

Recurrent Nosocomial Outbreaks of Multidrug-Resistant Gram-Negative Bacilli in Neonatal Intensive Care Units: A Narrative Review

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ABSTRACT

Background: Neonatal Intensive Care Units (NICUs) are recognized as high-risk settings for outbreaks caused by Multidrug-Resistant (MDR) gram-negative bacilli, particularly *Pseudomonas aeruginosa*, *Acinetobacter* spp. and ESBL/carbapenem-resistant Enterobacterales.

Objective: To review current evidence on the epidemiology, environmental and device-related sources, contributing risk factors, and control strategies of NICU outbreaks caused by MDR gram-negative bacilli, and to relate them to the recurrent-outbreak pattern observed in every-day hospital practice.

Methods: Narrative review of literature indexed in PubMed/MEDLINE and institutional guidance documents, published mainly between 1995 and 2026, using the terms "neonatal intensive care unit", "outbreak", "multidrug resistance", "*Pseudomonas aeruginosa*", "*Acinetobacter*" and "Enterobacterales".

Conclusions: Recurrent NICU outbreaks share common features across settings: persistent environmental reservoirs (water sources, ventilatory-support equipment), coexistence of more than one MDR organism, and organizational gaps in staffing ratios and aseptic technique. Sustained environmental microbiological surveillance, equipment reprocessing audits and molecular typing capacity are central to breaking the recurrence cycle.

Keywords: Cross Infection; Disease Outbreaks; Intensive Care Units, Neonatal; Drug Resistance; Multiple; Bacterial; *Pseudomonas Aeruginosa*; *Acinetobacter*; Enterobacteriaceae

Introduction

Neonates admitted to intensive care, especially those born preterm, are particularly vulnerable to healthcare-associated infection because of immature host defenses, prolonged invasive devices and frequent contact with staff and shared equipment. A recent systematic review and meta-analysis identified 122 outbreaks across 42 countries over two decades, with bacteria accounting for the large majority of episodes and gram-negative organisms among the leading causes. Gram-negative non-fermenting bacilli and Enterobacterales are repeatedly implicated because of their capacity to persist on moist surfaces, tubing and contaminated solutions, together with increasing multidrug-resistance profiles that limit therapeutic options and raise case-fatality. Understanding the recurrent sources and or-

ganizational conditions that sustain these outbreaks, rather than only the acute investigation of a single episode, is essential for designing durable control programs in Obstetric-Neonatal hospitals.

Methods

A narrative literature search was conducted in PubMed/MEDLINE for reports and reviews of NICU outbreaks caused by gram-negative bacilli, complemented by institutional and international infection-control guidance (Centers for Disease Control and Prevention, Ministry of Public Health of Cuba). Reference lists of retrieved reviews were screened for additional relevant primary studies. Non-systematic, thematic synthesis was used given the descriptive purpose of this review [1-16].

Results and Discussion

Epidemiology and Burden

Reviews spanning 2015-2026 consistently describe gram-negative bacteria as the most frequently reported cause of NICU outbreaks, with *Pseudomonas aeruginosa* and *Acinetobacter* spp. among the predominant non-fermenting species, alongside ESBL- and Carbapenemase-Producing Enterobacterales. Case-fatality in these episodes is consistently higher than in outbreaks caused by more susceptible organisms, reflecting both host vulnerability and limited antimicrobial options.

Predominant Pathogens and Resistance Mechanisms

Extended-spectrum β -lactamase (ESBL)-producing *Klebsiella pneumoniae* and carbapenem-resistant Enterobacterales have been repeatedly implicated in NICU outbreaks worldwide, including reports of NDM-type carbapenemases in Latin American units. Retrospective series from tertiary hospitals confirm that a substantial proportion of gram-negative bacilli isolated from septic neonates now carry multidrug-resistance phenotypes, which complicates empirical therapy and increases dependence on last-line agents.

Environmental and Device-Related Reservoirs

Contaminated water sources, sinks and plumbing have been documented as recurrent reservoirs for *P. aeruginosa* outbreaks in NICUs, in some cases resolved only after structural modification of water-use practices. Ventilatory-support equipment-tubing, endotracheal tubes and humidification circuits-is similarly recognized as a vehicle for cross-transmission when reassigned between patients without adequate disinfection, a mechanism described across multiple outbreak reports and consistent with routine hospital experience.

Organizational and Care-Related Risk Factors

Beyond the causative organism, case-control studies identify non-compliance with nurse-to-patient staffing ratios, prior antimicrobial exposure, prolonged assisted ventilation and use of central or umbilical catheters as recurrent contributing factors for both the occurrence and the perpetuation of NICU outbreaks. These organizational deficiencies frequently coexist with the environmental reservoirs described above, compounding transmission risk.

Molecular Typing and Outbreak Investigation

Antibiotic susceptibility patterns alone can be misleading when delineating an outbreak: comparative experience shows that whole-genome sequencing more accurately identifies clonal relationships than phenotypic typing, and is increasingly regarded as necessary to confirm or rule out a common source between temporally or spatially clustered cases, particularly when isolates share a cubicle or device but differ subtly in resistance profile.

Control and Prevention Strategies

1. Structured, multidimensional action plans covering managerial, care-related, organizational, disciplinary and teaching-research domains.
2. Systematic (not only reactive) environmental microbiological surveillance of devices, tubing and water sources.
3. Reinforcement of hand hygiene and of the nurse-to-patient ratio during outbreak periods and beyond.
4. Equipment disinfection protocols between uses, irrespective of whether patients are unrelated or share a cubicle (e.g., twins).
5. Care bundles for central-line and ventilatory-device management, supported by periodic staff training.
6. Access to molecular typing to clarify transmission chains and guide targeted, rather than generic, control measures.

Conclusion

The recurrence of NICU outbreaks caused by MDR gram-negative bacilli within short intervals, in the same unit and often with the same species, points to environmental reservoirs that are not fully eradicated by the control measures instituted after a first episode, together with persistent organizational gaps in staffing and aseptic practice. Sustaining environmental surveillance over time, auditing equipment reprocessing, and incorporating molecular typing into outbreak investigation are consistent priorities across the reviewed evidence for reducing recurrence in neonatal units.

Declarations

Ownership Statement

The author holds 100% ownership of this work and is solely responsible for its authorship and preparation.

Conflicts of Interest

The author declares no conflicts of interest related to this research.

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