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HIV and malaria co-infection in Mumbai, western India

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ABSTRACT

Background & objectives: Conflicting reports exist regarding the HIV-1 infection on the risk of malaria. A transient almost one-log elevation in HIV viral load occurs during febrile malaria episodes. We prospectively studied malaria patients for HIV infection from Mumbai.

Methods: A total of 171 malaria patients and 28,749 normal voluntary blood donors were studied for their HIV status. Diagnosis of malaria was done by microscopical examination of blood. HIV screening was done by detection of HIV-1 & 2 antibodies by micro well ELISA using Enzaids & J Mitra kits followed by confirmation using western blot (Innogenetics, Belgium) analysis.

Results: Out of 171 malaria patients 13 (7.6%; Odds ratio= 4.45; p <0.0001) and 521 blood bank donors were found to be HIV reactive. Among 13 HIV reactive patients, eight patients were Elisa borderline reactive and western blot positive (p24), which may be due to cross-reactive antibodies. Five of 13 malaria patients found to be HIV-1 positive by ELISA and by western blot confirming HIV and malaria co-infection.

Conclusion: Our findings suggest that HIV-1 and malaria co-infection can't be ruled out in malaria endemic countries like India.

Key words HIV-1 co-infection; malaria; Mumbai; western India

INTRODUCTION

Malaria is endemic in many areas of India and repeated infections with *Plasmodium falciparum* and *P. vivax* occur. Malaria parasitemia differs in instances of asymptomatic and clinical malaria and the degree of parasitemia may influence the pathological and biochemical presentations in these patients[1,2]. Influence of therapy to avoid HIV on malaria infection is controversial. Available studies have limited sample sizes and failed to demonstrate any association of malaria with HIV among hospitalized patients from areas with stable malaria transmission[3]. It has been postulated that HIV infection alters clinical presentation of malaria[4]. Further, treatment failure of anti-malarials is reported in HIV patients[5,6] which also has been contradicted[7]. Fever, a major manifestation present both in HIV and malaria patients is not only due to infection, but also of many other common infections. An immune reconstitution syndrome along with adverse effects of antiretroviral drugs and other medicines lead to a febrile illness too[5,6]. The fact that people in malaria endemic areas may have asymptomatic malarial parasitemia that complicates the diagnosis of febrile illness in malaria and HIV co-infected patients.

Survivors suffer chronic immune activation on repeated infection with increased susceptibility even in HIV negative individuals[8]. High prevalence of HIV in Africa aggravates it to a greater extent. Malaria increases HIV viral load as much as 10-fold, increasing contagiousness of HIV infected persons and affecting the population epidemiology dynamics[9]. Individuals in malaria endemic areas have a higher probability of sexual contact with persons who are infected with both malaria and HIV, with high viral load. Models of malaria-HIV interaction estimate a three fold increase in HIV transmission in malaria endemic populations and increased malaria transmission due to HIV co-infection[9].

Our current understanding of the human immune response to malaria and HIV leads us to expect that either of the infection might influence the clinical course of the other. Many other types of infections are associated with at least a transient increase in HIV viral load. Hence, it is logical to expect malaria to do the same and potentially to accelerate HIV disease progression. On the other hand, the control of malaria parasitemia is immune mediated, and this prevents most malarial infections from becoming clinically apparent in semi-immune adults in endemic areas[10,11]. The immune deficiency caused by HIV infection should in theory, reduce the immune response to malaria parasitemia and, therefore, increase the frequency of clinical attacks of malaria.

However, as research evidence emerged from sub-Saharan Africa in the 1980s and 1990s[3], it soon became clear that malaria is not a typical opportunistic infection.

In fact, the interaction between HIV and malaria has proved to be remarkably subtle, and it is only in the past few years that a clearer picture of this association has begun to emerge. The current study describes the occurrence of malaria and HIV co-infection in hospitalized malaria adult patients of malaria in Mumbai.

MATERIAL & METHODS

A total of 171 malaria patients with high-grade fever (38–45°C) for 3–8 days admitted to the medicine ward of KEM Hospital at Mumbai were enrolled in the study. Blood samples (5 ml) were collected aseptically at the time of admission for full blood count, erythrocyte sedimentation rate (ESR) and peripheral smears (thick and thin films for malaria parasite examined by two experts for confirmation of species). The serum was separated and stored at –20°C. These patients were confirmed for the malaria parasite in peripheral blood smears and the density showed varied numbers (<1–5%). These malaria patients tested for HIV-1 & 2 antibodies by two independent ELISA assays (Enzaids & J Mitra kits) and confirmed by western blot assay (Innogenetics, Belgium) following the manufacturer's protocol. The controls were normal blood bank volunteer donors who tested for HIV-1 & 2 antibodies by ELISA kits confirmed by western blot. The local ethical committee approved the study.

RESULTS

Our results showed that 13 (7.6%) out of 171 malaria patients and 521 (1.81%) out of 28,749 blood bank donors were HIV-1 & 2 seroreactive (Table 1). Five of 13 malaria patients were confirmed to have HIV-1 infection, and the remaining eight patients showed borderline ELISA reactive results and indeterminate status on western blot analysis (Table 2). Our results of malaria and HIV-1 co-infection were highly significant.

Table 1. HIV testing in malaria patients and normal blood bank donors from Mumbai, India

Patient status	Malaria patients n =171 (*Pf*%)	Blood bank controls n =28,749 (*Pf*%)	OR	χ^2	EF	95% CI	*P*-value
Total HIV reactive	7.60 (13)	1.81 (521)	4.45	28.331	0.0582	2.51–7.901	< 0.0001
Malaria & HIV co-infection	2.92 (5)	0 (0)	1899.4	680.12	0.0291	104.53–34512	< 0.0001

Pf(%) phenotype frequency percentage; OR = Odds ratio; EF = Etiological fraction; CI = 95% confidence interval.

Table 2. ELISA and western blot results of HIV-1 positive malaria patients

ID n=171	First ELISA	Second ELISA	Western blot results										Remarks
			P17	P24	P31	gP41	P51	P55	P66	gP120	gP160	gP36	HIV-1
1	2.022	1.708	1+	3+	2+	2+	4+	1+	3+	1+	1+		Positive
2	0.497	0.055											
3	2.496	1.642		4+	2+	1+	3+	1+	3+	1+	1+		Positive
4	0.558	0.129		1+									
5	0.212	0.011	1+	1+									
6	2.422	1.446	2+	4+	1+	3+	3+		3+	1+	1+		Positive
7	1.721	1.453	1+	4+	2+	2+	4+	1+	4+	1+			Positive
8	0.226	0.092	1+	1+									
9	0.336	0.020	1+	2+									
10	0.424	0.115	1+	2+									
11	0.230	0.028		1+									
12	2.171	1.264		2+	1+	1+	3+	1+	3+	1+	1+		Positive
13	0.321	0.040		4+									

1+=Weak positive; 2+=Moderate positive; 3+ and 4+=Strong positive; 8 out of 13 patients were first ELISA positive and second one negative; 5 patients were both ELISA positive and confirmed in western blot for HIV-1.

DISCUSSION

Infection with HIV-1 causes progressive cellular immunosuppression, and any resulting impairment in the immune response to malaria might be associated with failure to prevent infection or to suppress parasitemia and clinical disease[12]. However, laboratory-based studies have found that although some components of the human immune response to *P. falciparum* are modified by HIV-1, others are unaffected[10]. On the other hand, *P. falciparum* has been shown to stimulate HIV-1 replication through the production of cytokines (interleukin-6 and tumor necrosis factor-α) by activated lymphocytes[13]. *Plasmodium falciparum* also increases the potential reservoir for HIV in the placenta by increasing the number of CCR5+ macrophages[14]. An important study from Malawi showed that HIV-1 plasma viral loads were significantly higher in patients with malaria infection than in those without, and these levels remained higher for up to 10 weeks after treatment[15]. The increases in viral load were highest in those with clinical malaria, high levels of parasitemia, and relatively high CD4 counts. Studies report that malaria may speed up the progression of HIV disease, and this is supported by a study from Uganda showing increased CD4 cell decline associated with episodes of malaria despite prompt treatment[11]. However, the true clinical impact of malaria on HIV progression remains to be determined[16].

In areas of stable malaria, transmission is intense and continuous, although seasonal variations may occur. Immunity develops early in life, and young children and pregnant women are at greatest risk of morbidity and mortality from malaria. In these areas, HIV-related immunosuppression may increase rates of malaria infection and clinical malaria disease, but does not increase the rates of severe or complicated malaria[17]. In regions of unstable malaria, transmission is intermittent and less predictable, and epidemics may occur. The disease burden is similar in all age groups because pre-existing anti malarial immunity is limited[18]. Thus, HIV co-infection has its impact on disease presentation, with an increased risk of complicated and severe malaria and death[18]. Studies of malaria and HIV interactions in children living in areas of stable malaria epidemiology have been inconclusive[19]. A study in rural Kwazulu-Natal, an area of unstable malaria, reported that HIV-infected children were more likely to experience severe disease, coma, and death[20]. More data are required to document any significant malaria and HIV interactions in children.

Malaria and HIV-1 are two of the most common infections in sub-Saharan Africa and, to a lesser extent, in other developing countries. An increased prevalence of malaria and increased parasite density in HIV-infected individuals could lead to increased malaria transmission affecting both HIV-positive and -negative individuals[17]. The increased risk of clinical malaria in HIV-positive subjects could increase the burden on clinical services in areas where HIV-1 is prevalent as observed in the present western Indian study.

In a region with an increased HIV-1 prevalence of 30%, such as parts of southern Africa, the population-attributable fraction could reach 20% for parasitemia[10] and 35% for clinical malaria. However, malaria tends to affect mainly children, men and pregnant women, especially in rural areas, whereas HIV is more common among sexually active adults in urban centers.

Our findings suggest that HIV-1 infection is associated with malaria in hyperendemic areas. Further, the study suggests that the fraction of febrile illness attributable to malaria is lower in HIV positive adults. HIV testing should be conducted in malaria patients as an evaluation for febrile illness in malaria and HIV endemic areas.

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