Role of Rapid diagnostic Tests for guiding therapy in partially treated malaria patients

Sarita Mohapatra[1,*], Bhawna Sharma[2], Manorama Deb[3]

[1]Assistant Professor, AIIMS, New Delhi, [2]Assistant Professor, ESI Medical College & Hospital, Faridabad [3]Director Professor, Vardhaman Mahavir Medical College & Safdarjung Hospital, New Delhi

***Corresponding Author:**
Email: saritarath2005@yahoo.co.in, saritarath2005@yahoo.co.in

Abstract

Background: Malaria is one of the major public health problems worldwide. Diagnosis of malaria by microscopy and/ or rapid antigen detection test is the standard practice all over world. In endemic areas, many rely on clinical or self-diagnosis and start the antimalarial treatment without a definite microbiological diagnosis. These patients with incomplete treatment may pose a challenge to clinician and microbiologist alike.

Methods: A total of 62 patients with history of incomplete treatment and clinically diagnosed as malaria were included in this study. Microbiological diagnosis of malaria is arried out by microscopy of the peripheral thin smear by giemsa stain and rapid antigen detection test (RDT).

Results: All the blood samples were positive (62/62) by RDT, whereas 40 exhibited presence of malaria parasites by microscopy. 22 samples were negative for parasitic forms irrespective of the test band intensity in RDT.

Conclusion: In developing countries like India, where malaria is endemic self-diagnosis and self-medication is a common practice. RDT found to be better tool for the confirmation of malaria diagnosis for the patients with incomplete antimalarial treatment history compared to microscopy.

Key words: Self-medication, Anti-Malarial, Malaria, Diagnostic Tool.

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Introduction

Diagnosis of malaria in the endemic areas is commonly done either by microscopy or rapid antigen detection test. To prevent unnecessary prescription or intake of antimalarial in malaria endemic regions, WHO introduced certain guidelines regarding malaria diagnosis.[1]As per these guidelines, parasitological confirmation in every suspected febrile case must be performed either by microscopy (where microscopy report can be provided within 24 hours) or by rapid detection test (RDT) (where the report is generated after 24 hours)before starting any anti-malarial drug.(1) The number of febrile cases during the post- Punctuation error monsoon period rapidly increases in this region.(2) Since both malaria and dengue were mosquito borne, the epidemiological pattern and the surge in the number of febrile cases in New Delhi (India) almost match. Clinical diagnosis plays major role to initiate antimalarial medication as microscopy is time consuming and needs expertise.(2) On the other hand due to high cost of RDTs and easy availability of drugs in the medical stores, many patients take go for sealant-malarial medication.(3-7) These patients with incomplete treatment remain challenging to meet the correct diagnosis as well as for the adherence of further course of treatment.

Aims and Objectives

The present study aims to compare the role of microscopy and RDT for diagnosis of malaria in patients with incomplete anti-malarial therapy. The objective of the study was to estimate the proportion of clinically diagnosed febrile patients or diagnosed at a later stage, which can be detected as malaria positive by either microscopy and/ or RDT based on the principle of immune-chromatographic assay after different time period of taking anti-malarial drugs.

Material and Methods

The work was a part of prospective observational study conducted in a tertiary health centre over a period of 4months (July to October, 2013). All the investigations done in the study were part of routine investigation procedure during the hospital stay for which patient's consent had already been taken. Patients with clinical diagnosis of malaria with history of incomplete antimalarial intake in recent past i.e. 24-48 hours before were included in this study. Clinically malaria in these patients was defined as axillary temperature ≥37.5°C during admission or in the previous 48hours. Blood samples were collected in EDTA vial and peripheral smears were received at the microbiological laboratory. The malaria diagnosis was done by microscopy of the peripheral thin smears, and RDT (Immune check, Genomics Pvt. Ltd., Hyderabad, India). All peripheral smears were giemsa stained and examined independently by three microbiologists. The

positive smears were reported for different malaria species and parasite count as per WHO guideline. The RDT based on Plasmodium vivax specific LDH (lactate dehydrogenase antigen), and Plasmodium falciparum specific HRP II (histidine rich protein) antigen, was performed simultaneously. Detailed clinical history, laboratory parameters, treatment history of every patient was obtained for analysis.

Result

During the 4 months (July to October, 2013) of study period 6657 samples were tested for malaria by microscopy and RDT. A total 259 malaria positive cases were diagnosed during the above period, of which 62 (24%)positive samples were received after starting the antimalarial. All the 62 cases found positive by rapid detection test whereas only 40out of 62 cases (55%) were reported positive by microscopy (Table 1). Among the 62 samples, 13 were as *P. falciparum*, 47 were *P. vivax* and 2 were mixed infection of *P. vivax* and *P. falciparum*. All the patients were febrile on admission or had history of fever within 48 hours prior to admission. Among the 62 patients, 22had anaemia (haemoglobin <7gm/dl), 61had thrombocytopenia (thrombocytopenia: platelet count < 1.5lakh/µl), 34 had hepato-splenomegaly and 14 had jaundice at the time of admission (Table 2). Four patients were diagnosed to be positive for enteric fever by widal test and one had dengue along with malaria. The RDT interpretation varies from 1+ to 4+ (3+: intensity of the test band equal to control band, 2+ and 1+: intensity of the test band less than control line, 4+: intensity of the test band more than the control band). The peripheral smears of these cases stained with giemsa found as either negative for malaria parasite or showing only gametocytes or with both sexual and asexual forms of malaria parasites (Table 3). 22 out of 62 samples found to be negative by microscopy irrespective of the test band intensity in the RDT.

Table 1: Comparison of RDT and microscopy for detection of malaria

Grading of ICT	RDT positive	Microscopy neg	Only gametocyte	Asexual forms
1+	25	14	9	2
2+	11	5	4	4
3+	24	9	9	10
4+	2	-	-	2
Total	62	28	22	18

Table 2: Association of various signs and symptoms with ICT and Microscopy

Symptoms and signs	ICT pos (n=62)	Microscopy positive (n=40)	Microscopy negative(n=22)
Fever	62	40	22
Anaemia	22	17	5
Thrombocytopenia	61	39	22
Icterus	14	10	4
Hepatosplenomegaly	34	23	11
Deranged LFT	30	21	9
Deranged RFT	11	8	3
GI symptoms	34	22	12
Delirium	10	5	5
Respiratory complication	10	5	5

Table 3: Relationship of parasitic load with number of medications

Parasite load	1 medication (%)	2 medications (%)	3 medications (%)	Total (%)
Negative	12 (33.3)	8 (38.1)	2 (40)	22 (35.4)
Only gametocyte	13 (36.1)	6 (28.5)	3 (60)	22 (35.4)
Asexual forms with gametocyte	11 (30.5)	7(33.3)	0 (0)	18 (29)
Total	36	21	5	62

Discussion

In India, Malaria is a leading cause of morbidity and mortality.[8] Prompt and correct diagnosis of malaria is necessary to start right treatment at the earliest possible time. It not only reduces over diagnosis but also decreases unnecessary administration of antimalarial. However, at the community level of malaria endemic countries, people are still dependent on the clinical diagnosis followed by self-medication. Hence, the correct treatment may not be administered

due to incomplete or inappropriate medication prior to the diagnosis. This study highlights the usefulness of RDTs in such case, which helps in correct diagnosis as well as in adherence to the malaria treatment. Fever is the most common symptom followed by gastrointestinal discomfort (nausea/ vomiting/ abdominal pain etc.). During the study the samples were received at different time interval after treatment with different combination of drugs as revealed by the patient. The anti-malarial varied from chloroquinine alone, artesunate combination therapy and artesunate with or without antibiotics. Few patients had taken 2/3 drug combination such as one anti-malarial with antipyretics /one antibiotics or two anti-malarial with one antibiotic. It was observed that the band intensity of the RDT did not correlate with the parasite load. (Table 1). The microscopy was negative irrespective of 2+/3+ band intensity of the test line. The patients with a history of 2 or 3 medication intake exhibited either negative or presence of only gametocytes by microscopy. However, the values are statistically not significant because of small sample size. Based on the RDT results patients received further course of anti-malarial and recovery were uneventful. In addition to the advantages of RDT being rapid, easy to perform and interpret, the lower detection limit of parasite by RDT is about 100 parasites/µl, whereas the lower detection limit of microscopy varies from 5 to 10 parasites to 100parasites/µl depending on the experience and expertise of the microscopist[9] single dose of anti-malarial treatment clears majority of the parasite from the blood circulation within 24 hours. Hence, to see parasites in peripheral blood smears after the start of anti-malarial remains challenging. On the other hand, antigen detection test based on LDH and HRPII remain positive for 2 to 3 and 28 days after the start of therapy, respectively.[9] Thus, in the remote areas where microscopy facility is not available, RDT can be performed by the healthcare worker or by the pharmacist. The above study highlights that the practice of self-medication may hamper diagnosis, delay clearance of the parasite (in case of inappropriate intake or low dose), may mask severity and may lead to drug adverse effect and drug resistance etc.

Conclusion

Prompt, correct and effective management is the strategy to reduce the malaria burden in the endemic areas and prevent further transmission and drug resistance. RDT based on antigen detection is an essential diagnostic tool for patients care for the correct and comprehensive diagnosis and treatment of malaria.

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