Risk Factors for Treatment Failure and Clinical Outcomes of Methicillin-Resistant *Staphylococcus aureus* Bacteremia in Children

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**Background**

- The epidemiology, outcomes, and risk factors for treatment failure associated with methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia in children have not been well described.
- Current IDSA guidelines extrapolate from adult studies to determine pediatric treatment recommendations, including goal vancomycin serum troughs of 15-20 mcg/mL.

**Objective**

- To determine the outcomes and risk factors for treatment failure in children hospitalized with MRSA bacteremia

**Methods**

- Study design: Retrospective cohort study
- Study sites: The Children’s Hospital of Philadelphia, The Johns Hopkins Hospital, and Primary Children’s Hospital
- Data source: Electronic health records
- Study population: Children ≤ 18y hospitalized 2007-2014 and with a blood culture positive for MRSA. Our primary analysis includes patients treated with vancomycin. We excluded patients with:
  - polymicrobial bloodstream infection
  - incomplete lab or drug data
  - recurrent episodes
- Outcome: Treatment failure, defined by any one of the following:
  - MRSA-attributable mortality within 30 days
  - Recurrence within 30 days of discontinuing antibiotics
  - Bacteremia > 3 days.
- Analysis: A multivariable logistic regression model for the probability of treatment failure incorporating random effects to account for correlation across institution, evaluating the following a priori selected variables:
  - Endovascular and catheter-related infections
  - Vancomycin serum trough (<10, ≥10mcg/mL)
  - Source control intervention (not needed, ≤ 3 d, delayed)
  - Critical illness (vasopressor use within 48h)

**Results**

- **Demographics (n=235)**
  - Institution
    - CHOP: 113 (48%)
    - JHH: 65 (28%)
    - Utah: 57 (24%)
  - Age, mean (sd): 6.6 yr (5.5)
  - Female: 99 (42%)
  - Black race: 86 (37%)
  - Comorbid medical conditions (any): 118 (50%)

- **Characteristics of infection**
  - Primary Source of Bacteremia
    - *Catheter-related* 55
    - *Skin soft tissue* 95
    - *Pneumonia* 38
    - *Endovascular* 9
    - *Other* 21

- **Hospital onset**
  - 51 (22%)

- **Critically ill**
  - 28 (12%)

- **Vancomycin MIC>1 mcg/mL**
  - 17 (7%)

- **First vancomycin serum trough**
  - <10 mcg/mL: 129 (55%)
  - 10-14.9 mcg/mL: 45 (19%)
  - ≥15 mcg/mL: 21 (9%)

- **Delayed initiation (≥2 days) of therapy**
  - 14 (6%)

- **Outcomes**
  - Treatment failure: 74 (32%)
  - Recurrence of bacteremia: 8 (3.4%)
  - Bacteremia > 3 days: 66 (28%)

- **Risk factors for treatment failure**
  - **Odds ratio (95% CI) p-value**
    - *Catheter-related* 0.40 (0.17-0.94) 0.04
    - *Endovascular infection* 5.96 (1.10-32.1) 0.04
    - *Vancomycin trough <10mcg/mL* 0.82 (0.42-1.62) 0.57
    - *Source control intervention*  
      - None needed [Ref]
      - Within 3 days 1.56 (0.63-3.86) 0.34
      - Delayed > 3 days 1.91 (0.73-5.0) 0.19
    - *Critical illness* 3.18 (1.22-8.28) 0.02

**Conclusions**

- Mortality in children with MRSA bacteremia was low.
- Median duration of bacteremia was 2 days, and 1/3 of bacteremia episodes persisted beyond 3 days.
- One-third of children with MRSA bacteremia experienced treatment failure.
- Children with catheter-related infections experienced lower rates of treatment failure, while children with endovascular infections experienced higher rates of treatment failure.
- First vancomycin serum trough level of <10 mcg/mL was not associated with treatment failure.