Skin and gut colonisation with *Staphylococcus haemolyticus* in term and preterm neonates

Hanna Kadri Metsvaht¹, Tuuli Metsvaht², Imbi Eelmäe³, Mirjam Merila³, Mari-Liis Ilmoja³, Irja Lutsar¹, Hiie Soeorg¹

¹Department of Microbiology, University of Tartu, Tartu, Estonia; ²Pediatric Intensive Care Unit, Tartu University Hospital, Tartu, Estonia; ³Department of Neonatology, Children’s Clinic, Tartu University Hospital, Tartu, Estonia; ⁴Pediatric Intensive Care Unit, Tallinn Children’s Hospital, Tallinn, Estonia

**Background**

- Among coagulase-negative staphylococci *Staphylococcus haemolyticus* (SH) is the second commonest cause of late-onset sepsis (LOS) in preterm neonates. Clones spread in NICUs has been described.
- SH colonisation is poorly described. Understanding the mechanisms of SH colonisation may hold potential to develop strategies for prevention of invasive infection.

**Aim**

To compare SH colonisation of healthy term and hospitalized preterm neonates in terms of:
- the prevalence and multilocus variable-number tandem-repeats analysis (MLVA) type distribution
- the prevalence of virulence factors

**Material and Methods**

- **Included neonates**
  - Preterm neonates in NICU who started BM feeding with own mother’s BM within the 1st week of life (n=49).
  - Healthy term exclusively BM fed neonates (n=20).
- **Sampling**
  - Skin swabs and stool samples from neonates and BM from mothers collected once a week.
- **Isolation of staphylococci**
  - Cultured onto mannitol salt agar incubated at 37°C for 48h.
  - 5 colonies picked.
- **Identification to the species level**
  - MALDI-TOF MS
- **Typing of *S. haemolyticus***
  - MLVA
- **Characterization of *S. haemolyticus***
  - mecA; IS256; icaA

**Results**

- **SH colonisation**
  - of preterm neonates was predominated by a few MLVA-types. These MLVA types also caused LOS.
  - of term neonates was more diverse with almost no overlap with NICU admitted preterm neonates

- **Median (range) gestational age and birthweight of included term and preterm neonates was 40 (39-40) and 28 (25-30) wks; 3651 (3324-3970) g**
- **Colonisation with SH was**
  - more likely in preterm than term neonates (45/49 vs 11/20; OR 9.2; 95%CI 2.4-35.5)
  - equally likely in gut and on skin (55/69 vs 51/69; OR 1.4; CI 0.6-3.1).
- **In unit A 15/19 and in unit B all neonates were colonised with SH (p=0.018294)**
- **621 isolates represented 41 MLVA-types, 32 present in preterm and 12 in term neonates, with only 3 colonising both term and preterm.**

- **MLVA-types colonising preterm compared with term neonates carried more likely virulence genes**
  - mecA (153/185 vs 1/27; OR 124.3; 95%CI 16-950)
  - IS256 (95/185 vs 0/27; OR 58; 95% CI 3-966)
  - None of tested isolates were icaA positive.
  - Five MLVA-types (Figure 1)
    - Colonised 69% (34/49) of preterm, but none of term neonates
    - Caused 7 episodes of LOS in 6 preterm neonates. (Table)

**Table: LOS cases.**

<table>
<thead>
<tr>
<th><strong>Patient</strong></th>
<th><strong>MLVA-type</strong></th>
<th><strong>Age during first isolation from blood (days)</strong></th>
<th><strong>Isolated from skin before LOS (days)</strong></th>
<th><strong>Isolated from gut before LOS (days)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>B10</td>
<td>14</td>
<td>7</td>
<td>=</td>
<td>*</td>
</tr>
<tr>
<td>B16</td>
<td>19</td>
<td>17</td>
<td>*</td>
<td>3</td>
</tr>
<tr>
<td>B20</td>
<td>13</td>
<td>10</td>
<td>4</td>
<td>*</td>
</tr>
<tr>
<td>B21</td>
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<td>5</td>
</tr>
<tr>
<td>B22</td>
<td>19</td>
<td>7</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>C07</td>
<td>19</td>
<td>15</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Each MLVA-type is presented in a different color. If MLVA-types colonised gut or skin prior to or at the same time as blood, it is colored accordingly.
= isolated on the same day as LOS
* isolated later than from blood or not fount on this site

**Conclusion**

- NICU environment may be responsible for higher colonisation with more virulent SH strains in preterm.
- Control of virulent NICU clones may hold potential to reduce the burden of invasive infections.

**Figure: MLVA-types colonising term and preterm neonates.** Each node represents a distinct MLVA-type and the size of the node is proportional to the number of isolates of the MLVA-type. Numbers in nodes represent 5 most common MLVA-types. MLVA-types yielding multiple bands in loci Sh1 and Sh2 (n=7) were excluded.

**SH – *Staphylococcus haemolyticus***

**BM – breast milk**

**LOS – late-onset sepsis**

**NICU – neonatal intensive care unit**

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