TITLE: DEFINING RISK MICROBIAL BIOMARKERS FOR EARLY DIAGNOSIS OF PRETERM BIRTH

AUTHORS: FREITAS, A.S.; DOBBLER, P.C.T.; TAKAGAKI, B.M.; ROESCH, L.F.W.

INSTITUTION: UNIVERSIDADE FEDERAL DO PAMPA, CAMPUS SÃO GABRIEL, RS (AV. ANTONIO TRILHA, 1847 – SÃO CLEMENTE, CEP 97300-000, São Gabriel – RS, BRAZIL)

ABSTRACT:

Preterm birth is the main cause of infant mortality before 4 weeks of life and the second largest cause of mortality until five years of age. Epidemiological and clinical natures of preterm birth are not yet fully understood but with the advance of knowledge and new molecular biology techniques microbial communities also gained prominence in the study of the etiology of various diseases including premature birth. This work aimed to establish relationships between the vaginal microbial community and the incidence of preterm delivery in pregnant women from southern Brazil. The study was carried out at the Hospital de Clínicas de Porto Alegre. A total of 72 vaginal swab samples were collected from mothers recruited during hospital admission for delivery. Among them, 23 delivered preterm babies (average gestational age (AGA) = 30.7 weeks) and 29 delivered term babies (AGA = 39.6). Another group of 20 mothers who had preterm delivery with no onset of labor were used as additional control group (AGA = 29.2) aiming at evaluating the effect of gestational time as possible confounder. The 16S rRNA gene (V4 region) was amplified and sequenced by using Next Generation Sequencing. Sequences were processed using the pipeline from the Brazilian Microbiome Project and library comparisons were performed using the phyloseq package in R and the online tools MicrobiomeAnalyst and BugBase. Permanova analyses didn't show any changes in vaginal microbiota during the last ten weeks of gestation. No significant difference between treatments was found in alpha and beta diversity analyses. Thirty-two different phyla were found in both groups. *Firmicutes* was present in lower abundance in preterm samples ($p < 0.05$), whereas *Bacteroidetes* and *Tenericutes* were increased in preterm samples. In a general way, metagenome prediction showed a higher presence of gram-positive in term samples, whereas gram-negatives were most increased in preterm. Random Forest analyses have shown *Peptoniphilus*, *Porphyromonas* and *Ureaplasma* as the best genera for identification of preterm birth when in high abundance. Besides, low levels of *Aerococcus* also have appeared as biomarkers of preterm birth. Based on this data, we can conclude that there are many differences between vaginal microbiota structure of pregnant women who had term and preterm delivery and it was possible to establish biomarkers for early diagnosis of prematurity.

Keywords: biomarkers, preterm birth, ribosomal 16S, vaginal microbiota.

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