

Clinical and immunological impact of malaria and prevalence of helminth infections during pregnancy

Thesis by: **Ayola Akim Adegnika**

Promotor: Prof. Dr. M. Yazdanbakhsh
Co-promotor: Prof. Dr. Peter. G. Kremsner

Institut für Tropenmedizin, Tübingen, Germany
Department of Parasitology, Leiden University Medical Center, Leiden, The Netherlands

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Abstract

In this thesis the immunological and clinical impact of pregnancy-associated malaria (PAM) and the prevalence of helminth infections during pregnancy were assessed.

PAM is one of the leading causes of low birth weight (LBW) but few studies have investigated this in much detail. Elevated levels of CRP in microscopically *Plasmodium falciparum*-positive pregnant women, but not in those with sub-microscopic infections compared to those free of *P. falciparum* infection were seen. In multivariate analysis, the presence of microscopic or sub-microscopic *P. falciparum* infection in pregnant women and age of mothers less than 21 years, but not CRP levels, were independent predictors for LBW.

PAM is known to modify fetal immunity. Most previous studies have been cross-sectional in nature and have focused on the priming of acquired immune responses *in utero*. In this context,

the influence of timing and/or duration of placental infection with *P. falciparum* are unknown, and changes to innate immune responses have not been studied extensively. In a longitudinal immuno-epidemiological study we found that the cells of neonates born to mothers with microscopic *P. falciparum* infections, particularly those with infection in the last month of pregnancy, had significantly altered responsiveness to Toll-Like Receptor (TLR) ligands such as lipopolysaccharide (LPS) and polyinosinic: polycytidylic acid (Poly I:C) in terms of IFN- γ and TNF- α production. Inversely cells of neonates born to mothers free of *P. falciparum* infection, to mothers who were successfully treated for malaria during pregnancy and to mothers with sub-microscopic *P. falciparum*, did not show these changes. An independent association between gravidity and cord blood mononuclear cells (CBMC) in response to the TLR ligands and to phytohemagglutinin (PHA) was also discerned.

Newborns weighing less than 2500 grams are often born to primiparous and *P. falciparum* infected women in Africa. In order to understand the immunological correlates of LBW, the responses of maternal peripheral as well as cord blood cells to PHA and LPS were examined. Peripheral blood mononuclear cells (PBMC) of mothers giving birth to LBW infants, in response to LPS, and CBMC of their LBW neonates, in response to PHA, produced significantly more IFN- γ compared to the PBMC and CBMC of the normal birth weight (NBW) groups in response to the respective stimuli. Malarial infection was also associated with LBW and immunological changes. Further analysis indicated that LBW, primiparity and PAM were independently associated with higher IFN- γ response of PBMC to LPS and of CBMC to PHA.

Gestation is a unique physiological state that carries with it several immunological well-recognized consequences and results in changing susceptibility to various diseases. In contrast to the well recognized excess vulnerability of pregnant women to *Plasmodium falciparum* infection, it is not known whether pregnancy is associated with a higher prevalence of helminth infection.

We investigated the prevalence of the intestinal helminth infections in pregnant women in a case-

control study design. In the study we found that pregnant women have a significantly higher prevalence of intestinal helminth infections compared to age and location matched non-pregnant controls. In multivariate analysis pregnancy status was independently associated with a risk of being infected with intestinal helminths.

Further clinical, immunological and epidemiological studies of co-infection of malaria and helminth parasites are needed to fully understand the impact of these pathogens in pregnancy.