STRONG CHILDREN'S RESEARCH CENTER

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ABSTRACT

Title: ***Chorioamnionitis Induces Distinct Inflammatory and Regulatory Cytokine Changes in Premature Infant Cord Blood***

Background: Preterm birth (<37 weeks gestation) affects approximately 15 million infants worldwide, each year, and is a primary cause of morbidity and mortality in neonates. Preterm delivery is strongly associated with intrauterine infection, known as chorioamnionitis (chorio) or acute inflammation of the fetal membranes. Fetal exposure to chorio is linked to poor outcomes and may contribute to preterm delivery itself. Preterm infants delivered in the setting of chorio have increased T-cell activation, as demonstrated by an increase in the expression of activation markers. In addition, when compared to term infants, preterm infants have shown an increased pool of previously activated T-cells. Enrichment for activated cells may also be present in sterile inflammation, suggesting T-cell activation resulting from an inflammatory cytokine milieu, as opposed to classic activation through cognate interaction. As of now, the inflammatory environment promoting T-cell activation is not well understood.

Objective: The purpose of this pilot study is to identify cytokines in umbilical cord blood relevant to T cell activation, that may be modulated by either chorio, gestational age at birth, or both. We expect to find that chorio-exposed preterm infants will have increases in pro-inflammatory cytokines and decrease in regulatory cytokines. We also expect to find a greater effect at lower gestational ages.

Results: Cytokines were measured by Luminex in umbilical cord blood from eight chorio-exposed preterm infants and compared to eight age-matched controls without prior exposure to chorio. We measured a significant elevation in cytokines involved in innate immunity (IL-6, GM-CSF), the Th1 response (TNF-a, MIP-1a, MIP-1b) and immune regulation (IL-10) in premature infants with chorio. Our results showed a general overlap in the inflammatory milieu in subjects with clinical chorio and those with histological chorio, with the exceptions of increases in MIP-1a, MIP-1b, and IL-1b in clinically diagnosed chorio, suggesting a more robust innate immune response in clinical chorio. We also determined that the relationship between gestational age and cytokine levels in cord blood is cytokine dependent, but when present, is greater at lower gestational ages.

Conclusion: Our findings suggest that the circulating inflammatory environment of premature infants exposed to chorio involves primarily innate immune response cytokines. Our results suggest that cytokines associated with T-cell activation in chorio-exposed infants are increased, and may be enhanced at younger gestational ages. Contrary to our expectations, regulatory cytokines are up-regulated in the setting of chorio, regardless of gestational age, which may indicate a failed effort to suppress an inflammatory response.