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Title: Effects of in utero exposure to SARS-CoV-2 on incidence of wheezing in the first 6 months of life

Study Purpose and Rationale

The COVID-19 pandemic has presented the healthcare system with unique challenges and raised several questions, including what impact exposure to SARS-CoV-2 has on pregnant women and their babies. To better understand these questions, the COMBO (COVID-19 Mother Baby Outcomes) project was created to determine the impact of both SARS-CoV-2 infections and the pandemic on mothers and babies.

While SARS-CoV2 has been shown not to infect babies via vertical transmission, it has been shown that maternal immune activation in response to viral infection can impact fetal brain development. It has been postulated that similar inflammatory or immune activation processes could impact respiratory system development. As the newest generation of babies are born to mothers with SARS-CoV-2 infection during pregnancy, it is crucial that we better understand potential short- and long-term impacts of in-utero exposure on children.

It has been shown that neonates exposed to SARS-CoV-2 in utero had higher rates of respiratory symptoms in the neonatal period, including higher rates of assisted ventilation at birth, intubation at birth, NICU admission, respiratory distress syndrome, mechanical ventilation, and persistent pulmonary hypertension.

We seek to follow infants exposed to SARS-CoV-2 in utero to determine if the exposure increases their propensity for wheezing in later infancy.

Study Design

Data will be collected by chart review of patients enrolled in the study and questionnaires.

Parents will be invited to complete surveys at 4 and 6 months of age. Parents will be compensated for survey completion. Survey questions include:

- 1) Since birth, has your child's chest ever made a wheezing or whistling sound?
If yes, parents will be asked to complete additional questions:
 - i. Since birth, how many illnesses has your child had that have been associated with wheezing or whistling in his/her chest? Number of illnesses:
 - ii. During how many of these illnesses did your child also have difficulty breathing? Number of illnesses:
 - iii. In the last 14 days, how many days has your child had wheezing or whistling in his/her chest?
 - iv. Number of days: Since birth, has your child wheezed when he/she did not have a cold?
 - v. Since birth, has a health care provider said that your child was wheezing?
 - vi. Have you given your child any medicine for the wheezing since birth? Please include prescribed, over-the-counter, or medications belonging to someone else.
- 2) Has your baby been diagnosed with COVID-19? Please specify if yes:

In the survey distributed at 6 months old, additional socioeconomic questions will be included in the questionnaire:

- 1) What is the highest level of education that you have completed?
- 2) How would you describe your ethnicity?
- 3) What is your race? Please select all that apply. Please select other if you do not identify with any of these. If other, please describe here:
- 4) During the LAST year, what was the total income of your household from all sources before taxes and other deductions? Your best guess is fine. (NOTE: this is confidential information and your name is not connected to this data).

Subject Selection

All women who gave birth at CHONY/Allen with documented history of SARS-CoV-2 infection at any time during pregnancy were contacted 2 weeks-6 months postpartum and invited to participate in study. For each mother with a history of SARS-CoV-2 infection, a mother without exposure and with baby of same sex, gestational age, mode of delivery, and approximate DOB is enrolled in the COMBO project. All subjects enrolled in the COMBO project will be invited to complete surveys about wheezing at the 4 and 6 month visit.

Statistical Procedures

Data will be categorical based on whether or not the child wheezed. Categorical data will be analyzed by chi square test. Exposure matching will be used to control for other factors that have been identified to be associated with increased risk of wheezing. Power analysis will be conducted using a p value of <0.05 for statistical significance and 80% power.

Study procedure

None.

Study Drugs

None.

Medical Device

None.

Potential Risks

Minimal risk to subjects.

Potential Benefits

Understanding possible sequelae of in utero exposure to SARS-CoV-2.

Limitations

The primary limitation of this study is that wheezing will be determined by parental report rather than healthcare providers' auscultation. Additionally, as with all studies conducted by parent report, the study may be limited by recall bias.

References

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