

# MALARIA IN HIV INFECTED PATIENTS: A MATCHED CASE-CONTROL STUDY IN A NON-ENDEMIC SETTING

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## Background

The impact of HIV infection on malaria is unclear in malaria non-endemic areas. In endemic territories, it has been reported to be a risk factor for acquiring malaria and inducing higher morbidity, parasitemia and malaria treatment failure. Nowadays as HIV-infected patients have a better quality of life and travel more, particularly as VFR (visiting friends and relatives) represent a large proportion of travelling HIV-infected patients, it is important to assess the impact of HIV on imported malaria.

## Methods

This monocentric retrospective case-control study collected data on HIV-infected patients with malaria defined as positive thick smears with *P.falciparum* identification on microscopy and matched them with 2 controls based on age, sex and ethnicity. Clinical and biological parameters were collected and compared and different severity scores were applied on our cohort.

## Results

We identified 47 cases and 94 controls. Malaria prophylaxis use and delay before medical contact did not differ between cases and controls. Comparing each of the WHO 2014 severity criteria, hyperparasitemia above 10% ( $p=0.006$ ), icterus ( $p=0.042$ ), acute renal failure ( $p=0.022$ ) and bacteraemia ( $p=0.014$ ) were significantly more present in HIV-infected patients, with a trend to more neuromalaria (12.8% versus 6.4%) (Table 1). HIV-infected patients were hospitalised more frequently and for longer periods. We observed more severity criteria when CD4 were lower, especially below 200/ $\mu$ L (Table 2). These differences in occurrence of severe malaria disappeared when patients with CD4 T-cells count  $>500/\mu$ L and VL $<50$  copies/mL ( $n=9$ ) were compared to controls but small size of this subgroup does not allow to draw firm conclusion. De novo HIV diagnosis was recognized in 17 percent of cases during the malaria episode.

Malaria severity criteria	Cases	Controls	p-value
Bacteraemia	6.4% (N= 3)	0	0.014
Neuromalaria	12.8% (N= 6)	6.4% (N=6)	0.214
Hyperparasitemia $>10\%^*$	12.8% (N= 6)	1.1% (N= 1)	0.006
Impaired consciousness*	8.5% (N= 4)	7.4% (N= 7)	1
Prostration*	2.1%(N= 1)	0	0.333
Convulsion*	2.1 % (N= 1)	0	0.333
Shock*	2.1% (N= 1)	2.1% (N= 2)	1
Severe bleeding*	0	0	-
Acidosis*	0	1.1% (N= 1)	1
Hypoglycaemia*	2.1% (N=1)	0	0.333
Anaemia*	2.1% (N= 1)	0	0.333
Acute renal failure*	25.5% (N= 12)	9.6% (N= 9)	0.022
Icterus*	14.9% (N= 7)	4.3% (N= 4)	0.042
Pulmonary oedema*	4.3% (N= 2)	1.1% (N=1)	0.257

Univariate exact Fisher test was used to calculate p-values.  
\*WHO 2014 criteria

Table 1. Malaria severity criteria : WHO 2014, neuromalaria

	HIV negative patients N=95	HIV positive patients N=47 (N=1 missing)			p-value
		CD4 $<200/\mu$ L N=12	CD4 200 – 500/ $\mu$ L N=22	CD4 $>500/\mu$ L N=13	
Bacteraemia	0	2 (20%)	1 (4.3%)	0	0.002
Missing data	47 (50.5%)	6 (60%)	7 (30.4%)	3 (21.4%)	
Neuromalaria	6 (6.4%)	0	5 (21.74%)	1 (7.1%)	0.108
Hyperparasitemia $>10\%^*$	1 (1.1%)	2 (20%)	3 (13.04%)	1 (7.1%)	0.006
Impaired consciousness*	7 (7.4%)	0	3 (13.04 %)	1 (7.1%)	0.727
Prostration*	0	0	1 (4.3%)	0	0.333
Convulsion*	0	0	1 (4.3%)	0	0.333
Shock*	2 (2.1%)	0	1 (4.3%)	0	0.707
Severe bleeding*	0	0	0	0	/
Acidosis*	1 (1.1%)	0	0	0	1
Hypoglycemia*	0	0	1 (4.3%)	0	0.333
Anemia*	0	1 (10%)	0	0	0.071
Acute renal failure*	9 (9.4%)	3 (30%)	7 (30.4%)	2 (14.3%)	0.03
Icterus*	4 (4.3%)	2 (20%)	4 (17.39%)	1 (7.1%)	0.042
Pulmonary oedema*	1 (1.1%)	1 (10%)	1 (4.3%)	0	0.139
Severe malaria WHO 2014	15 (15.96%)	5 (50%)	8 (34.8%)	3 (21.4%)	0.031

Univariate exact Fisher test was used to calculate p-values.  
\*WHO 2014 criteria

Table 2. Comparisons of HIV-positive patients according to their CD4 cell counts

## Conclusion

HIV infection has an impact on the imported malaria profile, as previously described in endemic areas. It is unclear if well controlled HIV-infected patients have a higher risk of developing severe malaria. HIV-infected patients should be particularly targeted for pre-travel advice and physicians should perform HIV testing during a malaria episode.