What is the cervical length measurement in pregnant women that best determines the risk for preterm birth?

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Introduction

We previously demonstrated associations between cervical length ≤25 mm and decreased vaginal fluid concentration of D-lactic acid and elevated TIMP1. Furthermore, low vaginal D-lactic acid and high TIMP-1 were surrogate biomarkers for the absence of Lactobacillus crispatus-dominance, and the presence of a Gardnerella vaginalis or Lactobacillus iners-dominated vaginal microbiota. We assessed whether these biomarker levels in pregnant women with a cervical length of ≤30 mm would be comparable to cervical length < 25 mm.

Methods

Cervical length was measured by vaginal ultrasound in 593 women at 18-24 weeks gestation. 83 with cervical length of ≤25 mm (G1); 76 with cervix >25 mm and ≤30 mm (G2) and 434 with cervical length >30 mm (G3). The vaginal microbiome composition was measured by amplification and analysis of the V1-V3 region of the gene coding for bacterial 16S ribosomal RNA. The concentrations of D-lactic acid and TIMP-1 in vaginal fluid were determined by ELISA. Women with cervix ≤25 mm were treated with vaginal progesterone and pessary. Antibiotics were prescribed when associated with sludge in amniotic fluid. Multiple comparisons between groups were evaluated by the Mann-Whitney test.

Results

We observed loss of L. crispatus dominance in Group 1 while the Group 2 exhibited a transitional bacterial profile between G1 and G3. Only G. vaginalis showed significant difference when compared the numerical bacterial dominance between groups (p = 0.041). The median (25%-75%) of TIMP-1 (ng/ml) was 2.8 (0.9-6.5); 1.8 (0.5-8.7); 1.1 (0.3-4.5) for G1, G2 in G3 respectively. The comparison between groups showed G1 vs G2, p = 0.768; G1 vs. G3 p = 0.003; G2 vs. G3, p = 0.020. The D-lactic acid (mM) concentration was 0.20 (0.04-1.32); 0.90 (0.09-1.94); 0.80 (0.12-2.43) for G1, G2 and G3 respectively and the comparison between G1 vs. G2, p = 0.024; G1 vs. G3, p < 0.01; G2 vs. G3, p = 0.449.

The spontaneous preterm birth rate was 13.6, 15.8, 6.0 in G1, G2 and G3 respectively. The Group 3 was significant difference compared with G1 and G2 (p = 0.019; p = 0.003).

Conclusion

The cervical length ≤30 mm, instead of ≤25 mm identified additional women at risk for preterm birth due to higher vaginal concentration of TIMP1 and lower of D-lactic acid associated with a shift of vaginal microbiome toward the increasing L. iners and G. vaginalis compared with women with cervical length higher than 30 mm.

Women with cervical length >25 mm and ≤30 mm showed a transitional vaginal environment associated with increase spontaneous preterm birth rate and therefore should be followed carefully and eventually treated.