Characterization and Treatments of Neonatal Late-Onset Sepsis: A Retrospective Analysis of The University of Utah Hospital Cases

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Background

Neonatal sepsis remains a significant cause of morbidity and mortality, particularly among preterm and low birth-weight infants. Late-onset neonatal sepsis is associated with microorganisms encountered after birth, usually nosocomial and usually caused by coagulase-negative staphylococcus.

Blood cultures are used to confirm sepsis; however, a negative result does not exclude the possibility of sepsis and a positive result could be caused by a contaminant.

The purpose of this analysis was to compare cohorts of suspected but unconfirmed to confirmed late-onset sepsis for differences in patient characteristics, outcomes, and treatment strategy, as well as describe causative agents.

Methods

Electronic health records were collected from neonates billed with and without (control) ICD9 code 771.81 (newborn sepsis) between January 1, 2006 and September 30, 2015 from the University of Utah Hospital.

Late-onset sepsis was considered suspected if a blood culture was ordered within 3 to 28 days of birth. Sepsis was confirmed if any culture was positive and unconfirmed if none were positive.

Cultures reported as *Micrococcus* sp , diptheroids sp., or gram-positive rods were excluded as contaminants. Coagulase-negative staphylococci required two cultures within 48h to confirm sepsis.

Antimicrobials were considered as treatment for sepsis if started within ±0.5 days of any culture. Started defined as not administered within previous two days.

Table 1: Patient Demographics

		Late Onset Sepsis	
	Control	Unconfirmed	Confirmed
n	**1487**	**265**	**57**
Male Gender (% of n)	778 (52.3)	130 (49.1)	28 (49.1)
Race (% of n)			
Caucasian	773 (52.0)	147 (55.5)	32 (56.1)
Asian	45 (3.0)	3 (1.1)	1 (1.8)
Pacific Islander	28 (1.9)	6 (2.3)	1 (1.8)
Black or African American	27 (1.9)	10 (3.8)	0 (0.0)
Native American	12 (0.8)	3 (1.1)	1 (1.8)
Other	164 (11.0)	25 (9.4)	4 (7.0)
Unknown	438 (29.5)	71 (26.8)	18 (31.6)
Ethnicity (% of n)			
Hispanic/Latino	389 (26.2)	44 (16.6)	13 (22.8)
Not Hispanic/Latino	595 (40.0)	134 (50.6)	22 (38.6)
Unknown	503 (33.8)	87 (32.8)	22 (38.7)

Results

Figure 1: Patient Characteristics and Outcomes

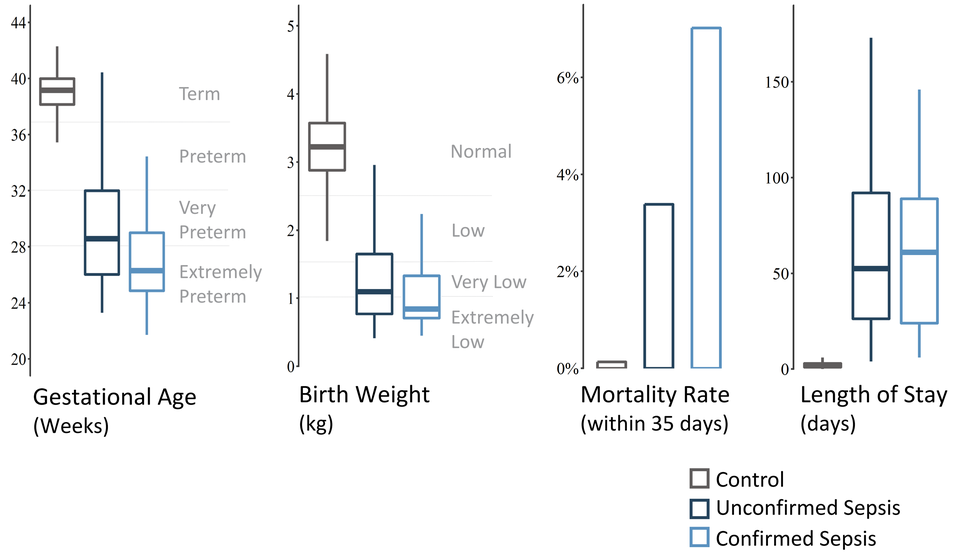
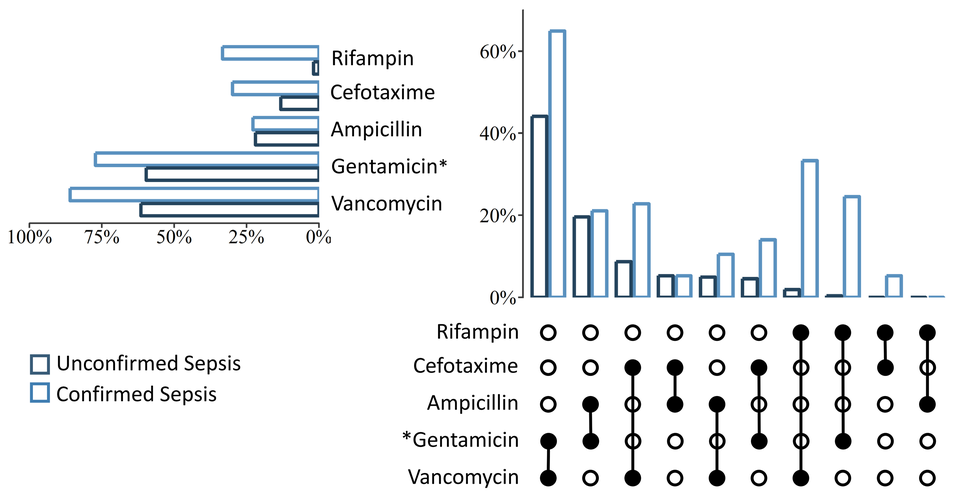


Figure 2: Antimicrobial Treatments and Treatment Combinations for Late-Onset Sepsis

A: Percentage of patients administered antimicrobial as treatment for sepsis.

B: Percentage of patients administered in combination for at least one day of treatment.



* Information on gentamicin is absent from the abstract due to an absence in the original database extraction.

Table 2: Microorganisms Isolated from Patients with Late-Onset Sepsis

Organism	n (%)
Coagulase-negative staphylococcus	27 (47.4)
Escherichia coli	8 (14.0)
Staphylococcus aureus	5 (8.8)
Enterococcus spp.	4 (7.0)
Viridans streptococci	3 (5.3)
Staphylococcus epidermidis	3 (5.3)
Unspecified cocci	3 (5.3)
Yeast	2 (3.5)
Klebsiella pneumoniae	2 (3.5)
Enterobacter spp.	2 (3.5)
Acinetobacter sp.	1 (1.8)
Citrobacter sedlakii	1 (1.8)

Findings/Conclusions

Neonates with confirmed compared to unconfirmed late-onset sepsis:

Had lower gestational age ($p^{\dagger} < 0.01$).

Had lower birth weight ($p^{\dagger} < 0.01$).

However, outcomes of mortality and length of stay were not significantly different between the two cohorts:

Rate of mortality ($p^{*} = 0.26$).

Length of stay ($p^{\dagger} = 0.78$).

Coagulase-negative staphylococci were the most prominent cause of late-onset sepsis (47%, Table 2), followed by *Escherichia coli (14%)*.

The most common treatments in both cohorts were vancomycin and gentamicin, usually in combination. Other combinations including vancomycin or gentamicin or were also common.

Rifampin was administered exclusively in conjunction with vancomycin and mostly in the confirmed cohort, likely to treat persistent coagulase-negative staphylococcus infections.

These conclusions cannot be generalized to all hospitals in the US or worldwide; however, these findings are in agreement with recently reported data for US-based hospitals.

* Fisher's exact test

† Mann-Whitney U test

Future Directions

Nearly all patients received gentamicin and vancomycin at some point; however, they were not all initiated near a blood culture order. The method of determining treatments for sepsis needs to be verified or improved.

Clinical signs and symptoms could be compared between the two cohorts. Efforts to accurately distinguish true cases of sepsis could reduce unnecessary treatment and improve antibiotic stewardship.