Exposure to Ureaplasma Is Associated with a Pro-Inflammatory State and Increased Risk of Nosocomial Sepsis in Very Immature Preterm Infants*

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Background: The pathogenicity of ureaplasma and its impact on inflammation-related neonatal morbidities remains controversial. **Objective:** To study the prevalence of ureaplasma colonization and infection in very preterm infants and its relationship with systemic inflammation and neonatal outcome.

Methods: Very low birth weight (VLBW) infants born before 30 weeks of gestation were prospectively enrolled at a neonatal intensive care unit of a tertiary care hospital. *Ureaplasma urealyticum* and *Ureaplasma parvum* were cultured from cord blood and initial ear swab, and PCR was performed on the DNA extracted. Multi-analyte immunoassay provided cord blood levels of TNF-α, IL-1β, IL-8, IL-12, IL-17, IL-10, IL-1ra, IFN-γ, IP10, MMP-8/9, MIP-1α/β, MCP-1, VEGF, G-CSF, ICAM-1 and VCAM-1 in addition to leukocyte counts, immature to total neutrophil (I:T) ratio and C-reactive protein levels. Using multivariable linear and logistic regression analyses, ureaplasma species were evaluated as risk factor for systemic inflammation, neonatal morbidity and mortality.

Results: Among 92 preterm infants enrolled, 36 were ureaplasma-positive, comprising 29/36 colonized infants: 15/36 with systemic and 8/36 with local and systemic infection. Ureaplasma-positive infants were more likely to have a history of vaginal delivery ($p = 0.024$) and maternal genital colonization with ureaplasma ($p = 0.003$) and candida ($p = 0.026$). Perinatal and baseline demographic characteristics did not otherwise differ among ureaplasma-positive and negative infants. Detection of ureaplasma was associated with higher I:T ratios ($p = 0.005$), increased ratios of pro-inflammatory cytokines to anti-inflammatory IL-10 (TNF-α/IL-10: $p < 0.001$, IL-8/IL-10: $p = 0.01$, IL-17/IL-10: $p < 0.001$), enhanced serum levels of IL-17 ($p = 0.033$) and MMP-8 ($p = 0.033$) and a 6.9-fold risk of nosocomial sepsis ($p = 0.015$).

Conclusions: Our study indicates a pro-inflammatory state and an increased risk of nosocomial sepsis in ureaplasma-positive VLBW infants.

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