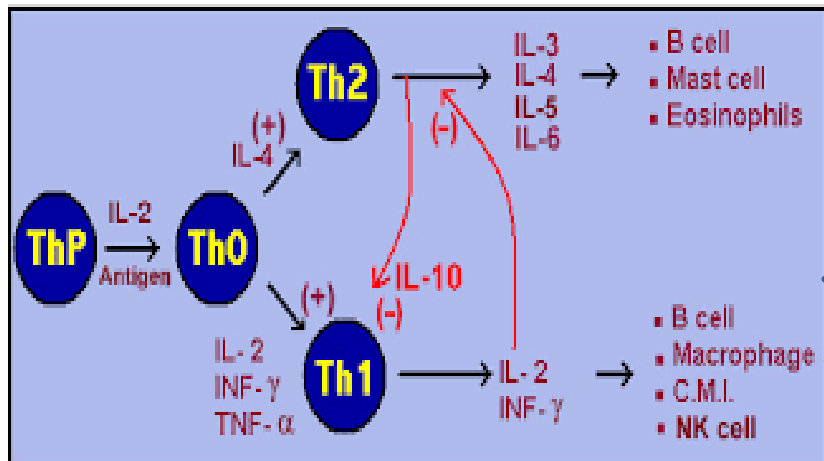


The role of chronic maternal helminths (*Schistosoma mansoni* and soil-transmitted helminths) infections on placental/congenital malaria among primigravidae and multigravidae women and their influence on infants/children underfives anti-malaria immune responses



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 Th₂ immune responses, characterized by increased activation and expansion of Th₂ CD4⁺ cells (including eosinophils, mast cells, basophils and antibody isotypes IgG1, IgG4 and IgE)
- This response is thought to negatively affect Th₁ 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

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-1₁₉)
 - iv. There is no difference in immune responses (measured in term of IgG₁ and IgG₃) against merozoites surface antigens (MSP-1₁₉) between children born from women co-infected with helminths (*S.mansoni/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

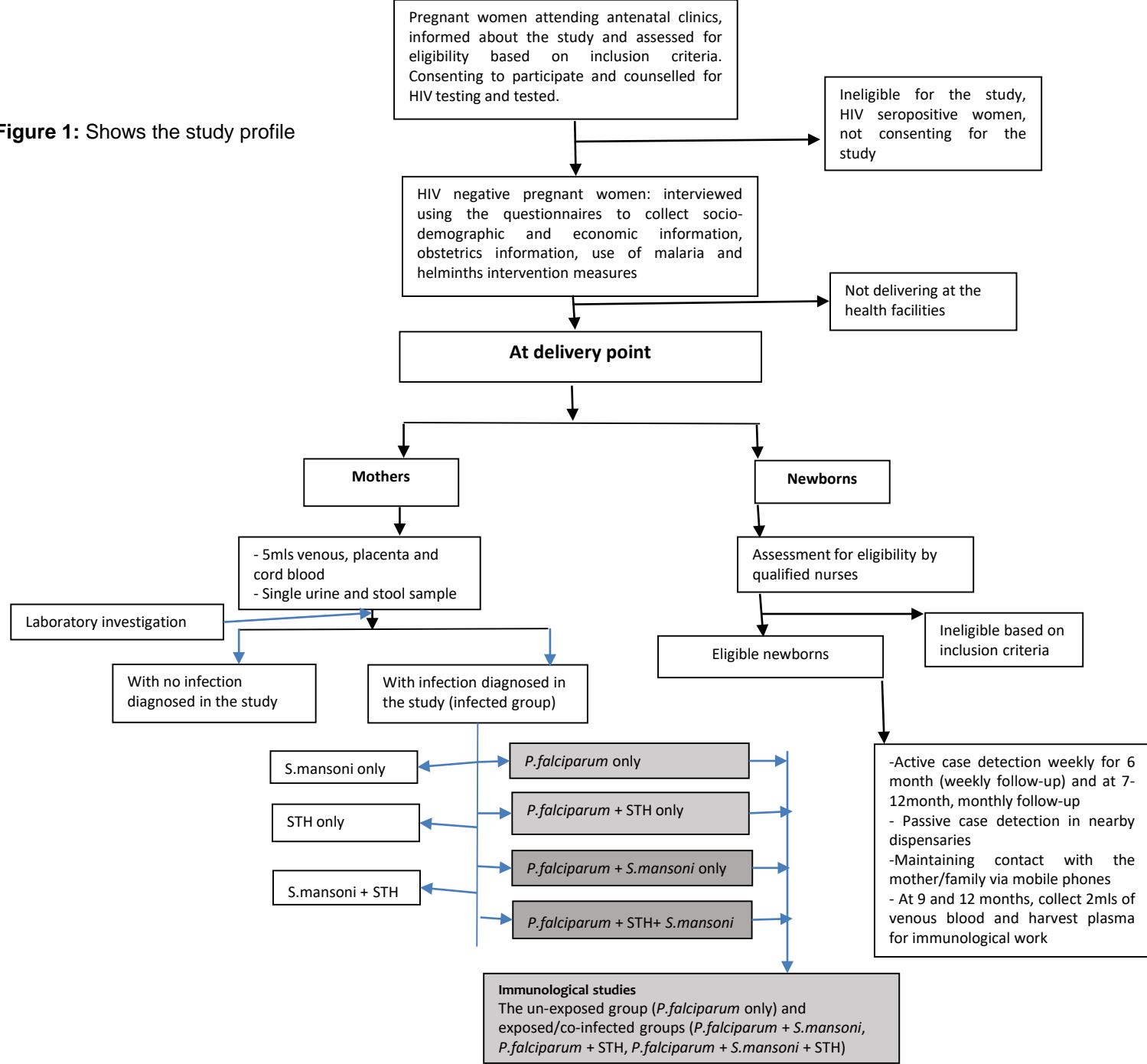
- i. To determine the prevalence of placental and peripheral malaria, *Schistosoma mansoni*, soil-transmitted helminths and their associated risk factors among primigravidae and multigravidae women
- ii. To determine the prevalence of congenital, clinical and asymptomatic malaria at birth among newborns 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.

Figure 1: Shows the study profile



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.mansoni* and *P.falciparum*

- Based on POC-CCA:- prevalence of *S.mansoni* infection was **63.4%** (95%CI: 58.5-68.3)
- Based on Kato Katz:- prevalence of *S.mansoni* 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.mansoni*
- **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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**Asanteni sana
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