



HIV-1 INFECTION INCREASES THE RISK OF SEVERE MALARIA IN SEMI- IMMUNE ADULTS IN ZAMBIA

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Background

HIV (low CD4 count) → Malaria

Parasitaemia



Clinical malaria



Severe Malaria*

Antimalarial drug use



Treatment efficacy



Hb levels



***Unstable Malaria:** 2-fold risk, 2 to 7-fold death risk

(Chirenda 2000, Khasniss, 2003, Grimwade 2004, Cohen 2005)



Objective

To assess if **HIV-1 & immune suppression** is a risk factor for **severe malaria** in semi immune adults



Methodology

- Study design: Matched Case Control
 - each confirmed severe malaria case
 - 2 matched controls
 - Uncomplicated malaria
 - Asymptomatic control
- Matching criteria: gender, age and area of residence and timing.
- HIV-1 infection and related immune suppression were explored
- Conditional logistic regression modelling



Case definition (WHO)

- Fever (or history of fever)
- & *P.falciparum* parasitaemia (>4,000/ μ l)
- & Absence of other evident causes
- & at least 1:
 - Impaired consciousness,
 - Severe anaemia,
 - Multiple convulsions (type 'grand mal '),
 - Jaundice,
 - Hypoglycaemia,
 - Hyperparasitaemia,
 - Renal impairment

**Uncomplicated
malaria attack**

**Severe
malaria attack**



Study location

- Luanshya Districts, Zambia
 - Meso-endemic
 - 11/2005-03/2007



Baseline results (1)

- HIV-1 prevalence:
 - Severe malaria cases : 27/29 (93.1%)
 - Uncomplicated malaria controls: 15/29 (51.7%)
 - Asymptomatic controls: 13/29 (44.8%)



Baseline results: cases

	HIV infection	
	HIV Infected N=27	HIV Negative N=2
Symptoms (%)		
Impaired consciousness (Glasgow Scale <11)	15 (56%)	0
Severe anemia (<7 g/dl) †	5 (19%)	0
Convulsions	6 (22%)	0
Jaundice	3 (11%)	1
Hypoglycaemia (<2.5mmol/L)	11 (41%)	0
Hyperparasitaemia (>100,000parasites/μL)	6 (22%)	0
Renal impairment	0 (0.0%)	0
White Blood cell count [mean*1000/μL (SD)]‡	6.9 (3.9)	4.2 and 8.7
Lymphocytes [% (SD)] ‡	25 % (11)	18 %
Monocytes [% (SD)] ‡	11 % (6)	5.2 %
Granulocytes [% (SD)] ‡	62 % (20)	76.8 %
Parasite density [geometric mean/UL (CI interval)]	43,314 (25,467-81,145)	11745 and 38942

†Anemia was never the sole inclusion criterion but was accompanied with impaired unconsciousness, convulsions and hyperparasitaemia



Risk analysis

Proportion HIV infected	N (%)	OR*	P*	OR	P*
Asymptomatic controls	13/29(45%)	1	-		
Uncomplicated malaria controls	15/29(52%)	1.3 (0.5- 3.7)	0.59	1	-
Severe malaria cases	27/29 (93%)	16.6 (2.5-111.8)	0.0005	12.6 (2.0-78.8)	0.0005
Proportion CD4 cell count <350/μL in HIV infected‡					
Asymptomatic controls	1/12 (8%)	1	-		
Uncomplicated malaria controls	11/14 (79%)	40.3 (> 1.3)	0.02	1	-
Severe malaria cases	19/23 (83%)	52.2 (> 1.8)	0.005	1.3 (0.2-7.1)	0.33

‡ CD4 count not measured in 4 CM, 1 UM and 1 AS due to technical constraints



Discussion

- CM is a rare event
- In routine practice: Uncomplicated + opportunistic infection?
- Asymptomatic also at risk
 - Prevention CTX for all HIV infected?
- CD4 count during malaria is biased



Conclusion

- HIV is a highly significant risk factor for severe malaria
- Severe malaria cases are more likely to have a CD4 count $<350/\mu\text{l}$
- In malaria–HIV-1 co-endemic areas, adults with severe malaria are likely to be co-infected with HIV-1



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