Association of Malaria and HIV-1-RNA in blood of adults in Rakai, Uganda

FINAL REPORT

May 2007

Aims and Background

The goal of this study was to assess the impact of malaria co-infection on HIV viral loads of infected individuals in Rakai, Uganda. Kublin and colleagues reported a higher median viral load among HIV-positive adults co-infected with malaria compared to HIV-positive adults not infected with malaria.[1] This has implications for heterosexual HIV transmission among HIV-sero-discordant couples since the HIV viral load has been shown to be a significant predictor of heterosexual HIV transmission.[2] We compared viral loads of HIV-positive individuals who were infected with malaria to HIV-positive individuals who were not infected to assess the impact of malaria infection on the HIV viral load levels of adults in Rakai, Uganda.

Sample and Methods

The study population is composed of 675 HIV-positive adults who were antiretroviral (ARV) naive. Approximately 151 individuals were pregnant women from a randomized trial of STD control for HIV prevention (MISS Cohort), whose blood samples were taken during the prepartum and postpartum visits, and 524 individuals were adult men and women in the Rakai Community Cohort Study.

Individuals with both a malaria result and HIV viral load test from the same visit were identified. For those missing one of the tests, slides and blood samples were identified and tested retrospectively. The HIV-1 viral load was quantified by reverse-transcriptase PCR (Amplicor HIV-1 Monitor 1.5 Assay, Roche Molecular Systems, Branchburg, NJ, USA), which reliably quantifies the predominant Ugandan HIV-1 subtypes A and D. Peripheral malaria was diagnosed with 20 μL serum using the malaria Binax NOW® ICT test (Binax, Inc., Portland, ME). The Binax test detects *P.falciparum* and *P.vivax* antigens in the blood up to two weeks following clearance of infection (sensitivity 80% compared to PCR and 94% to 100% compared to blood smear for detection of *P. falciparum*).[3-5]

Malaria "positive" was defined as those with a Binax "positive" band on the rapid test indicating acute, recent malaria infection. Viral load was log transformed to normalize its distribution for analysis. The analysis assessed log viral load 1) on a continuum and 2) with the median log viral load of 4.441 copies/mL as a threshold.

Results

As shown in Table 1, we found no significant difference in the median $\log_{10}$ HIV viral load levels for the total adult sample infected with peripheral malaria compared with those not infected with malaria (4.436 log copies/mL and 4.442 log copies/mL, respectively, Pearson Chi-Square test p=0.94). When stratified by pregnancy status, malaria infection was associated with higher viral load in pregnant women. The median log viral load for pregnant women with malaria is 4.417 copies/mL, compared to a median of 4.044 copies/mL among pregnant women without malaria (Pearson Chi-Square test p=0.01). There is no significant difference in the median viral load levels for the non-pregnant population.

Applying a generalized linear model, having peripheral malaria was associated with a 0.33 increase (95%CI 0.29-0.64) in $\log_{10}$ HIV viral load for pregnant women (Table 2). The effect among non-pregnant women is not statistically significant, nor is the effect among the total population is not statistically significant (p=0.93, p=0.70). In a logistic regression model, being above the median log viral load was not associated with malaria infection in the study population (Table 3). There was no association, even when stratifying for pregnancy status.

Conclusion

Current or recent malaria in HIV+ pregnant women is associated with a significantly higher viral load than in women without malaria infection. However, no association was observed between malaria and HIV viral load in the non-pregnant population.

Figures

Table 1: Median viral load

	Malaria Negative	Malaria Positive	p-value Chi-Squared	n
Total sample	4.442 [4.326, 4.522]	4.436 [4.277, 4.619]	0.94	675
Pregnant sample	4.044 [3.822, 4.314]	4.417 [4.212, 4.634]	0.01	151
Non-pregnant sample	4.495 [4.403, 4.609]	4.484 [4.162, 4.734]	0.91	524

Table 2: Generalized linear model of malaria status on log viral load

	Total Sample (n=675)		Pregnant Sample (n=151)		Non-pregnant sample (n=524)	
	coefficient (se)	p	coefficient (se)	P	coefficient (se)	p
Malaria Positive	.035 (.091)	0.70	.333 (.155)	0.03	-.010 (.111)	0.93

Table 3: Logistic regression of malaria status on being above the median viral load

	Total Sample (n=675)		Pregnant Sample (n=151)		Non-pregnant sample (n=524)	
	coefficient (se)	p	coefficient (se)	P	coefficient (se)	p
Malaria Positive	-.022 (.190)	0.91	.345 (.350)	0.32	-.057 (.233)	0.81

Reference List

1. Kublin JG, Patnaik P, Jere CS, Miller WC, Hoffman IF, Chimbiya N *et al*. Effect of Plasmodium falciparum malaria on concentration of HIV-1-RNA in the blood of adults in rural Malawi: a prospective cohort study. *Lancet* 2005;**365**:233-40.

2. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F *et al*. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N.Engl.J Med* 2000;**342**:921-9.

3. Farcas GA, Zhong KJ, Lovegrove FE, Graham CM, Kain KC. Evaluation of the Binax NOW ICT test versus polymerase chain reaction and microscopy for the detection of malaria in returned travelers. *Am.J.Trop.Med.Hyg.* 2003;**69**:589-92.

4. Wongsrichanalai C, Arevalo I, Laoboonchai A, Yingyuen K, Miller RS, Magill AJ *et al*. Rapid diagnostic devices for malaria: field evaluation of a new prototype immunochromatographic assay for the detection of Plasmodium falciparum and non-falciparum Plasmodium. *Am.J.Trop.Med.Hyg.* 2003;**69**:26-30.

5. Mockenhaupt FP, Ulmen U, von Gaertner C, Bedu-Addo G, Bienzle U. Diagnosis of placental malaria. *J Clin.Microbiol.* 2002;**40**:306-8.