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LITERATURE REVIEW

DETERMINANT FACTORS FOR CENTRAL LINE-ASSOCIATED BLOOD STREAM INFECTIONS (CLABSI) IN NEONATES

Faktor Determinan Central Line-Associated Blood Stream Infections (CLABSI) Pada Neonatus

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ABSTRACT

Background: CLABSI accounts for 70% of all hospitalized bloodstream infections, especially in premature infants. CLABSI in neonates can compromise the immune system and future quality of life. **Purpose**: This study aims to identify determinant factors associated with CLABSI in neonates. **Methods**: This research was a scoping review study of three international databases namely Science Direct, PubMed, and ProQuest from January 2021-April 2024. Keyword selection refers to PCC (Populations, Concepts, Categories), with the keywords used "factor" AND "associated" AND "CLABSI" AND ("neonate" OR "newborn") AND "hospital." The selection process is depicted with PRISMA-ScR. **Results**: A total of 14 articles met the criteria and objectives of the study. The articles obtained represented all continents, which were conducted in the Americas (29%), Europe (29%), Asia (29%), and Africa (13%). Risk factors for CLABSI in neonates are grouped into two, namely intrinsic and extrinsic factors. Prevention of CLABSI in neonates can be done by modifying extrinsic factors, namely with proper aseptic technique, supervision, and management strategies. **Conclusion**: The determinant factors of CLABSI in neonates include intrinsic factors (gestational age of <27 weeks or preterm, comorbidities, being born by cesarean section, low birth weight, being previously treated with antibiotics, and having underlying surgical conditions) and extrinsic factors (the type of catheter, the amount of catheter lumen, long duration of insertion, insertion location at the femoral and internal-jugular access site, parenteral nutrition, and large microbial colonization at the insertion site).

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ABSTRAK

Latar Belakang: *CLABSI mencakup 70% dari semua infeksi aliran darah yang dirawat di rumah sakit, terutama pada bayi prematur. CLABSI pada neonatus dapat membahayakan sistem imun dan kualitas hidup di masa mendatang.* ***Tujuan:*** *Penelitian ini bertujuan untuk mengidentifikasi faktor penentu yang terkait dengan CLABSI pada neonatus.* ***Metode:*** *Penelitian ini merupakan studi tinjauan cakupan dari tiga basis data internasional yaitu Science Direct, PubMed, dan ProQuest dari Januari 2021-April 2024. Pemilihan kata kunci mengacu pada PCC (Populations, Concepts, Categories), dengan kata kunci yang digunakan "faktor" DAN "berhubungan" DAN "CLABSI" DAN ("neonate" ATAU "newborn") DAN "hospital." Proses pemilihan digambarkan dengan PRISMA-ScR.* ***Hasil:*** *Sebanyak 14 artikel memenuhi kriteria dan tujuan penelitian. Artikel yang diperoleh mewakili semua benua, yang dilakukan di Amerika (29%), Eropa (29%), Asia (29%), dan Afrika (13%). Faktor risiko terjadinya CLABSI pada neonatus dikelompokkan menjadi dua, yaitu faktor intrinsik dan ekstrinsik. Pencegahan terjadinya CLABSI pada neonatus dapat dilakukan dengan memodifikasi faktor ekstrinsik, yaitu dengan teknik aseptik, supervisi, dan strategi penatalaksanaan yang tepat.* ***Simpulan:*** *Faktor determinan terjadinya CLABSI pada neonatus meliputi faktor intrinsik (usia gestasi <27 minggu atau prematur, penyakit penyerta, lahir dengan operasi caesar, berat badan lahir rendah, pernah mendapat pengobatan antibiotik, dan memiliki kondisi pembedahan yang mendasari) dan faktor ekstrinsik (jenis kateter, jumlah lumen kateter, lama pemasangan, lokasi pemasangan pada akses femoralis dan jugularis interna, nutrisi parenteral, dan kolonisasi mikroba yang besar pada lokasi pemasangan).*

INTRODUCTION

Central line-associated blood stream infection (CLABSI) is defined as a venous blood stream infection originating from a central line where no other source of infection is found in the patient. The most common type of central line is the peripherally inserted central line (PICC) (1). Although it has advantages such as prolonged use, reduced vascular damage, and convenience in placement and removal of access, it also has disadvantages and complications that often occur in the use of central venous access such as CLABSI (2).

The prevalence of CLABSI in 2020 was 0.08% (per 100 central line days) at ICUs in the United States (3). CLABSI leads to prolonged hospital stays, increasing the cost of care with a cost burden of approximately $46.000 per case (4). It has a mortality rate of 12%-15% and an in-hospital mortality odds ratio of 2.75 (5). CLABSI accounts for 70% of all hospitalized bloodstream infections, especially in premature infants (6). The prevalence of CLABSI in NICUs in developing countries is 2.6 – 60.0 cases per 1.000 days of central venous line use. This figure is 3-20 times greater than the incidence of CLABSI in developed countries (7).

Neonates have a high risk of infection due to thin skin, immature immunity, underlying critical illness, exposure to various antibiotics, and germ patterns present in the hospital (8). CLABSI in neonates not only compromises the immune system but also has an impact on the quality of life of the neonates in the future (9). CLABSI is one of the causes of the length of days of hospitalization, the amount of treatment costs, and the increased risk of death in neonates (5).

Understanding the risk factors for CLABSI is a key step in developing strategies to prevent and reduce CLABSI. Determinants of CLABSI in newborns include hand hygiene, aseptic technique, central line care, prevention of fungal infections, and nurse empowerment (10). On the contrary, this is different that double lumen catheters, prolonged hospitalization (≥14 days), abdominal surgery, and blood transfusion are determinants of CLABSI in newborns (11).

However, risk factors associated with CLABSI are still being studied. Several studies regarding the risk factors of CLABSI provide different results.

Therefore, this study aims to identify determinant factors associated with CLABSI in neonates. That way it can provide information about CLABSI risk factors comprehensively.

METHODS

Research Design

This study used one of the comprehensive literature review techniques called a scoping review. This design was chosen because it suits the purpose of this study which has a topic with a broad scope. Articles were obtained from three international databases namely Science Direct, PubMed, and ProQuest from January 2021 until April 2024. Keyword selection refers to PCC (Populations, Concepts, Categories). Population describes the participants involved (neonates), concept describes the concept of the research topic under study (determinant factor of CLABSI), and categories or contexts describe the setting according to the research question (hospital). So, the keywords used are "factor" AND "associated" AND "CLABSI" AND ("neonate" OR "newborn") AND "hospital."

Inclusion criteria include original articles in English, published between January 2021 and April 2024, available full-text and open access, and articles discussing the risk factors that cause CLABSI in neonates. Exclusion criteria were review and not original article, inaccessible in full-text, and research subjects were not neonates. Furthermore, researchers used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) diagram to describe the selection process of the data analyzed.

Risk factors for CLABSI in neonates are grouped into two, namely intrinsic and extrinsic factors according to the CLABSI Toolkit JCI (12). Intrinsic factors are patient characteristics that cannot be modified including age, sex, and underlying disease, while extrinsic factors are modifiable factors related to the insertion or maintenance of central venous catheters such as catheter type, insertion duration, insertion location, type of fluid administered through the central venous catheter, and microbial colonization at the insertion site.

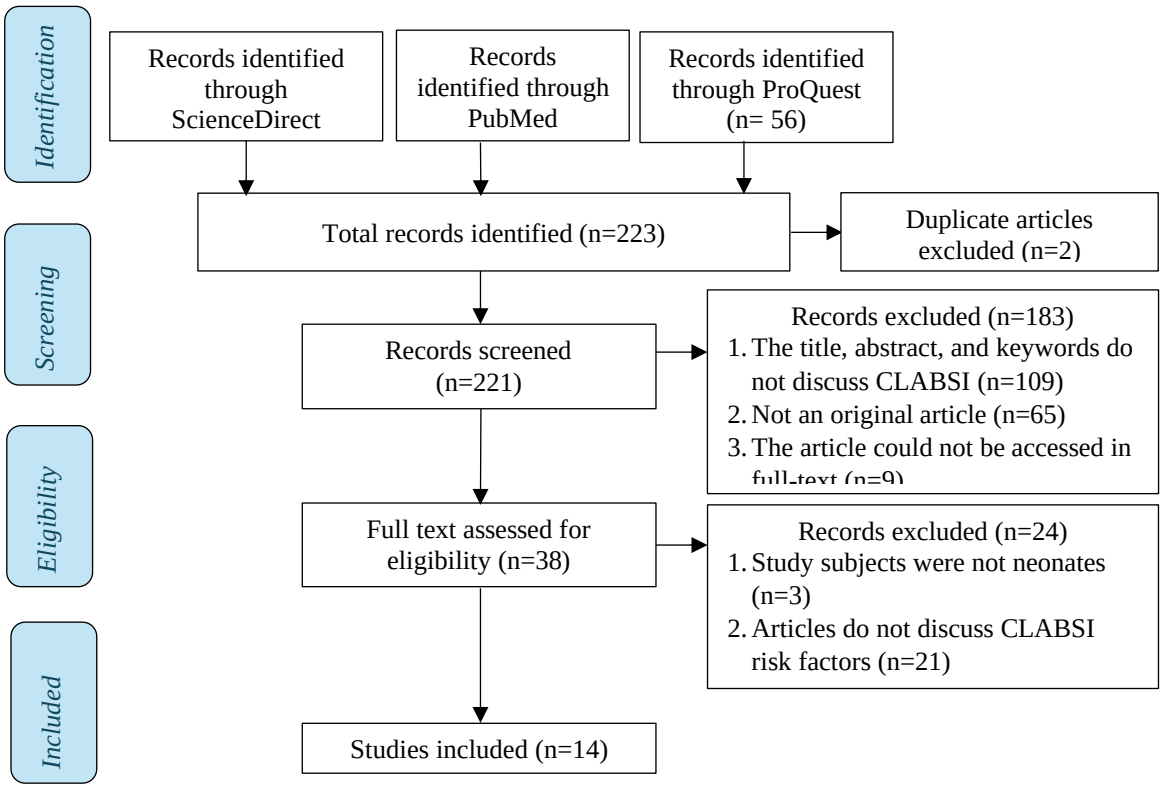

Figure 1. PRISMA-ScR

RESULTS

Based on a database search, 223 articles were obtained, 163 from ScienceDirect, four from PubMed, and 56 from ProQuest. After going through duplication screening, 221 articles were obtained which were screened first so that 183 articles were excluded because 1) the title, abstract, and keywords did not discuss the topic; 2) not an original article; 3) the article could not be accessed in full-text. Furthermore, in the second screening, 24 articles were excluded because 1) the research subjects were not neonates; 2) the article did not discuss CLABSI risk factors. A total of 14 articles met the criteria and in accordance with the research objectives (See Figure 1).

The articles found covered all continents, namely the Americas (29%), Europe (29%), Asia (29%), and Africa (13%). The article describes risk factors for CLABSI in neonates categorized as shown in Table 1.

Table 1
Matrix Literature Review

No	Author, Year	Country	Design	Respondent	Results
1	Nielsen et al. (2022)	Denmark	Cohort	382 infants admitted to a level III NICU.	Extrinsic risk: Prolonged CL dwell-time.
2	Hussain et al. (2020)	Pakistan	Quality improvement (QI) project	613 patients were admitted to tertiary care level 3 NICU who had central lines placed.	Intrinsic risk: Gestational age of <27 weeks. Extrinsic risk: Pathogens associated with CLABSI.
3	Durant et al. (2024)	South Texas	Retrospective case-control	All central line insertions (n=1.356) at NICU (Level IV, 67 beds) in a pediatric hospital.	Extrinsic risk: Implantable device, neck site placement, and device dwell time.
4	Jarraya et al. (2023)	Tunisia	Prospective observational	134 pediatric patients.	Intrinsic risk: Comorbidities, thrombocytopenia, and neutropenia. Extrinsic risk: Difficult insertion procedure.
5	Dramowski et al. (2021)	South Africa	Prospective study	712 babies hospitalized in a neonatal ward or NICU.	Intrinsic risk: Born by cesarean section, preterm, low birth weight, previously treated with antibiotics, and to have underlying surgical conditions. Extrinsic risk: Pathogen type (Gram-negative).
6	Zhang et al. (2021)	China	Retrospective study	103 premature infants underwent PICC insertion.	Extrinsic risk: Duration of antibiotics, parenteral nutrition infusion, and postnatal glucocorticoid exposure.

(Continued)

Table 1
Continued

No	Author, Year	Country	Design	Respondent	Results
7	Hu et al. (2021)	China	Case-control	386 newborns who underwent PICC catheterization in the neonatal department.	Intrinsic risk: Newborns with low birth weight. Extrinsic risk: Longer durations of PICC stay ≥21 days and femoral vein PICC insertion.
8	Khieosanuk et al. (2022)	Thailand	Prospective study	Neonates (aged < 1 month) and children (aged ≥ 1 month).	Extrinsic risk: Number of CVC lumen and place of catheter insertion.
9	Jansen et al. (2024)	Dutch	Retrospective observational cohort	2935 neonates born admitted to all nine Dutch NICUs over a two-year surveillance period.	Extrinsic risk: Longer central line dwell time, umbilical lines, and single rooms.
10	Picaud et al. (2024)	France	a single-center, before-and-after study	313 infants in NICU.	Extrinsic risk: The duration of central line use.
11	Durant et al. (2023)	United State	Retrospective cohort	1,356 in the NICU at a pediatric hospital in South Texas.	Intrinsic risk: very low birth weight. Extrinsic risk: Days admitted before line placement and implantable device.
12	Catho et al. (2023)	Switzerland	Prospective cohort	574 neonates.	Intrinsic risk: Birth weight. Extrinsic risk: a similar CABSI risk between venous and arterial umbilical catheters.
13	Rosenthal et al. (2023)	Latin American countries	Multicenter prospective cohort	29,385 patients were hospitalized in 58 ICUs of 34 hospitals in 21 cities in 8 Latin American countries.	Extrinsic risk: LOS before CLABSI acquisition, femoral and internal-jugular access site.
14	Torres-Muñoz et al. (2023)	Columbia	Observational cross-sectional	226 device-associated infections.	Intrinsic risk: infants with a weight lower than 1000 g Extrinsic risk: Infection by gram-negative bacteria.

DISCUSSION

CLABSI is a laboratorially proven bloodstream infection originating from a central catheter line in such patients for more than two days (27). Intrinsic risk factors for CLABSI in neonates include gestational age of <27 weeks (14) or preterm (17), comorbidities (16), born by cesarean section (17), low birth weight (17,19,23,24,26), previously treated with antibiotics, and having underlying surgical conditions (17). Prematurity, previously treated with antibiotics, and having underlying surgical conditions may lead to a longer stay in NICU and also independently increase the risk of CLABSI. In addition, the high risk of CLABSI is associated with difficult catheter insertion in children with comorbidities, especially children with severe thrombocytopenia.

An intrinsic factor found in many articles is low birth weight. Neonates have low immunity and poor resistance to infections. Therefore, they are a high-risk group for HAIs. The defense function of newborns with birth weight ≤ 1500 grams is not perfect, and this will increase the risk of CLABSI. Premature infants with very low birth weight were found to have increased infections caused by gram-negative bacteria. This is associated with a higher risk of mortality (20–23).

Extrinsic factors include the type of catheter (21,24), the number of catheter lumens (20), duration of insertion (13,19,21,22), insertion location (19,20,25), type of fluid administered through the central venous catheter (18), as well as colonization microbes that are abundant at the installation site (14,17,26). Catheter types consist of venous umbilical catheter, arterial umbilical catheter, and PICC. Of all the types of catheters in newborns, umbilical catheter has the highest infection rate. The arterial umbilical catheter is often removed earlier than the venous umbilical catheter due to the risk of non-infectious complications such as thromboembolic events. Patients using PICC catheters are mostly children or tumor patients. The vascular elasticity of these patients is generally poor. Quite often, this makes the insertion procedure difficult and increases the risk of CLABSI (16). Articles have also shown that the greater the number of lumens, the greater the likelihood of infection (20).

Currently, many hospitals do not have clear regulations on the duration of catheter insertion. In the NICU, prolonged CL dwell time is an independent risk factor for CLABSI.

In the first 18 days after catheterization, the incidence of CLABSI increases by 14% per day, and 19-35 days after catheterization the incidence of CLABSI will not increase again, but the incidence of CLABSI will increase by 33% daily at 36-60 days after catheterization (20,24,28). The location of catheter insertion also has a great influence on the risk of CLABSI. Catheterization of the femoral vein is prone to blood embolism, so the femoral vein should be avoided for catheter insertion (19). The femoral route is more likely to be chosen than the jugular route in the most severe patients. Compared to the internal jugular route, the risk of catheter colonization is significantly higher in the femoral route. However, femoral and internal jugular access both lead to almost the same risk of catheter infection (25).

The type of fluids administered through central venous catheters associated with CLABSI is parenteral nutrition (18). The association between parenteral nutrition and infection may be due to device colonization (14,17,26). Infections are caused by microorganisms originating from the fluid when the device is inserted or after insertion. However, if catheter care is performed routinely, the risk of infection will be reduced (26). Therefore, the insertion during nutrition administration should be done in a sterile manner and checked for discoloration or not, before giving parenteral therapy (28).

Based on the above risk factors, prevention of CLABSI in neonates can be done by modifying extrinsic factors. This suggests that adequate protocols are required to maintain catheter hygiene both before and after insertion. For neonates, a PICC catheter type is recommended, which is a less invasive technique compared to SVCs or totally implantable venous-access ports (TIVAPs). In addition, the operator is required to be highly skilled and experienced in using the catheter to avoid difficult insertion procedures. This may lower the risk of the number of lumens, insertion duration, as well as device colonization.

CONCLUSION

Risk factors for CLABSI in neonates include intrinsic and extrinsic factors. Intrinsic factors include gestational age of <27 weeks or preterm, comorbidities, being born by cesarean section, low birth weight, being previously treated with antibiotics, and having underlying surgical conditions. Extrinsic factors include the type of catheter, the number of catheter lumens, the long

duration of insertion, femoral and internal-jugular access site, parenteral nutrition, and microbial colonization at the insertion site.

CONFLICT OF INTEREST

There is no conflict of interest for this study.

AUTHOR CONTRIBUTION

MHN took part in the concept, methodology, compiled articles, and analysis. SM guided during research and edited. DH gave advice and suggestions by reviewing.

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