Could mother intrapartum RDW, leukocytosis and elevated CRP predict early neonatal infection or sepsis?

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Infection, sepsis and mother laboratory findings

- The aim of study was to determine could the intrapartum maternal laboratory exams of the:
  - Red cell distribution width (RDW)
  - Leukocytes (L)
  - C-reactive protein (CRP)

Predict early newborn infection or sepsis
Newborn laboratory findings

- Diagnosis of neonatal sepsis may be difficult because clinical presentations are often nonspecific, bacterial cultures are time-consuming

- Laboratory tests lack sensitivity and specificity

- Role of procalcitonin (PCT), C-reactive protein (CRP), interleukin (IL)-6, IL-8 and tumor necrosis factor-alpha (TNF-alpha)

- TNF-alfa and PCT used in practice for diagnosis of neonatal sepsis
Infection and Sepsis

- Early onset sepsis develops in the first 2-3 days after birth
- Late onset sepsis develops within 3-7 days after birth
- Neonatal sepsis is caused by bacteria. The infant may come in contact with bacteria during:
  - Pregnancy
  - Birth
  - Environment after birth
Focus was on the RDW

Last reports of possible connection RDW with sepsis in adults as in newborn or neonatal sepsis


Intent was check if there were changes in RDW, L or CRP in mothers whose newborns had early infection or sepsis

Infection from the mother may pass to the newborn trans - placentary or throught birth canal during delivery
Infection, Sepsis

- Early onset sepsis is caused by an infection from the mother. It may pass to the infant from the placenta or birth canal during birth.
- Antibiotics may be given to high risk mothers, during labour. They have been able to prevent early onset bacterial sepsis in some infants.
- Late onset sepsis is caused by bacteria from the caregiving environment.

✓ Male babies have a greater risk for neonatal sepsis than female babies
Definition, instruments

- Infection an Sepsis was diagnosed based on the standard formulated by the International Joint Conference of Pediatric Sepsis.


- ARCHITECT - C 8200 automatic blood cell analyzer was used
Laboratory RDW, L, CRP

- The more RDW is, the more uneven the red blood cell size is, and the higher the volume heterogeneity is.

- Recent studies found that RDW can taken as a “marker” of death in critical patients.


- It can be used independently to predict the risk of death in critical patients.
Material and Methods

- Relationship between laboratory findings (RDW, L, CRP) intrapartum of the in three groups of the mother`s were analysed

- Only newborns who admitted neonatal intensive care unit (NICU - Split University Hospital) with diagnosis of infection and sepsis (early onset) were included in study

- From January 2007 to July 2015 yr.
Material and Methods

- Three groups of mother`s in delivery were compared
  - Group (0) Control group – mothers who delivered normal healthly newborn up to 34 weeks of pregnancy (control were randomised on recommendation of statistician) N = 145
  - Group (1) Infection group – newborns with infection (NICU – diagnosis) N = 51
  - Group (2) Sepsis group – newborns with early onset sepsis (NICU – diagnosis) N = 33
Material and Methods

- Mother’s obstetrical history
- Delivery course and outcome were assessed
- Laboratory findings intrapartum
- In statistical analysis were used:
  - Kruskal – Wallis test,
  - Mann-Whitney test,
  - Chi-squared test (p-value smaller than 0.05)

Control group size and randomisation were made under control of statistician
# Results

<table>
<thead>
<tr>
<th></th>
<th>Group (0)</th>
<th>Group (1)</th>
<th>Group (2)</th>
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</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>145</td>
<td>51</td>
<td>33</td>
</tr>
<tr>
<td><strong>Mean value – RDW</strong></td>
<td>14,0</td>
<td>13,9</td>
<td>22,7</td>
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<tr>
<td><strong>RDW – Conf. interval (CI)</strong></td>
<td>13,7 – 14,2</td>
<td>13,6 – 14,2</td>
<td>5,2 – 40,1</td>
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<tr>
<td><strong>Leukocytes (L) mean</strong></td>
<td>11,8</td>
<td>14,3</td>
<td>10,1</td>
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<tr>
<td><strong>Leukocytes – CI</strong></td>
<td>11,4 - 12,3</td>
<td>12,9 - 15,6</td>
<td>7,8 - 12,3</td>
</tr>
<tr>
<td><strong>CRP mean</strong></td>
<td>5,4</td>
<td>16,7</td>
<td>20,7</td>
</tr>
<tr>
<td><strong>CRP – CI</strong></td>
<td>4,6 – 6,2</td>
<td>8,5 – 25,1</td>
<td>5,7 – 35,7</td>
</tr>
</tbody>
</table>
Results

- Between all three groups RDW values were not statistically different ($\chi^2 = 3.25, p = 0.196$)

- Leukocytes was also not statistically different between groups ($\chi^2 = 3.8, p = 0.121$)

- Values of the CRP were statistically different ($\chi^2 = 29.2, p < 0.001$)
**Results**

- Mann-Whitney test did not found statistically significant difference between values of CRP and Leukocytes in infection and sepsis ($Z = 0.69; p = 0.54$)

- Statistically significant difference was found for CRP between infections and control ($Z = 4.9$ a $p < 0.001$)

- Statistically significant difference for CRP also found between control and sepsis ($Z = 3.3; p = 0.001$)

- For CRP area under curve were $0.679$, $95\%$ (CI : $0.613 – 0.782$); $p < 0.001$ for specificity of $95\%$

- **But sensibility was lower than 25.5 % for CRP**
Green – Control (0) Yellow – Infection (1) Red – Sepsis (2)
Conclusion

- RDW were elevated in sepsis but did not reach statistically significance

- Leukocytes also did not reach statistically significance difference

- CRP were statistically significance elevated but with very low sensitivity for infection and sepsis (about only 25%)
Conclusion

- New paper (2014) \(^4\) conclude significant risk of early sepsis in case of mother CRP (\(\geq 15\) mg/L)


- Jeon et all concludes : “In newborn of high CRP mother, the clinician may be alerted to earlier evaluation for possible neonatal infection”

- Our work did not prove this opinion
Conclusion

- Work from (2005)\(^5\) Interleukin IL-6, IL-8 in maternal blood was indicative of intrauterine environmental threats


- Serial Ultrasonographic Examination of the Fetal Thymus in the Prediction of Early Neonatal Sepsis in Preterm Premature Rupture of Membranes\(^6\)

Diocletian palace builded by roman emperor
Diocletian A.D. 305 year
World's most powerful man in the time 1700 years from today
Croatia, Split University Clinic of the Obstetrics and Gynecology