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Does maternal SARS-CoV-2 infection or SARS-CoV-2 vaccination trigger an inflammatory response in the fetus?

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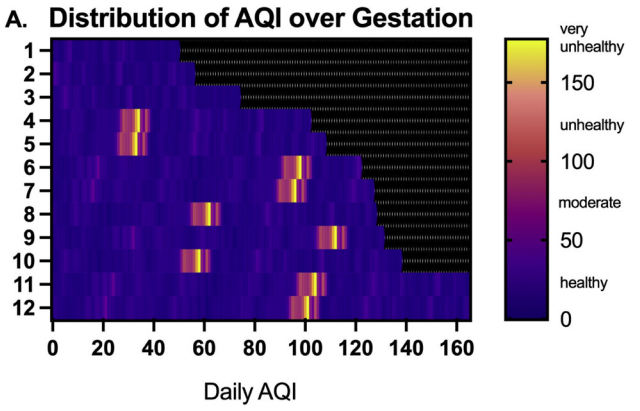

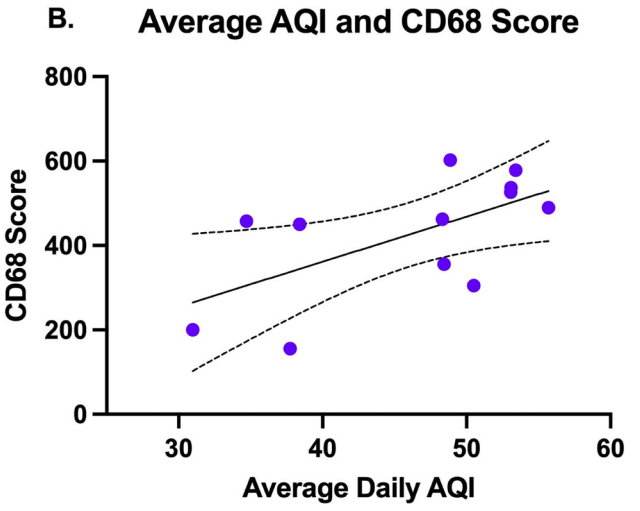

33 Risk-based care management implementation reduces preterm birth disparities in North Carolina

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OBJECTIVE: In 2011, NC Medicaid implemented the Pregnancy Medical Home (PMH) program that includes risk-based care management to improve birth outcomes. The objective of this study is to determine if intensive pregnancy care management for the highest risk pregnant people is associated with a reduction in PTB.

STUDY DESIGN: This was a retrospective quasi-experimental observational study, 1/2016-12/2017. We included pregnant people with Medicaid who were categorized as highest risk per a "Maternal-Infant Impactability Score" (MIIS). In 2017, the MIIS was created and validated using PMH historical data to identify people most likely to benefit from intensive care management and was implemented to guide care management resources. This highest risk cohort had ≥3 priority risk factors: prior spontaneous PTB, hypertension, smoking, substance abuse, mental health disorder, domestic violence, housing instability, and food insecurity. Intensive care management was defined as greater than 5 face-to-face encounters. The PTB rate (< 37 weeks' gestation) was compared by (a) receipt of intensive pregnancy care management; (b)year of pregnancy − 2016 (year prior to implementation of the MIIS) versus 2017 (year after implementation of the MIIS) and stratified by race.

RESULTS: 3,565 pregnant people were included (Table 1). The PTB rate was 18.3%. Intensive pregnancy care management as compared to no intensive care management was associated with lower PTB rates among Black and White pregnant people (Black: 16.9% vs. 26.0%, p< 0.0001; White: 12.3% vs. 17.8%, p< 0.001). PTB rate was significantly lower in the year following implementation of the MIIS as compared to the year prior for Black pregnant people (20.1 vs. 24.4%, p< 0.05), but not for White pregnant people (15.5% vs. 15.6%).

CONCLUSION: Intensive pregnancy care management is associated with lower rates of PTB for Black and White pregnant people. Focusing care management resources on those most likely to benefit is a promising strategy to reduce PTB rates and associated disparities.

Table 1. Demographic Characteristics of Pregnant People with Medicaid who participate the Pregnancy Medical Home in NC, 2016-2017

Characteristics	Black	White	Total
N	1536	2029	3565
Nulliparous	18%	21%	20%
Average Age of Mother	27.9	27.4	27.6
High School diploma or higher	68%	65%	66%
Food Insecurity	26%	26%	26%
Unstable housing	13%	8%	10%
Intimate Partner Violence	37%	37%	37%
Mental Health Condition	66%	79%	73%
Drug or Alcohol Use (past and present)	85%	85%	85%
Smoking	60%	74%	68%
Hypertension	55%	43%	48%
History of Spontaneous Preterm Birth	25%	22%	23%
Average Number of Risk Factors	3.7	3.7	3.7

Table 2. PTB Outcomes Among Black and White Pregnant People who Participate in the Pregnancy Medical Home: Results from Two Different Methodologies

(a) PTB rates by receipt of intensive pregnancy care management					
Race	Intensive Pregnancy Care management	N	Mean number of risk factors	PTB Rate	p-value
Black	No	861	3.65	26.0%	<.0001
	Yes	675	3.70	16.9%	
White	No	1,183	3.74	17.8%	<.001
	Yes	846	3.75	12.3%	
(b) 2016 (year prior to MIIS) vs. 2017 (year of MIIS implementation)					
Race	Year	N	Mean number of risk factors	PTB Rate	p-value
Black	2016	679	3.66	24.4%	<.05
	2017	857	3.67	20.1%	
White	2016	945	3.74	15.6%	0.97
	2017	1,084	3.74	15.5%	

34 Does maternal SARS-CoV-2 infection or SARS-CoV-2 vaccination trigger an inflammatory response in the fetus?

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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 SAR-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 optinal timing of maternal SARS-CoV-2 mRNA immunization to maximize transplacental antibody transfer?

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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 term 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

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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.