Scoping review protocol: Nosocomial infections in neonatal care: a scoping review of published surveillance case definitions

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Introduction

Nosocomial infections (NI), otherwise known as healthcare-associated infections, are defined by the World Health Organization (WHO) as an infection occurring in a patient in the process of care in a hospital or other health care facility, which was not incubating or present at the time of admission. This includes infections appearing after discharge but acquired in the health care facility as well as occupational infections among health care workers of the facility⁽¹⁾. Bacteria are the most common group of pathogens that cause NI⁽²⁾. NI continue to be a serious public health issue worldwide even though it is estimated that approximately one third of these infections could be prevented by effective infection prevention programs⁽³⁾. Critically-ill infants admitted to the neonatal intensive care unit (NICU) in particular, are at an increased risk of neonatal nosocomial infections (NNI) due to impaired host-defense mechanisms, concomitant medical conditions, prolonged hospitalizations and frequent and long-lasting use of invasive medical devices⁽⁴⁾.

NNI are associated with significant morbidity and mortality. The type of morbidity is determined by the type of NNI. For example, an episode of hospital-acquired meningitis may lead to visual impairment, hearing loss, seizure disorder, mental retardation, cerebral palsy and learning disabilities^(5, 6) while an episode of ventilator-associated pneumonia may lead to chronic lung diseases⁽⁷⁾. Mortality rates are reported from 13% to 50% in neonates who experience one or more episodes of NNI, specifically those with a bloodstream infection or meningitis⁽⁸⁾. NNI impact the healthcare system by increasing the cost of healthcare, the length of hospital stay and the use of medical resources.

There is a wide variation in the reported incidence rate of NNI. For example, in the United States NNI incidence rates vary from 6% to more than 40%, but internationally incidence rates have been reported up to 69%⁽⁹⁻¹⁴⁾. This wide variation in incidence rates may be partially explained by the lack of standardized NNI surveillance case definitions⁽¹⁵⁾ and the population at risk. Specifically, for NNI various definitions are used for differentiation between

early onset (perinatal acquired) and late onset (nosocomial acquired) infection. For example, criteria established by the US National Healthcare Surveillance Network (NHSN) in partnership with the Centers for Disease Control and Prevention (CDC) include 48 hours as the cutoff time⁽¹⁶⁾ while the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network applies a period of three days⁽¹⁰⁾. On top of that, neonatal textbooks typically use five to seven days^(8, 17). Moreover, there are several different elements available for defining NNI case definitions such as specific diagnostic and clinical factors. Most reports use a positive culture, whether blood, urine or spinal fluid⁽⁹⁻¹⁴⁾. However, some other studies also include neonates with only clinical symptoms of infection who had negative cultures⁽¹⁸⁾. Furthermore, there are different ways to report NNI. For example, neonates with a central venous line and a positive blood culture are reported either as the number of positive blood cultures per catheter days or as a percentage of the population⁽¹⁹⁾. Evidently, the use of different surveillance case definitions may hamper reliable comparisons of NNI incidence rates on both a national and international level.

The surveillance of NNI has been shown to be an indispensable tool in infection control. It is used for defining patients who are at risk, to facilitate preventive measures and quality improvement and to detect best practice management and prevention strategies, with the ultimate aim to improve neonatal outcomes⁽²⁰⁾. The methods that are used in published literature consist of manual, semi-automatic and automatic approaches. Through manual surveillance, patient charts are reviewed by hand while applying a case definition to detect NNI. With semiautomatic surveillance, selected cases are manually chart reviewed and 'risk cases' are selected through an electronic algorithm. Via automatic surveillance, there is no manual evaluation and a standardized definition is applied by using available electronic data⁽²¹⁾. The surveillance method used affects the degree in which certain surveillance criteria can be applied. For example, clinical criteria are suitable for manual surveillance but less appropriate for automated surveillance. Therefore, it is important that the surveillance criteria are adapted to the chosen surveillance method.

NNI surveillance data are often incomparable due to differences in defining, identifying and reporting NNI⁽¹⁹⁾. To generate reliable and valid surveillance data, standardized surveillance using uniform and unambiguously defined surveillance case definitions for the different NNI subtypes is required. As a first step towards standardized NNI surveillance, we aim to provide an overview of the available NNI surveillance case definitions in current literature and the different surveillance methods (manual, semiautomatic, automatic) used. Subsequently, we will suggest uniform NNI surveillance case definitions per subtype with the most frequently included elements.

Objectives and research question

Objectives:

1. To systematically review published surveillance case definitions for NNI in low, middle and high resource settings in the past two decades. This includes providing an overview of the surveillance case definitions of NNI subtypes, including:
 - a. Bloodstream infection (BSI)
 - b. Central-line associated bloodstream infection (CLABSI)
 - c. Ventilator-associated pneumonia (VAP)
 - d. Hospital-acquired pneumonia, not-ventilator associated (HAP)
 - e. Urinary tract infection (UTI)
 - f. Catheter-associated Urinary Tract Infections (CAUTI)
 - g. Hospital-acquired meningitis
 - h. Surgical site infections (SSI)
2. To evaluate published active surveillance methods for the detection of NNI.

Research questions:

1. Which case definitions have been used for surveillance of neonatal nosocomial infections in low, middle and high resource settings in the past two decades?
2. Which surveillance methods have been used for the detection of NNI: manual/semi-automatic/automatic?

Methods

The review protocol has been written conform the guidelines of the Joanna Briggs Institute (JBI) manual⁽²²⁾ and will be registered within the Open Science Framework (OSF) database. The proposed scoping review will be performed according to the PRISMA-ScR checklist and the PRISMA flowchart for scoping reviews^(23, 24). Research objectives, inclusion and exclusion criteria and methodological strategies are defined before study commencement.

Inclusion and exclusion criteria

The following inclusion and exclusion criteria will be used.

Inclusion criteria:

- Articles describing neonates born at all gestational ages who are admitted to neonatal hospital care.
- Articles have to provide the surveillance case definitions for neonatal nosocomial infections.
- Only studies published in English, German or Dutch.
- Only studies that are published between 2000 and 2020.

Exclusion criteria:

- Studies only reporting on infant populations after discharge of neonatal hospital care.
- Studies only reporting infections that were present at the time of admission at the neonatal care.
- Studies only reporting infections caused by viruses and fungi/yeasts.
- Studies only reporting infections caused by group B streptococcus
- Conference abstracts and research meetings, since these generally lack a clear description of definitions.

Search strategy for identification of studies

A comprehensive list of search terms will be used for each database including key words such as: neonates, nosocomial infection and epidemiological monitoring as well as spelling alternatives and related terms. This list is made with the help of an experienced librarian and conform the Peer Review of Electronic Search Strategies (PRESS) 2015 Evidence-Based Checklist⁽²⁵⁾.

Search strategy:

"Cross infection"[MeSH] OR "Catheter-Related Infections"[Mesh] OR "Pneumonia, ventilator associated" [MeSH] OR "Healthcare-Associated Pneumonia" [MeSH] OR "Urinary Tract Infections"[Mesh] OR "Neonatal Sepsis" [Mesh] OR "Meningitis" [MeSH] OR "Surgical Wound Infection" [MeSH] OR Cross infection*[TIAB] OR Urinary tract infection*[TIAB] OR Meningitis [TIAB] OR Pachymeningitis [TIAB] OR Nosocomial infection*[TIAB] OR Bloodstream infection* [TIAB] OR Bacterial infection*[TIAB] OR Sepsis [TIAB] OR (Ventilator [TIAB] AND complication*[TIAB]) OR Pneumonia [TIAB] OR ((Health care [TIAB] OR healthcare [TIAB] OR hospital [TIAB] OR ventilator [TIAB] OR central line [TIAB] OR catheter [TIAB] OR surgical [TIAB] OR post-operative [TIAB]) AND infection*[TIAB]) OR HAP [TIAB] OR HABSI [TIAB] OR HABSIs [TIAB] OR LOS [TIAB] OR CLABSI [TIAB] OR CLABSIs

[TIAB] OR CABS [TIAB] OR CRBS [TIAB] OR BSI [TIAB] OR VAP [TIAB] OR UTI [TIAB]
OR CAUTI [TIAB] OR CAUTIs [TIAB] OR SSI [TIAB] OR SSIs [TIAB]

AND

"Intensive Care Units, neonatal"[MeSH] OR "Infant, newborn"[MeSH] OR NICU*[tiab] OR
Infant*[TIAB] OR Newborn*[TIAB] OR Neonat* [TIAB] OR Baby [TIAB] OR Babies [TIAB]

AND

"Epidemiological monitoring"[MeSH] OR "Sentinel Surveillance"[Mesh] OR
"epidemiology"[MeSH] OR "benchmarking"[MeSH] OR "infection control"[MeSH] OR "Cross
infection/prevention and control"[MeSH] OR "Infections/epidemiology"[Mesh] OR
Epidemiological monitoring [TIAB] OR surveillance [TIAB] OR benchmarking [TIAB] OR
infection control [TIAB] OR epidemiology [TIAB]

This search strategy is suitable for PubMed(Medline) and will be adjusted for Embase,
Cochrane library and Web of Science. Gray literature and unpublished studies will not be
searched given the broad topic.

Source of evidence selection

The search strategy will be applied in PubMed (Medline), EMBASE, Cochrane collaboration
and Web of Science. All the results will be imported to EndnoteX9 and duplicates will be
excluded. The eventually articles, without the duplicates, will be imported into Rayyan. Using
this program, titles and abstracts will be independently reviewed against the selection criteria
and will be marked as "clearly not eligible" and "possibly eligible" by two reviewers.
Discrepancies will be resolved by discussion and consensus with a third party. Studies
classified as "clearly not eligible" will be excluded and all studies classified as "possibly
eligible" will be moved to the full-text review. Two reviewers will again independently review
the full-text articles against the selection criteria. References of the included full-text articles
will be hand searched. Again discrepancies will be resolved by discussion and consensus
with a third party. Through different labels in Rayyan the reason for exclusion will be
maintained for every excluded article.

Data extraction and synthesis

Data extraction will be performed on included articles using a pilot tested data file. Basic
information such as title, first author, country, and year of publication will be collected. The
country of origin of the studies are divided into low, middle or high income countries
according the World Bank country income classifications⁽²⁶⁾. The surveillance case definitions
will be presented narrative and in the form of multiple tables. These tables will give an
overview of the included elements in the surveillance case definitions per NNI subtype.

Discussion

The strength of a scoping review is the use of a transparent and reproducible procedure.
Through publishing this scoping review protocol in OSF, we strengthen the clarity and
transparency of the research. Any alterations to this protocol will be reported in the final
published scoping review.

This scoping review focuses on the lack of standardized NNI surveillance case definitions on
national and international level. It aims to provide a broad overview of the surveillance case
definitions used to define NNI that can be found in the published literature. This overview will
include the most frequent elements used in surveillance NNI case definitions for every NNI

subtype. This study will provide a starting point for the development of standardized surveillance case definitions. These standardized surveillance case definitions are needed to justify, monitor and refine best practice management and infection prevention strategies. Ultimately, this will lead to reduction of NNI incidence rates which will potentially result in shorter hospitalization, less morbidity and lower hospital costs.

Limitations

Our planned review comes with some limitations. Although we search different databases and hand search references we will miss some studies. First because we do not search gray literature and secondly not all full-text will be available so we will have to reach out to authors and they may not respond and we might miss some relevant work. We may not be able to make a conclusion including a surveillance case definition with the most frequent elements used for every subtype if there are too few published studies which contain a surveillance case definition.

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