Leveraging Culture Data to Justify a 24-Hour Antibiotic Duration in Early Onset Sepsis

Erlinda Manalo, MD; Shengda Ma, PharmD; Betty Vu, PharmD; Gina Rosito, PharmD; Lise Bashe, CLS; Erika Bezdecheck, RN; Danielle Lombardi, RN; Melanie Lombardi, RN

Abstract

Introduction: Most bacterial pathogens in blood cultures (BCx) are identified within 24 hours, yet many centers utilize a 36 to 48 hour duration for empiric antibiotics in early onset sepsis (EOS). We established a 24-hour duration for EOS antibiotics based on review of culture data and improvement in culture time to incubation.

Methods: A multidisciplinary antimicrobial stewardship team reviewed all neonatal blood cultures from 2019 to 2023. Culture time to incubation (TTI), time to positivity (TTP) and turnaround time (TAT) were analyzed. Each positive blood culture was reviewed to determine whether the organism was a true bacterial pathogen or contaminant.

Results: A total of 3,182 blood cultures were collected for EOS episodes with a positivity rate of 0.82% (n=26). Of the positive cultures, 58% (n=15) were definitive bacterial pathogens and 42% (n=11) considered contaminants. Median TTP was 10.1 hours in gram-negative organisms (n=8) and 17.5 hours in gram positive organisms (n=18). Median TTP in contaminants were 20.5 hours (IQR, 19.4-31.9). No definitive bacterial pathogens exceeded TTP greater than 24 hours.

Conclusion: Analysis of five years of culture data revealed all definitive bacterial pathogens were identified within 24 hours. Gram-negative pathogens had shorter TTP compared to gram-positive organisms. TTI was reduced via targeted interventions. Consequently, we have adopted a 24-hour duration for empiric antibiotics in EOS based on these findings.

Introduction

Early antibiotic exposure raises the risk of dysbiosis, resulting in adverse outcomes for infants, especially preterm ones, and has been associated with necrotizing enterocolitis, bronchopulmonary dysplasia, late-onset sepsis, and mortality. Despite most pathogens being identified within 24 hours, many centers still use a 36-to-48-hour duration for empiric antibiotics in early-onset sepsis (EOS). Short-course regimens are gaining traction, but changing established practices is challenging, as neonatologists often prescribe antibiotics to asymptomatic infants out of concern for missed infections.

At Sutter Medical Center Sacramento (SMCS), a NICU antimicrobial stewardship team comprised of a neonatologist, pharmacists, clinical laboratory scientist, and nurses, was formed to review data and implement interventions aimed at reducing antibiotic exposure. This quality improvement project focuses on a data-driven approach to supporting a 24-hour duration for empiric antibiotics in EOS.

Methods

- This was a quality improvement project based on retrospective review of culture data. Data from 4,859 blood cultures collected in the NICU were extracted from electronic health records over a span of five years.
- A multidisciplinary team reviewed all blood cultures drawn from infants less than 72 hours of age admitted to the SMCS NICU from 2019 to 2023.
- Culture-related delays were identified in each of the following timeframes: time to incubation (TTI), time to positivity (TTP), and turnaround time (TAT).
- Interventions to reduce TAT included: special labeling of cultures from NICU for expedited processing, increased frequency of reporting from every 24 hours to every 8 hours for negative blood cultures, and increased frequency of courier routes between laboratories.
- Per standard NICU policy, prior to starting antibiotics, 1 mL of blood was drawn and inoculated into a bioMérieux BACT/ALERT® PF Plus media bottle.
    - All blood cultures were transported via courier to a centralized system laboratory off site.
    - Blood cultures were subsequently incubated in bioMérieux BACT/ALERT® 3D for up to 5 days or until detected positive.
    - When the blood culture was determined to be positive, the blood was plated on to solid agar media for culture and a rapid PCR identification panel was performed.

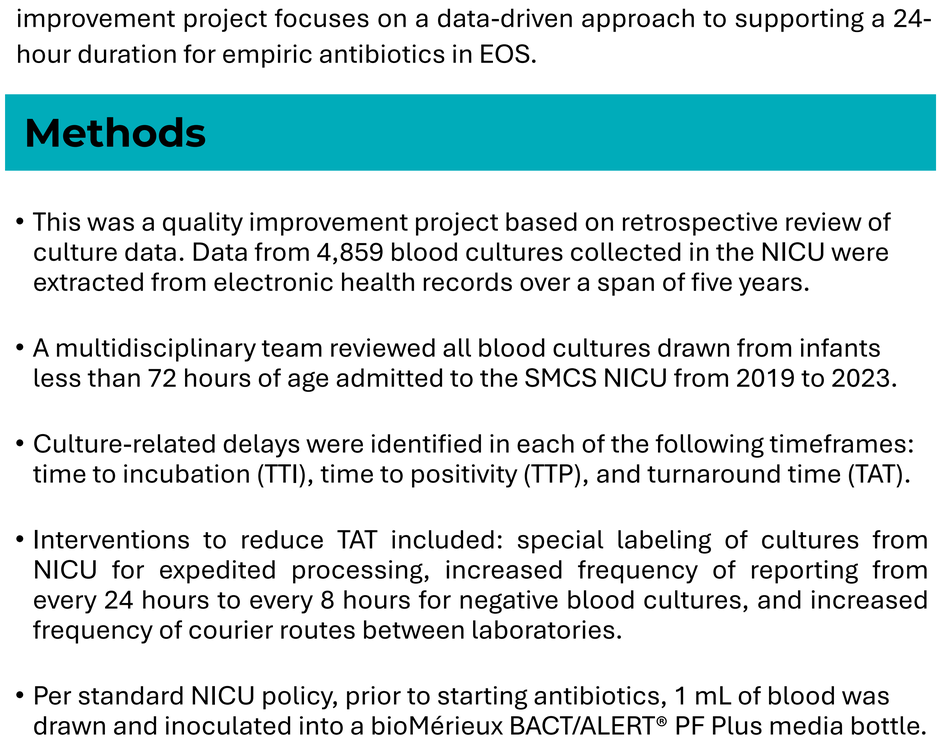

FIGURE 1. FLOW CHART OF BCx COLLECTION AND PROCESSING AT SMCS

Results

During a five-year period, 4,859 blood cultures were collected in our NICU, with 3,182 (65.4%) drawn for suspected EOS episodes. Twenty-six of these cultures were positive, with a similar distribution observed between term and preterm populations (**Table 1**). The majority of these cultures were drawn from neonates born to mothers with negative group-B *Streptococcus* (GBS) status (**Table 1**).

TABLE 1. BASELINE DEMOGRAPHICS OF EOS NEWBORNS WITH POSITIVE BLOOD CULTURES (TOTAL N = 26)

	Pathogenic (N=15) No. (%n/N)	Contaminant (N=11) No. (%n/N)	Overall (N=26) No. (%)
Gestational Age, weeks, mean (SD)	33.1 (±7)	36.2 (±4.1)	34.4 (±6)
Degree of Prematurity, weeks GA			
</=28	5 (33)	1 (9)	6 (23)
29-33	2 (13)	2 (18)	4 (15)
34-36	1 (7)	1 (9)	2 (8)
>/=37	7 (47)	7 (64)	14 (54)
Birth Weight, kg, mean (SD)	2.21 (±1.3)	2.72 (±1)	2.42 (±1.2)
Birth Weight Distribution			
</= 750 grams	4 (26)	0 (0)	4 (15)
751 – 1000 grams	1 (7)	0 (0)	1 (4)
1001 – 1500 grams	0 (0)	2 (18)	2 (8)
1501 – 2500 grams	3 (20)	3 (27)	6 (23)
>2500 grams	7 (47)	6 (55)	13 (50)
Method of Delivery			
Spontaneous Vaginal Delivery	6 (40)	6 (55)	12 (46)
Cesarian Section	8 (53)	4 (36)	12 (46)
VBAC, Spontaneous	1 (7)	0 (0)	1 (4)
Vaginal, Vacuum (Extractor)	0 (0)	1 (9)	1 (4)
Maternal GBS Status			
Negative	13 (86)	7 (64)	20 (77)
Positive	1 (7)	0 (0)	1 (4)
Unknown	1 (7)	4 (36)	5 (19)

VBAC= Vaginal birth after a cesarean; GBS=Group B *Streptococcus*; TTP = Time to Positivity; CoNS = Coagulase-negative *Staphylococcus*

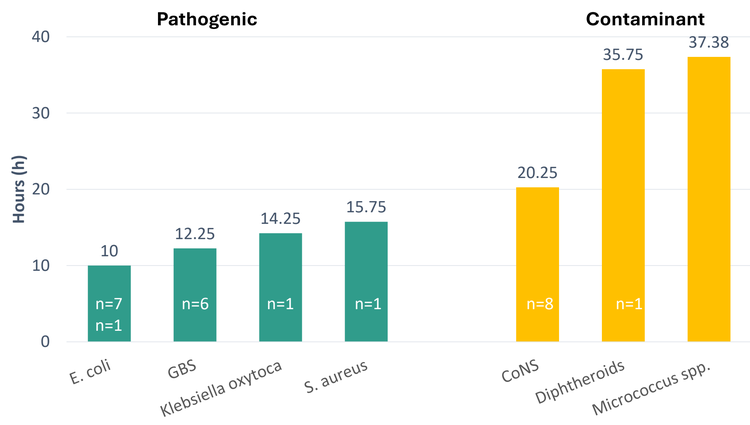

FIGURE 2. MEDIAN TTP OF POSITIVE BCx RESULTS (2019-2023), N=26

Of the positive cultures, 58% (n=15) were definitive bacterial pathogens and 42% (n=11) were determined to be contaminants (**Table 2**). Median TTP was 10.1 h in gram-negative organisms (n=8) and 17.5 h in gram positive organisms (n=18). *Escherichia coli* and GBS were the most common isolates (**Figure 2**). Uncommon isolates included methicillin-resistant *Staphylococcus aureus* (n=1) and *Klebsiella oxytoca* (n=1).

Eleven contaminants were isolated (**Figure 2**). Five had a TTP of less than 24 h, all of which grew coagulase-negative *Staphylococcus* (CoNS). Repeat blood cultures were all negative, and 2 patients received additional antibiotics while awaiting culture results. Contaminants with TTP greater than 24 h included *Micrococcus spp* (n=2), CoNS (n=2), and diphtheroids (n=1).

TABLE 2. DESCRIPTION OF SMCS NICU BLOOD CULTURES COLLECTED OVER FIVE YEARS (N=4859)

	2019 (n=955)	2020 (n=934)	2021 (n=993)	2022 (n=1026)	2023 (n=951)	Total (n=4859)
Total No. Of EOS BCx Collected	624 (65)	621 (66)	625 (63)	652 (64)	660 (69)	3182 (65)
Positive EOS BCx, No.	5	2	5	8	6	26
Pathogens, No.	3	0	3	6	3	15
Median TTP, (IQR) *h*	13.8 (11.1-14)	N/A	9.8 (9.1-10.4)	9.8 (8.2-12.6)	12 (11.1-13.1)	10.8 (9-13.6)
TTP >24 h, *No.*	0	N/A	0	0	0	0
Contaminants, No.	2	2	2	2	3	11⁺
Median TTP, (IQR) *h*	27 (23.5-30.5)	28 (21.6-34.4)	24.3 (21.5-27)	28.1 (24.3-31.9)	20.5 (18.4-22.6)	20.5 (19.4-31.9)
TTP >24 h, *No.*	1	1	1	1	1	6*

⁺TTP <24h: CoNS (n=6); polymicrobial (n=1)
**Micrococcus spp*. (n=2); CoNS (n=3); Diphtheroids (n=1)

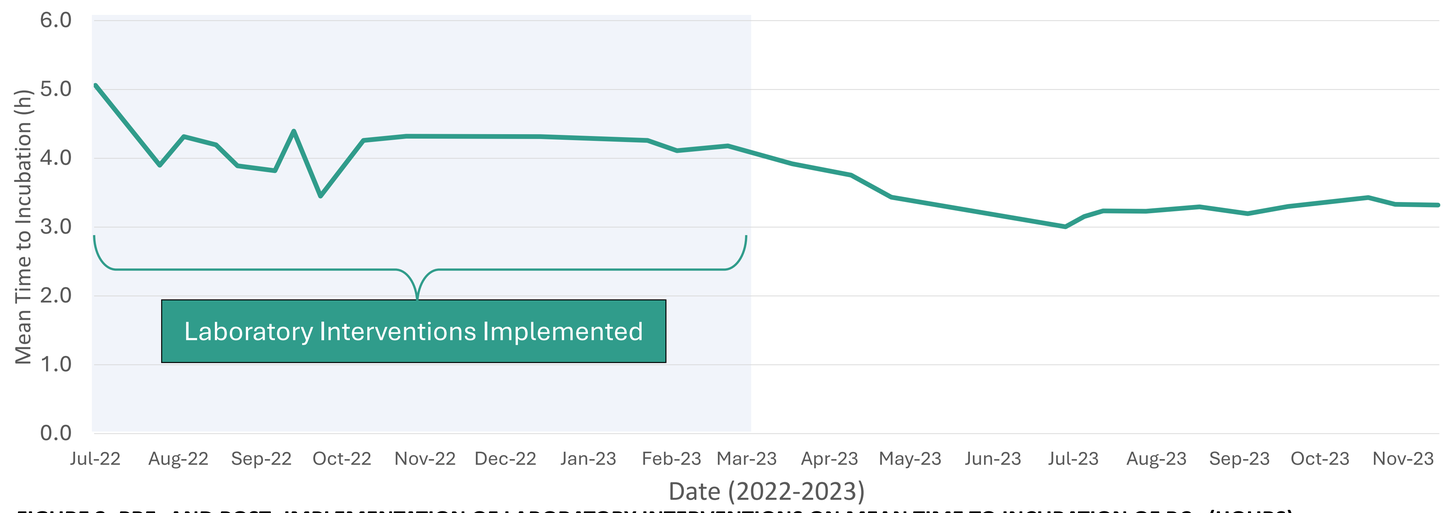

FIGURE 3. PRE- AND POST- IMPLEMENTATION OF LABORATORY INTERVENTIONS ON MEAN TIME TO INCUBATION OF BCx (HOURS)

Prospective TTI tracking began in July of 2022 (**Figure 3**). In 2022, 503 blood cultures were analyzed with mean TTI of 4.3 h. After targeted interventions, mean TTI was reduced to 3.2 h in 2023 with 952 blood cultures analyzed.

Discussion

- Analysis of five years of NICU culture data revealed that all definitive bacterial pathogens were identified within 24 hours. Using a mean TTI of 3.2 h in 2023, all definitive pathogens met our target 24-hour window for positivity even when TTI is added to TTP.
- Our data highlights the importance of tracking time to incubation, a key piece that is not commonly discussed in other stewardship projects. With the increasing implementation of centralized laboratories requiring courier transport, potential delays in culture transport for incubation can lead to false-negative culture results and may skew time to positivity data.
- By including a microbiology laboratory specialist as a key stakeholder in this project, we were able to implement targeted interventions to decrease delay in TTI from 4.3 h to 3.2 h.
- CoNS with TTP under 24 hours were not considered definitive pathogens as the clinical course did not support true infection. This may be reflective of inadequate aseptic technique when drawing cultures and highlights opportunities for education.
- Ongoing tracking of TAT, TTP, and TTI have reinforced our confidence in implementing a 24-hour EOS rule-out. Additionally, focusing on patients who restart antibiotics within 5 days provides reassurance that a shortened duration is appropriate.
- Future direction of this project includes analyzing the effects of reduced early antibiotics on late onset sepsis, necrotizing enterocolitis, and chronic lung disease. Sutter Health Laboratory recently invested in an automated blood culture system that minimizes temperature fluctuations during incubation, which will shorten TTP.
- This project is one of many interventions implemented by our NICU antimicrobial stewardship team. Other areas of focus include reducing unnecessary blood culture collections, adherence to sepsis risk calculators to avoid antibiotic use, creating an annual antibiogram, and creating a durations of therapy guide for infections in the NICU.

References

Scan QR code using your mobile device to review poster references.