BRIEF REPORT

Accurate Clinical Diagnosis of Malaria in a Postflood Epidemic: A Field Study in Mozambique

Brian W. Loveridge, MD; John R. Henner, DO; Frank C. Lee, DO

From the Department of Emergency Medicine, Wright State University School of Medicine, Dayton, OH.

Objective.—To determine the positive predictive value (PPV) of a clinical diagnosis vs laboratory testing for malaria in a remote field setting following a natural disaster.

Methods.—During an observational study, as part of a disaster response in Mozambique, patients were clinically diagnosed and treated for malaria. The population included native tribes in remote areas and displaced persons in refugee camps representing all age groups, male and female. The diagnosis was made if patients exhibited at least 3 of the following historical features: fever, chills, headache, and nausea/vomiting (N/V). In addition they had to have either a tactile fever or palpable spleen. At the conclusion of the mission, 28 patients were prospectively tested with an antigen-capture assay for *P. falciparum* to determine the PPV of clinical diagnosis vs definitive laboratory testing.

Results.—During the study period, 1215 of 4064 (30%) patients were diagnosed with malaria based on clinical presentation. On our final day, 28 consecutive patients with a clinical diagnosis of malaria were tested using an antigen-capture assay for *P. falciparum*. Of those, 25 tested positive—yielding a PPV of 89% (CI 0.78–1.01).

Conclusion.—In a remote field setting where malaria is endemic/epidemic, diagnosis of malaria based on selected historical and physical findings is possible with a high positive predictive value.

Key words: malaria, diagnosis, disaster medicine, tropical medicine, antigen-capture assay

Introduction

Authorities from the World Health Organization continue to report the endemic nature of malaria in South Africa, with 50 000 cases in 1999, accompanied by hundreds of deaths.¹ After the massive flooding of the Limpopo and Save Rivers, Mozambique faced calamity. As media coverage of the daring helicopter rescues dominated the news, a greater threat emerged. Floodwaters receded and exposed vast areas of new mosquito habitat. The Mozambican government reported a “high degree” of malaria in the refugee camps, with United Nations reporting tens of thousands of new cases among flood victims.¹

As medical teams were flown into remote areas by helicopter, diagnosis and treatment of malaria became a significant concern. Our team developed a set of historical and physical examination findings to make a clinical diagnosis of malaria. Examination of blood smears was not practical in this setting. Using an antigen-detection assay specific for *Plasmodium falciparum*, we tested patients in an observational study to evaluate our clinical diagnostic approach.

Materials and Methods

This was a prospective, nonblinded, observational field study of suspected malaria patients after the February 2000 flooding in the region of Chibuto, Mozambique. Investigators were volunteers for a humanitarian mission during March–April 2000. Included with our supplies were 28 malaria test kits. We decided to test our clinical diagnosis of malaria against the antigen-capture assay for *P. falciparum*. Patients consisted of males and females of all age groups. They were divided into pediatric (0–16 years) and adult (>16 years) groupings for reporting purposes. Patients were seen in remote areas, and treating physicians were flown by helicopter to reach areas inaccessible by ground. Translators were recruited in the city of Chibuto and flown with the physicians to facilitate communication with the various tribes of the area. Formal Institutional Review Board approval was not possible, given the nature of this disaster-relief effort. But consent was obtained from either the caregivers or the patients before testing, and confidentiality was maintained.

Clinical diagnosis of malaria was made if patients ex-

Table 1. Observational data during humanitarian medical patient encounters. Number of patients encountered in each category, including those diagnosed clinically with malaria (see criteria for diagnosis in "Materials and Methods" section)

	Children	Women	Men	Total
Total no. of patients	2009	1488	567	4064
Clinical malaria	819 (41%)	303 (20%)	93 (16%)	1215 (30%)

hibited at least 3 of the following historical features: fever, chills, headache, and nausea/vomiting. They also had to have at least 1 of the following physical exam findings: tactile fever or palpable spleen. There were no exclusionary criteria. In infants and children, historical information was obtained from a parent or guardian. Patients with concurrent diseases (ie, worm infestation, schistosomiasis) were treated for both malaria and any secondary diagnosis encountered. These criteria were applied and validated by 3 physicians.

Subsequent testing for *P falciparum* was done using the KAT-Quick Malaria Rapid Test, Kat Medical (Pty) Ltd, Ansfere, South Africa. This simple antigen-capture assay detects the presence of specific soluble protein, histidine-rich protein II, released from red blood cells infected with *P falciparum*. Manufacturer's studies compared the Kat-Quick Malaria Test with standard thick and thin smear testing along with polymerase chain reaction analysis and reported a sensitivity of 96% and specificity of 99.7%.² On the final field day, consecutive patients with a clinical diagnosis of malaria were tested with the antigen-capture assay. Packaging instructions were followed in strict detail, and the positive and negative controls functioned appropriately in all 28 test kits used.

Results

In 3 weeks, 4064 patients were treated at various camps throughout the Chibuto region. A total of 2009 children, 1488 women, and 567 men were treated for a variety of

conditions. Table 1 shows that clinical diagnosis of malaria was made in a high percentage of people in our study group. In the pediatric population, 41% (819/2009) were diagnosed with malaria. In the adult population, 20% of women (303/1488) and 16% of men (93/567) were diagnosed with malaria. In total, 30% (1215/4064) of patients were clinically diagnosed with malaria. Table 2 shows that the positive predictive value of a clinical diagnosis was 89% when using the antigen-capture assay for *P falciparum* (CI, 0.78–1.01).

These tests were done on a total of 23 children, 4 women, and 1 man. The negative tests included a 3-year-old female with a history of fever, chills, nausea/vomiting, and a tactile fever with palpable spleen; a 48-year-old male with history of fever, chills, nausea/vomiting, and a palpable spleen (terminal hematuria was also noted); and finally, a 45-year-old female with history of fever, chills, and headache with a tactile fever. Unfortunately, follow-up was not possible because we often spent only 1 day at a given locale. But all patients with a clinical diagnosis of malaria were treated with sulfadoxine/pyrimethamine.

Discussion

After the flooding of Mozambique in early 2000, more than 14 000 individuals were rescued by helicopter as they fled to higher ground, according to the World Food Program.³ Our observational data suggest that the 400 000+ displaced refugees suffered a great deal from malaria. Whereas official government figures are lacking, the World Food Program estimated that tens of thousands were affected by malaria.³ Our data presumptively support this claim, with nearly 1 of every 3 patients evaluated being diagnosed clinically with malaria. As expected, children faced the greatest risk (40% diagnosed with malaria) and the most serious sequelae. Numerous infants had to be transported to the local hospital for aggressive care of dehydration and malnourishment, and at least 1 death was attributed to malaria. Prior studies indicate a malaria-attributable morbidity of 9.8% in infants compared with 1.3% in children 1–4 years of age, and 0.6% in children aged 5–9 years.⁴ Furthermore,

Table 2. Prospective observational evaluations of the clinical diagnosis of malaria compared with the antigen-capture assay for *Plasmodium falciparum*. Of 28 consecutive patients meeting the clinical criteria who were tested, 25 patients were found positive for *P falciparum* antigen

Clinical malaria	Positive assay	PPV*
28	25	89% (CI, 0.78–1.01)

*PPV indicates positive predictive value.

malaria is among the leading causes of stillbirth as well as maternal mortality in Maputo, Mozambique.^{5–7}

Although this was a preliminary observational attempt to quantify our clinical judgment, the criteria performed well in the setting of a malarial epidemic. The positive predictive value of clinical criteria was 89% as confirmed by the antigen-capture assay. Three patients who met the clinical diagnosis of malaria tested negative in our study. They may have had *Plasmodium ovale*, *Plasmodium malariae*, or *Plasmodium vivax* because the antigen assay does not cross-react with different species of plasmodium.² Likewise, other infectious etiologies such as influenza, shigella, salmonella, cholera, etc, could have been the causative agents in these negative studies.

Other reports^{8,9} found that a combination of rectal temperature elevation, splenomegaly, and nailbed pallor was 85% sensitive and 41% specific for malaria. Furthermore, they found that a mother's report of a febrile child was 93% sensitive and 21% specific for the diagnosis. Although tactile fever is not ideal for determining core body temperature, it is still reported to be a useful first step in determining who should be referred for further testing.⁹

Furthermore, other clinical guidelines have been used in locations where definitive testing is either impracticable or impossible.¹⁰ There is wisdom in simplifying the diagnostic evaluation in disaster medicine especially when the disease in question has such serious sequelae. This was our experience, when each day a helicopter would transport our team and supplies to a remote locale that could not be reached by ground transport. Blood smear analysis was impracticable if not impossible. Even if this testing could be done, it would expose providers to blood from a high-risk human immunodeficiency virus-infected community. Hence, a clinical diagnosis was preferred.

Under the flood conditions, with new mosquito breeding grounds, the baseline rate of malaria increased to epidemic proportions. In addition, malnutrition and close living quarters also raised the risk of acquiring malaria among refugees.³ These factors may explain the high positive predictive value of our clinical diagnostic criteria.

The greatest limitation in our study was limited access to malaria test kits. Increasing the number of subjects in the study would have added statistical power and narrowed the confidence intervals. In future studies, it would be prudent to add a control group to assess the baseline endemic rate of malaria. It would also have

been ideal if we had been able to test our criteria vs thick and thin blood smears. But we were in less than ideal circumstances, and the antigen-capture study (much like a urine pregnancy test) has a reported sensitivity and specificity of greater than 95%.²

Despite these limitations, our preliminary results show a high positive predictive value when using historical and physical examination criteria to diagnose malaria in a remote jungle setting. Further investigation is needed to validate these criteria before widespread application is undertaken.

Acknowledgments

The authors thank Humedica International for their support of this humanitarian mission and Dr Roger Pacholka for his unrelenting efforts to provide relief to those without access to medical care.

References

1. Sidley P. Malaria epidemic expected in Mozambique. *BMJ*. 2000;11:669.
2. Le DC, Cong LD, Morozov VP, Rabinovich SA. KatQuick malaria test—Method for express diagnosis of falciparum malaria. Its effectiveness and specificity. *Proceedings of the 26th Annual Conference of Parasitology*. Bloemfontein, South Africa: Society of South Africa; 2000.
3. World Food Program. Report No. 09, March 3, 2000. Available at: www.wfp.org/report/2000/000303.htm.
4. Smith T, Hurt N, Teuscher T, Tanner M. Is fever a good sign for clinical malaria in surveys of endemic communities? *Am J Trop Med Hyg*. 1995;52:306–310.
5. Axemo P, Liljestrand J, Bergstrom S, Gebre-Medhin M. Aetiology of late fetal death in Maputo. *Gynecol Obstet Invest*. 1995;39:103–109.
6. Granja AC, Machungo F, Gomes A, Bergstrom S, Brabin B. Malaria-related maternal mortality in urban Mozambique. *Ann Trop Med Parasitol*. 1998;92:257–263.
7. Granja AC, Machungo F, Gomes A, Bergstrom S. Adolescent maternal mortality in Mozambique. *J Adolesc Health*. 2001;28:303–306.
8. Redd SC, Kazembe PN, Luby SP, et al. Clinical algorithm for treatment of *Plasmodium falciparum* malaria in children. *Lancet*. 1996;347:223–227.
9. Nwanyanwu OC, Ziba C, Redd SC, Luby SP. Palpation as a method of fever determination in Malawian children who are less than 5 years old: how reliable is it? *Ann Trop Med Parasitol*. 1997;91:359–363.
10. Cherian T, Steinhoff MC, Simoes EA, John TJ. Clinical signs of acute lower respiratory tract infections in malnourished infants and children. *Pediatr Infect Dis J*. 1997;16:490–494.