Placental Pathology in SARS-CoV-2 Positive Mothers

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I have nothing to disclose.
• Preliminary studies of placental pathology in SARS-CoV-2 mothers at New York Presbyterian Hospital
  o Early data (Baergen & Heller)
  o Prospective cohort study at NYP (Prabhu et al)
  o NYP- Brooklyn Methodist (Zhang et al)
  o Combined data from NYP Brooklyn Methodist & NYP WCM
  o Complement (Mulvey et al)
Initial Study
Baergen & Heller Pediatr Devel Pathol 2020

• 100% of patients admitted to L&D tested for Covid-19
• Placental pathology was reviewed on Covid-19 positive mothers
• All infants also tested within 24 hours of life
• Initial review of first 20 cases
  o 9/20 cases with lesions of fetal vascular malperfusion (FVM)
  o All low grade
  o All segmental
Fetal vascular thrombosis
Intramural fibrin deposition
Avascular Villi
Villous stromal-vascular karyorrhexis
Other pathology

- 5 patients with maternal vascular malperfusion (1 with FVM)
- 7 patients with meconium-filled macrophages in membranes
- 3 cases of chronic villitis (one with obliterate vasculopathy, one with FVM)
- 1 case of hypercoiled cord with marginal insertion (no FVM)
- 1 case of furcate cord insertion with FVM
Clinical

- 2 patients with severe PEC (1 with MVM)
- One patient with fever (+ for FVM)
- One patient with pneumonia and acute hypoxia (+FVM and MVM)
- One patient readmitted from SOB (+FVM)
- One patient with chronic diabetes (no pathology)
- One patient with hypertension (+FVM, chronic villitis)
**Prabhu et al BJOB 2020**

- Epidemiology of Covid-19 positive mothers
- Across 3 NYP medical centers
- 100% of pregnant women were tested for SARS CoV-2 via nasopharyngeal swab PCR prior to delivery during the time period of the study (approx. 6 months)
- Neonates were also tested after delivery
- 675 women admitted with positive rate of 10.4% (n=70)
- 55 patients (78.6%) asymptomatic
- Symptoms (n=15)
  - Cough most common – 7 patients (46.7%)
    - 5 patients (33.3%) fever after initially being afebrile
    - 7 patients developed fever after initially being asymptomatic
• One patient at 37 weeks gestation was transferred to the intensive care unit (ICU) due to an increasing oxygen requirement in the setting of multifocal pneumonia and pulmonary edema
• Two other women developed oxygen requirements
• No patients required mechanical ventilation
• One fetal demise in an asymptomatic patient with uncontrolled diabetes
• Comorbidities were significantly increased in positive patients
  o Chronic hypertension (p=0.006)
  o Pregestational diabetes (p=0.021)
  o Obesity (p=<0.001)
• All neonates were tested via RT-PCR and were negative
• Placental pathology on 29 cases
• Control placentas were reviewed during the same time period (6 months, n=106)
• Placentas were evaluated for the presence of:
  o Fetal vascular malperfusion
  o Maternal vascular malperfusion
  o Acute chorioamnionitis
  o Chronic villitis
  o Presence of meconium
  o Umbilical cord abnormalities
  o Chorangiosis
  o Other placental abnormalities
From Prabhu et al *BJOB (in press).*

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>FVM</td>
<td>14 (48.3%)</td>
<td>12 (11.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MVM</td>
<td>8 (27.6%)</td>
<td>33 (31.1%)</td>
<td>0.82</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>3 (10.3%)</td>
<td>16 (15.1%)</td>
<td>0.92</td>
</tr>
<tr>
<td>Chronic villitis</td>
<td>5 (17.2%)</td>
<td>13 (12.3%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Meconium staining</td>
<td>18 (62.1%)</td>
<td>33 (31.1%)</td>
<td>0.004</td>
</tr>
<tr>
<td>UC abnormalities</td>
<td>1 (3.4%)</td>
<td>17 (16.0%)</td>
<td>0.12</td>
</tr>
</tbody>
</table>
From Zhang et al AJOG MFM *(in press)*

- Placental pathology in Covid-19 positive mothers
- 74 positive patients, 290 negative controls
- No significant difference in placental pathology between groups
  - Decidual vasculopathy
  - Infarcts
  - Abruption
  - Chorioamnionitis
  - Meconium
  - Thrombosis
  - Avascular villi
  - Villitis
  - Cord issues
  - Massive perivillous fibrin deposition/maternal floor infarction
• Covid-19 positivity had a negative correlation with
  o History of preeclampsia (p=0.003)
  o History of category 2 fetal heart tracing (p<0.001)
  o Cesarean delivery (p=0.048)
  o Significance unclear
• 53 placentas with Covid-19 positive mothers were tested for SARS-CoV-2 by ISH
• 2 of 53 positive (3.8%).
• One of ISH positive placentas
  o Neonate tested positive for Covid-19 via nasopharyngeal swab PCR
  o Asymptomatic and discharged home
Combined Cases WCM
(unpublished data)

• Cases from original studies at NYP-WCM
• Cases reported from NYP-WCM Brooklyn Methodist
• Additional cases since publication
• 196 cases/193 controls
## Clinical characteristics

<table>
<thead>
<tr>
<th>COVID19</th>
<th>Negative</th>
<th>Positive</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>(N=193)</td>
<td>(N=196)</td>
<td></td>
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</tr>
<tr>
<td>Gestational age</td>
<td>39.0 [38.0;40.0]</td>
<td>39.0 [37.0;40.0]</td>
<td>0.052</td>
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<tr>
<td>Delivery</td>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>- Cesarean</td>
<td>83 (43.0%)</td>
<td>58 (29.6%)</td>
<td></td>
</tr>
<tr>
<td>- Vaginal</td>
<td>110 (57.0%)</td>
<td>138 (70.4%)</td>
<td></td>
</tr>
<tr>
<td>Category 2 (NRFH)</td>
<td></td>
<td>&lt;0.001</td>
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</tr>
<tr>
<td>absent</td>
<td>148 (76.7%)</td>
<td>188 (95.9%)</td>
<td></td>
</tr>
<tr>
<td>present</td>
<td>45 (23.3%)</td>
<td>8 (4.1%)</td>
<td></td>
</tr>
<tr>
<td>IUGR</td>
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<td>0.444</td>
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</tr>
<tr>
<td>-</td>
<td>183 (94.8%)</td>
<td>187 (96.9%)</td>
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</tr>
<tr>
<td>+</td>
<td>10 (5.2%)</td>
<td>6 (3.1%)</td>
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<tr>
<td>IUFD</td>
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<td>0.726</td>
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</tr>
<tr>
<td>-</td>
<td>190 (98.4%)</td>
<td>189 (97.4%)</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>3 (1.6%)</td>
<td>5 (2.6%)</td>
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### Placental Pathology

<table>
<thead>
<tr>
<th>Condition</th>
<th>Covid-19</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Negative</td>
<td>Positive</td>
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</tr>
<tr>
<td>FVM</td>
<td>184 (95.3%)</td>
<td>156 (79.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>9 (4.7%)</td>
<td>40 (20.4%)</td>
<td></td>
</tr>
<tr>
<td>MVM</td>
<td>177 (91.7%)</td>
<td>163 (83.2%)</td>
<td>0.017</td>
</tr>
<tr>
<td></td>
<td>16 (8.3%)</td>
<td>33 (16.8%)</td>
<td></td>
</tr>
<tr>
<td>Meconium</td>
<td>115 (59.6%)</td>
<td>125 (63.8%)</td>
<td>0.456</td>
</tr>
<tr>
<td></td>
<td>78 (40.4%)</td>
<td>71 (36.2%)</td>
<td></td>
</tr>
<tr>
<td>Abruptio</td>
<td>189 (97.9%)</td>
<td>191 (97.4%)</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>4 (2.1%)</td>
<td>5 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>110 (57.0%)</td>
<td>152 (77.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>83 (43.0%)</td>
<td>44 (22.6%)</td>
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<tr>
<td>Acute Funisitis</td>
<td>150 (77.7%)</td>
<td>179 (91.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>43 (22.3%)</td>
<td>17 (8.7%)</td>
<td></td>
</tr>
<tr>
<td>Chronic villitis</td>
<td>148 (76.7%)</td>
<td>156 (79.6%)</td>
<td>0.568</td>
</tr>
<tr>
<td></td>
<td>45 (23.3%)</td>
<td>40 (20.4%)</td>
<td></td>
</tr>
<tr>
<td>Cord issue</td>
<td>179 (92.7%)</td>
<td>171 (87.2%)</td>
<td>0.102</td>
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<td></td>
<td>14 (7.3%)</td>
<td>25 (12.8%)</td>
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Pathogenesis –
Mulvey et al Ann Diagn Path (in press)

• Possible complement mediated
• Study of 5 placentas of Covid-19 positive mothers
• All had evidence of FVM
• None showed increased complement expression by IHC
• Viral RNA and viral spike protein was negative in all cases

?The finding of vascular thrombosis without complement deposition may reflect the systemic nature of COVID-19’s procoagulant effects unrelated to systemic complement activation.
Final Comments

- Additional studies needed to address:
  - Discrepancies in different studies
  - Vertical transmission
  - Pathogenesis
References


