#### NICHD **NEONATAL RESEARCH NETWORK**

# Impact of Maternal COVID-19 on **Outcomes of Extremely Preterm Infants in** the Neonatal Intensive Care Unit

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#### Speaker: Emily A. Messick, DO

- I have no financial relationship to disclose or conflict of interest to resolve.
- This presentation will not involve discussion of unapproved or off-label, experimental or investigational use of a drug.

# **COVID-19 During Pregnancy**

- COVID-19 during pregnancy is associated with preterm birth and stillbirth
- In term neonates, clinical manifestations of COVID-19 vary widely:
  - Asymptomatic infection
  - Fever, cough, hypoxemia, respiratory distress or pneumonia
  - GI symptoms (feeding difficulties, diarrhea, emesis)
  - Rare: Disseminated intravascular coagulation, neurological manifestations, multisystem inflammatory syndrome, death
- Less is known about vertical transmission and NICU outcomes in extremely preterm infants exposed to maternal SARS-CoV-2 infection during gestation



- To determine the prevalence of SARS-CoV-2 detection among mothers who delivered preterm infants <29 weeks' gestation
- 2) To determine the rate of vertical transmission
- 3) To describe possible association(s) of maternal COVID-19 infection during pregnancy with adverse NICU outcomes

## Methods

- Prospective observational study: 3/1/2020 5/31/2022
- 15 centers of the NICHD Neonatal Research Network
- Inborn infants: birth weight 401-1000 grams and/or
  <29 weeks' gestation</li>
- Born to mothers tested for SARS-CoV-2 during pregnancy
- Maternal and infant testing for SARS-CoV-2 was performed per center's infection prevention policy

## Methods

- Pertinent maternal and infant demographic, clinical, laboratory, and NICU outcome data were recorded
- Infant outcomes were compared between infants born to mothers with and without SARS-CoV-2 infection during pregnancy
- Data analyzed using nonparametric Kruskal-Wallis test for continuous outcomes and Chi-square/Fisher's Exact test for categorical outcomes

#### Results



# **Results: Reason for Maternal COVID Testing**

- 3252 mothers tested
  for SARS-CoV-2 at a
  mean (±SD) of 25 (±37)
  days before delivery
- 47% tested at delivery

|                              | Maternal SARS-CoV-2 |      |  |
|------------------------------|---------------------|------|--|
|                              | Infection           |      |  |
|                              | Yes                 | No   |  |
| No. of mothers               | 230 (7%)            | 3022 |  |
| <b>Reason for testing:</b> * |                     |      |  |
| Screening                    | 62%                 | 95%  |  |
| Symptomatic                  | 34%                 | 3%   |  |
| Exposure                     | 4%                  | 1%   |  |
| Other                        | <1%                 | <1%  |  |

\*22 (<1%), not known

## **Results: Reason for Infant COVID Testing**

|                           | Maternal SARS-CoV-2 Infection |             |  |
|---------------------------|-------------------------------|-------------|--|
|                           | Yes (n=230)                   | No (n=3022) |  |
| No. of infants            | 257 (7%)                      | 3362 (93%)  |  |
| No. of infants tested     | 141 (55%)                     | 979 (29%)   |  |
| Reason for testing:       |                               |             |  |
| Mother suspect/has COVID  | 62%                           | 8%          |  |
| Exposure (other than mom) | 4%                            | 13%         |  |
| Clinical signs/symptoms   | 13%                           | 29%         |  |
| Screening                 | 20%                           | 50%         |  |
| Other                     | 1%                            | 1%          |  |

### **Results: Maternal Characteristics**

|                                  | Maternal SARS-CoV-2 Infection |                     | n-value |
|----------------------------------|-------------------------------|---------------------|---------|
|                                  | Yes (n=230)                   | No (n=3022)         | p-value |
| Age (years; median, IQR)         | 30 (25 <i>,</i> 34)           | 29 (25 <i>,</i> 34) | 0.94    |
| Race:                            |                               |                     | 0.27    |
| Black                            | 39%                           | 39%                 |         |
| White                            | 45%                           | 49%                 |         |
| American Indian/Alaska Native    | 1%                            | 1%                  |         |
| Asian                            | 2%                            | 4%                  |         |
| Native Hawaiian/Pacific Islander | 1%                            | 1%                  |         |
| Ethnicity:                       |                               |                     | <0.01   |
| Hispanic                         | 23%                           | 18%                 |         |
| Not Hispanic                     | 73%                           | 80%                 |         |

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#### **Results: Maternal Characteristics**

|                           | Maternal SARS-CoV-2<br>Infection |             | p-value |
|---------------------------|----------------------------------|-------------|---------|
|                           | Yes (n=230)                      | No (n=3022) |         |
| Multiple gestation        | 11%                              | 15%         | 0.11    |
| Diabetes before pregnancy | 7%                               | 5%          | 0.35    |
| Diabetes during pregnancy | 6%                               | 6%          | 0.99    |
| Pre-eclampsia             | 43%                              | 38%         | 0.16    |
| Magnesium sulfate         | 86%                              | 84%         | 0.34    |
| Antenatal steroids        | 89%                              | 89%         | 0.96    |

#### **Results: Maternal Characteristics**

|                                  | Maternal SARS-CoV-2<br>Infection |             | p-value |
|----------------------------------|----------------------------------|-------------|---------|
|                                  | Yes (n=230)                      | No (n=3022) |         |
| Preterm premature ROM            | 35%                              | 46%         | <0.01   |
| Prolonged ROM ( $\geq$ 18 hours) | 19%                              | 28%         | <0.01   |
| Histologic chorioamnionitis      | 34%                              | 45%         | <0.01   |
| Clinical chorioamnionitis        | 12%                              | 16%         | 0.15    |
| C-Section                        | 70%                              | 68%         | 0.48    |

### **Results: Neonatal Infection and Vertical Transmission**

|                       | Maternal SARS-CoV-2 Infection |             |  |
|-----------------------|-------------------------------|-------------|--|
|                       | Yes (n=230)                   | No (n=3022) |  |
| No. of infants        | 257                           | 3362        |  |
| No. of infants tested | 141 (55%)                     | 979 (29%)   |  |
| Infant SARS-CoV-2:    |                               |             |  |
| Positive:             | 2 (1.4%)                      | 5 (0.5%)    |  |
| ≤ 72 hours            | 2                             | 1           |  |
| >72 hours             | 0                             | 4           |  |
| Negative              | 99%                           | 99%         |  |

#### **Vertical Transmission Rate: 1.4%**

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### **Results: Infant Characteristics**

|                                   | Maternal SARS-CoV-2 Infection |             |         |
|-----------------------------------|-------------------------------|-------------|---------|
|                                   | Yes (n=230)                   | No (n=3022) | p-value |
| No. of infants                    | 257                           | 3362        |         |
| Gestational age (wk; median, IQR) | 27 (24, 28)                   | 26 (24, 28) | 0.10    |
| Birth weight (g; median)          | 830                           | 810         | 0.30    |
| APGAR, 1 min (median)             | 4                             | 4           | 0.53    |
| APGAR, 5 min (median)             | 7                             | 7           | 0.24    |
| Head circumference (cm; median)   | 24                            | 23.5        | 0.09    |
| Small for gestational age         | 20%                           | 18%         | 0.47    |

### **Results: Infant Outcomes**

|                     | Maternal SARS-CoV-2 Infection |             | p-value |
|---------------------|-------------------------------|-------------|---------|
|                     | Yes (n=230)                   | No (n=3022) |         |
| No. of infants      | 257                           | 3362        |         |
| IVH (Gr III/IV)     | 14%                           | 14%         | 0.82    |
| Seizures            | 2%                            | 1%          | 0.56    |
| Early-onset sepsis  | 4%                            | 2%          | 0.34    |
| Antibiotics ≥5 days | 18%                           | 23%         | 0.17    |
| Late-onset sepsis   | 15%                           | 18%         | 0.28    |

## **Results: Infant Outcomes**

|                                | Maternal SARS-CoV-2<br>Infection |              | p-value |
|--------------------------------|----------------------------------|--------------|---------|
|                                | Yes (n=230)                      | No (n=3022)  |         |
| No. of infants                 | 257                              | 3362         |         |
| NEC                            | 15%                              | 11%          | 0.06    |
| BPD                            | 52%                              | 53%          | 0.76    |
| Any ROP                        | 57%                              | 61%          | 0.30    |
| Severe ROP (≥Stage 3)          | 16%                              | 13%          | 0.24    |
| NICU duration (d; median, IQR) | 80 (56, 118)                     | 87 (54, 120) | 0.46    |

## **Results: Infant Mortality**





- Among a large cohort of extremely preterm infants, the prevalence of maternal SARS-CoV-2 infection during pregnancy was 7%.
- The vertical transmission rate of SARS-CoV-2 was low at 1.4%.
- There was no identified association between maternal COVID-19 infection during pregnancy and adverse in-hospital infant outcomes.

## Neonatal Research Network Centers: 2016-2023

- Brown University
- Case Western Reserve University
- Cincinnati Children's Medical Center
- Duke University
- Emory University
- Nationwide Children's Hospital, The Ohio State University
- RTI International
- Stanford University

- University of Alabama at Birmingham
- University of Iowa
- University of New Mexico
- University of Pennsylvania
- University of Rochester
- University of Texas Southwestern
- University of Texas Health Science Center at Houston
- University of Utah

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#### **Questions?**



#### Abstract



#### NRN Abstracts

