

INVESTIGATING THE IMPACT OF *SCHISTOSOMA HAEMATOBIIUM* INFECTION ON IMMUNITY TO *PLASMODIUM FALCIPARUM* MALARIA IN POPULATIONS FROM BURKINA FASO

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INTRODUCTION

Several studies indicate that infection with helminths might modulate the immune response towards intracellular pathogens including Plasmodium in areas of co-endemicity (Salgame et al., 2013 Nat Immunol). We recently reported that in rural villages of Burkina Faso the seroprevalence of *Strongyloides stercoralis*, *Wuchereria bancrofti* and *Schistosoma haematobium* was 5%, 16% and 63% respectively, in line with estimates of infection prevalence in the region for the three parasites (Mangano et al., 2020 Acta Tropica).

The aim of the present investigation was to assess the impact of serological markers of *S. haematobium* infection on the prospective risk of *Plasmodium falciparum* parasitaemia among study populations, using a repeated cross-sectional surveys design (Mangano et al., 2015 J Inf Dis).

METHODS

IgM and IgG against *S. haematobium* Soluble Worm Antigen Protein (SWAP) and Soluble Egg Antigen (SEA) were measured by an in-house ELISA protocol (Mutapi et al., 1997 Parasite Immunol) in plasma samples collected from N=452 subjects. Statistical analysis was performed using STATAv13. Descriptive analysis to assess variation in prevalence and levels of *S. haematobium*-specific antibodies according to age, sex and ethnicity was conducted using logistic (Results 1) and linear (Results 2) regression respectively. Association analysis between the presence of *S. haematobium*-specific antibodies at baseline and the number of *P. falciparum* infections measured by microscopy over 5 surveys was conducted using Poisson regression adjusting for age, sex, ethnicity and haemoglobin genotype (Results 3).

Table 1: Logistic regression of positivity for anti-*S. haematobium* antibodies according to age, sexe and ethnicity

Positivity for anti- <i>S. haematobium</i> antibodies	OR	95% CI	p-value
Age (years)	1.10	1.06	<0.0001
Sexe (Female vs Male)	0.71	1.16	
Ethnicity (Non-Fulani vs Fulani)	1.26	2.23	0.414
		0.12	
	0.26	0.58	0.001

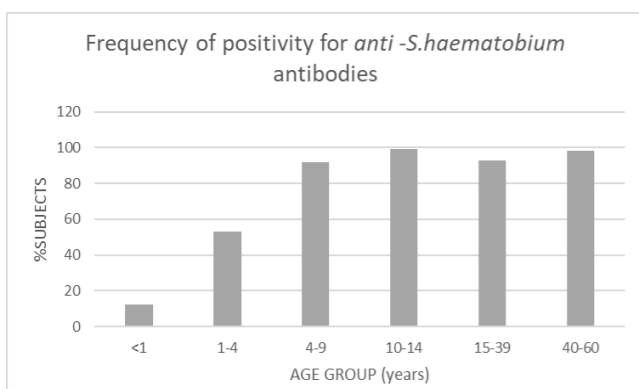


Fig.1: Frequency of positivity for anti-*S. haematobium* antibodies according to age group

RESULTS 1

The frequency of subjects seropositive for both anti-SWAP and anti-SEA Ig (IgM and/or IgG) increased with age, did not show differences among females and males, and was higher in Fulani than Non-Fulani. These results suggest that seropositivity for *S. haematobium*-specific antibodies could be used as a marker of cumulative exposure to infection. Differences between populations could be explained by a higher frequency of contact with contaminated water in the Fulani as a result of their pastoral activity.

Table 2: Linear regression of antibody levels according to age sex ethnicity (OR, 95% CI, p-value)

Antibodies	age (years)	sexe (female vs male)	ethnicity (Non-Fulani vs Fulani)
Anti-SWAP IgM	1.00 (0.99 1.00); p=0,20	0.99 (0.98 1.01); p=0,70	0.99 (0.98 1.01); p=0,70
Anti-SWAP IgG	0.99(0.99 1.00); p=0,40	0.98 (0.97 0.99); p=0,02	1.00(0.99 1.01); p=0,48
Anti-SEA IgM	0.99(0.99 1.00); p=0,05	0.99(0.98 1.00); p=0,29	0.99 (0.98 1.01); p=0,96
Anti-SEA IgG	0.99(0.99 0.99); p=0,001	0.96(0.95 0.98); p<0,0001	1.02(1.01 1.04); p=0,001

RESULTS 2

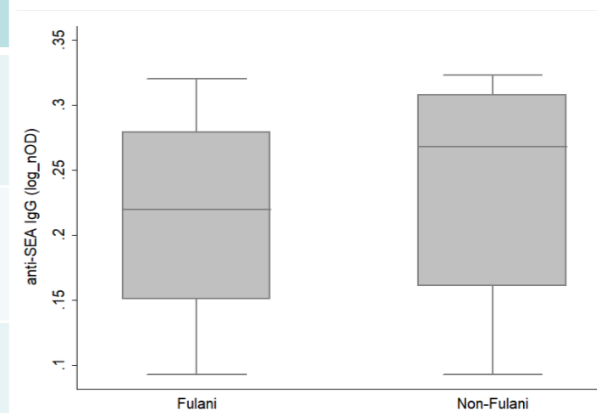


Fig.2: Levels of anti-SEA IgG according to ethnicity

It is noteworthy that levels of anti-SEA IgG were lower in Fulani than Non-Fulani, confirming previous observations (Mangano et al., 2020 Acta Tropica) and suggesting that lighter *S. haematobium* infections occur in the malaria-resistant population (Modiano et al., 1996PNAS).

Table3: Association of positivity for anti-*S. haematobium* antibodies with number of *P. falciparum* infections over time

Number of <i>P. falciparum</i> infections over time	IRR	95% CI	p-value
anti-SWAP IgM	1.2	1.04 1.37	0.009
anti-SWAP IgG	1.1	0.99 1.30	0.05
anti-SEA IgM	1.1	0.97 1.31	0.094
anti-SEA IgG	1.1	0.97 1.29	0.104
anti- <i>S. haematobium</i> Ig	1.3	1.09 1.56	0.004

RESULTS 3

Association analysis showed a significant increase in the incidence of *P. falciparum* infections among anti-*S. haematobium* seropositive subjects.

CONCLUSION AND PERSPECTIVES

Results of association analysis are in line with those of a systematic review and meta-analysis indicating an association between *S. haematobium* infection and increased prevalence of *P. falciparum* asymptomatic malaria (Degarage et al., 2016 Plos Neg Trop).

To support interpretation of these results a cohort study will be conducted in the study area to identify humoral correlates of prevalence and intensity of *S. haematobium* infection. Also, the immunomodulatory activity of *S. haematobium* candidate proteins - H-IPSE (Pennington et al., 2017 Infect Immun) and tetraspanins (Sotillo et al., 2019 Plos Neg Trop Dis) - will be investigated by testing their effect on cytokine production by Dendritic Cells *in vitro* and on the course of *P. berghei* infection *in vivo*.

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