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## Review

## A systematic review of nosocomial waterborne infections in neonates and mothers

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## ABSTRACT

**Background:** Water is an important, overlooked, and controllable source of nosocomial infection. Hospitalized neonates and their mothers are particularly vulnerable to nosocomial waterborne infections. Our objectives through this systematic review were to: investigate water sources, reservoirs, and transmission routes that lead to nosocomial waterborne infections in neonates and their mothers; establish patient risk factors; compile measures for controlling outbreaks and recommended strategies for prevention; and identify information gaps to improve guidelines for reporting future outbreaks.

**Methods:** We searched PubMed, Web of Science, Embase, and clinicaltrials.gov. Peer-reviewed studies reporting contaminated water as a route of transmission to neonates and/or their mothers were included.

**Results:** Twenty-five studies were included. The most common contaminated water sources in healthcare facilities associated with infection transmission were tap water, sinks, and faucets. Low birthweights, preterm or premature birth, and underlying disease increased neonatal risk of infection. Effective control measures commonly included replacing or cleaning faucets and increased or alternative methods for hand disinfection, and recommendations for prevention of future infections highlighted the need for additional surveillance.

**Discussion/conclusion:** The implementation of control measures and recommended prevention strategies by healthcare workers and managing authorities of healthcare facilities and improved reporting of future outbreaks may contribute to a reduction in the incidence of nosocomial waterborne infections in neonates and their mothers.

## 1. Introduction

Nosocomial infections are a persistent challenge worldwide. In the United States, they affect up to 10% of all hospitalized patients (Anaissie et al., 2002). Nosocomial infections contribute to morbidity and mortality, and increase financial burdens and length of stay for patients in low-, middle-, and high-income countries (Anaissie et al., 2002; Ducel et al., 2002; Hassan et al., 2010). Water systems are significant and controllable sources of nosocomial infections that are often inadequately managed in healthcare facilities (HCFs) (Anaissie et al., 2002; Cunliffe et al., 2011; Exner et al., 2005). In large, urban HCFs such as hospitals, patients may be exposed to poorly designed or managed systems, leading to increased risks of disease outbreaks (Cunliffe et al., 2011). In smaller, rural facilities in low- and middle-income countries (LMICs), there may be limited access and availability of water or use of unsafe water sources and unsafe stored water

(Bartram et al., 2015; Shields et al., 2015; World Health Organization and UNICEF, 2015).

Inadequate management of HCF water systems can lead to nosocomial infections in more vulnerable hospitalized populations, including those that are immune-compromised, are old, or have underlying diseases (Ducel et al., 2002). Neonates and their mothers are particularly vulnerable. Surveillance studies show 15–20% infection rates in neonatal intensive care units (NICU). Neonates with risk factors such as low birthweights are especially predisposed to infection due to poor immune defenses and intrusive life support systems (Baltimore, 1998). A point prevalence survey of 29 NICUs in the United States showed an infection rate of 11.4%, while individual NICU nosocomial infection rates ranged from 6% to 25%. Multicenter studies in Europe ranged from 8% to 10% (Sohn et al., 2001).

Postpartum sepsis is the leading cause of direct maternal death in the United Kingdom, and a growing source of morbidity and mortality

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in the United States (Bauer et al., 2013). Nulliparous women, women with multiple births, and women with chronic conditions are at a higher risk of developing infections after pregnancy (Knowles et al., 2015), though the large majority of the 6.0% observed postpartum infection rate manifest after hospital discharge (Yokoe et al., 2001). In 2013, estimates suggest 430,000 neonatal deaths were caused by sepsis or other infection (Oza et al., 2015).

Exposure to nosocomial pathogens can lead to a variety of adverse health outcomes in neonates and their mothers. Infections can occur in the bloodstream, lower respiratory tract, and urinary tract, and can increase mortality (Anaisie et al., 2002; Ducel et al., 2002; Sohn et al., 2001).

Prior systematic reviews have described studies of waterborne nosocomial infections, but there is a need for an up-to-date, comprehensive review that highlights the vulnerability of this population in particular. Experts and supporting actors call for improvements in water, sanitation, and hygiene (WASH) in HCFs to improve maternal and neonatal health and reduce morbidity and mortality rates (Velleman et al., 2014). However, there is insufficient characterization of the impact of waterborne nosocomial infections on maternal and neonatal health.

We systematically reviewed the scientific literature to better understand the causes of and prevention strategies for waterborne nosocomial infections on neonatal and maternal health. The primary objectives were:

- What are the most common water sources, reservoirs, and transmission routes that lead to nosocomial infections in neonates and their mothers?
- What are the patient risk factors in nosocomial waterborne infections in neonates and their mothers?
- What measures and strategies are effective in controlling ongoing outbreaks or recommended for preventing future outbreaks of nosocomial waterborne infections in neonates and their mothers?
- What information gaps exist in the literature on nosocomial waterborne infections in neonates and their mothers?

In addition to addressing these topics, we propose a set of reporting guidelines for nosocomial waterborne infections to improve consistency and better inform practice and research.

## 2. Methods

A systematic review was conducted of studies reporting waterborne infections of neonates and their mothers in HCFs.

### 2.1. Eligibility

Studies were included based on the following criteria: reported symptomatic clinical disease; reported on HCFs where deliveries could occur; and contained primary data. Editorials, reviews, and studies exclusively reporting colonization of patients without infection were excluded. Studies exclusively reporting *Legionella pneumophila* species as the infectious microbe were also excluded due to recent literature review pertaining to *Legionella* (see Leiblein et al., 2016). There was no limit on the date of publication.

### 2.2. Definitions

Neonates are defined as children under 28 days old (World Health Organization, 2014). When age was not specified, patients referred to as “newborn” or “neonate” or treated in the neonatal or nursery unit of a hospital were characterized as neonates. Water sources, reservoirs and transmission routes included tap water, peripherals (e.g. faucets, sinks, shower heads), water baths, water used to prepare aqueous solutions, and water used in humidifiers, ventilators, and incubators. HCFs

included hospitals, outpatient clinics, and nursery facilities.

### 2.3. Search strategy

We used the initial stages of a search strategy employed in a previous systematic review of nosocomial waterborne infections in patients of all ages (Li et al., 2016).

Peer-reviewed studies were identified through PubMed, Web of Science, Embase, and clinicaltrials.gov. The following search statements were used: (waterborne OR water) AND (health facilities OR “health care facilities, manpower, and services” OR hospitals OR hospital OR “Hospital Design and Construction” OR hospital-acquired OR nosocomial) AND (disease outbreaks OR infection control OR “Cross Infection” OR “Disease Reservoirs”).

Three independent reviewers using Cochrane’s Covidence online software screened the titles and abstracts of studies obtained from searches. Studies independently approved by two of three reviewers were included in the next stage of screening. Conflicts between the three reviewers were resolved by one of these reviewers. Full texts of selected studies were screened in two stages: initially for the reasons for exclusion as described above, and subsequently to limit the review to neonates and/or mothers as an affected population. The references lists of included studies were searched for additional eligible studies. The search was updated on March 17, 2016.

### 2.4. Data extraction

The following data were extracted from included studies: setting (HCF type and country information), microbial testing (including temporality and antimicrobial susceptibility); water sources, reservoirs and transmission routes tested; non-water environmental reservoirs tested; conclusion about cause of infection; length of study; number of neonates and/or mothers affected; risk factors for infected patients; other populations affected (including staff and infants older than 28 days); outcomes for neonates, mothers, and other populations; implemented control measures; recommended prevention strategies.

### 2.5. Synthesis of results

Extracted data were tabulated to compare and summarize findings. Due to the heterogeneity of the results, meta-analysis was not performed.

## 3. Results

### 3.1. Search results and study characteristics

The screening process and results are summarized in Fig. 1. This resulted in 16 studies satisfying the inclusion criteria for nosocomial infections of neonates. No studies were found that reported exclusively on infection of mothers. A review of the references of included articles identified nine previously unidentified articles that were included after full text review. One additional study was excluded on the basis it reported on the same outbreak as another included study (Cabrera and Davis, 1961; George et al., 1961). Metadata for the 25 included studies are listed in Table 1 and a summary of the extracted data in Table 2. Based on the synthesized findings and the identified information gaps, a list of criteria for the reporting of waterborne nosocomial infections is proposed in Table 3.

The included articles were published between 1951 and 2016, with study lengths ranging from two weeks to six years. Most studies were case series (n = 17, 68%), followed by case-control studies (n = 3, 12%). All 25 studies took place in inpatient hospital settings, specifically in the neonatal unit, nursery, or neonatal intensive care unit. The hospitals had different managing authorities, most commonly university hospitals (n = 14, 56%). The studies were from 17 countries;

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