COVID Illness in the Pregnant Mom: How Does it Affect the Fetus?

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Division of Pediatric Infectious Diseases
04/21/2022
Educational Objectives

(1) To provide general information on the biology and epidemiology of SARS-COV-2 infection in pregnancy and repercussions to the infant.

(2) To describe the status of the pandemic in pregnant women and infants and knowledge to date.

(3) To review main research questions pertaining to COVID-19 in pregnancy and perinatal/ neonatal COVID-exposure.

(4) To present work in progress and preliminary study results of the COMP Study at UCLA
Disclosure

• Neither I nor any member of my immediate family has a financial relationship or interest (currently or within the past 24 months) with any proprietary entity producing health care goods or services consumed by, or used on, patients related to the content of this CME activity.

• I do not intend to discuss an unapproved/investigative use of a commercial product/device.
Congenital infections

• Infections and illnesses in pregnancy are common.
• Pregnancy renders women more susceptible to:
  • CMV primary infection
  • HIV primary infection
  • Syphilis
• Or associated with worse outcomes in:
  • Influenza
  • Measles
  • Coccidiodomycosis
Introduction

Pregnant women face increased risk of infection due to:

1. Immunologic paradox of pregnancy
2. Physiologic changes in pregnancy
3. Gender dynamics that impact transmission

Mor et al. PMID: 28627518
Introduction
Pathogenesis of congenital infections

- Infected mother
  - Transplacental
  - Ascending infection/ ruptured membranes at delivery

- In utero- fetus/ infant
  - Acute death
  - Persistent infection
  - Recovery from infection
  - Late sequelae/ chronic illness

- Child
  - Late death
  - Recovery
Development of the fetal brain and gestational age of infection

1st trimester: 2nd trimester: 3rd trimester/peripartum:

• Rubella
• Zika
• CMV
• VZV
• CMV
• Toxo
• HIV
• HSV
• VZV
• CMV
• Toxoplasm
• T. pallidum

Screening for congenital infections recommended for:

• Infants who are small for gestational age (IUGR).
• Infants with high risk maternal history.
• All infants with congenital defects.

Infants who are small for gestational age (IUGR).
• Infants with high risk maternal history.
• All infants with congenital defects.
## Types of coronaviruses

### Table 1. History of Human Coronaviruses

<table>
<thead>
<tr>
<th>Coronavirus</th>
<th>Year(s) Identified</th>
<th>First Identification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alpha coronavirus: group 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCoV-229E</td>
<td>1960s</td>
<td>Boy with cold, United Kingdom: B814 isolate; medical students with colds, Chicago, Ill. 229E (note: B814 isolate described here not further propagated)</td>
</tr>
<tr>
<td>HCoV- NL63</td>
<td>2004</td>
<td>7-month-old and 8-month-old infants with bronchiolitis in the Netherlands</td>
</tr>
<tr>
<td><strong>Beta coronavirus group 2, lineage A</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCoV-OC43</td>
<td>1967–1972</td>
<td>Acute respiratory infections in adults at the National Institutes of Health</td>
</tr>
<tr>
<td>HCoV-HKU1</td>
<td>2004</td>
<td>71-year-old man with pneumonia in Hong Kong</td>
</tr>
<tr>
<td><strong>Beta coronavirus group 2, lineage B</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SARS-CoV</td>
<td>2003–2004</td>
<td>Humans with severe pneumonia in China; natural host, Chinese horseshoe bats; presumed intermediate host, palm civet</td>
</tr>
<tr>
<td>SARS-CoV-2</td>
<td>2019–2020</td>
<td>Adults with acute respiratory distress syndrome/pneumonia from Wuhan, China; potential bat origin and related to SARS-CoV</td>
</tr>
<tr>
<td><strong>Beta coronavirus group 2, lineage C</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle East respiratory syndrome-CoV</td>
<td>2012</td>
<td>Adults with acute respiratory distress syndrome in Saudi Arabia; dromedary camel as reservoir/intermediary</td>
</tr>
</tbody>
</table>

Abbreviations: HCoV, human coronavirus; SARS, severe acute respiratory syndrome.
Viral infections in Pregnancy

• During the 1918-1919 influenza pandemic
  - Higher mortality rates 5.7/1,000 vs 4.9/1,000
  - 50% higher chances of developing pneumonia
  - Higher rates of miscarriages and premature birth

• During the 2009 H1N1 influenza pandemic, pregnant women were disproportionately impacted and required high rates of ECMO
  - They represented 1% of the population; however, accounted for 5% of the deaths
Influenza in Pregnancy

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>pregnancy Events</th>
<th>pregnancy Total</th>
<th>no pregnancy Events</th>
<th>no pregnancy Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buda 2010</td>
<td>138</td>
<td>514</td>
<td>5933</td>
<td>120030</td>
<td>10.2%</td>
<td>7.06 [5.80, 8.59]</td>
</tr>
<tr>
<td>Echavarria 2010</td>
<td>1</td>
<td>5</td>
<td>77</td>
<td>270</td>
<td>5.0%</td>
<td>0.63 [0.07, 5.70]</td>
</tr>
<tr>
<td>Gilca 2011</td>
<td>10</td>
<td>20</td>
<td>157</td>
<td>367</td>
<td>8.8%</td>
<td>1.34 [0.54, 3.29]</td>
</tr>
<tr>
<td>Gonzales-Candelas 2011</td>
<td>46</td>
<td>102</td>
<td>653</td>
<td>1300</td>
<td>9.9%</td>
<td>0.81 [0.54, 1.22]</td>
</tr>
<tr>
<td>Harris 2010</td>
<td>9</td>
<td>14</td>
<td>22</td>
<td>79</td>
<td>7.9%</td>
<td>4.66 [1.41, 15.47]</td>
</tr>
<tr>
<td>Jamieson 2009</td>
<td>11</td>
<td>34</td>
<td>218</td>
<td>5435</td>
<td>9.2%</td>
<td>11.45 [5.51, 23.78]</td>
</tr>
<tr>
<td>Kwan-Gett 2009</td>
<td>4</td>
<td>11</td>
<td>66</td>
<td>554</td>
<td>7.7%</td>
<td>4.23 [1.20, 14.82]</td>
</tr>
<tr>
<td>Lenzi 2012a</td>
<td>162</td>
<td>352</td>
<td>884</td>
<td>2175</td>
<td>10.2%</td>
<td>1.25 [0.99, 1.56]</td>
</tr>
<tr>
<td>Orellano 2010</td>
<td>87</td>
<td>124</td>
<td>4171</td>
<td>6742</td>
<td>10.0%</td>
<td>1.45 [0.98, 2.14]</td>
</tr>
<tr>
<td>Poepli 2011</td>
<td>8</td>
<td>15</td>
<td>335</td>
<td>525</td>
<td>8.4%</td>
<td>0.65 [0.23, 1.82]</td>
</tr>
<tr>
<td>Poggensee 2010</td>
<td>25</td>
<td>160</td>
<td>527</td>
<td>16957</td>
<td>Not estimable</td>
<td></td>
</tr>
<tr>
<td>Sevencan 2011</td>
<td>12</td>
<td>18</td>
<td>11</td>
<td>59</td>
<td>7.9%</td>
<td>8.73 [2.68, 28.37]</td>
</tr>
<tr>
<td>Vasoo 2010</td>
<td>3</td>
<td>4</td>
<td>45</td>
<td>95</td>
<td>4.8%</td>
<td>3.33 [0.33, 33.20]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>1213</strong></td>
<td><strong>137631</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>491</strong></td>
<td><strong>12572</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 1.21; \chi^2 = 229.19$, df = 11 ($P < 0.000001$); $I^2 = 95$
Test for overall effect: $Z = 2.52$ ($P = 0.01$)

**Total (95% CI)**

<table>
<thead>
<tr>
<th></th>
<th>pregnancy Events</th>
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</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 1.21; \chi^2 = 229.19$, df = 11 ($P < 0.000001$); $I^2 = 95$
Test for overall effect: $Z = 2.52$ ($P = 0.01$)
Test for subgroup differences: Not applicable
Respiratory Pathogens in Pregnancy

Highly-pathogenic beta-coronaviruses: SARS-CoV-1 and MERS

SARS-CoV-1: 25% maternal mortality rate

MERS: 30% infant mortality rate

>50% rate of miscarriage in both

>80% rate of preterm birth in both
Pregnancy and SARS-CoV-2

- SARS-CoV-2 infection causes more severe disease in pregnant women compared to age-matched non pregnant women
  - Higher risk for hospitalizations and mechanical ventilation
  - Higher risk of mortality
  - Higher risk of preterm birth
- Maternal immune response to infection can have protective effects on neonatal health by transfer of COVID19 specific antibodies (IgG) trans-placentally
  - Infants are born with immunity
- Viral infections during perinatal and postnatal periods has a wide range in effects of fetal and neonatal development
  - Effects on developing fetal and neonatal brain and the development of the immune system
Estudos mostram fator de alto risco

À inflamagista do IESS Ana Luiza Oliveira como caso que os idosos que já não estão mais internados, possivelmente já não tem efetivo de vacinação. O professor dos jovens, muitos com consolidação, predominam nas UTIs e as gestantes estão entre eles. A situação de gravidade excessiva é mais grave e se envolve em gestantes do que em mulheres de outras faixas etárias. Já uma pesquisa do Centro de Controle e Prevenção (CDC) mostra 400 mil pessoas com coronavírus e 10% de mortes. A doença é de alta mortalidade e as pacientes estão entre os pacientes mais graves. A resistência à infeção e a recuperação são mais associadas à Covid-19 de casos leves, interrompidas e terapêuticas.

Temos perder meu filho, minha vida. Tudo o que via eram máscaras.

Agora os jovens predominam nas UTIs e as gestantes estão entre eles.

Na linha de frente, com a mão na barra.

Não há compreensão de que o coronavírus pode ser transmitido durante a infecção. Na inflamação, a infeção não pode ser feita, com consequências ainda incertos. Na linha de frente do tratamento de gestantes desde o início da pandemia, o laboratório e o estudo da infectologia estão se esforçando para entender a criança e o tratamento adequado.
Epidemiology

• 2-4% of the infected population have died

• Very contagious - transmitted via respiratory droplets, though it can be airborne in some circumstances.
  • 1 person can infect on average 2.0-2.5 individuals at a time. With the Delta strain estimates are 8 to 9 people infected by 1 individual.
  • Reproduction number of the virus can be decrease if appropriate measures are taken:
    • Masking, cancellation of social gatherings, stay-at-home policies, and universal symptom screenings.

• Pregnant women and neonates are 2 populations at risk for serious complications related to COVID19
  • Pregnancy allows for physiologic changes
  • Neonates have immature immune systems
Clinical Presentation, Diagnosis, Outcomes in Pregnant Women

- COVID19 may exacerbate comorbidities common to pregnancy which can lead to preterm birth

- Pregnant women infected with COVID19 need to be closely monitored

- COVID19 infection is not an indication for delivery.
Pregnant women may be at increased risk for severe illness from COVID-19 compared with non-pregnant women.

CDC.GOV

Pregnant women and their families should take steps to stay healthy and reduce their risk for getting COVID-19.

bit.ly/MMWR62520

MMWR
Epidemiology and High-Risk Groups

Data collected from standardized case reporting forms and via the voluntary National Notifiable Disease Surveillance System.

From January 22 – October 3, pregnancy data was available for 35.5% of all cases in women aged 15 – 44 (reproductive age).

Data available for 409,462 women in the US with PCR-confirmed SARS-CoV-2 infection. 23,434 were pregnant and 30% Latina.

Multivariate analysis by pregnancy status:

- ICU admission: adjusted RR 3.0 (2.6 – 3.4)
- Invasive ventilation: adjusted RR 2.9 (2.2 – 3.8)
- ECMO: adjusted RR 2.4 (1.4 – 5.0)
- Death: adjusted RR 1.7 (1.2 – 2.4)

Zambrano et al.
• 706 pregnant women with COVID-19 diagnosis and 1424 without this diagnosis.

• Women with COVID-19 at higher risk for:
  • Preeclampsia- eclampsia  RR 1.76  95% CI 1.27 – 2.43
  • Severe infections  RR 3.38  95%CI 1.63 – 7.01
  • ICU admission  RR 5.04  95% CI 3.13 - 8.10
  • Pre-term birth  RR 1.59  95%CI 1.30 – 1.94
  • Perinatal mortality/morbidity RR 2.14  95%CI 1.66 – 2.75

**CONCLUSIONS AND RELEVANCE** In this multinational cohort study, COVID-19 in pregnancy was associated with consistent and substantial increases in severe maternal morbidity and mortality and neonatal complications when pregnant women with and without COVID-19 diagnosis were compared. The findings should alert pregnant individuals and clinicians to implement strictly all the recommended COVID-19 preventive measures.
Clinical Presentation of Coronavirus Disease 2019 (COVID-19) in Pregnant and Recently Pregnant People

Yalda Afshar, MD, PhD, Stephanie L. Gaw, MD, PhD, Valerie J. Flaherman, MD, Brittany D. Chambers, PhD, MPH, Deborah Krakow, MD, Vincenzo Berghella, MD, Alireza A. Shamshirsaz, MD, Adeline A. Boatin, MD, MPH, Grace Aldrovandi, MD, Andrea Greiner, MD, Laura Riley, MD, W. John Boscardin, PhD, Denise J. Jamieson, MD, and Vanessa L. Jacoby, MD, MAS, on behalf of the Pregnancy CoRonavIrus Outcomes RegIsTrY (PRIORITY) Study

<table>
<thead>
<tr>
<th>Symptom</th>
<th>n (%)</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st symptom (check only 1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>118 (20)</td>
<td>17–23</td>
</tr>
<tr>
<td>Sore throat</td>
<td>95 (16)</td>
<td>13–19</td>
</tr>
<tr>
<td>Body aches</td>
<td>72 (12)</td>
<td>10–15</td>
</tr>
<tr>
<td>Fever</td>
<td>69 (12)</td>
<td>9–14</td>
</tr>
<tr>
<td>Headache</td>
<td>45 (8)</td>
<td>6–10</td>
</tr>
</tbody>
</table>
Maternal outcomes and risk factors for COVID-19 severity among pregnant women


Pregnant women may be at higher risk of severe complications associated with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which may lead to obstetrical complications. We performed a case control study comparing pregnant women with severe coronavirus disease 19 (cases) to pregnant women with a milder form (controls) enrolled in the COVI-Preg international registry cohort between March 24 and July 26, 2020. Risk factors for severity, obstetrical and
COVI-PREG
International COVID-19 and Pregnancy Registry

An international registry for emergent pathogens and pregnancy

1079 pregnant women enrolled

1033 pregnant women enrolled with available SARS-CoV-2 test result and maternal outcomes

526 with a positive SARS-CoV-2 RT-PCR test and maternal outcomes

92 with severe maternal outcomes

3 patients with ongoing pregnancy > 37 WG

2 patients with completed pregnancy > 42 WG and unreported outcomes

669 pregnant women with obstetrical outcomes

18 spontaneous abortions < 14 WG or legal voluntary termination of pregnancy

95 patients with ongoing pregnancy < 37 WG

26 patients with ongoing pregnancy > 37 WG

26 patients with completed pregnancy > 42 WG and unreported outcomes
### Obstetrical/Neonatal outcomes

#### Severe maternal outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n (%)</th>
<th>95% CI</th>
<th>No / Mild adverse maternal outcomes</th>
<th>n (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy outcomes &gt; 14 WG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Livebirth</td>
<td>75 (92.6)</td>
<td>84.6-97.2</td>
<td></td>
<td>658 (98.1)</td>
<td>96.7-99.0</td>
</tr>
<tr>
<td>Fetal loss &gt; 14 WG</td>
<td>6 (7.4)</td>
<td>2.8-15.4</td>
<td></td>
<td>13 (19.4)</td>
<td>10.4-32.9</td>
</tr>
<tr>
<td>Termination of pregnancy</td>
<td>1 (1.4)</td>
<td>0.0-6.7</td>
<td></td>
<td>2 (0.3)</td>
<td>0.0-1.1</td>
</tr>
<tr>
<td>Obstetrical outcomes among live births</td>
<td>75</td>
<td></td>
<td></td>
<td>658</td>
<td></td>
</tr>
<tr>
<td>GA at delivery (Weeks gestation)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median GA (IQR)</td>
<td>37 (34-38)</td>
<td>39 (38-40)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown GA at delivery</td>
<td>6 (8.0)</td>
<td>3.0-16.6</td>
<td></td>
<td>17 (25.8)</td>
<td>15.1-41.0</td>
</tr>
<tr>
<td>Obstetrical management</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All vaginal deliveries</td>
<td>22 (29.3)</td>
<td>19.4-41.0</td>
<td></td>
<td>447 (67.9)</td>
<td>64.2-71.5</td>
</tr>
<tr>
<td>Vaginal delivery after spontaneous onset of labour</td>
<td>10 (13.3)</td>
<td>6.6-23.2</td>
<td></td>
<td>280 (42.6)</td>
<td>38.7-46.4</td>
</tr>
<tr>
<td>Vaginal delivery after induction of labour</td>
<td>12 (16.0)</td>
<td>8.6-26.3</td>
<td></td>
<td>167 (25.4)</td>
<td>22.1-28.9</td>
</tr>
<tr>
<td>Caesarean sections – no (%)</td>
<td>53 (70.7)</td>
<td>59.0-80.6</td>
<td></td>
<td>203 (30.9)</td>
<td>27.3-34.5</td>
</tr>
<tr>
<td>Elective caesarean sections – no (%)</td>
<td>21 (28.0)</td>
<td>18.2-39.6</td>
<td></td>
<td>85 (12.9)</td>
<td>10.5-15.7</td>
</tr>
<tr>
<td>Emergency pre-labor caesarean sections – no (%)</td>
<td>12 (16.0)</td>
<td>8.6-26.3</td>
<td></td>
<td>16 (2.4)</td>
<td>1.4-39.2</td>
</tr>
<tr>
<td>In labour caesarean sections after induction</td>
<td>12 (16.0)</td>
<td>8.6-26.3</td>
<td></td>
<td>52 (7.9)</td>
<td>6.0-10.2</td>
</tr>
<tr>
<td>In labour caesarean sections after spontaneous</td>
<td>8 (10.7)</td>
<td>4.7-19.9</td>
<td></td>
<td>50 (7.6)</td>
<td>5.7-9.9</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0.0)</td>
<td>0.0-4.8</td>
<td></td>
<td>8 (1.2)</td>
<td>0.5-2.4</td>
</tr>
<tr>
<td>Preterm birth among pregnancy with exposure &lt; 37 WG</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All preterm birth &lt; 37 WG – no (%)</td>
<td>32 (62.7)</td>
<td>48.1-75.9</td>
<td></td>
<td>78 (35.9)</td>
<td>29.6-42.7</td>
</tr>
<tr>
<td>Iatrogenic birth among preterm birth – no (%)</td>
<td>26 (81.3)</td>
<td>63.6-92.8</td>
<td></td>
<td>49 (62.8)</td>
<td>51.1-73.5</td>
</tr>
<tr>
<td>Unknown – no (%)</td>
<td>0 (0.0)</td>
<td>0.0-10.9</td>
<td></td>
<td>1 (1.3)</td>
<td>0.0-6.9</td>
</tr>
<tr>
<td>Unknown GA at delivery</td>
<td>0 (0.0)</td>
<td>0.0-7.0</td>
<td></td>
<td>3 (1.4)</td>
<td>0.3-4.0</td>
</tr>
<tr>
<td>Preterm birth among pregnancy with exposure &lt; 34WG</td>
<td>27</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All preterm birth &lt; 34 WG – no (%)</td>
<td>14 (51.9)</td>
<td>31.9-71.3</td>
<td></td>
<td>24 (20.3)</td>
<td>13.5-28.7</td>
</tr>
<tr>
<td>Iatrogenic birth among preterm birth – no (%)</td>
<td>12 (85.7)</td>
<td>57.2-98.2</td>
<td></td>
<td>14 (58.3)</td>
<td>36.6-77.9</td>
</tr>
<tr>
<td>Unknown – no (%)</td>
<td>0 (0.0)</td>
<td>0.0-23.2</td>
<td></td>
<td>0 (0.0)</td>
<td>0.0-14.2</td>
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<tr>
<td>Unknown GA at delivery</td>
<td>0 (0.0)</td>
<td>0.0-12.8</td>
<td></td>
<td>2 (1.7)</td>
<td>0.2-6.0</td>
</tr>
</tbody>
</table>
The number of maternal deaths in 2 months due to COVID-19 in Brazil was 10% of the annual maternal death rate in the country.
<table>
<thead>
<tr>
<th>Prevalence of selected comorbidities</th>
<th>Recovery</th>
<th>Death</th>
<th>p-value$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>41</td>
<td>13</td>
<td>0.002</td>
</tr>
<tr>
<td>No</td>
<td>573</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Missing/Unknown (%)$^a$</td>
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Epidemiology and High-Risk Groups
Brazil reels from expectant mother tragedies

More infectious Covid variant and lack of adequate access to already stretched care take toll

MICHAEL POOLER AND CAROLINA PULICE
SÃO PAULO

Following two difficult pregnancies, it seemed it might be luckier for Vanessa de Oliveira Silveira. But in her 34th week of gestation, she began to feel unwell and developed a cough. A coronavirus test returned positive, and breathing became difficult.

“She said that she was afraid to die, of having a coronavirus (birth) and the baby not surviving,” said Douglas Silveiro, her husband. “Vanessa, 33, who died during an emergency operation to deliver her baby in March. Her death is one of hundreds of such tragedies to strike families in Brazil, leading to a mortality rate among new or soon-to-be mothers that has alarmed doctors and public health experts.

In total, more than 1,500 pregnant or post-partum women have succumbed since the start of the pandemic, said the Brazilian Obstetric Observatory.

“Before the pandemic began, we already had a maternal death rate of 5.3 for every 100,000 babies born alive, which is considered extremely high,” said Rossana Puçinelli Vieira Francisco, a professor at the University of São Paulo’s department of obstetrics and gynecology, who leads the research.

“It is not possible to say for sure that Brazil is where pregnant and post-partum women die the most by Covid, as there are not many population studies on death by Covid in these women,” added Francisco. “But we cannot say the numbers here are very high.”

Overall, maternal deaths in Brazil averaged 10 each week during 2020, according to the observatory. This year, that has quadrupled to above 46, as mortality in the population doubled.

Many explanations proposed echo those for the country’s wider virus disaster, which has already claimed more than a million lives. The death toll is the second-highest in absolute terms after the US, and seventh on a per capita basis, according to FT analysis. In the case of mothers to be, experts blame a strained healthcare system, inadequate and unequal provision of services, a lack of training in treating such patients

28

The pandemic exacerbated maternal mortality in Brazil

Pregnancies and post-partum deaths in Brazil

Source: Brazilian Obstetric Observatory

Recovered

Died

2020

2021

4,000

2,000

1,600

1,000

800

600

400

200

0

7.4% died

16.7% died

1.0% died

2.0% died

4.0% died

6.0% died

Source: Brazilian Obstetric Observatory

Pregnant women were more vulnerable … Black and poor women died more

‘Pregnant women were more vulnerable … Black and poor women died more,’ said Marcelo Otto, a doctor and coordinator at the Brazilian Society of Infectology.

Treatment involves finely balanced clinical decisions. Douglas Silveiro said: “One of the doctors told me they didn’t know why the caesarean didn’t happen earlier. If they had, it would have been more effective.”

Fabiana Aves Sousa, fromCeará state in the northeast, had an emergency caesarean at almost 30 weeks after contracting coronavirus. Her son is “full of health”, but she said: “There were several mothers with Covid. And many did not survive childbirth.”

Many health professionals cite a failure of public health policy as a factor.

Critics accuse the government of lax, even negligent, attitudes to the pandemic that has contributed to its spread.

Fears are rising about the Delta variant, too. About 74 per cent of Brazil’s population of 121m is fully immunised and health minister Marcelo Queiroga announced last week the resumption of jobs for some expectant and new mothers. “More than 2.5m women are expected to benefit,” he tweeted.
COVID-19 and pregnancy

Based on what we know at this time, pregnant people are at an increased risk for severe illness from COVID-19 compared to non-pregnant people. Additionally, pregnant people with COVID-19 might be at increased risk for other adverse outcomes, such as preterm birth.
Treatment

Remdesivir: recommended for pregnant women if they meet criteria otherwise, although excluded from trials

Dexamethasone: recommended for pregnant women who meet criteria (require supplemental oxygen or ventilatory support)

Convalescent Plasma: pregnant women were eligible in 2 clinical trials, good safety data

Monoclonal Antibodies: placental transfer may be expected
Vaccine
Pregnant women were excluded from the major vaccine trials (Pfizer, Moderna, AstraZeneca, Johnson & Johnson, Novavax)
CDC Recommends Pregnant Women Get Coronavirus Vaccine

The Centers for Disease Control and Prevention recommends that pregnant women get vaccinated against COVID-19, the agency’s director said Friday during a White House coronavirus briefing.

Previously, the CDC followed the guidance laid out by leading maternal health organizations that said pregnant women should be offered vaccines if they want one and providers should not withhold vaccines from them but should discuss available data. The CDC has said that evidence shows pregnant women are at higher risk of severe COVID-19 infection.

COVID-19 vaccines and neglected pregnancy

Pradip Dashraath, Karin Nielsen-Saines, Shabir A Madhi, *David Baud

www.thelancet.com Published online August 27, 2020

The development of an effective COVID-19 vaccine is a global health priority. Pregnant women, who are at increased risk of adverse outcomes from COVID-19, would be additionally harmed if they were unable to access evidence-based chemoprophylaxis from vaccine trials. WHO’s global commitment to fair access to COVID-19 vaccines should, therefore, include pregnant women. Accordingly, we advocate that pregnant women should be included in the phase 3 trial protocols of adenovirus-vectored vaccines and also protein-based vaccines (eg, NVX-
Can SARS-Cov-2 be transmitted from the mother to the newborn?

What are the short and long term neonatal outcomes?
• It is still unclear if the virus can be transmitted during pregnancy from mother to child.
• There are several reports of newborns who were found to be positive shortly after birth, but unclear if they were infected right after being born or before.
• Infants who contract the virus tend to do well and do not develop pneumonia.
• They do tend to shed the virus for a number of weeks.
• The virus has been identified in the placenta of women who had miscarriages because of complications of COVID-19.
Maternal Transmission to the Newborn

Transmission rate
- Intrauterine transmission while low, is possible
- 1-3% of births to U.S mothers with active infection

(AAP National registry for perinatal COVID19 infection)

Horizontal transmission>>> Vertical Transmission

Sankaran et al. Neoreviews 2021
Transplacental Transmission of SARS CoV-2 appears to be rare

In 66 placentas tested in women with confirmed COVID-19, SARS CoV-2 was not present in any.

Studies have suggested in utero transmission rates vary from 0 to 4.3%
After a handful of cases in Ireland, clinicians there are warning that the virus might infect the placenta in very rare instances and cause fetal distress, but a rise in stillbirths has not been seen in epidemiological studies.

Estimates are quite hard at the moment, in terms of working out the true risk, but we think we are seeing one in one hundred to one in two hundred cases [of stillbirth] in women with [COVID-19].

—Keelin O’Donoghue, Cork University Maternal Hospital

Cases of necrotic placentas reported from 6 cases in Ireland where women experienced miscarriages.
Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study

Nan Yu*, Wei Li*, Qingling Kang, Zhi Xiong, Shaoshuai Wang, Xingguang Lin, Yanyan Liu, Juan Xiao, Haiyi Liu, Dongrui Deng, Suhua Chen, Wanjiang Zeng, Ling Feng, Jianli Wu

<table>
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<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>Patient 6</th>
<th>Patient 7</th>
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<td>Discharged</td>
<td>Discharged</td>
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<td>Discharged</td>
<td>Discharged</td>
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<tr>
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<td>Normal</td>
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<td>Normal</td>
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<tr>
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<td>3350</td>
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<td>3000</td>
<td>3500</td>
<td>3300</td>
<td>3250</td>
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<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<td>Negative</td>
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<td>Not tested</td>
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<td>28</td>
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<td>Neonatal complications</td>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

None of the women were admitted to intensive care. Normal=no respiratory symptoms or fever or neonatal complications, such as neonatal respiratory distress syndrome, feeding abnormalities, or abnormal growth or development. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Table 2: Maternal and neonatal outcomes of seven patients with COVID-19

Shifting perception of infant outcomes
88,159 infants in Sweden from 3/20 – 3/21
2323 (1.6%) to SARS CoV-2 + mothers
Prematurity rate:
  + mothers: 8.8%, neg mothers: 5.5%

Maternal positivity associated with:
  - Infant admission: OR 1.5 (1.26-1.70)
  - Infant resp distress: OR 2.4 (1.50-3.84)
  - Any resp disorder: OR 1.4 (1.07-1.90)
  - Hyperbilirubinemia: OR 1.47 (1.13-1.90)

Infant mortality not different between groups.
21 infants (1%)+ for SARS CoV-2 in the neonatal period.
Neonates with SARS-CoV-2 Infection

• Early onset neonatal COVID19 (between 2-7 days)
  • Mainly asymptomatic but can have mild, moderate or severe symptoms
  • Labs- leukocytosis, lymphopenia, thrombocytopenia and elevated inflammatory markers
  • Tx: supportive

• Late onset neonatal COVID19 (>7 days)
  • Mainly symptomatic- fever, coryza, respiratory symptoms, apnea, poor feeding, vomiting and lethargy.
  • Many have negative PCR test results in the hospital after birth
  • CXR- ground glass changes
  • Labs: leukocytosis, thrombocytopenia, elevated lactate, elevated CRP, and lymphopenia. DIC may also occur.
Multisystem Inflammatory Syndrome in Children (MIS-C)

- Characterized by fever, elevated inflammatory markers, and high levels of pro- and anti-inflammatory cytokines.

- Children present with symptoms related to:
  - CV system: Shock, LV dysfunction, elevated cardiac enzymes, coronary artery abnormalities
  - GI system: Nausea, vomiting, diarrhea
  - Mucocutaneous symptoms resembling Kawasaki disease

- Can Neonates have MIS-C?
  - Rare but possible
Neonatal MIS-C

Multisystem Inflammatory Syndrome in Children Associated With Severe Acute Respiratory Syndrome Coronavirus-2 in an 8-Week-Old Infant

Esther Orlianski-Meyer 1, Dotan Yoqev 1,2, Adi Auerbach 3, Orli Meaoed 2,4, Daniel Glikman 5.

Maternal SARS-CoV-2 Infection Associated to Systemic Inflammatory Response and Pericardial Effusion in the Newborn: A Case Report

Andressa R O Lima 1, Cynthia C Cardoso 2, Priscilla R B Bentim 1, Carolina M Voloch 2,

MULTISYSTEM INFLAMMATORY SYNDROME IN A CHILD ASSOCIATED WITH CORONAVIRUS DISEASE 19 IN THE BRAZILIAN AMAZON: FATAL OUTCOME IN AN INFANT

Emmerson Carlos Franco de Farias, a,1* Maria Cleonice Aguiar Justino, b and Mary Lucy Ferraz Maia Fiuza de Mello a

COVID-19–Related Potential Multisystem Inflammatory Syndrome in Childhood in a Neonate Presenting as Persistent Pulmonary Hypertension of the Newborn

David Geffen School of Medicine

UCLA Health
Rare cases of virus identified in cord blood by PCR.

- Cytokine release syndrome (CRS)
  - High level of immune activation + inflammatory cytokines
  - Hyaline membrane & lymphocytes in lungs on autopsy of COVID-19 patient
Neonatal Management

Only case reports of SARS-CoV-2 detected in breastmilk

Primary concern with breastfeeding is transmission via respiratory droplets

CDC recommends frequent handwashing and feeding, with discussion with clinical team regarding risks/benefits
Is Breastfeeding Safe?

• Similar guidelines have also transitioned to encourage breastfeeding.
  
  • No evidence to suggest that it poses an increase risk that an infant tests positive when nursed.

• Replicable virus has not been conclusively demonstrated to be present in breast milk.
Maternal-infant separation if Covid19+?

- Evidence has accumulated and guidance has shifted from safety preference of temporary maternal-infant separation to one that encourages infants to room in with mothers.
- Mother healthy enough to provide self care
- Appropriate prevention precautions

**Monthly Percentage of Infants Separated vs. Non-Separated**

- % Separated
- % Not Separated

AAP SOPNM National Registry 2020
Why are so many babies dying of Covid-19 in Brazil?

By Nathalia Passarinho and Luis Barrucho
BBC Brazil

Why Is Covid Killing So Many Young Children in Brazil? Doctors Are Baffled

Experts believe Brazil’s overloaded hospital system and uneven access to health care are among the reasons babies and small children are succumbing to the virus at a high rate.

Dr. Marinho, who is leading a study tallying the death toll among children based on both suspected and confirmed cases, estimates that more than 2,200 children under 5 have died since the start of the pandemic, including more than 1,600 babies less than a year old.

“We are seeing a huge impact on children,” said Dr. Marinho. “It’s a number that’s absurdly high. We haven’t seen this anywhere else in the world.”
What about pediatric long term outcomes?
The present work builds upon a large collaborative effort initiated during the ZIKV epidemic in Brazil in 2015-2016.

In utero Zika exposure and neurodevelopmental outcomes

**Table 1** Characteristics of ZIKV-exposed neonates and neurodevelopmental assessments

<table>
<thead>
<tr>
<th>Cognitive function</th>
<th>Language function</th>
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<td>% below average</td>
<td>% below average</td>
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<tr>
<td>28</td>
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<td>13</td>
<td>8.3</td>
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<td>8</td>
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</tr>
<tr>
<td>4</td>
<td>1.9</td>
</tr>
<tr>
<td>2</td>
<td>0.9</td>
</tr>
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<td>2</td>
<td>0.9</td>
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</table>

- Language function most affected, 35% of children below average.
- Improved neurodevelopment in female children, term babies, children with normal eye exams and maternal infection later in pregnancy.
- ASD identified in 2% of children.

**Figure 1.** Individual Scores on the Bayley-III Scales at 12 to 18 Months of Age, According to Neuroimaging Results.

**Neuroimaging and neurodevelopment:**

A significant association was noted between normal brain imaging and higher Bayley-III scores, but neuroimaging failed to predict developmental delay in 16% of children and normal development in 2% of cases.

88 women with rash during pregnancy, 72 (82%) ZIKV PCR+ in blood, urine or both

* 125 pregnancies with known outcomes; 117 live births in 116 pregnancies (one set of twins)
We can identify surrogate markers of abnormal pregnancy outcomes in Zika:

- Extensive multiplexing analysis of 69 cytokines in 74 pregnant patients revealed that CXCL10, CCL2, and CCL8 chemokines specifically associated with symptomatic ZIKV+ infection during pregnancy.
- Distinct immune profiles were detected at different trimesters in ZIKV-infected pregnant women.
- CCL2 levels and its inverse correlation with CD163, TNFRSF1A, and CCL22 levels was associated with ZIKV-induced abnormal birth outcomes.

Suan-Sin Foo,¹ Weiqiang Chen,¹ Yen Chan,² Wai-Suet Lee,¹,³ Shin-Ae Lee,¹ Genhong Cheng,⁴ Karin Nielsen-Saines,⁵ Patrícia Brasil,⁵ and Jae U. Jung¹

*JCI Insight.* 2018;3(21):e124152. [https://doi.org/10.1172/jci.insight.124152.](https://doi.org/10.1172/jci.insight.124152.)
Maternal Immune Activation (MIA) During Pregnancy and Implications to the Fetus

- Epidemiological data and animal data implicating maternal immune activation in pregnancy and CNS disorders: ASD, Schizophrenia and Cerebral Palsy
- MIA can affect fetal brain development
  - Changes in brain structure and function
  - Neuronal dysfunction and behavioral phenotypes
- Mechanisms:
  - Maternal and fetal immune dysregulation: Cytokines/chemokines
  - “2 Hit Hypothesis”
  - Early vs Late infection in pregnancy

If fetus is in MIA environment infant may be more susceptible to infection-2 hit hypothesis
Maternal Immune Activation (MIA) and Implications to the Fetus

- Zika Virus turned **public attention** to the detrimental effects of maternal infection
  - Risk of microcephaly
- Historic outbreaks of flu, MMR, Polio correlate with increases in neuropsychiatric illnesses.
  - 1964 Rubella pandemic, incidence of ASD and Schizophrenia rose from 1% to 13 and 20%
- Majority of pregnancies will lead to a healthy offspring, and the resulting CNS disorders often do not appear for many years after birth.
  - Dx of Autism can be made starting at 2 years of age
  - Schizophrenia- mid to late 20’s
Potential risk for neurodevelopmental disorders in neonates

Pregnant women with COVID infection have high IL-6 levels which in turn can influence placental-fetal interactions and subsequently fetal brain development.

Advocating for collaborative research to explore the mechanisms underlying breakdown in fetal neurodevelopment during maternal infection.

How prenatal maternal stress impacts fetal epigenetic and neurodevelopmental programming leading to offspring psych disorders later in life.
COVID Outcomes Mother-Infant Pair Study (COMP Study)

A study of immuno-pathogenesis in mother-infant pairs affected by SARS Cov2 infection in Los Angeles and Rio de Janeiro, started on 4/4/2020
COVID Outcomes Mother-Infant Pair Study (COMP Study)

An observational study evaluating clinical outcomes, viral shedding and immune responses in mother-infant pairs affected by COVID-19

Objectives:

1. To characterize clinical, obstetrical and neurodevelopmental outcomes in mother-infant pairs with SARS CoV-2 infection from the time of maternal infection/ birth up to 36 months of follow-up.

2. To evaluate viral shedding in the first month after infection and humoral immune responses over 3 years in mother-infant pairs.

3. To evaluate chemokine-cytokine proteomics and T cell responses (single-cell RNAseq) in mother-infant pairs during the time of acute infection in pregnancy until 3 years postpartum.

Specimens collected at the time of acute infection, labor and delivery, 6 months and 12 months, 24 and 36 months post-partum in mother-infant pairs.
COMP Study

- **Population** (Original sample size): 100 mother-infant pairs affected by COVID-19 and 100 mother-pair controls.

- **Enrolling study sites**: UCLA & Fiocruz (Brazil); both sites have IRB approval, functioning Redcaps and are actively recruiting.

- **Study enrollment to date**: n = 605 pregnancies
  - UCLA: **205** pregnancies
  - Rio: **400** pregnancies

- Variable disease expression, some mothers required ICU care, a small group ECMO. Maternal deaths and fetal demise reported.
The systemic inflammatory landscape of COVID-19 in pregnancy: Extensive serum proteomic profiling of mother-infant dyads with in utero SARS-CoV-2

Graphical abstract

Authors
Suan-Sin Foo, Mary Catherine Cambou, Thalita Mok, ..., Rashmi Rao, Jae U. Jung, Karin Nielsen-Saines

Table 1. Demographics and clinical characteristics of mother-infant dyads infected with SARS-CoV-2 during pregnancy

<table>
<thead>
<tr>
<th></th>
<th>All women, N = 93</th>
<th>Asymptomatic, N = 12 (12.9%)</th>
<th>Mid/moderate, N = 61 (65.6%)</th>
<th>Severe/critical, N = 20 (21.5%)</th>
<th>P</th>
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<td>33 (19-40)</td>
<td>34 (16-44)</td>
<td>33 (18-44)</td>
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<td>Latina</td>
<td>44 (47.3)</td>
<td>4 (33.3)</td>
<td>26 (45.9)</td>
<td>12 (60.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White</td>
<td>23 (24.7)</td>
<td>3 (25.0)</td>
<td>17 (27.9)</td>
<td>3 (15.0)</td>
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<tr>
<td>Black/African American</td>
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<td>2 (16.7)</td>
<td>2 (3.3)</td>
<td>4 (20.0)</td>
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<tr>
<td>Asian/other</td>
<td>18 (19.4)</td>
<td>3 (25.0)</td>
<td>14 (23.0)</td>
<td>1 (5.0)</td>
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<td>Insurance, N (%)</td>
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<td>Public</td>
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<td>5 (41.7)</td>
<td>21 (34.4)</td>
<td>11 (55.0)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>56 (60.2)</td>
<td>7 (58.3)</td>
<td>40 (65.6)</td>
<td>9 (45.0)</td>
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<td>Occupation, N (%)</td>
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<td>1 (8.3)</td>
<td>13 (21.3)</td>
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<td>Other</td>
<td>77 (82.8)</td>
<td>11 (91.7)</td>
<td>48 (78.7)</td>
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<tr>
<td>Parity, median (range)</td>
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<td>3 (1-6)</td>
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<td>3 (1-7)</td>
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<td>Gestational age at diagnosis, N (%)</td>
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<td>1st trimester</td>
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<td>15 (24.6)</td>
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<td></td>
</tr>
<tr>
<td>2nd trimester</td>
<td>31 (33.3)</td>
<td>2 (16.7)</td>
<td>17 (27.9)</td>
<td>12 (60.0)</td>
<td></td>
</tr>
<tr>
<td>3rd trimester</td>
<td>44 (47.3)</td>
<td>9 (75.0)</td>
<td>29 (47.5)</td>
<td>6 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Table 1. Continued</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>--------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A. Maternal demographics and medical history (N = 93)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All women, N = 93</td>
<td>Asymptomatic, N = 12 (12.9%)</td>
<td>Mild/moderate, N = 61 (65.6%)</td>
<td>Severe/critical, N = 20 (21.5%)</td>
<td>P</td>
<td></td>
</tr>
<tr>
<td>Complications during the course of pregnancy pre-delivery, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>9 (12.8)</td>
<td>2 (16.7)</td>
<td>3 (6.8)</td>
<td>4 (28.6)</td>
<td>0.10</td>
</tr>
<tr>
<td>Hypertensive disorder</td>
<td>23 (32.9)</td>
<td>3 (25.0)</td>
<td>14 (31.8)</td>
<td>6 (42.9)</td>
<td>0.61</td>
</tr>
<tr>
<td>Late pregnancy and postpartum complications, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal growth restriction</td>
<td>11 (15.7)</td>
<td>2 (16.7)</td>
<td>8 (18.2)</td>
<td>1 (7.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>6 (8.6)</td>
<td>1 (8.3)</td>
<td>3 (6.8)</td>
<td>2 (14.3)</td>
<td>0.05</td>
</tr>
<tr>
<td>Postpartum hemorrhage</td>
<td>11 (15.7)</td>
<td>0 (0.0)</td>
<td>5 (11.4)</td>
<td>6 (42.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Preeclampsia/HELLP</td>
<td>11 (15.7)</td>
<td>3 (25.0)</td>
<td>6 (13.6)</td>
<td>2 (14.3)</td>
<td>0.72</td>
</tr>
<tr>
<td>Preterm rupture of membranes</td>
<td>4 (5.7)</td>
<td>0 (0.0)</td>
<td>2 (4.5)</td>
<td>2 (14.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (5.7)</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
<td>3 (21.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>Mode of delivery/pregnancy endpoint, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSVD</td>
<td>33 (47.1)</td>
<td>6 (50.0)</td>
<td>25 (56.8)</td>
<td>2 (14.3)</td>
<td>0.10</td>
</tr>
<tr>
<td>C-section</td>
<td>25 (35.7)</td>
<td>5 (41.7)</td>
<td>14 (31.8)</td>
<td>6 (42.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>Vacuum-assisted vaginal delivery</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
<td>0 (0.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (5.7)</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
<td>3 (21.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>Miscarriage/termination/fetal loss</td>
<td>7 (10.0)</td>
<td>1 (8.3)</td>
<td>3 (6.8)</td>
<td>3 (21.4)</td>
<td>0.72</td>
</tr>
<tr>
<td>Miscarriage (&lt;20 weeks)</td>
<td>2 (2.9)</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
<td>1 (7.1)</td>
<td>0.30</td>
</tr>
<tr>
<td>Fetal loss (≥20 weeks)</td>
<td>2 (2.9)</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
<td>1 (7.1)</td>
<td>0.30</td>
</tr>
<tr>
<td>Pregnancy termination</td>
<td>2 (2.9)</td>
<td>0 (0.0)</td>
<td>1 (2.3)</td>
<td>0 (0.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Maternal-fetal demise</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (7.1)</td>
<td>0.30</td>
</tr>
<tr>
<td>Pregnancies resulting in live births (N = 70)</td>
<td>63 (90.0)</td>
<td>11 (91.7)</td>
<td>41 (93.2)</td>
<td>11 (78.6)</td>
<td>0.28</td>
</tr>
<tr>
<td>No. multiple gestations</td>
<td>5 (7.1)</td>
<td>1 (8.3)</td>
<td>2 (4.5)</td>
<td>2 (14.3)</td>
<td>0.46</td>
</tr>
<tr>
<td>No. infants born as of March 1, 2021</td>
<td>69 (98.6)</td>
<td>13 (18.57)</td>
<td>43 (61.43)</td>
<td>13 (18.57)</td>
<td>0.46</td>
</tr>
<tr>
<td>C. Infant outcomes with associated O-link data (N = 45), N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All women</td>
<td>14 (31.1)</td>
<td>0 (0.0)</td>
<td>8 (28.6)</td>
<td>6 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Asymptomatic, N = 11 (24.44%)</td>
<td>5 (12.5)</td>
<td>1 (9.1)</td>
<td>4 (14.3)</td>
<td>0 (0.0)</td>
<td>0.58</td>
</tr>
<tr>
<td>Mild/moderate, N = 28 (62.22%)</td>
<td>13 (41.7)</td>
<td>1 (9.1)</td>
<td>6 (21.4)</td>
<td>6 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe/critical, N = 6 (13.34%)</td>
<td>6 (100)</td>
<td>1 (9.1)</td>
<td>6 (21.4)</td>
<td>6 (100)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Association of SARS-CoV-2 Infection With Serious Maternal Morbidity and Mortality From Obstetric Complications

Tori D. Metz, MD, MS; Rebecca G. Clifton, PhD; Brenna L. Hughes, MD, MS; Grecio J. Sandoval, PhD; William A. Grobman, MD, MBA; George R. Saade, MD; Tracy A. Manuck, MD, MS; Monica Longo, MD, PhD; Amber Sowles, BSN, RN; Kelly Clark, BSN, RN; Hyagriv N. Simhan, MD; Dwight J. Rouse, MD; Hector Mendez-Figueroa, MD; Cynthia Gyamfi-Bannerman, MD, MS; Jennifer L. Bailit, MD, MPH; Maged M. Costantine, MD; Harish M. Sehdev, MD; Alan T. N. Tita, MD, PhD; George A. Macones, MD; for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units (MFMU) Network

Table 2. Maternal and Neonatal Outcomes for Individuals With and Without a Positive SARS-CoV-2 Test Result

<table>
<thead>
<tr>
<th>Maternal outcomes</th>
<th>SARS-CoV-2 positive, No. (%)</th>
<th>Difference (95% CI)</th>
<th>Relative risk (95% CI)</th>
<th>Adjusted relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n = 2352)</td>
<td>No (n = 11,752)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary composite outcome of death or serious morbidity from hypertensive</td>
<td>316 (13.4)</td>
<td>1076 (9.2)</td>
<td>4.2 (2.8 to 5.6)</td>
<td>1.45 (1.29 to 1.64)</td>
</tr>
<tr>
<td>disorders of pregnancy, postpartum hemorrhage, or non-SARS-CoV-2 infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death (any cause)</td>
<td>5 (0.2)</td>
<td>0</td>
<td>3.6 (2.4 to 4.8)</td>
<td>1.56 (1.35 to 1.79)</td>
</tr>
<tr>
<td>Hypertensive disorders of pregnancy$^b$</td>
<td>238 (10.1)</td>
<td>761 (6.5)</td>
<td>3.6 (2.4 to 4.8)</td>
<td>1.56 (1.35 to 1.79)</td>
</tr>
<tr>
<td>Postpartum hemorrhage$^c$</td>
<td>61 (2.6)</td>
<td>282 (2.4)</td>
<td>0.1 (−0.5 to 0.8)</td>
<td>1.06 (0.81 to 1.40)</td>
</tr>
<tr>
<td>Infection other than SARS-CoV-2$^d$</td>
<td>55 (2.3)</td>
<td>103 (0.9)</td>
<td>1.4 (0.8 to 2.1)</td>
<td>2.61 (1.88 to 3.63)</td>
</tr>
</tbody>
</table>
Maternal demographics and clinical characteristics of COMP U.S. study participants excluding 27 controls (N = 177)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Maternal Age (Range)</td>
<td>32 (16 - 56)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Latina</td>
<td>47.7%</td>
</tr>
<tr>
<td>White</td>
<td>23.6%</td>
</tr>
<tr>
<td>Black</td>
<td>6.4%</td>
</tr>
<tr>
<td>Asian</td>
<td>12.1%</td>
</tr>
<tr>
<td>Mixed/Other</td>
<td>10.2%</td>
</tr>
<tr>
<td>COVID-19 Severity</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>11.9%</td>
</tr>
<tr>
<td>Mild/Moderate</td>
<td>71.7%</td>
</tr>
<tr>
<td>Severe/Critical</td>
<td>16.4%</td>
</tr>
<tr>
<td>Trimester of Diagnosis</td>
<td></td>
</tr>
<tr>
<td>1st</td>
<td>13.0%</td>
</tr>
<tr>
<td>2nd</td>
<td>34.5%</td>
</tr>
<tr>
<td>3rd</td>
<td>52.5%</td>
</tr>
<tr>
<td>Cardiovascular Co-Morbidities</td>
<td></td>
</tr>
<tr>
<td>Hypertensive Disorder</td>
<td>24.2%</td>
</tr>
<tr>
<td>Pre-Eclampsia</td>
<td>14.0%</td>
</tr>
</tbody>
</table>
Figure 1. Residence of patients with severe/critical Covid-19 superimposed on a map of Economic Hardship Index

Los Angeles, CA

1st quartile (least) 2nd quartile 3rd quartile 4th quartile (most) Excluded** Other Unincorporated LAC

* Score based on ACS 2012 5-Year estimates ** Population below 10,000
Geographic, Social and Epidemiologic Predictors of SARS-CoV-2 Infection in Youth in Southern California

Youth under 25 years of age living in the ZIP codes reflective of the most disenfranchised populations in LA county were proportionally most affected by COVID-19 early in the pandemic.
COVID Outcomes Mother-Infant Pair Study (COMP Study)
An observational study evaluating clinical outcomes, viral shedding and immune responses in mother-infant pairs affected by COVID-19

Sera immunoprofiling of COVID-19-positive pregnancies

Jae Jung, PhD

Olink proteomics multiplex (1536-plex)

➢ Maternal sera (n = 93)
➢ Infant’s sera (n = 45)
➢ Cord sera (n = 32)

High-throughput sera proteome multiplexing (1440 proteins)

COVID19 mother-infant cohort

Maternal blood
Healthy (n = 18)
COVID19+ (n = 79)

Maternal blood
Healthy (n = 14)
COVID19+ (n = 49)

Infant blood
Healthy (n = 7)
COVID19-exposed (n = 45)

Cord blood
Healthy (n = 14)
COVID19-exposed (n = 32)
COVID-19 induced robust immune activation during pregnancy

- ~1400 sera cytokines screened
- 125 cytokines significantly altered in COVID-19 pregnancies
- Severe/Critical pregnancies displayed distinct immune signatures

 Musk Mother

Healthy controls

COVID-19-positive

Healthy controls

Asymptomatic

Mild

Severe/critical

Fold change relative to control
Infants of Severe/Critical COVID-19 mothers reveal strikingly unique immune profiles

➢ ~1400 sera cytokines screened
➢ 120 cytokines significantly altered in COVID-19-exposed infants
➢ Infants of Severe/Critical COVID-19 mothers displayed distinct immune signatures
A. COVID19 mother-infant cohort

- Initial diagnosis
- Delivery

Maternal blood:
- Healthy (N = 14)
- COVID19+ (N = 49)
- COVID19-exposed (N = 32)

Infant blood:
- Healthy (N = 7)
- COVID19-exposed (N = 45)

Cord blood:
- Healthy (N = 14)
- COVID19-exposed (N = 45)

High-throughput sera proteome multiplexing (1440 proteins)

B. Canonical pathways: Symptomatic COVID19

- Neuroinflammation Signaling Pathway
- Hepatic Fibrosis Signaling Pathway
- Cardiac Hypertrophy Signaling (Enhanced)
- NF-kB Signaling
- Regulation Of The EMT By GF Pathway
- p38 MAPK Signaling
- Role of PKR in IFN Induction and Antiviral Response
- Production of NO and ROS in Macrophages
- Type 1 Diabetes Mellitus Signaling
- Coronavirus Pathogenesis Pathway
- Crosstalk between DCs and NK Cells
- Colorectal Cancer Metastasis Signaling
- Osteoarthritis Pathway
- IL-15 Production
- STAT3 Pathway

Legend:
- Mild/Moderate
- Severe/Critical
- Z-SCORE

Healthy and COVID19-exposed infants

- Mild/Moderate
- Asymptomatic
- Moderate
- Severe
- Critical
Highly upregulated cytokines

Proinflammatory cytokines significantly altered in COVID19-affected pregnancies
Comparison of proteomic profiles of neonatal blood at day 1 of life compared to cord blood and maternal blood. Very little overlap. Cytokines do not cross the placenta.
Respiratory Distress in Neonates Exposed to Maternal SARS-CoV-2 Infection In Utero

Jessica S. Creton 1, Sophia Finn Tien 1, Mary Catherine Cambou 1, Sophia Paikou 1, Thalia Wong 1, Jenny Mei 1, Viviana Fajardo 1, Debika Bhattacharya 1, Grace Albavardani 2, Iara Kimm 2, Rashmi Ibo 2, Trevor Fuller 2, Patricia Brasil 2, Karin Nielsen-Saines 2

1 University of California Los Angeles, CA, United States 2 Hucrtrz, Rio de Janeiro, Brazil

Background

- Respiratory Distress is one of the most common causes of admission to the NICU
- Neonates with respiratory distress have 2-4 times higher fatality rate than those without respiratory distress
- Respiratory Distress affects approximately 1-2% of term infants, with a higher incidence among pre-term infants
- Studies have shown a high prevalence of respiratory distress in infants born to mothers with COVID-19 during pregnancy

Objective

- To characterize the multifactorial associations leading to Respiratory Distress (RD) in neonates born to mothers diagnosed with COVID-19 during pregnancy

Methods

- The COVID-19 Outcomes in Mother-Infant Pairs (COMP) study is a longitudinal cohort of mother-infant dyads diagnosed with SARS-CoV-2 during pregnancy in Los Angeles, California and Rio de Janeiro, Brazil.
- Respiratory Distress was defined as at least 2 of the following: RR>60/min, retractions, nasal flaring, central cyanosis.
- Sera proteomics profiling was performed using Olink Explore 1536, a high-multiplex, high-throughput protein biomarker platform that utilizes Proximity Extension Assay (PEA) technology coupled with next generation sequencing for readout of >1400 cytokines.
- Normalized protein expressions (NPFx) values for all proteins were retrieved from Olink after sequencing and validated using real-time PCR.

Results

<table>
<thead>
<tr>
<th>Table 1. Maternal/Infant Demographics and Clinical Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Gestational Age</td>
</tr>
<tr>
<td>Birth</td>
</tr>
<tr>
<td>Length</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Neonatal Abnormalities</td>
</tr>
<tr>
<td>Apgar Score</td>
</tr>
<tr>
<td>Trimester of Cord Diagnosis</td>
</tr>
<tr>
<td>First Trimester</td>
</tr>
<tr>
<td>Second Trimester</td>
</tr>
<tr>
<td>Third Trimester</td>
</tr>
</tbody>
</table>

- Medical History Prior to Covid

<table>
<thead>
<tr>
<th><strong>Comorbidities</strong></th>
<th><strong>Maternal</strong></th>
<th><strong>Infant</strong></th>
<th><strong>P Value</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>1 (10%)</td>
<td>2 (10%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>3</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Congenital Heart Disease</td>
<td>0</td>
<td>0</td>
<td>0.01</td>
</tr>
<tr>
<td>Asthma</td>
<td>2 (10%)</td>
<td>2 (10%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Autoimmune Disease</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Autism Spectrum</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
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<tr>
<td>Cerebellar Atrophy</td>
<td>0</td>
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<tr>
<td>Cystic Fibrosis</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Sickle Cell Disease</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Other Genetic Disorders</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
</tbody>
</table>

- Cytokines Associated with Respiratory Distress

<table>
<thead>
<tr>
<th><strong>Cytokines</strong></th>
<th><strong>Infant</strong></th>
<th><strong>P Value</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-2</td>
<td>0.3 (20%)</td>
<td>0.01</td>
</tr>
<tr>
<td>IL-4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>IL-6</td>
<td>0 (10%)</td>
<td>0.01</td>
</tr>
<tr>
<td>IL-10</td>
<td>1 (20%)</td>
<td>0.01</td>
</tr>
<tr>
<td>IFN-gamma</td>
<td>2 (20%)</td>
<td>0.01</td>
</tr>
<tr>
<td>TNF-alpha</td>
<td>2 (20%)</td>
<td>0.01</td>
</tr>
<tr>
<td>IL-12</td>
<td>1 (20%)</td>
<td>0.01</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>1 (20%)</td>
<td>0.01</td>
</tr>
<tr>
<td>CXCL10</td>
<td>0</td>
<td>0.01</td>
</tr>
<tr>
<td>CXCL11</td>
<td>0</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Conclusions

- Overall, infants born to COVID-19 mothers with more severe/critical disease and cytokine storm exhibited more pronounced immune alterations as compared to infants born to mothers with asymptomatic disease.
- The rate of RD in infants born to COVID-19 mothers was higher than baseline.
- In addition, several serum factors were identified as potential biomarkers for prenatal SARS-CoV-2 infection and neonatal RD.
- Immunological evaluations of term COVID-19 exposed infants who developed RD identified:
  - High levels of IL-18, IL-1β, and CASP1, indicative of an activated NLRP3 inflammasome pathway.
  - High levels of TREM2, known to promote macrophage survival and viral-induced lung pathogenesis.
  - Increased IL6 levels that degrade glycosaminoglycans, and decreased AGR3, which is essential in regulating ciliary beat frequency in the airway.
- Therefore, these proteins are potential pathogenic factors implicated in RD associated with prenatally COVID-19-exposure in term infants and should be further explored.
- Infants exposed to COVID-19 in utero should be carefully assessed for RD at birth.

The details and resources of the COMP study can be found at PMID: 34722228.
General Movement Assessment (GMA)

- Non-invasive, video-based assessment
- Identify neurological deficits
- Enables referral of infants at risk
- Long term relevance for the later development of cognitive, speech-language and motor function.

General movement assessments (GMA) at 3 to 5 months identify poor neurodevelopment at 12 months, specificity 96%, sensitivity 70% in infants exposed to maternal Zika

Einspieler et al. Jama Netw Open 2019

There are tools for early identification of children at risk for poor neurodevelopment
Neuromotor function in infants exposed to Prenatal SARS-CoV-2 infection using the General Movement Assessment Tool

Viviana Fajardo-Martínez1, Dajie Marschik2, Sophia Paio1, Thalia Mok1, Mary C. Cambou1, Rashmi Rao1, Patricia Brasil3, Fatima Ferreira3, Trevon Fuller3, Debika Bhattacharya4, Christa Einspieler4, Peter Marschik2, Karin Nielsen-Saines1

1 University of California Los Angeles, Los Angeles, CA, United States, 2 Georg-August-University of Göttingen, Germany, 3 Fiocruz, Rio de Janeiro, Brazil, 4 Medical University of Graz, Austria

Background
- The long-term neurodevelopmental impact of the SARS-CoV-2 pandemic on prenatally exposed infants is still unknown.
- Early life is a critically important and vulnerable period for neurodevelopment.
- Studies have shown an association between acute respiratory virus infections such as SARS-CoV-1 and Influenza and increased risk of neurodevelopmental disorders in offspring including cerebral palsy, autism spectrum disorder and schizophrenia.
- The Prechtl General Movement Assessment (GMA) is a reliable screening tool for identifying infants at risk for neuromotor deficits. GMA was Introduced in 1990 and has been increasingly utilized in the screening of motor dysfunction. It is non-invasive, cost effective and highly reliable tool.
- Between 3 to 5 months post-term age, GMAS appear as fidgety movements, small movements of the neck, trunk, and limbs in all directions and of variable acceleration indicating a normal neurodevelopmental development. Abnormal fidgety movements with exaggerated amplitude, speed and jerkiness may point to neurological deficits, but it is the absence of fidgety movements that is strongly related to the development of severe neurological deficits.

Objectives
- To assess the integrity of the developing nervous system by analyzing the neuromotor repertoire at 3-5 months postterm age in infants exposed to SARS-CoV-2 infection in utero using GMA.
- The COVID-19 outcomes in Mother-Infant Pairs (COMP) study is a longitudinal cohort where infants prenatally exposed to SARS-CoV-2 during any trimester in pregnancy were recruited in Los Angeles, and Rio de Janeiro, Brazil between March 2020 to the present.
- Infants exposed to SARS CoV-2 in utero were matched 1:1 by gestational age, gender, and age at video recording to normal, pre-pandemic neurotypical controls from the Univ Graz database.

Results
- 114 SARS CoV-2 exposed infants were evaluated using the general movement assessments (GMAs) by video recordings, lasting 2-3 minutes, of active wakefulness lying in supine position without manipulation.
- Motor Optimality score (MOS) were generated for each infant, based on age-specific movement repertoire, postural patterns, and movement character.
- The reported median MOS for typically developing infants (neurotypical infants) is 26.
- Among the 114 infants, MOS ranged from 9-28, with a median of 23, and IQR 21-24.
- 8 infants (7%) scored between 9-16 points
- 8 infants (7%) scored between 17-19 points
- 79 infants (69%) scored between 20-24 points
- 20 infants (17%) scored between 25-28 points
- 29 preterm infants (born before 37 weeks) had a median MOS score of 23 (IQR 21-24). There were 4 multiple-births (10 infants).
- An average MOS of 20 points or higher is seen as non-pathological. This was the case in most infants within the cohort.
- 14.0% of babies had scores lower than 20 and should be closely followed.

Conclusions
- Compared to controls, COVID-exposed infants had lower MOS scores, less frequent age adequate repertoires, a higher frequency of abnormal movement patterns and abnormal postural patterns, and more frequent alterations in movement character. Associations between MOS score and maternal disease severity or with trimester of maternal infection were not statistically significant.
- Lower median scores could reflect heightened stress caused by infection during pregnancy and the deviance may be transient, with normal outcomes for most infants, but this remains to be seen.
- SARS CoV-2 in utero exposed infants require long term follow-up. (GMA)

Table 1. Motor Optimality Scores (MOS) of 114 infants grouped by maternal Covid-19 disease severity and trimester of maternal infection in pregnancy. Numbers indicate the range of MOS in the cell. Italic formatted number indicate the cell mean and (median). d = 0.09.

Table 2. Clinical Characteristics and Motor Behavior at 3-5 Months Post-term age

"Details of the COMP study can be found at PMID34723226"
Maternal & infant antibody responses and placental antibody transfer at labor & delivery to SARS-CoV-2 infection / vaccination in pregnancy

Enrollment during pregnancy following acute infection
Diagnosis: NP RT-PCR or serology

Maternal blood
COVID19+ (n = 164)

Labor & Delivery

Maternal blood
COVID19+ (n = 134)

Infant blood
COVID19-exposed (n = 113)

Cord blood
COVID19-exposed (n = 97)

ELISA:
Anti-SARS-CoV-2 IgA, IgG, and IgM

Diagnosis Date-to-Delivery Interval:
Median (IQR) = 74 (31-123) Days
## Serology of Mother-Infant Dyads Infected with SARS-CoV-2 During Pregnancy

<table>
<thead>
<tr>
<th>Anti-SARS-CoV-2 IgG, IgM, and IgA</th>
<th>Maternal Serum at L&amp;D</th>
<th>Cord Blood</th>
<th>Infant Serum at Birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 134</td>
<td>N = 97</td>
<td>N = 113</td>
<td></td>
</tr>
<tr>
<td>N (%) of Total</td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td>IgG + Total</td>
<td>114 (85)</td>
<td>81 (98)</td>
<td>87 (77)</td>
</tr>
<tr>
<td>IgM+ Total</td>
<td>120 (90)</td>
<td>10 (12)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>IgA+ Total</td>
<td>108 (81)</td>
<td>10 (12)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>IgG (+) / IgM (+)/ IgA (+) (all 3 present)</td>
<td>97 (72)</td>
<td>6 (7)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Seronegative</td>
<td>6 (4)</td>
<td>13 (13)</td>
<td>26 (23)</td>
</tr>
</tbody>
</table>

*Transplacental IgG transfer was high following natural in utero SARS-CoV-2 infection correlating with timing of infection prior to delivery. Maternal vaccination & severe COVID-19 yielded higher Ab levels in mothers and infants at delivery. 50% NAb was present in 68% of mothers & 42% of infants tested*
**a**

COVID-19 diagnosis date-to-delivery interval vs transplacental transfer ratio

![Graph showing the relationship between COVID-19 diagnosis date-to-delivery interval and transplacental transfer ratio. The Pearson correlation coefficient (R) is 0.2251.](image)

**b**

Transfer ratio stratified by trimester of pregnancy of COVID-19 diagnosis

![Box plots showing transfer ratio stratified by trimester of pregnancy.](image)
Maternal antibody levels at L&D stratified by COVID-19 Disease Severity

- **IgG**
  - Asymptomatic: $N = 17$
  - Mild/Moderate: $N = 89$
  - Severe/Critical: $N = 19$
  - $P = 0.0002$
  - $P = 0.0001$ \(P = 0.6455\)

- **IgM**
  - Asymptomatic: $N = 17$
  - Mild/Moderate: $N = 89$
  - Severe/Critical: $N = 19$
  - $P = 0.0389$
  - $P = 0.0546$ \(P = 0.6907\)

- **IgA**
  - Asymptomatic: $N = 17$
  - Mild/Moderate: $N = 89$
  - Severe/Critical: $N = 19$
  - $P = 0.0031$
  - $P = 0.0210$ \(P = 0.2565\)
Comparison of mother-infant antibody responses at L&D to maternal vaccination and SARS-CoV-2 natural infection

- **Maternal**
  - IgG at L&D
  - IgM at L&D
  - IgA at L&D

- **Infant**
  - IgG at birth

Statistical significance:
- P = 0.0002
- P = 0.1161
- P = 0.0276
- P = 0.0001
Conclusions

• Pregnancy confers an increased risk of infection due to dynamic immunologic changes that facilitate fetal growth

• COVID-19 in pregnancy may be associated with increased risk of maternal ICU admissions, ARDS, and adverse pregnancy outcomes

• Minority and disenfranchised pregnant women are disproportionately impacted by COVID-19 as a result of systemic inequities.

• Pregnant women with severe/critical COVID-19 exhibit distinct immune signatures that may explain clinical manifestations.

• Nearly all clinical trials excluded pregnant women, although remdesivir, dexamethasone, monoclonal antibodies and convalescent plasma are still recommended when appropriate.

• SARS-CoV-2 vaccines were not tested in pregnant women, but should be offered to all pregnant individuals.

• Low risk of SARS CoV-2 MTCT, but long term infant follow-up recommended.
Pregnant women in this cohort with severe/critical disease were more likely to be Latina, have public insurance, and have at least one underlying medical condition, reflective of systemic racism/inequities.

SARS-CoV-2 infection re-shaped maternal immunity at delivery, potentially promoting late pregnancy- and postpartum-related complications.

SARS-CoV-2 infection in pregnancy appears to trigger NF-κB-dependent proinflammatory immune activation.

Cytokines do not appear to cross the placenta.

Neonates with in-utero exposure to severe/critical COVID-19 maternal disease exhibited dysregulated Wnt signaling, which may impact immunity and neurodevelopment.
Take home points

- Pregnant women are at higher risk of developing COVID-19 related complications and their infants are at risk of being premature and having respiratory distress at birth, even if not infected.

- Mother to child transmission of SARS CoV-2 is rare.

- Infants born to women who had COVID-19 in pregnancy should be followed closely for neurodevelopment, regardless of whether the mother has severe illness.

- Maternal antibodies to COVID-19 cross the placenta and protect the fetus when the mother was vaccinated or had moderate to severe illness. Vaccination confers the highest antibody levels to the infant.

- By six months of age, maternal antibodies to SARS CoV-2 transferred to the infant have waned.
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Any questions?