Bloodstream Infections

Epidemiology and Resistance

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KEYWORDS

• Antibiotic stewardship • Central-line–associated bloodstream infection
• Infection control • Multidrug resistance • Neonate • NICU

KEY POINTS

- Among hospitalized infants, bloodstream infections are associated with increased mortality, as well as increased length of stay, health care costs, and adverse neurodevelopmental outcome in survivors.
- Risk factors for bloodstream infections include prematurity, indwelling catheters or other medical devices, exposure to prolonged empiric antibiotic therapy, acid-blocking medications, or steroids, and overcrowding or understaffing.
- Gram-positive organisms, particularly coagulase-negative *Staphylococcus*, account for most bloodstream infections, but gram-negative and *Candida* infections are associated with higher morbidity and mortality.
- Drug-resistant bacteria account for an increasing proportion of infections and outbreaks in the neonatal intensive care unit. Good antibiotic stewardship and infection prevention practices are of paramount importance to slow the increase in resistant organisms.

INTRODUCTION

Bloodstream infections (BSI) are a common cause of morbidity and mortality in neonatal intensive care units (NICUs) worldwide. **Table 1** highlights the adverse outcomes associated with BSI in infants, including increased length of stay, poor neurodevelopmental outcome, and higher mortality.[1–5] BSI can be divided into early-onset or late-onset sepsis (LOS), with LOS occurring greater than 3 days after delivery. The purpose of this review is to focus on the epidemiology of BSI in the NICU, with a focus on prevention.

Disclosures: The authors have no financial disclosures or conflicts of interest to report.
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Clin Perinatol 42 (2015) 1–16
http://dx.doi.org/10.1016/j.clp.2014.10.002 perinatology.theclinics.com
0095-5108/15/$ – see front matter

Table 1
Selected adverse outcomes associated with bloodstream infection in very low-birth-weight infants in the neonatal intensive care unit

Adverse Outcome	Study	Adjusted Effect
Mortality	Stoll et al.[1] (1996)	2.4-fold increase (17% vs 7%)
	Stoll et al.[2] (2002)	2.6-fold increase (18% vs 7%)
	Makhoul[53] (2002)	2.0-fold increase (17% vs 9%)
Poor neurodevelopmental outcome	De Haan[90] (2013)	OR 4.8 (1.5–15.9), for gram-negative BSI[a]
	Mitha[4] (2013)	OR 2.2 (1.5–3.1)[b]
	Schlapbach[91] (2011)	OR 3.2 (1.2–8.5)[b]
	Stoll[5] (2004)	OR 1.4 (1.3–2.2)[a]
Length of stay	Stoll et al.[1] (1996)	19–22 d mean increase
	Stoll et al.[2] (2002)	18.6 d mean increase
	Makhoul[53] (2002)	27 d mean increase
	Atif[92] (2008)	9.2 d mean increase
Increased cost	Payne et al.[3] (2004)	$54,539 mean increase
	Donovan[93] (2013)	$16,800 mean increase

All studies adjusted for gestational age.
Abbreviation: OR, odds ratio.
[a] Bayley-II motor or cognitive score less than 85, blindness, deafness, or cerebral palsy.
[b] Cerebral palsy.

EPIDEMIOLOGY AND DEFINITIONS

In addition to early-onset and late-onset, BSI in the NICU frequently are further categorized to facilitate benchmarking rates between and within hospitals. Hospital-acquired BSIs (HABSI) are defined by the Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN) as BSI not present on admission, in which blood culture yields a proven pathogen at least once or a possible pathogen (ie, coagulase-negative *Staphylococcus* [CoNS]) on 2 or more occasions.[6] BSI may be associated with infection at another site, such as necrotizing enterocolitis (NEC) or a urinary tract infection. BSIs may also be associated with an indwelling catheter. These "central-line–associated" BSI (CLABSIs) are a subset of HABSI and are defined by the NHSN as HABSIs in which the initial positive culture occurs at least 2 days after the placement of a central line that is in situ or was removed less than 2 days before the positive culture, and the positive blood culture is not attributable to infection at another site.[6] Traditionally, CLABSIs are reported as occurrences per 1000 central-line–days. By monitoring CLABSI incidence rates, institutions can improve their prevention efforts and their quality of care. In 2010, the Patient Protection and Affordable Care Act created a policy of non-reimbursement for hospital charges that result from CLABSI care.[7] Data suggest that CLABSI rates are underreported. Relying on physician coding to identify CLABSI is unreliable because of different interpretations of criteria for BSI.[8,9] Furthermore, adjudicating whether a possible CLABSI is a contaminant or may be "attributable to infection at another site" can be subjective, and discordance has been demonstrated between trained professionals reviewing the same case.[10–12] For these reasons, it has been suggested that HABSIs may be a more generalizable method for reporting BSI in the NICU setting.[13] Others have recommended the use of an adjusted CLABSI rate that takes gestational age or severity of illness into account; currently, CLABSI reporting to the NHSN is stratified only by birth weight.[14–16]