HHS Public Access

Author manuscript

Pediatr Infect Dis J. Author manuscript; available in PMC 2024 February 01.

Published in final edited form as:

Pediatr Infect Dis J. 2023 February 01; 42(2): 152–158. doi:10.1097/INF.0000000000003736.

Serratia Infection Epidemiology Among Very Preterm Infants in the Neonatal Intensive Care Unit

Sarah A. Coggins, MD[1,2], **Erika M. Edwards, PhD, MPH**[3,4], **Dustin D. Flannery, DO, MSCE**[1,2,5], **Jeffrey S. Gerber, MD, PhD, MSCE**[2,5,6], **Jeffrey D. Horbar, MD**[3,4], **Karen M. Puopolo, MD, PhD**[1,2,5]

[1]Division of Neonatology, Children's Hospital of Philadelphia, Philadelphia, PA, USA

[2]Department of Pediatrics, University of Pennsylvania, Philadelphia, PA, USA

[3]University of Vermont, Burlington, VT, USA

[4]Vermont-Oxford Network, Burlington, VT, USA

[5]Center for Pediatric Clinical Effectiveness, Children's Hospital of Philadelphia, Philadelphia, PA, USA

[6]Division of Infectious Diseases, Children's Hospital of Philadelphia, Philadelphia, PA, USA

Abstract

Background: *Serratia spp*. are opportunistic, multi-drug resistant, gram-negative pathogens, previously described among preterm infants in case reports or outbreaks of infection. We describe *Serratia* late-onset infection (LOI) in very preterm infants in a large, contemporary, nationally-representative cohort.

Methods: In this secondary analysis of prospectively-collected data of preterm infants born 401–1500 grams and/or 22–29 weeks' GA from 2018–2020 at 774 Vermont Oxford Network members, LOI was defined as culture-confirmed blood and/or cerebrospinal fluid infection >3 days after birth. The primary outcome was incidence of *Serratia* LOI. Secondary outcomes compared rates of survival and discharge morbidities between infants with *Serratia* and non-*Serratia* LOI.

Results: Among 119,565 infants, LOI occurred in 10,687 (8.9%). *Serratia* was isolated in 279 cases (2.6% of all LOI; 2.3 *Serratia* infections per 1000 infants). Of 774 hospitals, 161 (21%) reported at least one *Serratia* LOI; 170/271 (63%) of cases occurred at hospitals reporting 1 or 2 *Serratia* infections and 53/271 (20%) occurred at hospitals reporting ≥5 *Serratia* infections. *Serratia* LOI was associated with a lower rate of survival to discharge compared to those with non-*Serratia* LOI (adjusted relative risk 0.88, 95% CI 0.82, 0.95). Among survivors, infants with

Corresponding Author: Dr Sarah A. Coggins, Children's Hospital of Philadelphia, Division of Neonatology (2 Main NW), 3401 Civic Center Blvd, Philadelphia PA, 19104, USA. cogginss@chop.edu; phone: 215-590-1653.

AUTHOR CONTRIBUTIONS

SAC contributed to study design and interpretation of results, drafted the initial manuscript, and reviewed and revised the final manuscript. EME contributed to study design, data verification, interpretation of results, performed statistical analyses, and critically reviewed the manuscript. DDF, JDH, and KMP contributed to study design, interpretation of results, and critically reviewed the manuscript. JSG contributed to interpretation of results and critically reviewed the manuscript. All authors approved the final manuscript as submitted.

Serratia LOI had higher rates of tracheostomy, gastrostomy, and home oxygen use compared to those with non-*Serratia* LOI.

Conclusions: The incidence of *Serratia* LOI was 2.3 infections per 1000 very preterm infants in this cohort. Lower survival and significant morbidity among *Serratia* LOI survivors highlight the need for recognition and targeted prevention strategies for this opportunistic nosocomial infection.

Keywords

Serratia ; bacteremia; late-onset sepsis; preterm; infant

INTRODUCTION

Serratia spp. are opportunistic gram-negative bacteria and an important cause of nosocomial infection in neonatal intensive care units (NICUs). *Serratia* infection has been estimated to account for 1–2% of bloodstream infections (BSIs) among NICU patients in the United States (US) and Germany(1–3), and up to 15% of BSIs among a group of NICUs in Europe(4). BSIs are the most common manifestation of neonatal *Serratia* disease, but meningitis, urinary tract infections (UTIs), respiratory tract infections, and conjunctivitis due to *Serratia* also occur(5). Although most reports of neonatal *Serratia* infection arise from single centers and describe infectious clusters or outbreaks in small cohorts(6,7,16,17,8–15), endemic patterns of sporadic infections are also described(18). Environmental reservoirs are heavily implicated in *Serratia* transmission, with outbreaks in NICUs traced to medical equipment, water sources, as well as colonized patients and hospital personnel(19).

Risk factors for neonatal *Serratia* infection are common to most forms of hospital-acquired infection among preterm infants, including low birth weight, mechanical ventilation, and presence of central catheters(2,6,12,18,19). Although *Serratia* infections can be mild in some hosts, neonatal *Serratia* BSIs have been associated with increased duration of hospitalization, higher healthcare costs, and higher all-cause and *Serratia*-attributable mortality, with an 18% case-fatality rate in one cohort of very-low birth weight infants(2,3). Ventriculitis and multiple abscess formation complicating *Serratia* meningitis can both result in devastating neurologic damage(20). There are limited available surveillance data to inform current patient- and center-level burdens of *Serratia* infections and related outcomes among very preterm infants in the United States. Therefore, the objectives of this study were to describe the epidemiology of late-onset *Serratia* infections among very preterm infants, and to evaluate the relationship between *Serratia* infections, survival, and discharge morbidities, within a large, contemporary, nationally-representative cohort.

METHODS

Data Source and Study Population:

Vermont Oxford Network (VON) is a nonprofit, voluntary worldwide community of practice dedicated to improving the quality, safety, and value of newborn care through a coordinated program of data-driven quality improvement, education, and research. VON maintains a prospective database describing NICU care of infants born <1500 grams. We utilized that database to perform a secondary cohort study of infants admitted to 774 participating VON

centers from January 1, 2018, to December 31, 2020. The study population included infants born with birth weight 401–1500 grams and/or gestational age of 22–29 weeks. Infants who died or were transferred from the participating center by day 3 after birth were excluded. For study infants, data were collected from birth until hospital discharge, death, or first birthday (whichever came first); infants transferred after day 3 were tracked to determine their ultimate disposition and length of stay. The Institutional Review Board at the University of Vermont determined that use of the VON database for this analysis was not human subjects research.

Study Definitions

Late-onset infection (LOI): LOI was defined as isolation of a prespecified bacterial or fungal pathogen from blood and/or cerebrospinal fluid (CSF) cultures obtained >3 days after birth(21). We were not able to distinguish LOI due to bacteremia versus meningitis. Recurrent and/or polymicrobial LOI episodes were included in the analysis. Coagulase-negative staphylococci (CoNS) LOI episodes were included if pathogens were isolated from blood or CSF, accompanied by at least one clinical sign of generalized infection, and ≥5 days of antibiotic therapy.

Exposures: All eligible preterm infants were included in analysis of the primary outcome (incidence of *Serratia* LOI). For assessment of secondary outcomes among infants with LOI, the exposure of interest was *Serratia* versus non-*Serratia* LOI.

Outcomes: The primary outcome was incidence of late-onset *Serratia* infections per 1000 eligible very preterm infants during the study period. Secondary outcomes included survival to discharge and morbidities among surviving infants with *Serratia* vs. non-*Serratia* LOI, including discharge with tracheostomy, gastrostomy (or jejunostomy), supplemental oxygen (defined as fraction of inspired oxygen >0.21), and any enteral human milk feeding. Technology dependence at discharge is an important patient-oriented outcome and is associated with increased risk of hospital readmission, healthcare resource utilization, and financial burden(22–24).

Covariates: Covariates of interest were defined per the VON Manual of Operations(21). Infant demographic characteristics included sex, race, ethnicity, gestational age at birth, birth weight, and presence of a congenital anomaly. Small for gestational age (SGA) status was defined as birth weight <10th percentile, per the Fenton growth chart(25). Maternal and delivery characteristics included: maternal hypertensive disorders (including pre-eclampsia), maternal diabetes of any type, chorioamnionitis, delivery mode, and maternal receipt of antenatal corticosteroids. Morbidities of prematurity included chronic lung disease (CLD, receipt of supplemental oxygen at 36 weeks' postmenstrual age), severe intraventricular hemorrhage (IVH, grade 3–4), severe retinopathy of prematurity (ROP, stage 3–5), and necrotizing enterocolitis (NEC)(21). All morbidities occurred prior to NICU discharge or death. Length of stay was defined as the number of days elapsed between birth and hospital discharge or death. NICU level of care is defined using centers' responses to the VON membership survey as: Type A (required to transfer infants for assisted ventilation based on infant characteristics or duration of ventilation required), Type B (provide

mechanical ventilation without limitations on duration, no major surgery performed), and Type C (provide mechanical ventilation without limitations on duration, and major surgery performed, excluding cardiac surgery requiring bypass), and Type D (provide mechanical ventilation without limitations on duration and major surgery performed, including cardiac surgery requiring bypass)(26,27). Geographical regions were defined by US Census Bureau classifications.

Statistical Analysis

We determined the incidence of late-onset *Serratia* per 1000 eligible very preterm infants, and *Serratia* prevalence among all infants with LOI (stratified by gestational age and study year). Demographics, clinical characteristics, and outcomes were compared between infants with *Serratia* and non-*Serratia* LOI. To study the association of *Serratia* vs non-*Serratia* LOI with the secondary study outcomes, we used logistic regression with generalized estimating equations, adjusted for clustering of infants within hospitals and for multiple covariates (gestational age, SGA status, sex, delivery mode, inborn status, and presence of congenital anomalies). Risk ratios were estimated using the Poisson distribution with a log link function. The primary non-*Serratia* LOI comparison group was composed of LOI due to all non-*Serratia* bacteria (including CoNS) and fungi. To ensure comparison between infections of similar morbidity, in sensitivity analyses we compared infants with *Serratia* LOI versus those with (1) bacterial non-*Serratia* LOI, excluding infections with CoNS (an organism that may cause less severe infection among preterm infants(28,29)) and fungi, and with (2) non-*Serratia* gram-negative LOI. Finally, we described the distribution and hospital characteristics associated with *Serratia* infections occurring at VON centers. All analyses were performed using SAS version 9.4.

RESULTS

Of 119,565 eligible very preterm infants, 10,687 (8.9%) had at least one episode of LOI, and of those, 279 (2.6%) were infected with *Serratia*. The overall incidence of *Serratia* LOI was 2.3 infections per 1000 very preterm infants (95% confidence interval [CI] 2.1, 2.6). Cohort demographic and clinical characteristics are presented in Table 1. Median gestational age was similar among infants with *Serratia* and non-*Serratia* LOI (25 weeks, interquartile range [IQR] 24, 27), and lower compared to infants with no LOI (30 weeks, IQR 29, 32). Median birth weight was also similar among infants with *Serratia* and non-*Serratia* LOI, and was lower compared to infants with no LOI. Infants with *Serratia* LOI had a higher prevalence of CLD (73% vs 62%) and severe ROP (72% vs 62%) compared to infants with non-*Serratia* LOI, with similar rates of NEC and severe IVH between the two groups.

Rates of LOI due to *Serratia* increased with decreasing gestational age and birth weight, but did not differ by year of birth (Table 2). Infants with *Serratia* were more likely to have multiple distinct episodes of LOI or episodes of polymicrobial LOI; 35% of infants with *Serratia* had LOI due to ≥2 pathogens, compared to 13% of infants with non-*Serratia* LOI.

Of 774 participating hospitals, 161 (21%) reported at least one late-onset *Serratia* infection during the three-year study period (see Table, Supplemental Digital Content 1). Of 279 *Serratia* LOI episodes, 271 occurred at VON centers and were included in the center-level

analysis. The majority of *Serratia* LOI episodes (170/271, 63%) occurred at 137 hospitals reporting only 1 or 2 *Serratia* infections during the study period; 54/271 (20%) *Serratia* LOI episodes occurred at 9 hospitals reporting ≥5 *Serratia* infections. Hospitals reporting *Serratia* infections were more frequently located in the southern United States, were teaching institutions offering higher levels of neonatal and surgical care, and had higher annual admissions (Table 3).

The overall proportion of infants surviving to discharge was similar between infants with *Serratia* and non-*Serratia* LOI (75% vs 78%, respectively). However, survival was significantly lower among infants with *Serratia* after adjusting for potential confounders, including gestational age (adjusted risk ratio [aRR] 0.88, 95% CI 0.82, 0.95) (Table 4).

In adjusted analyses describing discharge morbidities among LOI survivors, infants with *Serratia* LOI were more likely to be discharged with tracheostomy (aRR 2.8, 95% CI 1.7, 4.6) and gastrostomy (aRR 1.8, 95% CI 1.4, 2.4), compared to infants with non-*Serratia* LOI due to any bacteria or fungi. At discharge, *Serratia* LOI was associated with increased risk for supplemental oxygen use (aRR 1.3, 95% CI 1.1, 1.5) and decreased likelihood of any enteral human milk feeding (aRR 0.64, 95% CI 0.5, 0.8) among survivors, compared to surviving infants with non-*Serratia* LOI (Table 4).

In a sensitivity analysis, adjusted survival among infants with *Serratia* LOI was not different compared to infants with non-CoNS bacterial LOI, and was higher compared to infants with other gram-negative LOI (see Tables, Supplemental Digital Content 2 and 3). Compared to infants with non-CoNS bacterial LOI, infants with *Serratia* had significantly higher associated risk of discharge with gastrostomy. There were no statistical differences in the risk of discharge morbidities when comparing infants with *Serratia* LOI versus other gram-negative LOI.

DISCUSSION

In this large, contemporary, nationally-representative cohort, *Serratia* accounted for 2.6% of LOI episodes among very preterm infants, similar to rates reported in earlier US-based cohorts(1,2). We further demonstrate that invasive *Serratia* LOI is not rare, and that infection with this opportunistic pathogen is associated with lower survival and increased morbidity at discharge, compared to infants infected with non-*Serratia* pathogens.

This study provides new insights into the association of *Serratia* LOI with morbidity and mortality risks in very preterm infants. Technology dependence at discharge is an important patient-oriented outcome with a multifactorial risk profile. LOI is associated with (and may modify) risk of severe BPD, via inflammatory-mediated pathways (30–32), and has been independently associated with tracheostomy placement in preterm infants(33). BPD, growth failure, and neurodevelopmental impairment are all identified risk factors for gastrostomy placement in preterm infants; all of these conditions have are further associated with antecedent LOI (22,34–36). Although *Serratia* accounts for a low proportion of neonatal infections and has variable pathogenicity in infants (ranging from asymptomatic colonization to invasive disease)(5,19,37), we identified lower survival and higher risks

of discharge morbidities (tracheostomy, gastrostomy, and supplemental oxygen) associated with *Serratia* LOI, compared with non-*Serratia* LOI. These findings were attenuated when restricting the comparison group to non-CoNS bacterial LOI; although mortality was equivalent, excess morbidity risk associated with *Serratia* LOI remained. A final comparison was restricted to infants with *Serratia* LOI versus other gram-negative LOI, given higher mortality associated with gram-negative LOI (compared to gram-positive or CoNS LOI) (3,38–40). Infants with *Serratia* LOI had slightly higher survival and similar risks of discharge morbidities compared to infants with other gram-negative LOI, underscoring the virulence of this opportunistic pathogen among preterm infants.

While *Serratia* infections account for a small percentage of all invasive neonatal LOI, our center-level analysis demonstrates that this infection burden is distributed across 21% of all hospitals reporting data to VON. Our study reinforces prior work identifying *Serratia* infections as more frequently occurring in large, academic NICUs offering complex medical and surgical services(2), likely reflecting a more chronically ill patient population with longer lengths of stay and higher technical care utilization(2,6,15,18,41). Although most published neonatal *Serratia* literature describes infections occurring in outbreak patterns, center-level data from our study suggest that *Serratia* LOI largely occurs sporadically. Most *Serratia* LOI (170/271, 63%) occurred in hospitals that reported ≤2 *Serratia* infections over the three-year study period; however, the nine highest-burden *Serratia* hospitals (≥5 episodes of *Serratia* LOI, 1% of all 774 hospitals) accounted for 20% (54/271) of infections. *Serratia* cases appeared to occur more commonly in NICUs offering higher levels of service. Among 108 type D NICUs, 48 (44%) did not have a *Serratia* LOI during the study period – though given the sporadic infection pattern, it is difficult to identify type D units with no *Serratia* LOI due to chance, versus those without *Serratia* LOI due to particularly effective infection prevention procedures. Hospitals reporting *Serratia* or non-*Serratia* LOI were proportionally more commonly located in the southern US; this geographic distribution has been similarly reported at the patient level(2), though it should be noted that neither study reports geographic distribution of patients and hospitals without LOI. Further elucidation of *Serratia* epidemiology by US geographic region may require national surveillance, including consideration of hospital-wide *Serratia* burden in addition to NICUs. We acknowledge that this study may underestimate outbreak patterns, as we exclusively studied *Serratia* bacteremia and meningitis and thus did not capture other infections (e.g., conjunctivitis, UTIs) that are also reported in *Serratia* outbreaks.

Serratia species are intrinsically resistant to beta-lactam antibiotics and carry inducible beta-lactamase resistance via chromosomal *ampC* genes. Depending on the degree of *ampC* expression, beta-lactamases variably reduce the bactericidal capacity of third-generation cephalosporins and piperacillin-tazobactam (commonly-used empiric antibiotics in NICUs) against *Serratia*(42). In a large cohort study of neonatal sepsis in low- and middle-income countries, *Serratia* was the second-most common gram-negative pathogen and accounted for 6% of all neonatal sepsis cases. Whole-genome sequencing of bacterial isolates in that study demonstrated concerning rates of antimicrobial resistance genes, including extended-spectrum beta-lactamases (ESBLs) and carbapenemases(43). In the face of rising *Serratia* incidence among pediatric(2) and adult(44) populations, as well as increasing antimicrobial resistance rates due to ESBL-producing *Enterobacterales*, renewed attention to *Serratia*

infection prevention is needed to mitigate infectious burdens and use of reserve antibiotics for resistant isolates.

Reduction of *Serratia* infection burden in NICUs requires both patient- and unit-level strategies for surveillance and decontamination. The prevalence of invasive *Serratia* disease in NICUs across the US likely reflects even higher underlying colonization rates that are potentially amenable to infection control measures. Epidemiologic surveillance within NICUs experiencing *Serratia* outbreaks has identified neonatal *Serratia* colonization, particularly in the gastrointestinal tract, as the most important infectious reservoir. Single-unit colonization rates amidst *Serratia* outbreaks are reported to range widely (28–69% of screened infants)(10,12,45,46), with isolates identified in feces and in swabs of eye, throat, umbilicus, and rectum(10,45–47). Conversion rates from *Serratia* colonization to clinical infection, which ranged from conjunctivitis to bacteremia/meningitis, varied from 11–28%(10,12,47,48). Active surveillance for *Serratia* may enable rapid initiation of enhanced hand hygiene and environmental cleaning procedures in the setting of colonization or clinical outbreaks. Reichert *et al.*(49) calculated pathogen-specific risks of additional BSIs among preterm infants in the same NICU once an index case was isolated; though its incidence density was low, *Serratia* had the highest associated risk of producing additional incident BSIs among all organisms analyzed (relative risk 77.5, 95% CI 41, 146), suggesting the potential value of initiating enhanced containment measures if index cases are detected. Approaches to reducing *Serratia* transmission within NICUs have largely focused on improving hand hygiene; efforts to cohort colonized/infected infants, institute contact precautions, and reduce nursery overcrowding are also described(10,12,47,50). Enhanced environmental cleaning is generally indicated; no consistent environmental reservoir is reported, but *Serratia* outbreaks in NICUs have been linked to sinks and water sources(51,52), incubator doors(51,53), laryngoscope blades(8), air conditioning ducts(17), and contaminated breast pumps(9), human milk(54), soap(7,55), and parenteral nutrition(56).

Strengths of this study include analysis of a large, nationally representative, contemporary cohort of very preterm infants admitted to both academic and community NICUs, supporting generalizability of our findings. However, we acknowledge study limitations. Infants with *Serratia* LOI were more likely to have LOI due to multiple organisms; however, the data reporting structure does not differentiate whether this was due to multiple distinct episodes of LOI growing different organisms, or a single polymicrobial LOI episode. It is therefore possible that multiple infectious episodes could have contributed to excess morbidity identified among patients with *Serratia* LOI. Our definition of LOI included bacteremia and meningitis, though we could not distinguish between these two types of infections. This definition did not include infections of the respiratory tract, urinary tract, and conjunctivae (all reported *Serratia* infection sites in preterm neonates(57)); therefore, the *Serratia* infection burden in this cohort could be underestimated. Because the VON dataset does not record the timing of positive blood cultures relative to infant birth, associations of LOI with some morbidities should be interpreted cautiously. For example, we cannot comment on potential causal associations of *Serratia* infection relative to onset of any morbidities of prematurity (e.g., CLD, ROP). *Serratia* LOI was associated with increased risks of discharge with tracheostomy and gastrostomy; it is possible that these procedures

could have occurred prior to LOI onset, though the majority (90%) of LOI in very preterm infants is reported to occur within the first two postnatal months(58,59), while tracheostomy and gastrostomy placements usually occur late in the NICU course among infants corrected beyond term postmenstrual age(60,61). As this study focuses on *Serratia* LOI among very preterm infants, we are unable to comment on *Serratia* epidemiology among infants born at higher gestations and birth weights. No antimicrobial susceptibility data were available, so we are unable to describe *Serratia* antibiotic resistance patterns in this cohort.

CONCLUSIONS

Serratia is a persistent cause of opportunistic invasive late-onset infections in NICUs, affecting 2.3 infants per 1000 very preterm births and occurring in 21% of neonatal units within this large cohort from the United States. Increased risks of death and morbidity among very preterm infants with *Serratia* LOI reinforce the need for recognition and targeted prevention strategies for this nosocomial infection.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

Thank you to our colleagues who submit data to the Vermont Oxford Network on behalf of infants and their families. The centers contributing data to this study are in listed Supplemental Digital Content 4.

Conflicts of Interest and Funding Sources:

Dr. Coggins reports receiving research funding from the National Heart, Lung and Blood Institute of the National Institutes of Health (T32HL007891). Dr. Edwards reports receiving salary support from Vermont Oxford Network. Dr. Flannery reports receiving research funding from the Agency for Healthcare Research and Quality (K08HS027468), from two contracts with the Centers for Disease Control and Prevention, and from the Children's Hospital of Philadelphia. Dr. Horbar is the President, Chief Executive and Chief Scientific Officer of Vermont Oxford Network, and is an unpaid member of the Vermont Oxford Network Board of Trustees. Dr. Puopolo reports receiving research funding from the National Institutes of Health, from two contracts with the Centers for Disease Control and Prevention, and from the Children's Hospital of Philadelphia. None of the authors have conflicts of interest to declare relevant to this study.

FUNDING SOURCES

Dr. Coggins reports receiving research funding from the National Heart, Lung and Blood Institute of the National Institutes of Health (T32HL007891). Dr. Flannery reports receiving research funding from the Agency for Healthcare Research and Quality (K08HS027468), from two contracts with the Centers for Disease Control and Prevention, and from the Children's Hospital of Philadelphia. Dr. Puopolo reports receiving research funding from the National Institutes of Health, from two contracts with the Centers for Disease Control and Prevention, and from the Children's Hospital of Philadelphia. The funders/sponsors had no role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscripts; or decision to submit the manuscript for publication.

CONFLICT OF INTEREST STATEMENT:

Authors' funding sources are listed above. Dr. Horbar is the President, Chief Executive Officer, and Chief Scientific Officer of Vermont Oxford Network (VON) and an unpaid member of the VON Board of Trustees. Dr Edwards receives salary support from VON. Drs Coggins, Flannery, Gerber, and Puopolo have indicated they have no potential conflicts of interest to disclose.

DATA AVAILABILITY

The dataset analyzed during the current study derives from the Vermont Oxford Network database and is not publicly available.

REFERENCES

1. Greenberg RG, Kandefer S, Do BT, Smith PB, Stoll BJ, Bell EF, et al. Late-onset Sepsis in Extremely Premature Infants. Pediatr Infect Dis J [Internet]. 2017 Aug;36(8):774–9. Available from: http://journals.lww.com/00006454-201708000-00014 [PubMed: 28709162]
2. Johnson A, Watson D, Dreyfus J, Heaton P, Lampland A, Spaulding AB. Epidemiology of Serratia Bloodstream Infections among Hospitalized Children in the United States, 2009–2016. Pediatr Infect Dis J. 2020;39(6):E71–3. [PubMed: 32091494]
3. Piening BC, Geffers C, Gastmeier P, Schwab F. Pathogen-specific mortality in very low birth weight infants with primary bloodstream infection. PLoS One [Internet]. 2017 Jun 1 [cited 2022 Feb 24];12(6). Available from: /pmc/articles/PMC5481023/
4. Raymond J, Aujard Y. Nosocomial Infections in Pediatric Patients A European, Multicenter Prospective Study. Infect Control. 2000;21(4):260–3.
5. Mahlen SD. Serratia infections: From military experiments to current practice. Clin Microbiol Rev [Internet]. 2011 Oct [cited 2022 Apr 5];24(4):755–91. Available from: https://journals.asm.org/journal/cmr [PubMed: 21976608]
6. Al Jarousha AMK, El Qouqa IA, El Jadba AHN, Al Afifi AS. An outbreak of Serratia marcescens septicaemia in neonatal intensive care unit in Gaza City, Palestine. J Hosp Infect. 2008;70(2):119–26. [PubMed: 18723246]
7. Buffet-Bataillon S, Rabier V, Bétrémieux P, Beuchée A, Bauer M, Pladys P, et al. Outbreak of Serratia marcescens in a neonatal intensive care unit: contaminated unmedicated liquid soap and risk factors. J Hosp Infect. 2009 May 1;72(1):17–22. [PubMed: 19246120]
8. Cullen MM, Trail A, Robinson M, Keaney M, Chadwick PR. Serratia marcescens outbreak in a neonatal intensive care unit prompting review of decontamination of laryngoscopes. J Hosp Infect. 2005 Jan 1;59(1):68–70. [PubMed: 15571857]
9. Gransden WR, Webster M, French GL, Phillips I. An outbreak of Serratia marcescens transmitted by contaminated breast pumps in a special care baby unit. J Hosp Infect. 1986 Mar 1;7(2):149–54. [PubMed: 2871077]
10. Montagnani C, Cocchi P, Lega L, Campana S, Biermann KP, Braggion C, et al. Serratia marcescens outbreak in a neonatal intensive care unit: crucial role of implementing hand hygiene among external consultants. BMC Infect Dis [Internet]. 2015 Jan 13 [cited 2022 Feb 24];15(1). Available from: /pmc/articles/PMC4301457/
11. Zingg W, Soulake I, Baud D, Huttner B, Pfister R, Renzi G, et al. Management and investigation of a Serratia marcescens outbreak in a neonatal unit in Switzerland – the role of hand hygiene and whole genome sequencing – R1, ARIC-D-17–00143. Antimicrob Resist Infect Control [Internet]. 2017 Dec 11 [cited 2022 Feb 24];6(1). Available from: /pmc/articles/PMC5725813/
12. Redondo-Bravo L, Gutiérrez-González E, San Juan-Sanz I, Fernández-Jiménez I, Ruiz-Carrascoso G, Gallego-Lombardo S, et al. Serratia marcescens outbreak in a neonatology unit of a Spanish tertiary hospital: Risk factors and control measures. Am J Infect Control. 2019;47(3):271–9. [PubMed: 30392995]
13. Samuelsson A, Isaksson B, Hanberger H, Olhager E. Late-onset neonatal sepsis, risk factors and interventions: an analysis of recurrent outbreaks of Serratia marcescens, 2006–2011. J Hosp Infect. 2014 Jan 1;86(1):57–63. [PubMed: 24332914]
14. Böhne C, Chhatwal P, Peter C, Ebadi E, Hansen G, Schlüter D, et al. Detection of Serratia marcescens in neonatal intensive care units requires a rapid and comprehensive infection control response starting with the very first case. GMS Hyg Infect Control [Internet]. 2021 [cited 2022 Feb 24];16:Doc12. Available from: /pmc/articles/PMC7983028/ [PubMed: 33796440]

15. Yeo KT, Octavia S, Lim K, Lin C, Lin R, Thoon KC, et al. Serratia marcescens in the neonatal intensive care unit: A cluster investigation using molecular methods. J Infect Public Health. 2020 Jul 1;13(7):1006–11. [PubMed: 31883745]
16. Polilli E, Parruti G, Fazii P, D'Antonio D, Palmieri D, D'Incecco C, et al. Rapidly controlled outbreak of serratia marcescens infection/colonisations in a neonatal intensive care unit, Pescara general hospital, Pescara, Italy, april 2011. Eurosurveillance [Internet]. 2011 Jun 16 [cited 2022 Feb 24];16(24):19892. Available from: https://www.eurosurveillance.org/content/10.2807/ese.16.24.19892-en [PubMed: 21699768]
17. Uduman SA, Farrukh AS, Nath KNR, Zuhair MYH, Ifrah A, Khawla AD, et al. An outbreak of Serratia marcescens infection in a special-care baby unit of a community hospital in United Arab Emirates: The importance of the air conditioner duct as a nosocomial reservoir. J Hosp Infect. 2002;52(3):175–80. [PubMed: 12419269]
18. Bizzarro MJ, Dembry LM, Baltimore RS, Gallagher PG. Case-control analysis of endemic Serratia marcescens bacteremia in a neonatal intensive care unit [Internet]. Vol. 92, Archives of Disease in Childhood: Fetal and Neonatal Edition. BMJ Publishing Group; 2007 [cited 2021 Jun 25]. p. F120. Available from: /pmc/articles/PMC2675455/ [PubMed: 17088342]
19. Voelz A, Müller A, Gillen J, Le C, Dresbach T, Engelhart S, et al. Outbreaks of Serratia marcescens in neonatal and pediatric intensive care units: Clinical aspects, risk factors and management. Int J Hyg Environ Health. 2010;213(2):79–87. [PubMed: 19783209]
20. Campbell JR, Diacovo T, Baker CJ. Serratia marcescens meningitis in neonates. Pediatr Infect Dis J [Internet]. 1992 Oct;11(10):881–6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/1408491 [PubMed: 1408491]
21. Vermont Oxford Network Manual of Operations: Part 2: Data Definitions and Infant Data Forms for Infants Born in 2018. Release 22. Burlington, VT: Vermont Oxford Network, 2017.
22. Warren MG, Do B, Das A, Smith PB, Adams-Chapman I, Jadcherla S, et al. Gastrostomy Tube Feeding in Extremely Low Birthweight Infants: Frequency, Associated Comorbidities, and Long-term Outcomes. J Pediatr [Internet]. 2019 Nov 1 [cited 2022 Jul 30];214:41. Available from: /pmc/articles/PMC6815700/ [PubMed: 31427096]
23. Powell J, Keltie K, Sims A, Richardson H, Brodlie M, Powell S. National Cohort Study of Health Care Resource Use After Pediatric Tracheostomy. JAMA Pediatr [Internet]. 2022 [cited 2022 Jul 30]; Available from: https://jamanetwork-com.proxy.library.upenn.edu/journals/jamapediatrics/fullarticle/2792413
24. DeMauro SB, Jensen EA, Bann CM, Bell EF, Hibbs AM, Hintz SR, et al. Home oxygen and 2-year outcomes of preterm infants with bronchopulmonary dysplasia. Pediatrics [Internet]. 2019 May 1 [cited 2022 Jul 30];143(5). Available from: /pmc/articles/PMC6564066/
25. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatr [Internet]. 2013 Apr 20 [cited 2022 May 13];13(1):59. Available from: /pmc/articles/PMC3637477/ [PubMed: 23601190]
26. Barfield WD, Papile LA, Baley JE, Benitz W, Cummings J, Carlo WA, et al. Levels of Neonatal Care. Pediatrics [Internet]. 2012 Sep 1 [cited 2022 Jul 29];130(3):587–97. Available from: /pediatrics/article/130/3/587/30212/Levels-of-Neonatal-Care [PubMed: 22926177]
27. Edwards EM, Horbar JD. Variation in use by NICU types in the United States. Pediatrics [Internet]. 2018 Nov 1 [cited 2022 Jul 29];142(5). Available from: /pediatrics/article/142/5/e20180457/81654/Variation-in-Use-by-NICU-Types-in-the-United
28. Cantey JB, Anderson KR, Kalagiri RR, Mallett LH. Morbidity and mortality of coagulase-negative staphylococcal sepsis in very-low-birth-weight infants. World J Pediatr [Internet]. 2018;14(3):269–73. Available from: 10.1007/s12519-018-0145-7 [PubMed: 29536341]
29. Jean-Baptiste N, Benjamin DK, Cohen-Wolkowiez M, Fowler VG, Laughon M, Clark RH, et al. Coagulase-Negative Staphylococcal Infections in the Neonatal Intensive Care Unit. Infect Control Hosp Epidemiol [Internet]. 2011 Jul [cited 2021 Jun 24];32(7):679–86. Available from: /pmc/articles/PMC3238054/ [PubMed: 21666399]
30. Natarajan G, Pappas A, Shankaran S, Kendrick DE, Das A, Higgins RD, et al. Outcomes of Extremely Low Birth Weight Infants with Bronchopulmonary Dysplasia: Impact of the Physiologic Definition. Early Hum Dev [Internet]. 2012 Jul [cited 2022 Jul 30];88(7):509. Available from: /pmc/articles/PMC3686277/ [PubMed: 22236557]

31. Jensen EA, Edwards EM, Greenberg LT, Soll RF, Ehret DEY, Horbar JD. Severity of bronchopulmonary dysplasia among very preterm infants in the United States. Pediatrics [Internet]. 2021 Jul 1 [cited 2021 Nov 11];148(1). Available from: /pediatrics/article/148/1/e2020030007/179948/Severity-of-Bronchopulmonary-Dysplasia-Among-Very
32. Adams-Chapman I Long-Term Impact of Infection on the Preterm Neonate. Semin Perinatol [Internet]. 2012;36(6):462–70. Available from: 10.1053/j.semperi.2012.06.009 [PubMed: 23177806]
33. Kurata H, Ochiai M, Inoue H, Ichiyama M, Yasuoka K, Fujiyoshi J, et al. A nationwide survey on tracheostomy for very-low-birth-weight infants in Japan. Pediatr Pulmonol [Internet]. 2019 Jan 1 [cited 2022 Jul 30];54(1):53–60. Available from: https://onlinelibrary-wiley-com.proxy.library.upenn.edu/doi/full/10.1002/ppul.24200 [PubMed: 30525314]
34. Mukhopadhyay S, Puopolo KM, Hansen NI, Lorch SA, Demauro SB, Greenberg RG, et al. Neurodevelopmental outcomes following neonatal late-onset sepsis and blood culture-negative conditions. Arch Dis Child - Fetal Neonatal Ed [Internet]. 2021 Sep 1 [cited 2021 Nov 11];106(5):467–73. Available from: https://fn-bmj-com.proxy.library.upenn.edu/content/106/5/467 [PubMed: 33478957]
35. Stoll BJ, Hansen NI, Adams-Chapman I, Fanaroff AA, Hintz SR, Vohr B, et al. Neurodevelopmental and growth impairment among extremely low-birth-weight infants with neonatal infection. JAMA [Internet]. 2004 Nov 17;292(19):2357–65. Available from: https://jamanetwork.com/ [PubMed: 15547163]
36. Flannery DD, Jensen EA, Tomlinson LA, Yu Y, Ying G-S, Binenbaum G. Poor postnatal weight growth is a late finding after sepsis in very preterm infants. Arch Dis Child - Fetal Neonatal Ed [Internet]. 2021 May 1 [cited 2021 Oct 24];106(3):298–304. Available from: https://fn-bmj-com.proxy.library.upenn.edu/content/106/3/298 [PubMed: 33148685]
37. Cristina ML, Sartini M, Spagnolo AM. Serratia marcescens Infections in Neonatal Intensive Care Units (NICUs). Int J Environ Res Public Health [Internet]. 2019 Feb 1 [cited 2022 Feb 24];16(4). Available from: /pmc/articles/PMC6406414/
38. Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK Jr., et al. Early and Late Onset Sepsis in Very-Low-Birth-Weight Infants from a Large Group of Neonatal Intensive Care Units. Early Hum Dev [Internet]. 2012 May [cited 2021 Aug 1];88(Suppl 2):S69. Available from: /pmc/articles/PMC3513766/ [PubMed: 22633519]
39. Tsai MH, Hsu JF, Chu SM, Lien R, Huang HR, Chiang MC, et al. Incidence, clinical characteristics and risk factors for adverse outcome in neonates with late-onset sepsis. Pediatr Infect Dis J. 2014;33(1):7–13.
40. Levit O, Bhandari V, Li FY, Shabanova V, Gallagher PG, Bizzarro MJ. Clinical and Laboratory Factors that Predict Death in Very Low Birth Weight Infants Presenting with Late-Onset Sepsis. Pediatr Infect Dis J [Internet]. 2014 [cited 2022 Aug 3];33(2):143. Available from: /pmc/articles/PMC3917323/ [PubMed: 24418836]
41. Friedman ND, Kotsanas D, Brett J, Billah B, Korman TM. Investigation of an outbreak of Serratia marcescens in a neonatal unit via a case-control study and molecular typing. Am J Infect Control. 2008;36(1):22–8. [PubMed: 18241732]
42. Tamma PD, Doi Y, Bonomo RA, Johnson JK, Simner PJ. A Primer on AmpC β-Lactamases: Necessary Knowledge for an Increasingly Multidrug-resistant World. Clin Infect Dis [Internet]. 2019 Sep 27 [cited 2022 Apr 5];69(8):1446. Available from: /pmc/articles/PMC6763639/ [PubMed: 30838380]
43. Sands K, Carvalho MJ, Portal E, Thomson K, Dyer C, Akpulu C, et al. Characterization of antimicrobial-resistant Gram-negative bacteria that cause neonatal sepsis in seven low- and middle-income countries. Nat Microbiol [Internet]. 2021 Apr 1 [cited 2021 Oct 24];6(4):512. Available from: /pmc/articles/PMC8007471/ [PubMed: 33782558]
44. Laboratory surveillance of Enterobacter spp., Serratia spp. and Citrobacter spp. bacteraemia in England, Wales and Northern Ireland: 2018. Heal Prot Rep [Internet]. 2019;13(29):1–23. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/825668/hpr2919_entrbctr.pdf

45. Casolari C, Pecorari M, Della Casa E, Cattani S, Venturelli C, Fabio G, et al. Serratia marcescens in a neonatal intensive care unit: Two long-term multiclone outbreaks in a 10-year observational study. New Microbiol. 2013;36(4):373–83. [PubMed: 24177299]
46. Moles L, Gómez M, Moroder E, Jiménez E, Escuder D, Bustos G, et al. Serratia marcescens colonization in preterm neonates during their neonatal intensive care unit stay. Antimicrob Resist Infect Control [Internet]. 2019 Aug 9 [cited 2022 Feb 24];8(1). Available from: /pmc/articles/PMC6688303/
47. Christensen GD, Korones SB, Reed L, Bulley R, McLaughlin B, Bisno AL. Epidemic Serratia marcescens in a neonatal intensive care unit: importance of the gastrointestinal tract as a reservoir. Infect Control. 1982;3(2):127–33. [PubMed: 7042624]
48. Escribano E, Saralegui C, Moles L, Montes MT, Alba C, Alarcón T, et al. Influence of a Serratia marcescens outbreak on the gut microbiota establishment process in low-weight preterm neonates. PLoS One [Internet]. 2019 May 1 [cited 2022 Feb 24];14(5). Available from: /pmc/articles/PMC6529157/
49. Reichert F, Piening B, Geffers C, Gastmeier P, Bührer C, Schwab F. Pathogen-specific clustering of nosocomial blood stream infections in very preterm infants. Pediatrics [Internet]. 2016 Apr 1 [cited 2022 Feb 24];137(4). Available from: /pediatrics/article/137/4/e20152860/81369/Pathogen-Specific-Clustering-of-Nosocomial-Blood
50. Johnson J, Quach C, Fshea MF. Outbreaks in the Neonatal Intensive Care Unit: A Review of the Literature HHS Public Access. Curr Opin Infect Dis. 2017;30(4):395–403. [PubMed: 28582313]
51. Bates CJ, Pearse R. Use of hydrogen peroxide vapour for environmental control during a Serratia outbreak in a neonatal intensive care unit. J Hosp Infect [Internet]. 2005 Dec;61(4):364–6. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0195670105001982 [PubMed: 16099537]
52. Milisavljevic V, Wu F, Larson E, Rubenstein D, Ross B, Drusin LM, et al. Molecular Epidemiology of Serratia marcescens Outbreaks in Two Neonatal Intensive Care Units. Infect Control Hosp Epidemiol. 2004 Sep;25(9):719–22. [PubMed: 15484794]
53. Jang TN, Fung CP, Yang TL, Shen SH, Huang CS, Lee SH. Use of pulsed-field gel electrophoresis toinvestigate an outbreak of Serratia marcescens infection in a neonatal intensive care unit. J Hosp Infect. 2001 May 1;48(1):13–9. [PubMed: 11358466]
54. Fleisch F, Zimmermann-Baer U, Zbinden R, Bischoff G, Arlettaz R, Waldvogel K, et al. Three Consecutive Outbreaks of Serratia marcescens in a Neonatal Intensive Care Unit. Clin Infect Dis [Internet]. 2002;767:767–73. Available from: https://academic.oup.com/cid/article/34/6/767/385207
55. Rabier V, Bataillon S, Jolivet-Gougeon A, Chapplain JM, Beuchée A, Bétrémieux P. Hand washing soap as a source of neonatal Serratia marcescens outbreak. Acta Pædiatrica [Internet]. 2008 Oct 1 [cited 2022 Feb 24];97(10):1381–5. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1651-2227.2008.00953.x
56. Arslan U, Erayman I, Kirdar S, Yuksekkaya S, Cimen O, Tuncer I, et al. Serratia marcescens sepsis outbreak in a neonatal intensive care unit. Pediatr Int [Internet]. 2010 Apr 1 [cited 2022 May 16];52(2):208–12. Available from: https://onlinelibrary-wiley-com.proxy.library.upenn.edu/doi/full/10.1111/j.1442-200X.2009.02934.x [PubMed: 19664012]
57. Downey LC, Benjamin DK, Clark RH, Watt KM, Hornik CP, Laughon MM, et al. Urinary tract infection concordance with positive blood and cerebrospinal fluid cultures in the neonatal intensive care unit. J Perinatol [Internet]. 2013 Mar [cited 2021 Nov 26];33(4):302. Available from: /pmc/articles/PMC3549035/ [PubMed: 22935772]
58. Boghossian NS, Page GP, Bell EF, Stoll BJ, Murray JC, Cotten CM, et al. Late-onset sepsis in very low birth weight infants from singleton and multiple-gestation births. J Pediatr [Internet]. 2013 Jun;162(6):1120–4, 1124.e1. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0022347612014230 [PubMed: 23324523]
59. Köstlin-Gille N, Härtel C, Haug C, Göpel W, Zemlin M, Müller A, et al. Epidemiology of Early and Late Onset Neonatal Sepsis in Very Low Birthweight Infants: Data from the German Neonatal Network. Pediatr Infect Dis J. 2021;40(3):255–9. [PubMed: 33538544]
60. Rane S, Bathula S, Thomas RL, Natarajan G. Outcomes of tracheostomy in the neonatal intensive care unit: is there an optimal time? J Matern Neonatal Med [Internet].

2014 Aug 9 [cited 2022 May 25];27(12):1257–61. Available from: https://www-tandfonline-com.proxy.library.upenn.edu/doi/abs/10.3109/14767058.2013.860438

61. Ng K, Lefton-Greif MA, McGrath-Morrow SA, Collaco JM. Factors That Impact the Timing and Removal of Gastrostomy Placement/Nissen Fundoplication in Children with Bronchopulmonary Dysplasia. Am J Perinatol [Internet]. 2021 May 31 [cited 2022 May 25]; Available from: http://www.thieme-connect.com.proxy.library.upenn.edu/products/ejournals/html/10.1055/s-0041-1730432

Table 1:

Maternal and infant demographics and clinical characteristics

	Serratia LOI			Non-*Serratia* LOI*			No LOI		
	N	***n***	***%***	***N***	***n***	***%***	***N***	***n***	***%***
Maternal Characteristics									
Maternal Race/Ethnicity									
Black non-Hispanic, %	278	107	38.5	10,281	3,552	34.5	107,685	33,532	31.1
Hispanic, %	278	53	19.1	10,281	2,121	20.6	107,685	20,885	19.4
White non-Hispanic, %	278	108	38.8	10,281	3,834	37.3	107,685	44,453	41.3
Other non-Hispanic**, %	278	10	3.6	10,281	774	7.5	107,685	8,815	8.2
Antenatal steroids, %	278	228	82.0	10,346	9,052	87.5	108,459	95,690	88.2
Chorioamnionitis, %	272	47	17.3	10,274	1,823	17.7	107,973	13,148	12.2
Hypertension, %	274	86	31.4	10,317	3,118	30.2	108,322	43,555	40.2
Diabetes, %	268	27	10.1	10,280	939	9.1	108,120	12,625	11.7
Multiple gestation, %	279	75	26.9	10,408	2,186	21.0	108,874	26,562	24.4
Vaginal delivery, %	279	67	24.0	10,406	3,459	33.2	108,861	26,722	24.5
Infant Characteristics									
Gestational age									
≤23 weeks, %	279	54	19.4	10,408	1,833	17.6	108,874	3,946	3.6
24–25 weeks, %	279	115	41.2	10,408	3,628	34.9	108,874	13,312	12.2
26–27 weeks, %	279	69	24.7	10,408	2,554	24.5	108,874	20,968	19.3
28–29 weeks, %	279	23	8.2	10,408	1,568	15.1	108,874	31,148	28.6
>29 weeks, %	279	18	6.5	10,408	825	7.9	108,874	39,500	36.3
Gestational age (median, Q1, Q3)			25 (24, 27)			25 (24, 27)			30 (29, 32)
Birth weight, grams (median [Q1, Q3])	279		705 (590, 900)	10,406		760 (610, 985)	108,873		1,140 (870, 1,350)
Small for gestational age, %	278	53	19.1	10,311	1,622	15.7	108,644	21,183	19.5
Male, %	279	145	52.0	10,405	5,719	55.0	108,857	54,065	49.7
Inborn, %	279	227	81.4	10,408	8,344	80.2	108,878	94,698	87.0
Congenital anomaly, %	279	30	10.8	10,404	846	8.1	108,866	5,613	5.2
Morbidities of Prematurity									
Necrotizing enterocolitis, %	279	46	16.5	10,400	1,683	16.2	108,862	4,161	3.8
Chronic lung disease, %	211	153	72.5	8,041	4,982	62.0	93,338	25,212	27.0
Retinopathy of prematurity, %	217	156	71.9	8,228	5,075	61.7	87,365	25,444	29.1
Intraventricular hemorrhage, %	276	123	44.6	10,136	4,353	42.9	100,148	23,466	23.4
Morbidities at Discharge									
Tracheostomy, %	279	17	6.1	10,396	351	3.4	108,851	683	0.6
Gastrostomy or jejunostomy, %	279	48	17.2	10,396	1,254	12.1	108,851	4,031	3.7
Oxygen at discharge, %	166	75	45.2	6,730	2,529	37.6	94,482	12,487	13.2
Human milk at discharge, %	174	46	26.4	6,792	2,538	37.4	94,580	49,079	51.9

	***Serratia* LOI**			**Non-*Serratia* LOI***			**No LOI**		
	N	***n***	***%***	***N***	***n***	***%***	***N***	***n***	***%***
Survival, %	274	206	75.2	10,258	8,030	78.3	108,323	102,789	94.9
Length of Stay, days [median, (Q1, Q3)]									
Overall	274		117 (72, 178)	10,235		102 (62, 140)	108,135		62 (41, 89)
Among survivors	206		136 (102, 187)	7,999		113 (86, 149)	102,596		64 (44, 91)
Among non-survivors	68		29 (13, 59)	2,226		21 (11, 46)	5,521		13 (6, 31)

N: total number of infants with data available

n: number of infants with given characteristic among total

*Infants with other late bacterial, CoNS, or fungal infection

**Includes Asian/Pacific Islander, Native American/Alaska Native, Other

Table 2:

Serratia incidence by study year and gestational age category among infants with any late infection

Category	All infants with LOI (n)*	Infants with *Serratia* LOI (n, %)	*Serratia* incidence rate per 1000 infants with any late infection (95% CI)
Overall	10679	279 (2.6)	26.1 (22.4, 30.4)
Year of Birth			
2018	3550	95 (2.7)	26.8 (20.6, 34.7)
2019	3651	98 (2.7)	26.8 (20.8, 34.6)
2020	3478	86 (2.5)	24.7 (18.8, 32.5)
Gestational Age (weeks)			
≤23	1884	54 (2.9)	28.7 (20.3, 40.3)
24–25	3739	115 (3.1)	30.8 (24.3, 38.9)
26–27	2623	69 (2.6)	26.3 (19.4, 35.6)
28–29	1591	23 (1.5)	14.5 (8.5, 24.4)
>29	842	18 (2.1)	21.4 (11.8, 38.4)
Birth Weight (grams)			
≤500	875	25 (2.8)	27.8 (16.8, 45.7)
501–750	4228	139 (3.2)	31.8 (25.7, 39.4)
751–1000	2844	70 (2.4)	24.0 (17.7, 32.5)
1001–1250	1465	34 (2.3)	22.7 (14.7, 34.9)
1251–1500	854	11 (1.3)	12.7 (6.0, 26.9)
≥1500	132	0 (0.0)	0.0

* Infants with *Serratia*, other late bacterial infections (including coagulase-negative *Staphylococcus*), or fungal infections.

Table 3:

Characteristics of Hospitals Reporting Neonatal *Serratia* LOI

	Hospitals with ≥1 *Serratia* Case		**Hospitals with No *Serratia* Cases**	
	N	**%**	***N***	**%**
NICU Type				
A	161	0.6	613	13.5
B	161	19.9	613	44.4
C	161	42.2	613	34.3
D	161	37.3	613	7.8
NICU beds - med (Q1, Q3)	161	40 (24, 60)	610	20 (12, 30)
Total NICU admissions - med (Q1, Q3)	159	691 (445, 964)	592	327 (218, 537)
Teaching hospital	161	70.2	601	44.3
Single family rooms				
≤ 10%	159	45.9	609	55.2
11–50%	159	8.2	609	4.4
51–90%	159	12.6	609	5.9
≥ 91%	159	33.3	609	34.5
Region				
Northeast	161	13.7	613	15.2
Midwest	161	18.6	613	21.4
South	161	53.4	613	33.6
West	161	14.3	613	29.9

N: total number of infants with data available.

Table 4:

Outcomes of *Serratia* vs non-*Serratia* late-onset infection

	***Serratia* LOI**			**Non-*Serratia* LOI[1]**			**Adjusted risk ratio (95% CI)[2]**
	N	***n***	***%***	***N***	***n***	***%***	
Survival to discharge	274	206	75.2	10,258	8,030	78.3	0.88 (0.82, 0.95)
Among survivors discharged home:							
Tracheostomy placement	279	17	6.1	10,396	351	3.4	2.78 (1.68, 4.59)
Gastrostomy or jejunostomy placement	279	48	17.2	10,396	1,254	12.1	1.83 (1.41, 2.38)
Oxygen at discharge	166	75	45.2	6,730	2,529	37.6	1.29 (1.08, 1.54)
Human milk at discharge	174	46	26.4	6,792	2,538	37.4	0.64 (0.50, 0.83)

N: total number of infants with data available

n: number of infants with given characteristic among total

1: Includes all non-*Serratia* late bacterial LOI (including coagulase-negative *Staphylococcus*) and fungal LOI

2: Adjusted for clustering of infants within hospitals, and for gestational age in weeks, small for gestational age status, sex, mode of delivery, inborn status, and presence of a congenital anomaly