ABSTRACT

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OBJECTIVE: To look for evidence of HCA in spontaneous preterm labour by histopathological examination of the placenta and correlate early neonatal mortality with severity to HCA.

METHODOLOGY: The study consists of all women who are admitted with spontaneous preterm labour pain and after delivery placental examination was done.

RESULTS: 60 cases were studied, 33 were late preterm (55%), 15 were moderate (25%), 8 very preterm (13%) and 4 extreme preterm (7%). Percentage of HCA in each group was 15, 80, 75.8, 100 respectively. Mean gestational age and mean birth weight of HCA group (n=27) was 31.40±1.13 and 1706.40±227.58 and without HCA (n=33) was 34.51±0.54 and 2245.90±162.47 respectively. The maternal total leucocyte count was significantly high in HCA group. Maternal CRP was raised in 26 patients of which 22 had HCA. Neonatal mortality was 3 amongst 60, 3 of the babies had HCA.

CONCLUSION: In our study, we found that HCA is significantly correlated with lower gestational age, lower birth weight, higher maternal total leucocyte count, higher maternal CRP, thus suggesting that maternal inflammation could be one of the causes of spontaneous preterm birth.

Preterm delivery, defined as delivery occurring before 37 weeks' gestation. The rate of preterm delivery has increased 20 percent since 1990; recent increases have been associated primarily with late preterm (i.e., 34 to 36 weeks' gestation) deliveries.¹

Based on gestational age at delivery preterm births is subdivided into: infants born preterm are delivered before 37 completed weeks of gestation. Late preterm births between 34 and 36 weeks and 6 days of gestation. Moderate preterm are delivered between 32 and 33 weeks and 6 days of gestation.²

Before 32 weeks gestation there is a significant increase in Infant Mortality Rates. Preterm birth is a major cause of infant mortality and morbidity and is associated with long-term adverse sequelae like cerebral palsy and visual, hearing, and learning problems.³

Chorioamnionitis is a common cause of preterm birth. Chorioamnionitis may manifest as a clinical condition defined by maternal fever, leukocytosis, tachycardia, uterine tenderness, and preterm rupture of membranes.⁴ Chorioamnionitis can be subclinical, which is considered to be the most common manifestation and is defined histologically by inflammation of the chorion, amnion, and placenta.⁵

If placental tissue histology shows presence of histological evidence of subclinical chorioamnionitis, it can be confirmed and this could substantiate the need of prophylactic antibiotics in spontaneous preterm labour. Since prematurity is the commonest cause of neonatal mortality in India and there are only a very few studies that appear normal on gross examination, two right placenta were examined for the presence of histological chorioamnionitis in Indian population, we have undertaken this study.

AIMS AND OBJECTIVES

Primary objective - To look for evidence of subclinical chorioamnionitis in spontaneous preterm labour by histopathological examination of the placenta.

Secondary objective - To correlate early neonatal mortality in preterm deliveries with severity to subclinical chorioamnionitis

METHODOLOGY

This descriptive study is being conducted in the Department of Obstetrics and Gynaecology and Pathology, Jubilee Mission Medical College and Research Institute in a time period of December 2015 to October 2017.

During this period 60 preterm pregnant women who were admitted in labour room with spontaneous preterm labour were selected using inclusion and exclusion criteria. A detailed history was obtained from these patients as per proforma. Complete clinical examination was done. Immediately after delivery, the placenta was taken and kept in formalin. This was then sent to the department of pathology for further fixation followed by grossing and examined for evidence of Histological Chorioamnionitis (HCA).

Placenta examination protocol

Placentas were formalin fixed and gross examination was done using standard protocols. During the examination, the size, shape, consistency and completeness of the placenta were determined, and the presence of accessory lobes, placental infarcts, hemorrhage, tumors and nodules were noted.

The umbilical cord was assessed for length, insertion, number of vessels, thromboses, knots and the presence of Wharton’s jelly. The color and luster of the fetal membranes were evaluated, and the membranes were examined for the presence of large (velamentous) vessels.

Nine tissue samples embedded in paraffin blocks for microscopic assessment:

- two extraplacental membrane samples,
- two umbilical cord samples (one proximal and one distal to disc insertion), and
- five full-thickness disc samples, one the cord insertion, one in central tissue that appear normal on gross examination, two from central tissue, and one at the margin.

Definitions of histologic chorioamnionitis

Placental tissue components (i.e., cord, plate, and extraplacental membrane; extraplacental membrane only)

(i.e., at least one high-powered field with a polymorphonuclear leukocyte inflammatory pattern;)

- >10 polymorphonuclear leukocytes = Grade 1
- >30 polymorphonuclear leukocytes = Grade 2
- >100 polymorphonuclear leukocytes = Grade 3

Severity of chorioamnionitis will be compared to neonatal mortality that occurs before corrected gestational age of 40 weeks.
INCLUSION CRITERIA
Women within gestational weeks 24 through 36 weeks, singleton pregnancy, maternal age of 18 or more years, with spontaneous preterm delivery with or without membranes rupture was enrolled in this study

EXCLUSION CRITERIA
With known congenital anomaly in fetus and uterine anomaly in mother, associated pregnancy induced hypertension or diabetes in pregnancy.

SAMPLE SIZE = 60

RESULTS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total n=60</th>
<th>With HCA Chorioamnionitis</th>
<th>Without HCA Chorioamnionitis</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) [independent t test]</td>
<td>25.66±4.8</td>
<td>26.70 ± 1.99</td>
<td>24.81 ± 1.68</td>
<td>0.14</td>
</tr>
<tr>
<td>Booked</td>
<td>51</td>
<td>20</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Unbooked[fischer exact test]</td>
<td>9</td>
<td>7</td>
<td>2</td>
<td>0.06</td>
</tr>
<tr>
<td>Primi</td>
<td>28</td>
<td>14</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Multi[fischer exact test]</td>
<td>32</td>
<td>13</td>
<td>19</td>
<td>0.60</td>
</tr>
<tr>
<td>Mean gestational age (weeks)</td>
<td>33.11±2.6</td>
<td>31.40±1.13</td>
<td>34.51±0.54</td>
<td>0.0001</td>
</tr>
<tr>
<td>Median gest age</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extreme preterm</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Very preterm</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Moderate preterm</td>
<td>15</td>
<td>12</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Late Preterm</td>
<td>33</td>
<td>5</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>PPROM [fischer exact test]</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>0.74</td>
</tr>
<tr>
<td>Male</td>
<td>36</td>
<td>15</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>24</td>
<td>17</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Mean birth weight (gms) [independent t test]</td>
<td>2003.13±571.38</td>
<td>1706.40±227.58</td>
<td>2245.90±162.47</td>
<td>0.0001</td>
</tr>
<tr>
<td>Neonatal death [fischer exact test]</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0.08</td>
</tr>
<tr>
<td>Total Leukocyte count (cells/mm3)</td>
<td>15660.16±6401.19</td>
<td>18937.40±2490.82</td>
<td>12978.78±1888.44</td>
<td>001</td>
</tr>
<tr>
<td>CRP Positive [fischer exact test]</td>
<td>26</td>
<td>22</td>
<td>4</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Out of the 60 cases with spontaneous preterm labor studied, 33 were late preterm (55%) , 15 were moderate preterm(25%), 8 very preterm (13%) and 4 extreme preterm(7%). Percentage of HCA in each group was 15 in late preterm, 80 in moderate preterm, 75 in very preterm, 100 in extreme preterm. The mean gestational age of HCA group (n=27) was 31.40± 1.13 and that of without HCA (n=33) was 34.51 ± 0.54 which was found to be statistically significant.

The mean birth weight in HCA group was 1706.40± 227.58 vs without HCA 2245.90±162.47. The maternal total leucocyte count in HCA group was 18937.40± 2490.82 and without HCA group was 12978.78 ± 1888.44 which was statistically significant, and maternal CRP was found to be raised in 26 patients of which 22 had HCA.

Neonatal mortality was 3 amongst 60, 3 of the babies had HCA.

DISCUSSION AND CONCLUSION
Intrauterine infection is one of the frequent causes of preterm birth. Prostaglandins that stimulate uterine contractility are thought to be produced by the microbial endotoxins and proinflammatory cytokines. Intrauterine infection/inflammation not only causes preterm labor, but is also associated with PROM and decreased response to tocolytics.

In our study 45% of all spontaneous preterm delivery had evidence of HCA, which was higher than the other 2 studies where the incidence was 23.25% and 35.5%. The incidence of HCA is reported as 60-80%, 40-50%, and 5-30% in deliveries at gestations less than 28 weeks, between 29 and 34 weeks, and greater than 34 weeks, respectively by Lahra M. M. et al. In the present study, HCA rate was also found to be inversely related to week of delivery. This rate was especially noteworthy in deliveries below 34 weeks, where the incidence was 100%, 83.3% and 80% in extreme preterm, very preterm and moderate preterm respectively. The higher incidence of HCA in our study might have been because of the difference sample selection criteria and demographics.

The mean maternal age in our study was 26.70 ± 1.99 years, 24.81 ± 1.68 years respectively for mothers with and without HCA respectively. This was lesser than the similar studies by Erdemir G et al and Wu H et al. This might be because of the difference in demographics and sociocultural background of the mothers.

In our study HCA was more in unbooked cases and this was statistically significant.

In our study the mean gestational age of the HCA mothers(31.40± 13.13 weeks) were significantly lower than that of non HCA group (34.51 ± 0.54 weeks). Similar studies by Wu H et al and Erdemir G et al also showed statistically significant decrease in mean gestational age in HCA group.

Mean birth weight of the babies born to HCA mothers were significantly lesser than that of non HCA group. Similar study by Erdemir G et al also showed significant decrease in the birth weight. In a study by Wu H et al the mean birth weight of the babies in HCA group was lower than the other group but this difference was not statistically significant. The possible reason for this lower mean birth weight is because HCA group had significantly lower gestational age.

The mean total leucocyte count of mothers with HCA was significantly higher in our study. Other studies by Wu H et al also showed increase in total leucocyte count in the mothers with placental inflammation. But those differences were not statistically significant. Similar study by Erdemir G et al also showed higher total leucocyte counts in mothers with HCA and this difference was statistically significant.

In our study the HCA group had higher CRP positivity rates compared to non HCA group. This difference was statistically significant. In similar studies by Wu H et al and and Erdemir G et al, the mean CRP values were higher in mothers with placental inflammation. Maternal blood leucocyte count, CRP and IL-6 values, and glucose and cytokines in the amniotic fluid are biochemical parameters suggested for the diagnosis of CA, but their use in clinical evaluation is quite limited. Sensitivity of maternal CRP value for intrauterine infection was found to be 27%, with a specificity of 80%, and maternal serum CRP level is not affected by antenatal steroids. Yoon et al reported that maternal CRP and leucocyte count were significantly higher in CA, but amniotic fluid leucocyte count was more sensitive.

In our study there were three neonatal deaths in HCA group and none in the other. However this difference was not statistically significant. Erdemir G et al in similar study showed a significantly higher mortality rate in neonates born to mothers with HCA. Ogunyemi et al reported that pregnant women with HCA give birth earlier (at approximately 28.4 weeks); neonatal morbidities including BPD, PDA, IVH, and early neonatal sepsis are more frequent; and neonatal mortality is also higher in these infants.

In our study the incidence of preterm premature rupture of membranes (PPROM) was 1.3%, and that which had HCA was...
HCA was significantly correlated with lower gestational age, lower birth weight higher maternal CRP positivity, higher maternal WBC count. These findings further confirm the association between maternal inflammation and preterm deliveries

This being a non invasive and simple test can be done in all spontaneous preterm deliveries, as chorioamnionitis as such can be easily overlooked and undiagnosed unless it is confirmed by histopathological examination of placenta and the same shows evidence of HCA

However, the relationship of HCA with neonatal mortality has not been well understood and further studies have to be done in this area. Also duration of Preterm premature rupture of membranes and its relation with HCA is to be studied further.

References: