Title: Cervicovaginal Fluid (CVF) TNFα as a Biomarker for Preterm Birth

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Objective:
The prediction of preterm birth (PTB) is complex due to its multifactorial etiology. The inflammatory response through TNFα activation of the NFκB pathway is a proposed mechanism of preterm birth. TNFα can also be found in cervicovaginal fluid (CVF) in women who deliver preterm. We have demonstrated that cytokine profiles vary by obstetric history. The goal of our study was to examine CVF TNFα as a predictor of PTB in women discriminated by obstetric history.

Study Design:
This was a secondary analysis of a longitudinal multicenter study of women with singleton gestations. Maternal CVF specimens were collected in the first (5w0d-13w6d) and second (14w0d-26w6d) trimester and assayed for cytokine concentrations (IL-1a, IL-1b, IL-6, IL-8, IL-10, TNFα, CRP and MMP-8) using a multiplex beadlyte assay on a Luminex IS-100. Women were grouped by obstetric history: nulliparous, multiparous with history of PTB and multiparous without history of PTB. Women were followed throughout pregnancy and outcomes were obtained by medical record review. ROC analysis was used to determine an optimal cutpoint, chosen to maximize the Youden's distance and minimize the distance to the perfect (0,1), in predicting PTB.

Results:
Analysis included 217 women: 102 nulliparas (47%), 46 (21%) multiparous with a history of PTB, and 69 (32%) multiparous without history of PTB. Thirteen (28%) of those with a history of PTB had a recurrent PTB. Only TNF-α was found to be a potentially useful predictor of PTB and only in the subpopulation of women with a history of PTB. A ROC curve for women with history of PTB (Figure 1) was constructed and the cutpoint maximizing the Youden's index was 0.82 pg/ml; yielding a sensitivity of 92% and specificity of 63%. A ROC curve for women without a history of PTB was constructed for comparison (Figure 2).

Conclusion: (276)
CVF TNFα can be used as a predictor of PTB in women with a history of PTB. A proposed cutpoint for CVF TNFα could be 0.82 pg/ml with a sensitivity of 92% and specificity of 63%. A large validation study is warranted to assess the value of this biomarker in this subpopulation.

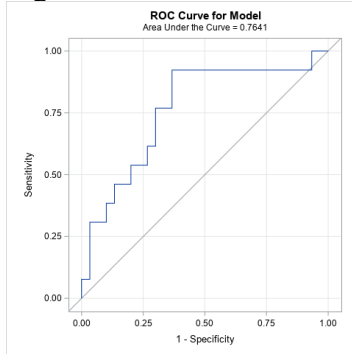Figure 1: ROC Curve for CVF TNFα in Multiparous Women with History of PTB

Figure 2: ROC Curve for CVF TNFα in Multiparous Women without History of PTB