Histopathologic Chorioamnionitis: Geodemographic and Clinical Predictors

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BACKGROUND

- Chorioamnionitis is an infection of fetal membranes that occurs in up to 10.5% of laboring women.
- Clinical chorioamnionitis:
  - Evidence of infection based on Maternal Fever and/or Tenderness, Tachycardia, Maternal Leukocytosis, OR foul-smelling amniotic fluid.1,2
  - Fever is considered the most predictive sign of chorioamnionitis, however its use to predict chorioamnionitis is imperfect.1
  - Fever is often caused by other entities which makes clinical diagnosis challenging.
- Histopathologic chorioamnionitis:
  - Evidence of infection or inflammation based on placental examination.1,2
  - Often considered the gold standard for diagnosis, however confirmation of chorioamnionitis is not available until after delivery.
- Ultimately, we rely on clinical signs at the time of delivery for the diagnosis of chorioamnionitis.
- However, studies have shown that the ability to identify histopathologic chorioamnionitis based on maternal fever is only 42% sensitive.3
  - Sensitivity increased to 60% when one other clinical sign was also present.3

PROBLEM

Fever, which is often used for the diagnosis of clinical chorioamnionitis, may be absent in histopathologic chorioamnionitis.

OBJECTIVE

To explore the associated risk factors and geographic distribution of histopathologic chorioamnionitis.

METHODS

STUDY DESIGN

- Retrospective study of mothers with babies born at Aurora hospitals, 2007-2013

- Cases = mothers with histology confirmed chorioamnionitis
- Controls = mothers without histology confirmed chorioamnionitis
- Randomly selected using statistical software
- Cases and controls (1:1 ratio) were only included in analysis if maternal age, race/ethnicity, clinical chorioamnionitis, and fetal status were identified (95.7% of original case population utilized).

STATISTICAL ANALYSIS

- Minitab Statistical software (Version 13, State College, PA) was utilized.
- Associations between maternal or neonatal variables and histopathologic chorioamnionitis were examined with:
  - Pearson chi-squared test of independence
  - Fisher's exact test
  - Mann-Whitney U test
  - Two-sample t-tests
- P values less than 0.05 were deemed statistically significant.
- Predictor variables significant on univariable analysis were included in multivariable logistic regression.

RESULTS

- Across all cases and controls (N=2,758), mothers of mean age 27.6 years and pre-pregnancy BMI 27.3 kg/m², were predominately White (53.6%), married (52.1%), multiparous (54.0%) and from 32XXX ZIF code group (54.9%). Neonates were of mean gestational age 37.7 weeks, male (53.5%) and primarily born vaginally (64.3%).
- 51.1% of those with histopathologic chorioamnionitis were febrile in labor (compared to 1.2% of controls, p<0.0001; Table 1).
- Fever in labor was only present among 26.3% of those with histopathologic chorioamnionitis who were <37 weeks gestation, 60.1% among those ≥ 37 weeks, p<0.0001 and 55.3% of multiparous mothers with HCA (vs. 41.4% among those who were multiparous; p<0.0001).
- Clinician suspicion of chorioamnionitis following placental delivery was 77.5% sensitive and 99.6% specific for prediction of histopathologic chorioamnionitis.
  - Positive predictive value 99.4%
  - Sensitivity higher in those <37 weeks gestation (83.3% vs. 75.3% among those ≥ 37 weeks, p=0.002)

CONCLUSIONS

- Our ability to identify those who are infected with chorioamnionitis before placental examination is significantly decreased in term (vs. preterm) gestations.
- Fever is absent in nearly half of all deliveries with histopathologic chorioamnionitis.
- Clinical definitions of chorioamnionitis that require fever for diagnosis will miss significant numbers of those with histopathologic chorioamnionitis.
- Clinical suspicion of chorioamnionitis following delivery of the placenta has high positive predictive value in our system, and may be useful to guide initial antibiotic treatment of the neonate.

Table 1: Predictors of Histopathologic Chorioamnionitis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Cases (N=1,384)</th>
<th>Controls (N=1,374)</th>
<th>Univariable OR (95% CI)</th>
<th>p-value</th>
<th>Multivariable OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age, mean (SD)</td>
<td>28.2 ± 5.8</td>
<td>27.7 ± 5.1</td>
<td>1.00 (0.63 - 1.58)</td>
<td>0.992</td>
<td>1.04 (0.65 - 1.66)</td>
</tr>
<tr>
<td>Pre-pregnancy BMI (kg/m²), median</td>
<td>25</td>
<td>25</td>
<td>1.03 (0.65 - 1.50)</td>
<td>0.002</td>
<td>1.08 (0.60 - 1.90)</td>
</tr>
<tr>
<td>Married, Y/N</td>
<td>Yes</td>
<td>No</td>
<td>1.04 (0.68 - 1.57)</td>
<td>0.014</td>
<td>1.04 (0.60 - 1.47)</td>
</tr>
<tr>
<td>Nature &amp; Race &amp; Ethnicity</td>
<td>778 (55.2)</td>
<td>583 (42.6)</td>
<td>1.54 (1.32 - 1.81)</td>
<td>0.0001</td>
<td>1.15 (0.87 - 1.50)</td>
</tr>
<tr>
<td>Non-White Race &amp; Ethnicity</td>
<td>722 (53.2)</td>
<td>549 (40.1)</td>
<td>1.67 (1.44 - 1.93)</td>
<td>0.0001</td>
<td>1.27 (0.96 - 1.68)</td>
</tr>
<tr>
<td>32XX ZIF code Group A</td>
<td>803 (63.9)</td>
<td>529 (39.1)</td>
<td>2.10 (1.80 - 2.51)</td>
<td>0.0001</td>
<td>1.50 (1.20 - 1.90)</td>
</tr>
</tbody>
</table>

- $P < 0.005$ for all variables.