The role of chronic maternal helminths (*Schistosoma mansoni* and soil-transmitted helminths) infections on placental/congenital malaria among primigravidae and multigravidae women and their influence on infants/children underfives anti-malaria immune responses

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Immune responses during pregnancy

- It is hypothesized that immune response during pregnancy shifts towards T-cell type-2 immune response characterized with increased activities of CD4+ T-cells and their related anti-inflammatory cytokines (interleukin-4, IL-5 and IL-10).

- The response is thought to down-regulates Th1 immune response (T-helper 1) and increases susceptibility of pregnant mothers to intracellular parasites such as malaria.

Brabin et al., 2004; Sappenfield et al., 2013; Abdoli et al., 2014
Immune responses during helminth infections

• During chronic helminths infections, there is a shift of immune responses towards Th$_2$ immune responses, characterized by increased activation and expansion of Th$_2$ CD4+ cells (including eosinophils, mast cells, basophils and antibody isotypes IgG1, IgG4 and IgE)

• This response is thought to negatively affect Th$_1$ immune response to intracellular pathogens such as malaria parasites

Anthony et al., 2007:Colley et al., 2011
Maternal malaria and newborns

• During pregnancy, maternal immune responses to *P. falciparum* infection also influence the offspring's immunity and response to *P. falciparum* infection (early childhood anti-malarial responses)

• Perhaps, *P.falciparum*-helminths co-infection during pregnancy may affect this immune response against malaria in early life

• If this is correct, then, infants born from mothers who are co-infected with PF/helminths are likely to experience more episodes of clinical and asymptomatic malaria

Moya-Alvarez et al., 2014
Hypothesis

• Maternal helminths infections exacerbates the Th₂ down-regulating effects on Th₁ immune response during pregnancy resulting in increasing susceptibility of pregnant women to *P.falciparum* parasite. Thus, co-infected mother will have:-

  i. higher placenta malaria (>20%)

  ii. Their newborns will have higher prevalence (>30%) of congenital malaria and have greater number of episodes of clinical and asymptomatic parasitaemia on follow-up

  iii. Their newborns will have lower immune responses (measured in term of IgG₁ and IgG₃ levels) against merozoites surface antigens (MSP-1₁ₙ)

  iv. There is no difference in immune responses (measured in term of IgG₁ and IgG₃) against merozoites surface antigens (MSP-1₁ₙ) between children born from women co-infected with helminths (*S.manson/P.falciparum* or STH/P.falciparum) and those from mothers infected only with *P.falciparum* parasite.
General objectives

- To determine the effect of maternal helminths (*Schistosoma mansoni* and soil-transmitted helminths) infections on placental/congenital malaria, and pregnancy outcomes among primigravidae and multigravidae women infected with malaria and their influence on infants/children underfives anti-malaria immune responses in North-western Tanzania
Specific objectives

i. To determine the prevalence of placental and peripheral malaria, *Schistosoma mansoni*, soil-transmitted helminths and their associated risk factors among primigravidae and multigravidae women

ii. To determine the prevalence of congenital, clinical and asymptomatic malaria at birth among newborns from primigravidae and multigravidae women with malaria infection co-infected or not with either *S. mansoni* or STH

iii. To determine the incidence of clinical and asymptomatic malaria during longitudinal follow-up among children born from primigravidae and multigravidae women with malaria infection co-infected or not with either *S. mansoni* or STH
iv. To determine the levels of protective malaria IgG antibodies (isotype IgG3) against merozoites surfaces antigens (MSP-1, MSP-2, MSP-3) in cord blood plasma of primigravidae and multigravidae women with malaria infection co-infected or not with *S. mansoni* or soil-transmitted helminths

v. To determine the levels of protective malaria IgG antibodies (isotype IgG3) against merozoites surfaces antigens (MSP-1, MSP-2, MSP-3) among children born from primigravidae and multigravidae women with malaria infection co-infected or not with either *S. mansoni* or soil-transmitted helminths

vi. To determine the effects of *P. falciparum* infection on anaemia and birth outcomes (birth-weight and pre-term delivery) among primigravidae women either co-infected or not with *S. mansoni* or soil-transmitted helminths
Materials and methods

- **Study area:** This study is conducted at Sengerema DDH
- **Study design:** This is a cross-sectional study
- **Study population and inclusion criteria:** The study population including of pregnant women attending for ANC and delivery at the selected hospital district hospital.
Pregnant women attending antenatal clinics, informed about the study and assessed for eligibility based on inclusion criteria. Consenting to participate and counselled for HIV testing and tested.

HIV negative pregnant women: interviewed using the questionnaires to collect socio-demographic and economic information, obstetrics information, use of malaria and helminths intervention measures.

At delivery point

Mothers

- 5mls venous, placenta and cord blood
- Single urine and stool sample

Newborns

Assessment for eligibility by qualified nurses

Eligible newborns

Ineligible based on inclusion criteria

Laboratory investigation

With no infection diagnosed in the study

With infection diagnosed in the study (infected group)

- Active case detection weekly for 6 month (weekly follow-up) and at 7-12 month, monthly follow-up
- Passive case detection in nearby dispensaries
- Maintaining contact with the mother/family via mobile phones
- At 9 and 12 months, collect 2mls of venous blood and harvest plasma for immunological work

Immunological studies

The un-exposed group (P.falciparum only) and exposed/co-infected groups (P.falciparum + S.mansonii, P.falciparum + STH, P.falciparum + S.mansonii + STH)
Data collections

- **Questionnaire:** The questionnaire will be used to collect socio-demographic, socio-economic information and obstetric information.

- **Diagnosis of malaria parasites:** Giemsa stained thick and thin smears, mRDT and real-time PCR for peripheral DBS, placental and cord blood.

- **Diagnosis of *Schistosoma mansoni* and STH:** Four Kato Katz thick smears will be prepared using a template of 41.7 mg, following a standard protocol, Formol-Ether Conc. And PCR for STH DNA in stool.

- **Diagnosis of *Schistosoma mansoni* circulating cathodic antigens:** commercially available rapid test (Rapid Medical Diagnostics, Pretoria, South Africa).
Data collections…..

• **Diagnosis of HIV-1:-** Bioline HIV-1/2 Rapid Test and Unigold rapid test

• **Measurements of malaria antibodies (IgG) response levels against a panel of merozoites surface antigens:** Children’s peripheral plasma samples, maternal peripheral and cord plasma samples will be tested by enzyme-linked immunosorbent assay

• **Determination of haemoglobin levels:** Haemoglobin concentration of each study participant will be determined using a portable haemoglobinometer (HemoCue B-Haemoglobin analyzer)
Prevalence data

• Based on the formal-ether concentration technique, 7.9% (95% CI: 5.2-11.5) had *S. mansoni* while 16.32% had STH.

• Of these women infected with STH, 4.2% had *T. trichiura*, 16.6% had *A. lumbricoides*, and 79.2% had hookworms.
RESULTS

Prevalence of *S.mansonii* and *P.falciparum*

- Based on POC-CCA:- prevalence of *S.mansonii* infection was 63.4% (95%CI: 58.5-68.3)

- Based on Kato Katz:- prevalence of *S.mansonii* infection was 9.68% (95%CI: 6.36-12.98)

- Prevalence of malaria in the mother’s peripheral blood was 34.6% (95%CI: 29.87-39.35)
Co-infections

• Using POC-CCA- 39% of the women were co-infected with *S. mansoni* and *P. falciparum*

• Using Kato Katz- 3% of the women were co-infected with *S. mansoni* and *P. falciparum*
RESULTS

• Overall, the prevalence of congenital /cord malaria was 22.82% (89/390, 95% CI: 18.6-27.0)

• Of the newborn diagnosed with congenital malaria, 74.2% were born from mothers who were co-infected with *P.falciparum* and *S.mansonii*

• 95.5% (85/89) of newborns who had cord malaria positive slides were born from mothers who had placental malaria (fisher exact=0.001).
Co-infections and risk of malaria

• Multigravidae women co-infected with *P.falciparum*-*S.mansoni* had higher prevalence of placenta malaria (53.8% versus 46.2%, \( P<0.03 \)).

• Malaria in pregnancy were mainly associated with being primigravidae AOR=1.88(95%CI: 1.003-3.49, \( P<0.04 \)).
Results

Maternal Hb

• In total, 55.9% (218/390) of the pregnant women were anaemic (Hb<11g/dL)
Conclusion

• Helminths infections especially *S. mansoni* and *P. falciparum malaria* are a public health concern in pregnant women

• Co-infections of *S. mansoni* and *P. falciparum* does occur in proportional of pregnant women

• There is a tendency of high prevalence PM in multigravidae women compared to primigravidae women (need follow-up)
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