Mid-trimester amniotic fluid pro-inflammatory biomarkers and the risk of spontaneous preterm delivery

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Objective
Intra-amniotic infection and inflammation remain a major cause of spontaneous preterm delivery (sPTD), mainly very preterm delivery (<32 weeks). We aimed to estimate the association between the concentrations of potential cytokines in mid-trimester amniotic fluid (AF) and the risk of subsequent sPTD.

Methods
We performed a case-control study nested in a large prospective cohort of asymptomatic pregnant women that underwent mid-trimester genetic amniocentesis between 15 and 23 weeks. Twenty-one women who subsequently delivered spontaneously before 35 weeks of gestation (cases) were paired with twenty-one women who delivered at term (controls). Magnetic bead-based multiplex immunoassays were used to quantify 48 potential cytokines in the AF samples. All analyses were performed by a technician blinded to clinical data. The association between AF cytokines levels and subsequent sPTD was examined using non-parametric statistical analyses.

Results
Cases and controls groups were comparable in terms of gestational age at amniocentesis (median of 16 weeks of gestation). We observed that AF levels of macrophage inhibitory factor (MIF) was significantly higher in the cases (median: 1,362 pg/ml) than in the controls (934 pg/ml, p=0.02). Looking specifically at the 10 cases who delivered before 32 weeks, we observed higher AF levels of MIF (median: 1,414 pg/ml) and IL-5 (0.33 vs 0.21 pg/ml, p=0.04) compared to the controls. High AF levels of IL-1β, IL-6, IL-8, and G-CSF were also observed in the cases, but the differences were not significant compared to the controls.

Conclusion
High concentrations of MIF and other potential biomarkers in mid-trimester AF are associated with an increased risk of sPTD.