

MALARIA, LEPROSY AND DAPSONE

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Abstract. Although the preventive action of dapsone against *P. falciparum* malaria was known for many years, there was no report about the incidence of *P. falciparum* malaria in leprosy patients treated with dapsone, especially from areas of Southeast Asia where both leprosy and malaria are endemic. Therefore, two clinic-based malaria surveys were undertaken at a gap of 12 years, comprising 506 lepromatous leprosy patients and 499 febrile nonleprosy control subjects. Both the surveys showed that the lepromatous patients treated with MDT had only *P. vivax* malaria (incidence comparable to the febrile nonleprosy controls) with complete freedom from *P. falciparum*. On the contrary, control subjects not taking any-leprosy drugs and staying with the leprosy patients at the same beggars' home, had both *P. vivax* and *P. falciparum* malaria. It is postulated that dapsone provided protection against *P. falciparum* among leprosy patients.

INTRODUCTION

In recent years, re-emergence of malaria, especially *P. falciparum* infection in India, despite the Indian Government's strong commitment to control it, is a matter of great concern. *P. falciparum* resistance to chloroquine and pyrimethamine-sulfadoxine is now widespread. It seems that neither insecticides nor antimalarial drugs are sufficient to control this disease (Sharma, 1996).

Leprosy-affected patients often suffer mild to moderate undernutrition due to food deprivation (Rao *et al*, 1986; 1987; Rao and Saha, 1986). They frequently develop pulmonary tuberculosis, when they become severely emaciated (Saha and Rao, 1989). Sexually transmitted diseases are rampant among them (Saha *et al*, 1990). Often they suffer from malaria and kala azar (visceral leishmaniasis). Recently, we reported concomitant kala azar and *P. vivax* malaria in an eight-year old Indian boy from Bihar with unstable indeterminate leprosy. Bihar plateau is a traditional home for kala azar, malaria and leprosy (Saha *et al*, 1998).

It has been long known that dapsone, the standard drug for treating leprosy, has substantial schizonticidal and gametocidal activity

against *P. falciparum*, including those resistant to chloroquine. However, it does not act against the asexual form of *P. vivax* (Manson, 1996). Recently a combination of dapsone and proguanil has proved effective for treating chloroquine-resistant *P. falciparum* malaria in Africa and is also being used successfully as a prophylaxis in Asia (Mshinda *et al*, 1996; Edstein *et al*, 1997).

The aim of the present study is to determine the incidence of *P. falciparum* and *P. vivax* in lepromatous leprosy patients taking MDT (containing 100 mg dapsone daily) and to compare it with the normal control subjects (not taking dapsone). In order to do this, a clinic-based malaria survey was carried out with two migrant populations (leprosy patients and normal control subjects) living in a beggars' home adjacent to the clinic in a periurban area of Delhi for the preceding year. Two surveys were conducted; the first in 1986-1987 and the second in 1999-2000.

MATERIALS AND METHODS

Human subject

Table 1 shows the grouping of human subjects; their ages varied from 17 to 72 years. The sex ratio was 3 males : 1 female.

People, their livelihood, survey area and its geography

Both leprosy patients and normal control

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subjects lived in a periurban area of Delhi, North India. They stayed in a beggars' home, administered by the Delhi Municipal Corporation. Beggars without leprosy (normal control subjects) as well as leprosy patients were kept in the beggars' home for one year and thereafter they were released. These people often move from one city to another to earn their livelihood from begging near temples or mosques, especially during festival days.

The survey area was at an average altitude of 210 m above sea level. The annual rainfall was 600 mm. Subsoil water was 0.6 m below ground level. The Jamuna River was joined by 17 major stormwater drains, carrying the sewage and sullage of the city. The area was a prolific breeding ground for *An. culicifacies*, the major vector of malaria in the periurban area of Delhi (Adak *et al*, 1999).

Laboratory methods

Diagnosis of leprosy and case holding: diagnosis of leprosy was based on clinical, bacteriological (slit skin smear test), histological findings and lepromin test (Rao *et al*, 1987). Histological classification was carried out on the Ridley and Jopling scale (Jopling, 1978). Only lepromatous leprosy patients taking MDT were included in the study. Their mean bacteriological index was 3.52. All were lepromin (late reaction) unresponsive. Urine samples from all patients were tested to detect dapsone and so identify defaulters (Jopling, 1978).

Malaria diagnosis: a total of 506 febrile and afebrile lepromatous patients from both the surveys taking 100 mg of dapsone daily and 499 control subjects with febrile episodes during the first and second surveys were subjected to blood-smear examination for malarial parasites. The slide positivity rates and the ratios of *P. falciparum* and *P. vivax* were determined. The results of the leprosy and control groups were compared.

RESULTS

The results of the two malaria surveys of 506 lepromatous patients at an interval of 12 years (164 in 1986-1987 and 342 in 1999-2000) re-

vealed that dapsone could certainly prevent *P. falciparum* malaria, but not *P. vivax* malaria in leprosy patients receiving MDT (Table 1). In the 2nd survey, 344 blood samples from febrile and afebrile leprosy patients were examined. Fifty-eight smears out of 342 samples (16.86%) tested positive for malaria. Out of these 58 smears, all were *P. vivax*. Curiously, two additional leprosy patients showed *P. falciparum* in slide examination during febrile episodes. Urine examination proved they were defaulters, who had not taken dapsone and thus were excluded from analysis. Six afebrile lepromatous patients (second survey) showed parasitemia, which needs explanation.

In the healthy control population, of the first survey (1986-1987) out of the 379 febrile subjects, 96 (25.32%) were smear-positive for malaria, 86 (22.68%) had *P. vivax* and 10 (2.64%) had *P. falciparum* malaria with a ratio of Pv : Pf of 8.6 : 1. Twelve years thereafter, during the second survey (1999-2000) out of 120 febrile normal controls, 28 (23.33%) were smear-positive, 19 (15.83%) had *P. vivax* and 9 (7.5%) had *P. falciparum* malaria, with a ratio of Pv : Pf as 2.1 : 1 (Table 1). These results showed that the incidence of *P. falciparum* malaria cases increased in the control population 12 years after the first survey ($\chi^2 = 5.87$; $p < 0.02$).

DISCUSSION

The *in-vitro* experiment of Yeo and associates (1997) gave support to our clinical observation that lepromatous patients taking MDT only contracted *P. vivax* malaria, but not *P. falciparum* malaria. These investigators added 500 ng dapsone to 50 μ l plasma samples containing *P. falciparum* isolates resistant to pyrimethamine and chloroquine, which increased the anti-malarial activity two to three times in comparison to proguanil-atovaquone (Wilairatana *et al*, 1997). Moreover, others had shown that a combination of dapsone with proguanil or chlorproguanil was effective in the treatment of chloroquine-resistant falciparum malaria in Africa and as a prophylaxis in Asia (Mshinda *et al*, 1996; Edstein *et al*, 1997; Wilairatana *et al*, 1997).

The high prevalence of *P. falciparum* in our control subjects was observed during the second

Table 1
Two surveys during 1986-1987 and 1999-2000 showing parasitemia in lepromatous leprosy patients and normal subjects living in the same periurban area of Delhi.

Survey	Area	Subjects	Febrile or afebrile	No. of slides examined	Slide positivity			Pv : Pf ration
					Total No. (%)	<i>P. vivax</i> No. (%)	<i>P. falciparum</i> No. (%)	
I (1986-1987)	Periurban area of Delhi	Lepromatous leprosy Patients taking daily 100 mg dapsone	Febrile ^a	124	39 (31.45)	39 (31.45)	Nil	All had vivax malaria
			Afebrile	40	Nil	Nil		
		Total	164	39 (23.78)	39 (23.78)	Nil		
		Control subjects (non leprosy)	379	96 (25.32)	86 (22.68)	10 (2.64)	8.6 : 1	
II (1999-2000)	Same	Lepromatous leprosy Patients taking daily 100 mg dapsone	Febrile ^a	200	52 (26)	52 (26)	Nil	All had vivax malaria
			Afebrile	142	6 (4.23)	6 (4.23)	Nil	
		Total	342	58 (16.86)	58 (16.86)	Nil		
		Control subjects (non leprosy)	120	28 (23.33)	19 (15.83)	9 (7.50)	2.1 : 1	
					p<0.05 ^b	p<0.02 ^c		

^aFever ranged from 36.5° - 39°C; duration from 1 to 3 days, with malaise, headache and vomiting.

^bDecreased compared to corresponding group of 1986-1987 survey.

^cIncreased compared to corresponding group of 1986-1987 survey.

survey because these subjects were beggars and moved from one city to another to earn their livelihood, especially during festivals. *P. falciparum* predominantly occurs in Orissa, Madhya Pradesh, Gujarat, the Indo-Bhutan border, Calcutta, Bombay, Panaji and Mangalore. Migrants transport new parasite strains and continue the spread of malaria wherever they settle (Pattanayak *et al*, 1994; Sharma, 1999).

The same may also explain that, although the slide positivity rates in lepromatous patients indicated a significant fall between 1986-1989 and 1999-2000, a similar trend of fall in malaria was not apparent in the control subjects, *ie* 25.32% (1986-1987) and 23.33% (1999-2000), despite a significant drop in the incidence of *P. vivax* (22.68% vs 15.83%; χ^2 ; $p < 0.05$) that was masked by the relative increase in *P. falciparum* (2.64% in 1986-1987 to 7.5% in 1999-2000).

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