

## COMMENT



# Infectious disease consultation in children with *S. aureus* Bacteremia: does it improve patient outcomes and quality of care?

Mohan Pammi<sup>1</sup>✉ and Sheldon L. Kaplan<sup>2</sup>

© The Author(s), under exclusive licence to the International Pediatric Research Foundation, Inc 2022

*Staphylococcus aureus* bacteremia is a serious invasive infection associated with significant mortality and morbidity. Quality-of-care indicators (QCI) that focus on diagnostics, monitoring, and treatment have been formulated in adults and infectious disease consultation improved adherence to these QCI and improved clinical outcomes. No such quality of care indicators have been established in children with *S. aureus* bacteremia. In this issue of *Pediatric Research*, Whittington et al. report their investigation of the impact of pediatric infectious disease consultation on adherence to six established QCI (adapted from adult QCI) and treatment failure in children with *S. aureus* bacteremia. ID consultation was associated with increased fulfillment of all 6 QCI and, the composite outcome of treatment failure was significantly lower in patients receiving ID consultation compared to those without (31 vs. 46%). Current evidence supports the recommendation that an ID consultation should be considered for all children with *S. aureus* bacteremia.

*Pediatric Research* (2022) 92:1502–1503; <https://doi.org/10.1038/s41390-022-02331-1>

*Staphylococcus aureus* bacteremia in children is one of the most common serious invasive infections in children and ranges from 1.5 to 3.5 per 1000 hospitalizations.<sup>1,2</sup> *S. aureus* bacteremia in children is associated with a mortality of 2–6% but reported as high as 15% in those with cardiac conditions, metastatic infections and prolonged hospitalizations.<sup>1,3–5</sup> Follow-up blood cultures documenting eradication of infection is necessary and in children, after two negative blood cultures in a well-appearing patient the risk of recurrence is low (<1%).<sup>3</sup> Recurrent or intermittent positive cultures were associated with endocarditis and osteomyelitis.<sup>3</sup> Guidelines for treating MRSA infections by the Infectious Disease Society of America have been published but not on MSSA infections.<sup>6</sup> In one study, best practice advisory associated with the electronic medical records increased infectious disease (ID) consultation and decreased time to optimal therapy in patients <21 years for *S. aureus* bacteremia.<sup>7</sup>

In adults with *S. aureus* bacteremia, there was more adherence to guidelines with decrease in mortality and morbidity by ID consultations.<sup>8,9</sup> Quality-of-care indicators (QCI) that focus on diagnostics, monitoring, and treatment have been formulated and adhering to these QCI is associated with improved clinical outcomes.<sup>10–13</sup> In adults, ID consultation confers a greater likelihood of management adhering to the QCI and decreased healthcare costs.<sup>8,12</sup> In an observational, pre and post bedside ID consult study of 571 adults from the United Kingdom, ID consultation was associated with a greater likelihood to identify a removable focus of infection, perform echocardiography, perform follow-up blood cultures, receive longer and combination

antimicrobial therapy and a trend towards decreased mortality at 30 days.<sup>14</sup>

In children, the impact of ID consultation on adherence to QCI and improved patient outcomes have been reported sparingly. Studies of children with *S. aureus* bacteremia in Australia and New Zealand demonstrated that ID consultation was associated with improved diagnostics, laboratory monitoring, and targeted antibiotic therapy and one with decreased mortality.<sup>4,15</sup> In the prospective study from Australia and New Zealand of 552 patients (where the indigenous population and low socioeconomic status were overrepresented), the incidence of *S. aureus* bacteremia was 4.4/100,000/year.<sup>15</sup> Predictors of mortality included prematurity, multifocal infection, necrotizing pneumonia, multiorgan dysfunction, and empiric vancomycin. In this study, ID consultation was associated with decreased mortality.<sup>15</sup> In another retrospective study from Australia, of 100 children with *S. aureus* bacteremia, 55 had ID consultation and 45 did not.<sup>4</sup> ID consultation resulted in improved appropriate directed therapy within 24 h (98.2 vs. 75.6%), and appropriate choice of antibiotics (98.2 vs. 82.2%), antibiotic dose (98.2 vs. 80%), and duration (94.5 vs. 53.3%).<sup>4</sup> Furthermore, control of source of infection and cure were more frequently achieved following ID consultation.<sup>4</sup> Another important predictor of mortality has been the use of empiric vancomycin, which emphasizes the importance of antibiotic stewardship and targeted therapy for *S. aureus* bacteremia.<sup>8,15–17</sup>

Results from the studies mentioned above may not be generalizable to the population in the USA due to epidemiology of the infection and health care systems. In this issue, Whittington

<sup>1</sup>Division of Neonatology, Department of Pediatrics, Baylor College of Medicine & Texas Children's Hospital, Houston, TX, USA. <sup>2</sup>Division of Infectious Diseases, Department of Pediatrics, Baylor College of Medicine & Texas Children's Hospital, Houston, TX, USA. ✉email: mohanv@bcm.edu

Received: 17 August 2022 Accepted: 19 August 2022

Published online: 5 October 2022

et al. report their investigation (PR-2022-0237) of the impact of pediatric ID consultation on adherence to six established QCLs and treatment failure in children with *S. aureus* bacteremia. The authors conducted this single-center study at St. Louis Children's Hospital from January 2011 to May 2018, which was an electronic medical health records review of relevant clinical and demographic factors. They included patients 0–24 years with *S. aureus* bacteremia ( $n = 306$ ). The primary exposure was ID consultation within 6 days of positive blood culture and secondary exposure was targeted antibiotic therapy based on the organism identification and antimicrobial susceptibility. The outcomes were six QCLs (proof of negative blood culture, indicated laboratory investigations, echocardiogram, source control, targeted antibiotic therapy, duration of targeted antibiotics) and treatment failure. Treatment failure was defined as a composite of all-cause mortality and/or hospital readmission within 90 days. The authors tried to account for potential confounding by severity of illness and other important factors by using propensity score methodology in the treatment failure analysis.

The authors report that, of the 306 patients with *S. aureus* bacteremia, 193 (63%) received ID consultation and the median time of ID consultation from positive blood culture was 3 days.

ID consultation was associated with increased fulfillment of all 6 QCLs when compared to the group without ID consultation, including proof-of-cure blood cultures (95 vs. 84%), all indicated laboratory studies (46 vs. 8%), echocardiography when indicated [e.g., structural heart anomalies or complicated bacteremia] (32 vs. 15%), source control when indicated (e.g., removal of infected central venous catheter or instrumentation (57 vs. 28%), targeted antibiotic therapy (92 vs. 71%), and appropriate duration of targeted antibiotic therapy in patients with bacteremia without a focus.

The composite outcome of treatment failure was significantly lower in patients receiving ID consultation compared to those without (31 vs. 46%). However, in propensity score-weighted analyses, risk of treatment failure (a composite of 90-day mortality and readmission) was similar among patients who did and did not receive ID consultation (few events and hence risk estimates were imprecise). Whittington's study is the first to report that ID consultation in children with *S. aureus* bacteremia resulted in greater likelihood of adherence to recommended QCLs leading to appropriate diagnostics, monitoring, and treatment, factors that have been associated with fewer rehospitalizations and deaths.

In the Whittington cohort, only 6 deaths (2%) were attributable to *S. aureus* bacteremia. We need better indicators than mortality for evaluating appropriate treatment for *S. aureus* bacteremia. QCLs may indicate the best ways to improve treatment success and decrease treatment failure. Hadano et al., in an adult retrospective study of pre- and post-mandatory ID consultation for *S. aureus* bacteremia in Japan, reported increased adherence to QCLs and decreased 30-day mortality after ID consultation.<sup>13</sup> They reported 6 QCLs, namely, follow-up blood culture on day 4, echocardiography, appropriate antimicrobial therapy, intravenous treatment for 14 days, early source control, and therapeutic vancomycin trough levels. There are no established QCLs in the treatment of *S. aureus* bacteremia in children. Whittington et al. adapted the 6 QCLs established for the adult population derived by Hadano et al. to assess diagnostic evaluation and treatment practices performed among children with *S. aureus* bacteremia.<sup>13</sup> However, obtaining vancomycin trough levels would not be expected to impact the outcome of bacteremia due to methicillin-susceptible *S. aureus* (MSSA) isolates and 66% of the patients in the study had MSSA bacteremia. The authors do not note the impact of ID consultation on the frequency of acute kidney injury associated with vancomycin administration.

The evidence for the benefits of ID consultations on adherence to QCLs and decreasing morbidity and mortality is compelling and supports the recommendation that an ID consultation should be considered for all children with *S. aureus* bacteremia.

## REFERENCES

- Hamdy, R. F. et al. Epidemiology of methicillin-resistant *Staphylococcus aureus* bacteremia in children. *Pediatrics* **139**, e20170183 (2017).
- Kumarachandran, G., Johnson, J. K., Shirley, D. A., Graffunder, E. & Heil, E. L. Predictors of adverse outcomes in children with *Staphylococcus aureus* bacteremia. *J. Pediatr. Pharmacol. Ther.* **22**, 218–226 (2017).
- Cardenas-Comfort, C., Kaplan, S. L., Vallejo, J. G. & McNeil, J. C. Follow-up blood cultures in children with *Staphylococcus aureus* bacteremia. *Pediatrics* **146**, e20201821 (2020).
- Duguid, R. C., Al Reesi, M., Bartlett, A. W., Palasanthiran, P. & McMullan, B. J. Impact of infectious diseases consultation on management and outcome of *Staphylococcus aureus* bacteremia in children. *J. Pediatr. Infect. Dis. Soc.* **10**, 569–575 (2021).
- Hamdy, R. F., Dona, D., Jacobs, M. B. & Gerber, J. S. Risk factors for complications in children with *Staphylococcus aureus* bacteremia. *J. Pediatr.* **208**, 214–220.e2 (2019).
- Liu, C. et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin. Infect. Dis.* **52**, e18–e55 (2011).
- Lloyd, E. C. et al. Impact of a best practice advisory for pediatric patients with *Staphylococcus aureus* bacteremia. *J. Pediatr. Infect. Dis. Soc.* **10**, 282–288 (2021).
- Buehrle, K., Pisano, J., Han, Z. & Pettit, N. N. Guideline compliance and clinical outcomes among patients with *Staphylococcus aureus* bacteremia with infectious diseases consultation in addition to antimicrobial stewardship-directed review. *Am. J. Infect. Control* **45**, 713–716 (2017).
- Robinson, J. O. et al. Formal infectious diseases consultation is associated with decreased mortality in *Staphylococcus aureus* bacteraemia. *Eur. J. Clin. Microbiol. Infect. Dis.* **31**, 2421–2428 (2012).
- Vogel, M. et al. Infectious disease consultation for *Staphylococcus aureus* bacteremia - a systematic review and meta-analysis. *J. Infect.* **72**, 19–28 (2016).
- Tissot, F. et al. Mandatory infectious diseases consultation for MRSA bacteremia is associated with reduced mortality. *J. Infect.* **69**, 226–234 (2014).
- Schmitt, S. et al. Infectious diseases specialty intervention is associated with decreased mortality and lower healthcare costs. *Clin. Infect. Dis.* **58**, 22–28 (2014).
- Hadano, Y. et al. Reduction of 30-day death rates from staphylococcus aureus bacteremia by mandatory infectious diseases consultation: comparative study interventions with and without an infectious disease specialist. *Int. J. Infect. Dis.* **103**, 308–315 (2021).
- Saunderson, R. B. et al. Impact of routine bedside infectious disease consultation on clinical management and outcome of *Staphylococcus aureus* bacteraemia in adults. *Clin. Microbiol. Infect.* **21**, 779–785 (2015).
- Campbell, A. J. et al. Pediatric *Staphylococcus aureus* bacteremia: clinical spectrum and predictors of poor outcome. *Clin. Infect. Dis.* **74**, 604–613 (2022).
- Messacar, K. et al. A handshake from antimicrobial stewardship opens doors for infectious disease consultations. *Clin. Infect. Dis.* **64**, 1449–1452 (2017).
- Sherbuk, J. E., McManus, D., Topal, J. E. & Malinis, M. Improved mortality in *Staphylococcus aureus* bacteremia with the involvement of antimicrobial stewardship team and infectious disease consultation. *Infect. Control Hosp. Epidemiol.* **40**, 932–935 (2019).

## COMPETING INTERESTS

S.L.K. is a co-investigator on a NIH study for which Dr. Fritz is a Principal Investigator.

## ADDITIONAL INFORMATION

**Correspondence** and requests for materials should be addressed to Mohan Pammi.

**Reprints and permission information** is available at <http://www.nature.com/reprints>

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.