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ORIGINAL ARTICLE

Malaria: Patterns of relapse and resistance

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Abstract Malaria constitutes persistent threat to the human health and remains a distinct cause of morbidity and mortality, 40% of the world population is at risk of exposure to this menace in 100 countries (WHO, 2001). Present data represents the registered cases of malaria in the hospitals and clinics in India. *Plasmodium vivax* and *Plasmodium falciparum* infections were recorded 63.86%, 66.06%, 62.58% and 36.13%, 33.93%, 37.41%, respectively, amongst individuals with symptoms of intermittent high fever for three days. Maximum transmission with highest slide positivity rates (SPR) 61.76% and 50.14% was periodically and strategically observed during September and October while lowest yearly transmission slide positivity rates (SPR) (19.60–24.07%) was estimated in the months of March and April. Average relapse rates (ARR) in *P. vivax* was recorded 17.1%. Short term relapses were more recurring than the long term in the ratio of 4:1. Eighty-eight patients who were administered with total of 1500 mg chloroquine and 75 mg primaquine through divided doses also showed relapse rate of 4.5%. Patients suffering from *falciparum* malaria showed resistance against chloroquine in 10.6% cases after getting 1500 mg chloroquine based on divided doses (i.e. 600 mg on day 1 and 300 mg after 8 h and followed by 300 mg daily for 2 days.)

1. Introduction

Malaria is a major burden for most resource-poor nations of the world. Between 200 and 500 million deaths attributable to malaria, most among the children of sub-Saharan Africa (Breman, 2001). In fact, 9 out of 10 cases of malaria occur in this region, while two third of remaining are concentrated in just six countries viz., India, Brazil, Sri Lanka, Vietnam, Cambodia and Solomon Island. The goal of eradicating malaria, once thought to be possible, was abandoned decades ago, and the present goal of malaria control is first to retard the accelerating rates of disease and death and then to "Roll Back Malaria".

In 1990s malaria re-emerged and took the lives of several thousand people (Sharma, 1996). Factors responsible for the re-emergence of malaria were vector resistance to insecticide and parasite's resistance to drug. In India 60–65% of the malaria infections are reported to be due to *Plasmodium vivax* and 30–35% due to *Plasmodium falciparum* (Adak et al. 1998). The worsening problems of drug resistance in many parts of the world and the limited number of antimalarial drugs available has increased difficulties for the development of anti-malarial drug policies and the provision of adequate disease management. It is now recognized that most endemic countries will

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have to face the unavoidability of some resistance to the antimalarial drugs used to treat uncomplicated malaria.

In India resistance of *P. falciparum* to chloroquine, the cheapest and the most frequently used therapeutic drug was first reported in the year 1973 from Diphu of Karbi-Analog district in Assam state. The reports on the resistance of *P. falciparum* to chloroquine and amodiaquine, first observed in 1960–1961 in Colombia and in Brazil (Bruce-Chwatt, 1985), were of greater consequence, since together with quinine these are the most valuable drugs for the treatment of acute malaria. Further reports on drug resistance came from Thailand, Malaysia, Cambodia, Phillipines, Indonesia, Vietnam, Laos, Burma and other areas of South-East Asia. Available information indicates that *P. falciparum* has given rise to formidable drug resistant strain in Asia. The problem of chloroquine resistance in *P. falciparum* is widespread and now it is leading towards multiple drug resistance against all major antimalarials (WHO, 1996).

2. Materials and methods

Present study is based on the malaria cases enrolled in Jawaharlal Nehru Medical College and a few other hospitals and clinics of Aligarh during the years 2001, 2002 and 2003. Blood smear were prepared from patients who attended hospitals and clinics, complained for fever and headache and were suspected of malaria. Thin and thick blood smears of patients were prepared by finger prick, stained with J.S.B. and Giemsa stains and microscopically examined under an oil immersion lens to see the positivity for malaria infection. From malaria positive cases, monthly prevalence of *P. vivax* and *P. falciparum* infections were recorded. Month-wise slide positivity rates (SPR) and slide *falciparum* rates (SFR) were worked out for the years 2001, 2002 and 2003. Resistant and relapse cases were also observed in *P. falciparum* and *P. vivax* infections, respectively.

For the study of relapse in *P. vivax,* one group of patients was treated by giving 1500 mg chloroquine base in divided doses (i.e. 600 mg on day 1 and 300 mg after 8 h followed by 300 mg daily for 2 days). The dose of child was adjusted according to his/her body weight. While patients in other group were administered 1500 mg chloroquine in the similar manner followed by 15 mg primaquine daily for 5 days and then followed up carefully. To determine the pattern of relapse in *P. vivax* each patient was identified individually by name, address and subsequent treatment. On reporting back blood smears were prepared from the patient and examined microscopically for the presence of malaria parasite and entered against his/her name.

The following criteria were used in classifying the patients into primary cases and non-relapse and relapse categories in the present study. Patient reporting for the first time (having no history of malaria) with acute illness and showing symptoms such as high fever, severe headache, loss of appetite, occasional vomiting and microscopic evidence of *P. vivax* infection were considered as primary cases. Some patients in this group who had no clinical symptoms of malaria or parasitological evidence of *P. vivax* infection following their primary infection during the entire period was considered as non-relapse cases. Those patients who reported back to the clinic within one month to one year with renewed clinical symptom (mild) along with a periodic alternate day fever (not observed in the primary cases) and found to be microscopically positive for *P. vivax* infection were considered as relapse cases. After medication if patient again suffered from malaria within 3 months with more regular paroxysm, he/she was treated as a case of short term relapse. But if it happened beyond 3 months then the case was considered as long term relapse. Cases of *P. vivax* who did not respond to 1500 mg of chloroquine and 75 mg primaquine was recorded as chloroquine resistant cases.

2.1. Drug resistance in *P. falciparum* infections

For drug resistance, patients who were positive for *P. falciparum* infections were given 1500 mg chloroquine base in divided doses (i.e. 600 mg on day 0, 300 mg after 8 h followed by 300 mg daily for 2 days). The dose of child was adjusted according to his/her body weight. Blood films of those patients who reported back with fever within 4 weeks of treatment were examined for *P. falciparum* infection. If found positive, such cases were recorded as chloroquine resistant cases. Level of resistance (i.e. RI, RII, RIII) was ascertained on the basis of late and early recrudescence.

3. Results

Tables 1–3 show month wise slide positivity rates and slide *falciparum* rates for the years 2001–2003 for *P.* vivax and *P.* falciparum infections observed in Aligarh. These tables also provide information on seasonal fluctuations of aforesaid species. *P.* vivax infection was predominant and was recorded in all months of the year, with almost similar seasonal patterns during the three successive years. *P.* vivax showed a gradual increasing trend from July onwards reaching a peak in September soon after the rainy season, and then showed a decline in December which continued until June. *P.* falciparum infections started gradual increasing in July–August and showed a peak in September and October and then decline November onwards with the on set of winter and continued to decline till June.

During 2001 out of 1473 slides examined, 487 were found positive for malaria of which 311 belonged to *P. vivax* and 176 to *P. falciparum*. In 2002 a total of 1369 slides were examined, out of which 498 were found positive for malaria of which 329 belonged to *P. vivax* and 169 to *P. falciparum*. In 2003 a total of 1428 slides were examined for malaria infection, out of which 580 were found positive. Slides showing positivity for *P. vivax* and *P. falciparum* were 363 and 217, respectively. During 2001–2003 overall percentage of *P. vivax* and *P. falciparum* were 63.86%, 66.06%, 62.58% and 36.13%, 33.93% and 37.41%, respectively (Table 4).

It was observed that malaria transmission was least from January to April. During the months of May, June and July transmission was low with slight fluctuating figures for the years 2001–2003 which was in accordance with the commencement of pre-monsoon shower that contributed slightly increased or decreased transmission rate in proceeding months. Increased rate of transmission was recorded July onwards, reaching a peak soon after rains in September and October followed by a sharp decline to a low level in December. During peak transmission season mean temperature and relative humidity ranged somewhere around 26–28 °C and 77–88%.