OBJECTIVE: SARS-CoV-2 infection triggers a significant maternal inflammatory response. There is a dearth of data regarding whether maternal SARS-CoV-2 infection or SARS-CoV-2 vaccination triggers an inflammatory response in the fetus. Fetal Inflammatory Response Syndrome (FIRS) has been described in other clinical conditions such as intraamniotic infection and has been defined as a cord blood Interleukin-6 (IL-6) level > 11 pg/mL. The objective of the study is to evaluate IL-6 levels in the cord blood of three delivering women: SARS-CoV-2 infection group, SARS-CoV-2 vaccinated group, and a control group.

STUDY DESIGN: A prospective case control study of a total of 61 pregnant women who presented for delivery at William Beaumont Hospital, Royal Oak, MI. All patients were tested for SARS-CoV-2 infection by polymerase chain reaction test (PCR). Three groups were evaluated: 22 pregnant women with positive SARS-CoV-2 PCR test (case group), 23 Pregnant women with negative SARS-CoV-2 PCR test (control group), and 16 pregnant women who had recent SARS-CoV-2 vaccination and a negative SARS-CoV-2 PCR test. At delivery, cord blood was collected for IL-6 levels.

RESULTS: IL-6 level (mean +/- SEM) was for the case group: 8.99 +/- 3.33 pg/ml, control group: 5.19 +/- 0.76 pg/ml, and vaccine group: 7.11 +/- 2.47 pg/ml. There was no statistical difference between the three groups with ANOVA p-value 0.51. Pairwise comparison also revealed no statistical difference with p-values for case versus control, case versus vaccine, and control versus vaccine being 0.52, 0.85, and 0.84 respectively.

CONCLUSION: IL-6, the most sensitive measure of inflammation in obstetric practice, did not identify increased inflammation in PCR negative newborns of vaccinated or SARS-CoV-2 infected mothers. Evaluation using other markers of possible intrauterine inflammation is warranted.

35 What is the optimal timing of maternal SARS-CoV-2 mRNA immunization to maximize transplacental antibody transfer?

Amihai Rottenstreich, Gila Zarib, Esther Oiknine-Djian, Olesya Vorontsov, Roy Zigron, Geffen Klein stern, Dana Wolf, Shay Porat
Hadassah Medical Center, Jerusalem, Israel

OBJECTIVE: We aimed to assess the optimal timing of maternal SARS-CoV-2 vaccination to maximize transplacental transfer and neonatal levels of SARS-CoV-2 antibodies.

STUDY DESIGN: Maternal and cord blood sera were collected following delivery after antenatal SARS-CoV-2 BNT162b2 mRNA vaccination. SARS-CoV-2 spike protein (S) and receptor binding domain (RBD)-specific, IgG levels and neutralizing potency were evaluated in maternal and cord blood samples.

RESULTS: The study cohort consisted of 228 parturients (median age, 31 years; median gestational age, 39.7 weeks): 57 (25.0%) immunized at second trimester (1st dose at 19-26 weeks), 83 (36.4%) immunized at early 3rd trimester (1st dose at 27-31 weeks), and 88 (38.6%) immunized at late 3rd trimester (1st dose at 32-36 weeks). All mother-infant paired sera were positive for anti-S- and anti-RBD-specific IgG. Anti-RBD-specific IgG concentrations in neonatal sera were higher following early 3rd trimester vaccination (median 9620 AU/mL) as compared to second (3970 AU/mL) and late 3rd trimester vaccination (6697 AU/mL) (P<0.001). The median placental transfer ratios of anti-S and anti-RBD specific IgG were increased following early 3rd (anti-S ratio:1.3, anti-RBD-specific ratio:2.3) and second trimester vaccination (anti-S ratio:1.5, anti-RBD-specific ratio:2.8) versus late 3rd trimester immunization (anti-S ratio:0.9, anti-RBD-specific ratio:0.7) P<0.001.

CONCLUSION: Early 3rd trimester as compared to second trimester and late 3rd trimester maternal SARS-CoV-2 immunization enhances transplacental antibody transfer and increased neonatal antibody levels. Our findings highlight that vaccination of pregnant women early in the third trimester may optimize neonatal seroprotection.

36 Assessment of SARS-CoV-2 serostatus and hypertensive disorders of pregnancy

Jourdan E. Triebwasser1, Miren B. Dhudasia2, Sagori Mukhopadhyay3, Dustin Flannery2, Madeline Pfeifer2, Emily Woodford2, Sigrid Gouma3, Scott Hensley3, Karen Puopolo3
1Perelman School of Medicine, University of Pennsylvania, Division of Maternal-Fetal Medicine, Philadelphia, PA, 2Children’s Hospital of Philadelphia, Division of Neonatology, Philadelphia, PA, 3Perelman School of Medicine, University of Pennsylvania, Department of Microbiology, Philadelphia, PA

OBJECTIVE: COVID-19 has been associated with hypertensive disorders of pregnancy (HDP). PCR testing underestimates the prevalence of exposure to SARS-CoV-2. We tested the hypothesis that exposure to SARS-CoV-2 increases the risk of HDP, using SARS-CoV-2 antibodies as well as PCR testing as evidence of infection.

STUDY DESIGN: This was a prospective cohort study of pregnant patients delivering at 2 urban tertiary care centers between 4/2020 and 12/2020. Seropositivity was defined as having SARS-CoV-2 antibodies (IgG, IgM, or both) using a previously validated ELISA. We also assessed COVID-19 infection by nasopharyngeal PCR tests performed clinically 1) for delivery admission (universal testing) and 2) anytime during pregnancy but >10 days prior to delivery admission. The primary outcome was HDP determined using previously validated diagnostic codes from medical charts. Chi-squared and rank-sum analyses were performed and p<0.05 was considered statistically significant.

RESULTS: Of 6680 deliveries, serology testing was performed on 6192 (92.7%), and 568 (9.2%) were seropositive. Compared to the seronegative group, the seropositive group was younger (Table, p<0.001), less likely to be non-Hispanic White (p<0.001), had higher gravidity (p<0.001), and had higher pre-pregnancy BMI (p<0.001). There were no differences in diabetes (p=0.93) or chronic hypertension (cHTN, p=0.45). There was no difference in incidence of HDP by seropositivity (147 [25.9%] vs. 1433 [25.5%], p=0.83), nor were there differences between groups in cHTN with superimposed preeclampsia (PEC) or PEC with severe features (Figure). 5856 (94.6%) had COVID-19 testing at delivery admission and 693 (11.2%) had COVID-19 testing during pregnancy. Positive PCR test at the time of delivery was not associated with HDP (32.2% vs. 25.5%, p=0.06) nor was testing during pregnancy (20.7% vs. 27.3%, p=0.18). Severity of HDP was not associated with COVID-19 infection by PCR at delivery (p=0.65) or PCR during pregnancy (p=0.52).

CONCLUSION: In a cohort with high incidence of HDP, we found no association between COVID-19 infection and HDP.
37 Gardnerella vaginalis induces matrix metalloproteinases in the cervicovaginal epithelium through TLR-2 activation

Kristin D. Gerson1, Lauren Anton1, Briana Ferguson2, Michal A. Elovitz2
1Hospital of the University of Pennsylvania, Philadelphia, PA, 2University of Pennsylvania, Philadelphia, PA

OBJECTIVE: Lactobacillus-deficient cervicovaginal (CV) microbial communities, as well as select anaerobes like Gardnerella vaginalis (GV), have been associated with adverse reproductive outcomes, including spontaneous preterm birth (sPTB). Mechanisms by which microbes drive these outcomes are not fully elucidated. As a gram-variable bacterium, GV peptidoglycan cell wall can activate TLR-2. We previously showed that high MMP-9 in CV fluid in pregnancy is associated with an anaerobic-rich CV microbiota, short cervix, and sPTB. We posit that GV induces MMPs in CV epithelial cells through TLR-2, which degrades the epithelial barrier leading to premature cervical remodeling and sPTB.

STUDY DESIGN: Ectocervical (ECTO), endocervical (ENDO), and vaginal (VK2) cells were treated with 10^5±0.5 CFUs live GV or Lactobacillus crispus (LC), a healthy CV bacteria, for 24 hours. For TLR-2 experiments, cells were pretreated with TLR-2 blocking antibody. An MMP Luminex panel was run on cell media for three biologic and two technical replicates per condition. Data were analyzed with a five-parameter logistic curve. One-way ANOVAs with Dunnet’s multiple comparisons tests were used.

RESULTS: GV induced MMP-1 in ENDO cells (p=0.01) and MMP-9 in ECTO, ENDO, and VK2 cells (p<0.001 for all) compared to non-treated controls. LC did not induce any MMPs compared to non-treated controls (Fig. 1). Epithelial cell specific effects were noted for MMP-9 with VK2 cells expressing increased levels compared to cervical cells (p<0.0001, Fig. 1). MMP-9 was selected for TLR-2 blocking experiments given induction in all cell lines after GV treatment. TLR-2 blockade mitigated GV induction of MMP-9 in cervical and VK2 cell lines (Fig. 2).

CONCLUSION: A common anaerobic microbe implicated in several adverse reproductive outcomes, including sPTB, can induce MMPs in the CV space. Uregulation of MMP-9 by GV occurs in a TLR-2 dependent fashion. These findings unveil mechanisms by which CV microbes influence host immune response and may compromise epithelial barrier integrity and promote cervical remodeling. SMFM/AAOGF (KG); 1R01HD102318, 5R01HD098867 (ME)