Clinical and Molecular Characteristics of Community-Acquired Methicillin-Resistant *Staphylococcus Aureus* Infections In Chinese Neonates

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S. aureus is the most common pathogen causing infections.

Diseases
- Local infection
  -- skin and soft tissue infections (SSTIs)
    cellulitis
    abscesses
    folliculitis
- Invasive infections
  necrotic pneumonia
  meningitis
  osteomyelitis
  endocarditis

**The most common pathogen causing infections in neonates.**
Introduction

• In the early 1990s, the widespread emergence of community-associated, methicillin-resistant *S. aureus* (CA-MRSA) has become a serious health problem worldwide.

• CA-MRSA is primarily associated with skin soft-tissue infections (SSTIs) and it leads to severe systemic infections such as sepsis and necrotizing pneumonia.

• Reported a continuous increase in the percentage of newborns with CA-MRSA infections, and an increasing number of serious infections, and even death
Aim of This Study

- Numerous countries, including the United States and Italy, have reported local neonatal CA-MRSA infections.
- However, these reports mostly involved small samples and single-center studies. Reports on CA-MRSA infection in Asia have been few.
- **This study presents the clinical features of CA-MRSA infections in Chinese neonates and the relationship between these clinical features and their molecular characteristic***
Patients and bacterial isolates

- 130 cases of CA-MRSA-infected neonates were identified among hospitalized patients in three regional children’s hospitals
- 2011 - 2013.
- Patients ≤ 28 days old were selected from the database.
- The isolates were recovered from:
  - pus,
  - sputum,
  - hydrothorax,
  - ascites,
  - blood,
  - cerebrospinal fluid.

**Case Definition**
- Patients with CA-MRSA infections were identified,
  - within 48h of hospitalization or
  - after 48h of hospitalization if clinical evidence, such as presence of symptoms upon hospital admission, indicated CA infection.
- Exclusion criteria included:
  - underlying illness that predisposes the patient to frequent hospitalizations or medical visits,
  - indwelling catheters or percutaneous medical devices,
  - hospitalization after birth (excluding birth).
General Information

- Of the 130 patients,
  - 63.1% male and 36.9% female.
  - The mean age: 16.5 D
- Time
  - Early-onset infection 16.2%
  - Late-onset infection 83.8%.
- The mean birth weight was 3292.2 g.
- Cesarean delivery was the main delivery route, accounting for 74.6% of all deliveries.
Disease Distribution

- Pneumonia: the most common infection 53.1%
- SSTI: 19.8%
  - Omphalitis, 38.5%
  - Impetigo (7, 26.9%)
  - Abscess (7, 26.9%)
  - Conjunctivitis (2, 7.7%)

- The remaining cases accounted for 26.9%,
  - Septicemia,
  - Empyema,
  - Meningitis,
  - Purulent peritonitis,
  - Purulent arthritis,
  - Pyogenic osteomyelitis.

35 cases (26.9%) were invasive infections
A total of 38 patients (29.2%) showed severe complications,
- The most common of which was respiratory failure 11.5%.
- Other complications included
  - septic shock 2.3%
  - heart failure 1.5%
  - coagulation defects 1.5%
  - toxicenteroparalysis 0.8%
  - myocardial damage 8.5%
  - liver damage 3, 2.3%
  - hearing damage 0.8%.
Treatment with Antibiotic

In the initial empiric antibiotic therapy.

- Third-generation cephalosporin (60, 46.2%),
- Second-generation cephalosporin (31, 23.8%),
- Cephalosporin combined with an enzyme inhibitor (29, 22.3%),
- Vancomycin (10, 7.7%)

The antibiotic changed 84.6% after culture results.

- Vancomycin: Common 101 (77.7%)
- Linezolid: 19 (14.6%)
- Cephalosporin combined with an enzyme inhibitor: 10 (9.1%)
# Clinical Features of Invasive and Non-invasive Infection

<table>
<thead>
<tr>
<th></th>
<th>Invasive n=35</th>
<th>Non-invasive n=95</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>M/F</td>
<td>28 (80%)</td>
<td>54 (56.8%)</td>
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<tr>
<td>Cesarean section</td>
<td>34 (97.1%)</td>
<td>63 (66.3%)</td>
<td>0.00</td>
</tr>
<tr>
<td>Premature birth</td>
<td>9 (25.7%)</td>
<td>2 (2.1%)</td>
<td>0.00</td>
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<tr>
<td>Fever</td>
<td>17 (48.6%)</td>
<td>26 (27.4%)</td>
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<tr>
<td>Jaundice</td>
<td>13 (37.5%)</td>
<td>16 (16.8%)</td>
<td>0.01</td>
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<tr>
<td>Multiple site infection</td>
<td>31 (88.6%)</td>
<td>12 (12.6%)</td>
<td>0.00</td>
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<tr>
<td>White blood cell count</td>
<td>19.9±14.6</td>
<td>12.7±4.9</td>
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<tr>
<td>CRP (&gt;8 mg/L)</td>
<td>25 (71.4%)</td>
<td>10 (10.4%)</td>
<td>0.00</td>
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<tr>
<td>Complication</td>
<td>16 (45.7%)</td>
<td>22 (23.2%)</td>
<td>0.01</td>
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<tr>
<td>Treated in the ICU</td>
<td>16 (45.7%)</td>
<td>13 (13.7%)</td>
<td>0.01</td>
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<tr>
<td>Apgar scoring</td>
<td>7.7±1.1</td>
<td>8.2±0.9</td>
<td>0.02</td>
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<tr>
<td>Birth weight</td>
<td>3062.9±833.0</td>
<td>3376.7±401.2</td>
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Risk factors for invasive CA-MRSA infection

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P</th>
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<tr>
<td>Cesarean section</td>
<td>15.6</td>
<td>1.6–152.6</td>
<td>0.02</td>
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<tr>
<td>Premature birth</td>
<td>9.2</td>
<td>1.7–50.3</td>
<td>0.01</td>
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<tr>
<td>Weight</td>
<td>1.0</td>
<td>1.0 – 1.1</td>
<td>0.06</td>
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<tr>
<td>Male</td>
<td>0.7</td>
<td>0.22 – 2.5</td>
<td>0.63</td>
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<tr>
<td>Apgar score</td>
<td>1.5</td>
<td>0.9 – 2.3</td>
<td>0.10</td>
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Logistic regression analysis

caesarean section and premature birth are risk factors for invasive CA-MRSA infection
### Molecular characteristic:

- 10 ST types were obtained
- ST59 (87, 66.9%), SCCmec type IVa (70.8%), SCCmecV (27.7%)
- spa type, t437
- Predominant CA-MRSA clonal
  - ST59-MRSA-SCCmecIVa-t437: 41.5%
  - ST59-MRSA-SCCmecV-t437: 20.0%

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<tr>
<th>Clonal Complex</th>
<th>MLST</th>
<th>SCCmec</th>
<th>Spa</th>
<th>n</th>
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<td>CC59</td>
<td>ST59</td>
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<td>t318</td>
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<td>10</td>
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<td>t078</td>
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</table>
Expression of *hla*, *psma*, *pvl*, and *RNAIII*

The *hla* expression in the ST59 higher **VS** ST910,

ST59-SCCmecV-t437 higher **VS** ST59-SCCmecIVa-t437

invasive higher **VS** non-invasive infections

The *RNAIII* expression in the ST59 higher **VS** ST910
Clinical Characteristic in SCCmec Type V and IVa of ST59

Invasive Infection

life-threatening complications
• This study is the first to present the clinical features of CA-MRSA infections among Chinese neonates, as well as the molecular characteristics and virulence gene expression in clinical isolates.

• CA-MRSA infections among neonates were:
  – More prevalent who were delivered via cesarean section
  – Mainly late-onset infections.
  – Pneumonia is the most common
  – Readily become invasive,
  – Involve multiple organs,
  – Often serious complications.
  – ST59 is the most predominant clone.
  – The pathogenic capacity of the SCCmec V clone may be stronger than that of SCCmecVIa.

• Additional studies must be conducted on this clone.