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Endemic parasitic infections during pregnancy and their impact on clinical and immunological outcomes in Gabon

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Summary

Parasitic infections during pregnancy pose a significant public health challenge in many areas of sub-Saharan Africa, where environmental and socioeconomic factors heighten exposure and vulnerability. Pregnant women are at increased risk of these infections, which can adversely affect both their health and the development of their unborn children. Despite the substantial burden of such infections, the effects of maternal parasitic infections, especially on neonatal immunity and early-life health outcomes, are not fully understood.

Chapter 1 provides an overview of the prevalence of parasitic diseases in pregnancy, focusing on key pathogens such as *Plasmodium spp.* and *Schistosoma spp.* It discusses their known impacts on maternal, foetal, and infant health. Additionally, the chapter highlights current knowledge gaps regarding the maternal and cord blood immune systems, antibody glycosylation patterns, and the potential effects on infants. This highlights the need for enhanced diagnostic methods and the integration of maternal infection monitoring into antenatal care. Finally, the chapter presents the rationale, objectives, and overall structure of the thesis, which aims to explore the clinical and immunological consequences of parasitic infections during pregnancy in endemic regions, such as Gabon.

Chapter 2 This chapter investigates the relationship between polyparasitic infections during pregnancy and adverse birth outcomes in newborns in Lambaréné, Gabon. By utilising clinical and parasitological data from a cohort of pregnant women monitored throughout gestation, the study highlights that co-infection with multiple parasites, particularly helminths and *Plasmodium falciparum*, is common and associated with low birth weight (LBW <2500g). The association was established through multivariate analyses, accounting for confounders such as anaemia, parity, and nutritional status. The findings emphasise the need for integrated parasite control strategies during pregnancy to improve birth outcomes in endemic areas.

Chapter 3 This chapter presents the study protocol for the freeBILy clinical trial, a prospective observational study designed to evaluate the diagnostic performance of circulating anodic antigen (CAA) detection for *Schistosoma haematobium* infections in pregnant women and their infants in Lambaréné, Gabon, using the Up-Converting Phosphor Lateral Flow Circulating Anodic Antigen (UCP-LF-CAA). The study addresses the limitations of conventional diagnostic tools, such as urine filtration and microscopy, particularly in low-intensity infections common during pregnancy. It describes the study design, recruitment strategies, inclusion criteria, and planned statistical analyses. The protocol also emphasises the importance of improving schistosomiasis diagnostics in maternal and child health programs in endemic areas.

Chapter 4 This chapter presents the results of the freeBILy study, where the accuracy of the UCP-LF-CAA urine test for detecting schistosomiasis in pregnant women was assessed. Conducted in an endemic area, the study compares the performance of this antigen-based test to the traditional diagnostic method of urine microscopy. The findings reveal that the UCP-LF-CAA test offers significantly improved sensitivity, especially for low-intensity infections, and can be suitable for use during pregnancy as a validated point-of-care test in the near future. The chapter discusses implications for diagnostic strategies in antenatal care and highlights the potential of non-invasive, highly sensitive tests in improving detection and treatment coverage.

Chapter 5 This chapter presents the clinical outcomes of the freeBILy-Gabon trial, a randomized, single-blinded, study assessing the safety and efficacy of praziquantel treatment in pregnant women infected with *Schistosoma haematobium*. The trial evaluates praziquantel's impact on maternal health, pregnancy outcomes, and parasite clearance. The results show that praziquantel is safe during pregnancy, with no major adverse events reported, and it is effective in reducing maternal anemia. The study provides evidence that supports WHO recommendations for routine treatment of schistosomiasis during pregnancy, and it emphasizes the importance of the integration of pregnant women in test-and-treat strategies in neglected tropical disease (NTD) treatment programs.

Chapter 6 This chapter explores how parasitic infections during pregnancy affect the glycosylation patterns of IgG antibodies in both mothers, their newborns and their infants of 9 and 12 months of age. Maternal and cord blood exhibited higher IgG galactosylation and lower fucosylation levels compared to infants, indicating a shift in glycosylation as the child matures. Furthermore, maternal infection status did not significantly influence the glycosylation patterns of their offspring. However, infants born to mothers with higher antibody galactosylation, also exhibited higher IgG galactosylation. These findings suggest that there might be some genetic influence on infants' antibody glycosylation profiles, but these become increasingly independent of maternal influence as exposure to the external environment increases. As IgG Fc galactosylation and fucosylation influences antibody functionality, further understanding of the changes in antibody glycosylation in vulnerable populations, particularly in low- and middle-income countries, might help the development of strategies to combat infectious diseases.

Chapter 7 Immunological profiles in umbilical cord blood show remarkable variations influenced by maternal infections during pregnancy, especially with malaria parasites and helminths. In this chapter, mass cytometry was used to investigate the immune cell composition of cord blood samples from newborns in Gabon (Africa) and the Netherlands (Europe) and how maternal parasitic infections during pregnancy influence the development and composition and functionality of immune cells in cord blood. The presence of placental malaria resulted in profiles in common with European samples, suggesting a potential shared immunological state resulting from pathogen-induced

versus sterile inflammation, respectively. In contrast, maternal helminth infections resulted in type 2 responses in cord blood, highlighted by increased ILC-2. The question of whether such alternations would have long-term consequences on the susceptibility of the children to infections or response to vaccines can be addressed by longitudinal follow up of such cohorts.

Chapter 8 Synthesizes the findings in this thesis, discussing the data generated on the multifaceted burden of parasitic infections during pregnancy in endemic regions, particularly in Gabon and suggesting directions for future research in terms of translating research into public health interventions. The findings highlight the impact of parasitic infections, and the need for better diagnostics and treatment programs. The work in this thesis provides the basis for developing targeted public health interventions to reduce the impact of parasitic infections on maternal and child health. Future interventions should incorporate improved diagnostic and treatment strategies into routine maternal health care programmes, complemented by a deeper immunological understanding to improve disease outcome. Moreover, translating these findings into policy requires effective communication and collaboration between researchers, health care providers and policy makers to significantly improve maternal and child health outcomes.