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Siroos Hozhabri
Aga Khan University

Stephen P. Luby
Aga Khan University

Mohammad H. Rahbar
Aga Khan University

Saeed Akhtar
Aga Khan University

Original Report

Clinical diagnosis of *Plasmodium falciparum* among children with history of fever, Sindh, Pakistan

Siroos Hozhabri,[1] Stephen P. Luby,[1,2] Mohammad H. Rahbar,[1,3] and Saeed Akhtar[1]

Objective: To identify clinical predictors for malaria and develop a clinical algorithm to more accurately identify malaria from non-malaria cases.

Methods: Four hundred thirty eight children aged 6–120 months attending the rural health center between August 15 and October 5, 1997, in Jhangara town of district Dadu, Sindh were recruited. A standard questionnaire was used to record symptoms and duration of child's illness. Each child was physically examined, had their axillary temperature measured, and blood samples were collected from which Giemsa stained thick and thin blood films were prepared and examined for presence of Plasmodium parasites. The sensitivity and specificity of several candidate algorithms for parasitemia were evaluated using various combinations of identified predictors.

Results: Twenty-six of 438 children (6%) were slide positive for malaria. An algorithm comprised of fever 3 days duration and (absence of cough or having rigors) had 100% sensitivity and 63% specificity for detecting *P. falciparum*.

Conclusion: In this low malaria prevalence region, restricting the diagnosis of malaria to persons who had >3 days of fever and absence of cough or rigors, remained highly sensitive but was more specific than current practice. If validated prospectively, this algorithm could reduce misdiagnosis and mis-treatment.

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INTRODUCTON

The Global Malaria Control Program[1] seeks to reduce morbidity and mortality from malaria by encouraging rapid diagnosis of malaria at the village level in developing countries, so that effective treatment can be administered quickly. Indeed, in a highly malarious area, malaria treatment is advised for all children with fever or a history of fever, whether or not other obvious causes are present.[2] In this context, health workers in Pakistan and other developing countries often do not determine the cause of fever before treating the patients for malaria,[3] and this may lead to a potentially high proportion of misdiagnosis and mistreatment of patients in areas with low malaria prevalence.[4] Data collected from four provinces in Pakistan in 1997 showed that only 2.7% of patients were slide parasite positive.[5] Such overdiagnosis and overtreatment of fever as malaria can lead to increased exposure of children to potentially toxic drugs.[6] The policy of the National Malaria Control Program of Pakistan is that children with fever, and no obvious source, should have blood smears examined microscopically, and patients with parasitemia should be treated.[5] However, microscopic diagnosis of parasitemia requires sufficient funding, expert personnel, and regular observation and maintenance, conditions which are inadequately available and economically unviable in developing countries, including Pakistan.[7] In this situation, utilization of a more specific clinical algorithm could help to improve the accuracy of diagnosis. We therefore undertook a study of children from a health clinic in rural Sindh, Pakistan, to evaluate the predictive potential of symptoms and clinical signs to establish clinical algorithms that might improve the clinical diagnosis of malaria in children in rural Sindh.

PATIENTS AND METHODS

Study setting

This cross-sectional survey was undertaken among children attending the outpatient clinic at the Jhangara rural health center between 15 August and 5 October 1997. Jhangara union council, Taluka Sehwan, is located in the middle of Dadu district. This union council consists of 64 villages with a population of about 16 000 near the bank of Manchhar Lake. This is the only health

[1]Department of Community Health Sciences, The Aga Khan University, Karachi, Pakistan; [2]The Centers for Disease Control and Prevention, Atlanta, GA, USA; [3]Michigan State University, East Lansing, MI, USA

Address correspondence to: Siroos Hozhabri, Department of Community Health Sciences, The Aga Khan University, Stadium Road, PO Box 3500, Karachi-74800, Pakistan.

E-mail: siroos.hozhabri@aku.edu

Corresponding Editorial Office: New York

facility in the area, and normally receives 50–100 patients daily.

Study population

The inclusion criteria for the study subjects were as follows: (1) children who attended the rural health center in Jhangara and had fever or history of fever during the last 2 weeks;[8] (2) willingness to participate; (3) age between 6 months and 10 years; and (4) no history of treatment with antimalaria drugs in the last 2 weeks.

Guardians of eligible children gave verbal informed consent to allow their children to be a part of the study. Using a pretested Sindhi translated questionnaire, we collected information on the patient's demographic characteristics and the reasons why he or she had been brought to the rural health center. A physician conducted a physical examination of the patient and looked for pallor, spleen enlargement, jaundice and other abnormalities. Axillary body temperature was measured using a standard mercury thermometer. Finally, capillary blood was sampled for thick- and thin-film examination. Blood films were stained with 4% Giemsa, and a trained technician identified and speciated malarial parasites. One hundred microscopic thick-film fields were examined under an oil immersion objective before the sample was declared malaria parasite negative.

Data analysis

The sensitivity and specificity of various combinations of clinical predictors were assessed to identify the most appropriate algorithm for the diagnosis of malaria.

Table 1. Distribution of signs and symptoms among the study subjects who attended the rural health center, Jhangara, August–October 1997 (N=429)

	%	*Plasmodium falciparum positive* %	*Plasmodium falciparum negative* %
Cough	36.5	0	100
Rigors	10	59	41
Diarrhea	24	29	71
Abdominal distention	8	0	100
Arthralgia	6	0	100
Vomiting	14	18	82
Major signs along with fever during physical examination			
Fever[a]	21	23	77
Pallor	28	35	65
Rash	8	0	100
Prickly heat	8	6	94
Splenomegaly	0.9	0	100
Hepathomegaly	0.7	0	100

[a]Fever≥37.5°C.

RESULTS

Analysis was restricted to the 438 patients for whom complete data were available. The median age of enrolled children was 24 months (range: 6–120 months); 57% of the children were boys. Guardians reported fever or history of fever as part of the illness in all children, although during physical examination only 128 (29%) had axillary temperature ≥ 37.5°C.

Among 26 children who were *Plasmodium* slide positive, 17 (65%) were positive for *P. falciparum* and 9 (35%) for *P. vivax*. Among the *P. falciparum*-positive children, 15 (88%) had scanty (1–10 parasites/100 fields) and 2 (12%) had moderate-density (10–100 parasites/100 fields) infection. Distribution of the signs and symptoms among the study subjects are presented in Table 1.

The optimum algorithm for prediction of *P. falciparum* infection included fever greater than 3 days in duration and absence of cough or rigors; this was 100% sensitive and 63% specific, and had 10% positive predictive and 100% negative predictive values.

DISCUSSION

Only 6% of the study population had any malaria, and only 4% had *P. falciparum*. An earlier report revealed that *P. falciparum* accounts for almost all of the malarial deaths worldwide.[9] A modified case definition for *P. falciparum* restricting diagnosis to those children with fever greater than 3 days in duration and absence of cough or rigors would have diagnosed all the children with *P. falciparum*, but excluded 63% of unnecessarily treated children. The clinical predictors of malaria identified in this study are consistent with studies in Kenya[10] and India[2] showing that fever less than 3 or 4 days in duration was not significantly associated with malarial parasitemia. In Papua New Guinea, patients who had cough were less likely to have *P. falciparum* infection,[11] and in the Philippines rigors represented a significant predictor of *P. falciparum* infection.[3]

Even though this proposed definition would have identified 100% of children infected with *P. falciparum* in this setting, steps to make the malaria case definition more specific will increase the risk of occasionally failing to identify a *P. falciparum*-infected child. However, when over 90% of the treated patients do not have the disease, the population is probably better served by greater attention to alternative diagnoses and the prevention of overtreatment.

Indeed, for an individual patient, the positive predictive value of the algorithm remained quite low, at 10%. Thus, even with an improved algorithm, health care workers should consider alternative diagnoses, and health policy makers should consider increasing the capacity for microscopic diagnosis.

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