Original Article

The Dilemma Of Malaria Diagnosis: How Accurate Are The Diagnostic Tools?

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Abstract

Background: Malaria represents a major health problem for the public as well as clinicians and diagnosticians, because many diseases have similar symptoms to the symptoms of malaria. This study aimed to determine the accuracy of malaria diagnosis both clinically and using various laboratory tests compared to the gold standard microscopy.

Materials and Methods: This is a descriptive, cross-sectional hospital-based study, conducted at the casualty of Atbara Hospital, in January 2011. Any patient clinically suspected to have malaria in this month was included. Demographic and clinical data was collected using a standardized pre-tested questionnaire. Each patient was diagnosed primarily by the clinician, mainly medical officers and houseofficers, investigated by a thick blood film stained by Giemsa stain in the hospital laboratory. We, thereafter, obtained blood samples from the same patient, made thick and thin films stained by Giemsa and Field stains in addition to rapid tests for malaria antigens and antibodies. For quality assurance, tests were reviewed by expert technicians in the State Reference Laboratory for Malaria. Giemsa thick blood film was taken as the gold standard. Results of the various diagnostic methods were compared.

Results: Two hundred patients volunteered to participate in this study. Females were 121(60.5%). The age range was from 7 months to 70 years, mean 25.85(±20.5). Only 5(2.5%) cases were confirmed positive for malaria. When compared to the gold standard test, giemsa thin film and Field stain showed 100% sensitivity and 100% specificity. The sensitivity and specificity of the blood film done by hospital laboratory was 80% and 99.5% respectively. While Rapid Antibody scored 60% and 89.7%, and for Rapid Antigen scored 80% and 96.9% for the sensitivity and specificity respectively. The clinical diagnosis was the least accurate method 80% sensitivity and 38.5% specificity.

Conclusion: The prevalence of malaria among symptomatic patients in Atbara hospital is low. The ICT antigen and antibody tests, as well as clinicians over diagnose malaria when compared to the blood film. A combination of Rapid Diagnostic Test (RDT) with thick blood film for suspected malaria cases is recommended.

Keywords: Malaria, Diagnosis, Blood film, Sudan.

Malaria is a major health problem in Sudan. In 2007, it was estimated that 5.7 million people were exposed to stable *falciparum* and to limited *vivax* malaria transmission in the northern states of Sudan[1-3]. However, the national malaria control program, with WHO's support, has reduced the number of malaria cases from more than four million in 2000 to less than one million in 2010. Between 2001 and 2010, the number of deaths due to malaria in Sudan was reduced by 75%[4].Establishing case definition of malaria is by identifying the asexual stages of plasmodium parasite in a stained blood film through the microscopic examination[59]. Yet, the gold standard, this method of diagnosis has many drawbacks[10-12]. Rapid Diagnostic Tests (RDTs) has recently been introduced, but their pros and cons in establishing diagnosis are ongoing[13-18]. The presumptive-approach, based on symptoms and signs alone, has been not been the

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recommended approach by WHO since 2010 [19-21]. Therefore, clinicians practicing in resource-limited tropical countries, are continuously challenged by a case with symptoms and signs that are common to many other febrile illnesses, for which the diagnosis of malaria has to be proved or excluded.

The aim of this work was to determine the accuracy of the various clinical and laboratory methods used in diagnosis of malaria in our settings.

MATERIALS AND METHODS:

Atbara Teaching Hospital (ATH) is the largest hospital in River Nile State (RNS), north Sudan. The total population of Atbara locality is about 140,000.

Study design: Descriptive, cross-sectional hospital based.

Sample size: 200 patients.

Sampling technique: Patients who attended the casualty of ATH in January 2011, and were diagnosed clinically initially as malaria then sent to hospital laboratory for confirmation were included.

Inclusion criteria: Any patient with the initial provisional diagnosis of malaria with or without other illness, for whom blood film for malaria was requested by the treating doctor in the casualty of ATH during study period, and volunteered to participate was included. From each case investigated in ATH laboratory, a finger prick blood sample was obtained for the research work.

Exclusion criteria: Patients for whom no malaria investigation was requested and any patient declined to consent for volunteering.

Samples: Selected cases were interviewed using interviewer-administered, standardized, pre-tested questionnaire that gathered demographic and clinical data. Blood sample were obtained using standard universal techniques. Thick and thin blood films were stained by giemsa and Field stains, Rapid Antibody and Antigen tests were done using products of Acon®, USA as described by the manufacturer.

Data Analysis:

Obtained data was double checked, validated, cleared and entered into SPSS version 20 computer program(IBM Statistics, Illinois, USA). Percentages were compared, sensitivity, specificity, negative and positive predictive values for the various tests were calculated.

Ethical Issues:

An ethical approval was obtained from the Ethical Committee, Faculty of Medicine, Nile Valley University. A written consent was obtained from each participant after explaining the research objective, procedures and possible risks. The same finger prick from which a blood sample was taken for the sake of diagnosis was used for obtaining blood samples used in the research.

RESULTS:

In this study that included 200 individuals 121 (60.5)% of them were femaleand 79 (39.5)% were male, with a female to male ratio of 1.5:1. The age range was from 7 months to 70 years, mean 25.85 (+20.5). Eighty-eight (44%) of patients were from rural districts outside Atbara. Table 1 shows the sociodemographic characteristics of study population.

The main symptoms that patients complain of were fever alone 58 (29.5)% or fever with other symptoms such as headache and

Table (1): The sociodemographic characteristics of study population

Characteristic	Variable	N	%
Age	≤10	65	32.5
	11 -20	26	13
	21 -40	60	30
	≥ 41	49	24.5
Sex	Male	79	39.5
	Female	121	60.5
Residence*	North districts	80	40
	South districts	19	9.5
	Central districts	13	6.5
	Rural areas	88	44

*North districts extend from Al Sayala to Khelaiwa.

*South districts extend from Al Dakhla to El Shargi

*Central districts are Al Morba'at and Mowrada

joint pain 28 (14)% . Table (2) displays main patients' complains. Prior to laboratory tests, 21% of patients were initially diagnosed as malaria by the clinician and 83(41.5)% were initially diagnosed as malaria with concurrent infection.

In the hospital laboratory, only 5(2.5%) of the results were reported as malaria positive following microscopical examination. Despite this result, 20 (10.0)% of cases received treatment for malaria (Table 2).

The result of the Giemsa thick film performed by the researchers identified 5(2.5)% positive and 195(97.5)% negative samples.

On thin films stained by Giemsa, 3(60%) samples were positive for *P. falciparum* and 2(40%) were positive for *P.vivax*.

When antibody RDT was used, 23(11.5)% of the samples were positive; and when antigen RDT used 10(5.0)% were positive for malaria. The sensitivity, specificity, positive predictive value and negative predictive value of each test are displayed in table (3).

DISCUSSION:

Correct diagnosis of malaria is crucial for proper treatment of patients and surveillance of the disease. However, laboratory diagnosis of malaria in Sudan is constrained by inadequate infrastructure, consumables and insufficient skilled personnel. Furthermore, the perceptions and attitude of clinicians on the quality of laboratory services also present a significant challenge in the utilization of the available services. Malaria can be a life-threatening disease in a vulnerable population if not treated. Therefore, a quick and accurate diagnosis is very important. To prevent unnecessary

Table (2): Clinical characteristics, past medical history and the clinical diagnosis of study population.

Characteristic	Variable	n	%
Symptom	Fever alone	59	29.5
	Headache	16	8.0
	Nausea	13	6.5
	Tiredness	11	5.5
	Other symptoms*	43	21.5
	Any combination of the above	58	29
Past history of malaria infection	Yes	165	82.5
	Never	35	17.5
Frequency of malaria infection in the past	Once	13	7.9
	More than once	152	92.1
Last time got malaria infection	One month or less	19	11.5
	2-6 months ago	29	17.6
	More than 6 months ago	117	70.9
Initial provisional diagnosis	Malaria	42	21
	Malaria with concurrent infection	83	41.5
	Other diseases**	75	37.5
Final clinical diagnosis	Malaria	20	10
	Bacterial infection	154	77
	Other diseases	26	13

*Other symptoms include: joint pain, backache, dizziness, dysuria, abdominal pain and diarrhea.
**In other diseases malaria is also investigated so as be excluded.

Table (3): The accuracy of various methods used for diagnosis of malaria, in comparison to gold standard test.

Method of diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Thick film in hospital lab	80	99.5	80	99.5
Thin film giemsa stain	100	100	100	100
Thick film Field stain	100	100	100	100
ICT Antigen	80	96.9	40	99.5
ICT Antibody	60	89.7	13	98.9
Clinical diagnosis	80	38.5	0.03	0.99

antimalarial treatments, it is important to confirm clinical suspicions with a good laboratory test.

In this study that included 200 individuals 60.5% of them were female and 39.5% were male Children under ten years of age represented (32%), 44% of the study population are from Peripheral districts of Atbara, 82% of the study population mention that they got malaria infection in their life, this is not surprising as Sudan is an endemic area for malaria.

In this study (58.5%) of patients suffered from fever, it is the main complain , either fever alone (29.5%) or with other symptoms (29%), this is also not astonishing as Sudan is one of the tropical countries with many infectious diseases that causes fever and other symptoms of malaria.

Only 2.5% of the study populationwere proved to have malaria by the gold standard test. This finding is consistent with that reported in acommunity-based studies in north Sudan[1]. This low infection rate may be attributed to effective malaria control program in the state, other reasons yet to be determined.

It is obvious that malaria occupies a larger area in minds of clinicians more than it really is among febrile patients. This is indicated by the finding that (21%) of patients were diagnosed before the laboratory test as malaria alone and (41.5%) as malaria with co-infection. There was little correlation between the clinical diagnosis and the laboratory result, so we can safely conclude that the clinical diagnosis alone of malaria is the least accurate of all methods used, simply because many diseases have similar symptoms to malaria.

However, 10.0% of the total cases were diagnosed as having malaria, a fourfold that reported by the laboratory results; this proofs the over diagnosis of malaria.

Two samples out of the 5 positive cases were positive for P.vivax species. This finding indicates that P.vivax is not uncommon as was thought before.

The sensitivity, specificity, positive and negative predictive value of thin film Giemsa stain and thick film Field stain are (100%) they are identical to the thick film stained by giemsa. Sensitivity of the thick film giemsa stain in hospital is relatively low (80%) compared to standard result but it has high specificity 99.5%.

To help detect malaria parasites in human blood promptly, rapid diagnostic tests were distributed to health facilities in villages of Sudan. The number of health facilities with rapid diagnostic tests has reached 3363 or 73% of the total targeted facilities[4]. RDTs had relatively low sensitivity resulting in high false positive rates according to many published studies[22].

The specificity of RDT Antibody in this study is low a finding that goes with other reports[23]. The specificity of the RDTs antigen in this study (96.9%) and sensitivity (80%) is similar to the results of other published studies[24].

Additionally in this study the diagnostic capacity of the ICT test was marked by the

presence of false positives. In extensive reviews on malaria RDT, these false positives have been linked with individuals that had been recently treated with anti malarial drugs and with the presence of the serum rheumatoid factor[7].

Both biological and operational factors that could have resulted in low sensitivity in this study were explored HRP2 is known to persist in the blood stream for several weeks and some loss of specificity might be due to patients with circulating antigens, but not live parasites that would be detected by microscopy[25].

The PPV of RDT Antibody is 13% that means there is only a 13% chance that a person with positive test result actually has malaria. And the NPV of the test is 98.9% that means there a 98.9% chance that persons with negative test result is indeed free of malaria. PPV of ICT Ag is 40% also that mean there is only a 40% chance that person has malaria and the NPP of ICT Ag is high 99.5%. Therefore, RDTs could be used as a supplementary diagnostic tool to aid evidence-based decision making in malaria treatment, putting in mind that a negative RDT is more reliable than a positive one.

Most patients who were diagnosed clinically as having malaria were proved to have no malaria parasites on microscopy. This clinical over-diagnosis of malaria, involving prescription of anti-malarial drugs to patients without evidence of parasitaemia is well documented[26]. Many factors are assumed to contribute to this problem including patient's, co-patients' and clinician's preference to feel relieved by a familiar diagnosis rather than to be upset by a long list of other febrile illnesses, many of them have no specific laboratory finding.

This study is not without limitations. The small sample size may not allow generalization to be made, also being across-sectional study may not reflect the real situation all over the year, as malaria prevalence is known to have seasonal variation. Besides the hospital based nature may hinder applying it to the whole community. However, this study is intended to shed light on the diagnostic accuracy of the tools used for diagnosis of malaria, so that further work may follow in many parts of our country.

In conclusion, this study determined the low prevalence rate of malaria among symptomatic individuals in Atbara and documents the overdiagnosis of malaria by clinicians and RDTs. A combination of RDT with thick blood film for suspected malaria cases is recommended.

Conflicts of interest: none declared.

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