always there is a 100% positivity. The present study showed 60% positivity while studies by Schiff et al[12]., showed a 50.8% positivity, while Rickman et al[13] showed 55.5% positivity.

In the present study, the sensitivity of PF test is 100% which is comparable to Sandrine Houzé et al.,[14]which showed sensitivity of 96% which is which is higher than the threshold of 95% recommended by the World Health Organization (WHO)[15] Most of the other studies whose sensitivity range from89% to 100%[16-20] The specificity in these studies range from 80% to 100%. The present study showed a specificity of 100%.

Thus the rapid immunochromatographic test, the PF test meets the criteria for an ideal diagnostic test as there was 100% result comparable to the gold standard test. Also the test results were available faster and it has not detected any false positive cases too, thus qualifying as a reliable test for the diagnosis of the deadly falciparum species.

The Positive predictive value(PPV) was 100 % in the study by Sandeep Arora[16] while other studies showed a range of 75-95%[16-20]. The present study too showed a PPV of 100 %. The negative predictive value was 100 % in the present study while some other studies had a range from 91-98.35%[16-21]

VI. Conclusion

Thus, the Parasight F test is one of the ideal tests for diagnosis as it is simple, sensitive, rapid, specific, easy to perform and does not require electricity for storage, does not require complicated equipments or trained personnel, thus proving as an effective tool in the battle against malaria. However, the limitation is the relative high cost of the kit, inability to indicate the severity of the infection and inability to detect the other species of plasmodium. But in the event of the complicated malaria which is more commonly due to falciparum malaria where rapid diagnosis and early management of the case is required to salvage life, this rapid diagnostic method proves to be a boon especially in remote and rural areas.

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