ORAL ABSTRACTS

848. Altered Fetal Cytokine Profiles Are Associated With Placental Malaria

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Session: 95. Global Diseases at Home and Abroad
Thursday, October 27, 2016: 2:00 PM

Background. Malaria during pregnancy threatens the health of mothers and newborns and may have long-lasting consequences on infant health. Our previous work shows that placental malaria is associated with increased risk of malaria in the infant. We hypothesize that this is due to priming of the fetal immune system toward down-regulatory responses as a consequence of maternal malaria infection.

Methods. We collected cord blood serum from children born to mothers with detailed antenatal histories and followed a subset of these children through the first year of life, collecting serum at 12 months of age. We used multiplexed electrochemiluminescent immunoassays (Meso Scale Discovery) to measure 11 cytokines (IL-1β, IL-2, IL-4, IL-6, IL-10, IL-12p70, IL-13, IFNgamma, TNFα, TGFβ and CRP). We analyzed cord serum from 26 infants born to mothers with no malaria during pregnancy, 26 born to mothers with peripheral malaria, 87 born to mothers with placental malaria, and 14 North American control infants never exposed to malaria.

Results. We observed that children born to mothers with chronic placental malaria had significantly higher levels of pro-inflammatory TNFα, anti-inflammatory IL-10 and CRP (a marker of inflammation) at birth as compared to children born to mothers with peripheral malaria during pregnancy ($p = 0.003$, $p = 0.001$, $p = 0.014$, respectively), no malaria during pregnancy ($p = 0.003$, $p = 0.037$, $p = 0.006$, respectively) or North American controls ($p = 0.002$, $p < 0.001$, $p = 0.045$, respectively). Children with above median levels of TGFβ (a cytokine associated with T regulatory cells [Tregs]) at birth had a shorter time to first malaria infection. Elevated cytokine levels normalized by one year of age.

Conclusion. We hypothesize that placental malaria causes chronic in utero inflammation with compensatory production of IL-10 and induction of Tregs. After birth, cytokine levels normalize, but Tregs may be maintained and downregulate effective immune responses to malaria resulting in increased risk of malaria during infancy. We are currently conducting flow cytometric studies on cord blood to further explore these hypotheses. Our results might inform the design and implementation of prenatal interventions to protect the health of pregnant women, newborns and infants from malaria.

Disclosures. **All authors:** No reported disclosures.

Open Forum Infectious Diseases 2016;1(S1):S1–68

DOI: 10.1093/ofid/ofw194