CLINICAL CASE DEFINITION OF MALARIA AT A SECONDARY LEVEL HOSPITAL IN NORTHERN INDIA

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Abstract. Malaria has re-emerged as a major public health problem in India. At present, under the National guidelines; all fevers are presumed to be due to malaria and chloroquine is given as presumptive treatment. This results in overtreatment. We did a pilot study to see whether some clinical predictors of malaria could be identified in the Indian setting. This case control study was done in a secondary level hospital. All those with fever who were smear positive for malaria were enrolled as cases and other patients fever who were smear negative for malaria served as the controls. All the factors under study were ascertained by a history or detailed clinical examination. A total of 41 cases and 95 controls were enrolled. Of the 41 cases, 35 were positive for *P. vivax* and six were positive for *P. falciparum.* After multivariate analysis, only splenomegaly (OR = 2.11; 95% CI = 1.27-3.50) and pallor (OR = 2.01; 95% CI=1.16-3.48) were significantly associated with malaria. It appears that history of fever along with one or both of these two signs can be a useful predictor of malaria in a secondary level hospital in India. The utility and feasibility of a similar approach in a field setting needs to be studied further.

INTRODUCTION

Malaria has re-emerged as a major public health problem in India. Epidemics of malaria are repeatedly being reported from different parts of India (Ministry of Health and Family Welfare, 1997). At present, under the Malaria Action Plan (MAP), National Malaria Eradication Program; all fevers are presumed to be due to malaria and chloroquine [10mg/kg body weight (BWt)] is given as presumptive treatment. In high risk areas (where chloroquine resistance is documented), the presumptive treatment comprises of a full dose of chloroquine (25 mg/kg BWt) and primaquine (0.75 mg/kg BWt) (NMEP, 1995). Since all fevers are not due to malaria, this definition has a high sensitivity but a low specificity. Use of this definition implies that false positives receive medication resulting in overtreatment.

There have been attempts to develop clinical case definitions or algorithms for identification of malaria patients (Redd *et al*, 1996; Rougemont *et al*, 1991). Most of these studies have been from high endemic areas of Africa and have dealt with only *Plasmodium falciparum* cases. These studies have identified fever at the time of visit, pallor and enlarged spleen as important predictors of malaria. Data from low endemic areas like India are not available. Also in India, *Plasmodium vivax* is more prevalent (Ministry of Health and Family Welfare, 1997). We did a pilot study to see whether the above mentioned factors can be used as clinical predictors of malaria in the Indian setting.

MATERIALS AND METHODS

The study was conducted in the Outpatients Department (OPD) of Civil Hospital, Ballabgarh which is run by the All India Institute of Medical Sciences, New Delhi. This is a secondary level hospital and the patients come from the nearby rural area and the urban locality including slums. As per the national guidelines, all patients with fever attending the OPD are advised a peripheral smear for malarial parasite and given chloroquine orally (NMEP, 1995),

Based on the previous study (Redd *et al*, 1996), sample size was calculated to detect odds ratio of 3.5 for splenomegaly and 2.5 for pallor. Based on our outpatient data, the prevalence of splenomegaly among the outpatients with fever was taken as 10% and the prevalence of pallor as 40%. At 5% significance level, with 3 controls per case and 70% power, the estimated sample sizes were 50 and 46 cases for splenomegaly and pallor respectively.

All outpatients attending on one particular day in the week during the period June to October 1997 (transmission season) were included in the study. Subjects were physically examined by the investigators (KA, SK). Duration of fever in days, history

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of chills and rigors, cough, loose stools and burning micturition were ascertained. Presence or absence of fever at the time of visit was measured by palpation method. Detailed clinical examination for conjunctival pallor, presence of rash, splenomegaly and hepatomegaly was carried out by the investigators who have more than ten years of experience.

Patients who tested positive for the malarial parasite on smear examination were labeled as cases and the rest served as controls. All the smears were examined by the laboratory technician at Ballabgarh who has received training for malaria work, and has more than ten years experience in malaria work. All slides positive for malaria and a proportion of negative slides, as a routine protocol under the National Malaria Eradication Program, were sent to the District Malaria Laboratory for confirmation.

The data were entered into DBase and univariate analysis done by EPIINF0 6. All the predictors were included into the logistic regression model using Statistix PC DOS version 2.0 (NH Analytical Software, 1987).

RESULTS

A total of 138 fever patients were registered. Two did not get their peripheral smear made and were therefore excluded from the study. Of the remaining 136, 41 were cases and 95 were controls. Of the 41 cases, 35 were positive for *Plasmodium vivax* and six were positive for *Plasmodium falciparum*. There were twenty -six males and eleven were children below 12 years of age. The results of univariate and multivariate analysis are shown in Table 1. Pallor and splenomegaly were found to be significantly associated with malaria in the univariate analysis. Fever at the time of visit, presence of chills with fever were not found to be associated with the diagnosis of malaria. Duration of fever (<4 days *vs* >3 days) and presence of any other illness was also not found to be associated with malaria. Reanalysis using seven days and fifteen days as cut off points for duration of fever did not show any significant association with malaria. Though, individually diarrhea, cough or burning micturition were not significantly associated with being a control, when all the three were combined as no other illness, the odds ratio in the univariate analysis was 0.49 (95% CI; 0.22 - 1.11) and was borderline significant ($p<0.06$). None of the study participant had rash on clinical examination.

After multivariate analysis, only splenomegaly (OR = 2.11; 95% CI = 1.27-3.50) and pallor (OR = 2.01; 95 CI = 1.16-3.48) were significantly associated with malaria.

DISCUSSION

This study was a preliminary one to onf the utility of clinical definition of malaria formulated in high endemic countries. These studies had identified fever of less than three days duration, fever at the time of examination, pallor and splenomegaly as important predictors of smear confirmed malaria. Our study found only pallor and splenomegaly to be significantly associated with a diagnosis of malaria. Duration of fever, presence of fever at the time of visit, associated chills and hepatomegaly were not associated with malaria.

Fever of >37.5°C for a period of less than three day with no obvious cause of fever was found to be strongly associated with malaria in a study in an endemic zone of West Africa (Rougemont *et al*, 1991). Usefulness of fever at the time of examination during the rainy season was also demonstrated in another study in Malawi (Redd *et al,* 1996). Our study did not find fever at the time of visit to be associated with malaria.

In our study, fever was ascertained by clinical examination. did not use a thermometer for measuring the temperature, as in real life clinical setting it is rarely used. Ascertainment fever by palpation is a less sensitive method as compared to measurement with a thermometer. Since, the impact of less sensitivity would be same on cases and controls, we do not expect any differential misclassification. Usefulness of fever at the time of examination is limited by the use of antipyretics by the patient before visiting the health facility.

Presence of cough, diarrhea or burning micturition did not rule out the possibility of malaria. Clinical pallor and splenomegaly were found to be significantly associated with a diagnosis of malaria in our study as in the previous studies. However, the strength of association (odds ratio) was lower.

Pallor was detected by examination of conjunctiva, since widespread use of nail polish, betel nut/tobacco chewing precluded any useful interpretation of nail bed or tongue hue examination. The prevalence of anemia in the study population is around 60% (unpublished data). Despite this, the presence of moderate and severe pallor was found to be significantly associated with the diagnosis of malaria.

Table 1
Predictors of malaria in a secondary level hospital at Ballabgarh, India.

Predictor	Prevalence (%) in controls	Odds ratio (95% CI)	
		Crude	Adjusted
Fever < 4 days	49	0.59(0.28-1.25)	0.69(0.29-1.62)
Febrile on visit	40	1.55(0.68-3.50)	1.42(0.60-3.35)
Chills	70	2.03(0.74-5.76)	1.54(0.55-4.30)
Presence of other illness*	59	0.49(0.22-1.11)	0.55(0.24-1.30)
Pollor	41	3.47(1.47-8.31)*	2.01(1.16-3.48)*
Splenomegaly	19	4.50(1.87-10.9)*	2.11(1.27-3.50)*
Hepatomegaly	8	2.64(0.81-8.64)	1.110.32-3.90)

*Other illnesses include cough, diarrhea and burning micturition.

In an area of high enemicity, prevalence of splenomegaly due to chronic malaria is high and therefore its utility in diagnosing acute malaria is limited. However, in the study area, as the edemicity of malaria was low, it was significantly associated with a diagnosis of malaria.

Our study used only microscopic examination of blood smear for the diagnosis of cases. This could result in misclassification due to presence of either asymptomatic parasitemia or of low parasite density. In endemic areas, asymptomatic parasitemia is common. Presence of a non-malarial cause of fever in asymptomatic parasitemic individuals could be falsely attributed to malaria. This would result in a control being classified as a case thus biasing the odds ratio towards unity. Asymptomatic parasitemia in a low endemic area like ours is uncommon and as most of the patients were having *Plasmodium vivax*, in which asymptomatic carriers are rare, we feel that this misclassification is unlikely in our study.

Level of parasitemia in the peripheral blood is lower in *Plasmodium vivax* infections as compared to *Plasmodium falciparum* infection. Most of the cases in our study were *Plasmodium vivax*. Thus the resultant lower parasitemia could have resulted in a case being missed by microscopy and thus being classified as a control.

Absence of any significant relationship between duration of fever, presence of fever at the time of smear could also be due to chance. This is more so because of the small sample size of the study. However, this study was planned only as a pilot study to confirm the results from high endemic areas.

Our study confirms the positive association of pallor and splenomegaly with malaria in a hospital setting. Therefore, it appears that history of fever along with one or both of these two signs can be a useful predictor of malaria. However, the validity of the criteria needs to be tested further. This study was done in a secondary level hospital with doctors having at least ten years of clinical experience in examining patients for pallor and splenomegaly. Caution needs to be expressed for its applicability in active surveillance being done by field level workers. In India, case finding of malaria is mainly done at domiciliary level by parahealth professionals. The utility and feasibility of a similar approach in a field setting needs to be studied further.

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