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PREVENTION OF CENTRAL VENOUS CATHETER-RELATED INFECTIONS: A RETROSPECTIVE SINGLE-CENTER STUDY COMPARING TWO DIFFERENT PERIODS

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1. INTRODUCTION

1.1 Catheter-Related Infections

1.1.1 Definition and epidemiology

The terminology used to describe infections related to intravascular catheters can be confusing because *catheter-related bloodstream infection* (CRBSI) and *central line–associated bloodstream infection* (CLABSI) are often used interchangeably, even though they have different meanings. CRBSI is a clinical definition used when diagnosing and treating patients, requiring specific laboratory tests to accurately identify the catheter as the source of the bloodstream infection (BSI). This approach involves specialized microbiological techniques—such as quantitative blood cultures or differential time-to-positivity—that are not available in all hospitals. Additionally, because catheters are not always removed for culture, and procedural compliance, like correctly labeling blood cultures, is not always consistently followed, establishing CRBSI in daily practice can be challenging. Therefore, simpler definitions are often used for surveillance purposes.

CLABSI is one such definition used by the CDC's National Healthcare Safety Network (NHSN). A CLABSI is defined as a primary BSI that occurs in a patient who had a central line within the 48 hours before infection begins, without any other identifiable source. This definition is easier to use and forms the basis for most surveillance systems, but it may overestimate the actual number of CRBSI cases because some BSIs come from other sources, such as pancreatitis or mucositis, which might not be recognized right away.

In summary, there are two main definitions used to describe catheter-related bloodstream infections. CRBSI is a clinical definition based on criteria that apply to a specific patient suspected of having an infection. It is used more often in research and occasionally in clinical care because it requires specialized microbiological methods to identify the catheter as the source of bacteremia directly. CLABSI, on the other hand, is a simplified definition designed for surveillance, which identifies BSIs in patients with central venous catheters (CVCs) when no other secondary source is evident. Although CLABSI can overestimate CRBSI incidence, refinements in the CDC

(Centers for Disease Control and Prevention) definition—such as the addition of mucosal barrier injury as a category for secondary sources—have helped to reduce this issue.

In recent years, additional pressures have affected how these definitions are used. In the United States, many states require public reporting of hospital CLABSI rates, and the Centers for Medicare and Medicaid Services impose financial penalties on hospitals with high CLABSI rates. These policy changes and financial incentives have prompted more detailed reviews of bloodstream infections within institutions and investigations into possible secondary sources that may not have been examined before. Simultaneously, concerns have arisen that somewhat subjective surveillance definitions, such as those from the NHSN, may be applied inconsistently, leading to the risk—whether intentional or not—of bias toward reporting lower CLABSI rates.

Because CLABSI is the most widely accepted definition for surveillance, public reporting, and quality initiatives, it is often the main focus of infection prevention strategies, and it is the focus of this study [1,2]. CLABSIs are among the most common and significant healthcare-associated infections in neonatal intensive care units (NICUs). The most frequently reported pathogens associated with CLABSI include coagulase-negative staphylococci, *Staphylococcus aureus*, Enterococci, and *Candida* species. Gram-negative bacilli represent a smaller but important proportion, accounting for 19% of cases reported to the CDC and 21% of those recorded in the Surveillance and Control of Pathogens of Epidemiological Importance (SCOPE) database.[1]

Four potential routes of catheter contamination have been identified in the literature. The most common pathway, especially for short-term catheters, is the migration of skin organisms from the insertion site through the subcutaneous tract and along the surface of the catheter, ultimately leading to colonization of the catheter tip. A second route involves direct contamination of the catheter or its connector through contact with contaminated hands, fluids, or devices. Less often, catheters may become infected via hematogenous seeding from another infection site. Finally, although rare, contamination of the infused solution itself can also cause infection.[1]

Several key factors influence the development of CLABSI. One important element is the material of the catheter itself, as certain surfaces may encourage microbial attachment. Host-related factors also contribute, particularly the deposition of proteins such as fibrin and fibronectin, which form a sheath around the catheter and serve as a substrate for microbial colonization. Additionally, the inherent virulence of the infecting organisms plays a significant role, with adherent microorganisms producing an extracellular polymeric substance (EPS) that supports biofilm formation and persistence. Some catheter materials may also have surface irregularities that further promote microbial adherence, especially for species such as *Staphylococcus epidermidis* and *Candida albicans*.[1]

1.1.2 Clinical impact (morbidity, mortality, costs)

According to a review in the New England Journal of Medicine, CLABSIs are linked to significant increases in morbidity, mortality, and healthcare costs. CLABSI results in longer intensive care unit (ICU) and hospital stays, with a median ICU stay of 24 days compared to 5 days for patients without CLABSI, and a median hospital stay of 45 days versus 11 days. The attributable increase in hospital costs is notable, with an adjusted excess fee of $11,971 per infection.

Mortality is also significantly higher; patients with CLABSI have a 51% mortality rate compared to 28% in those without infection. A meta-analysis cited in the review found an odds ratio for death of 2.75 (95% CI, 1.86 to 4.07) in patients with CLABSI versus those without. The review supports these findings by emphasizing the increased need for antibiotics, extended hospitalization, and the risk of severe complications associated with CLABSI, all of which add to the clinical and economic burden.[3]

1.2. Central Venous Catheters (CVCs)

1.2.1 Types of CVC

Vascular access refers to the placement of an endovascular device, whether for short-, medium-, or long-term use, in both acute and chronic patients. It is done for

diagnostic and therapeutic reasons, such as hemodynamic monitoring, blood sampling, infusion of fluids including blood products and parenteral nutrition, and the delivery of drugs like antibiotics, vasoactive agents, and pain medications. Vascular access devices are usually classified as central or peripheral, based on the final position of the catheter tip. Central access is defined when the catheter tip is at the atriocaval junction, in the upper third of the right atrium. Conversely, peripheral access is when the catheter tip is located in any vessel tributary of the superior or inferior vena cava.

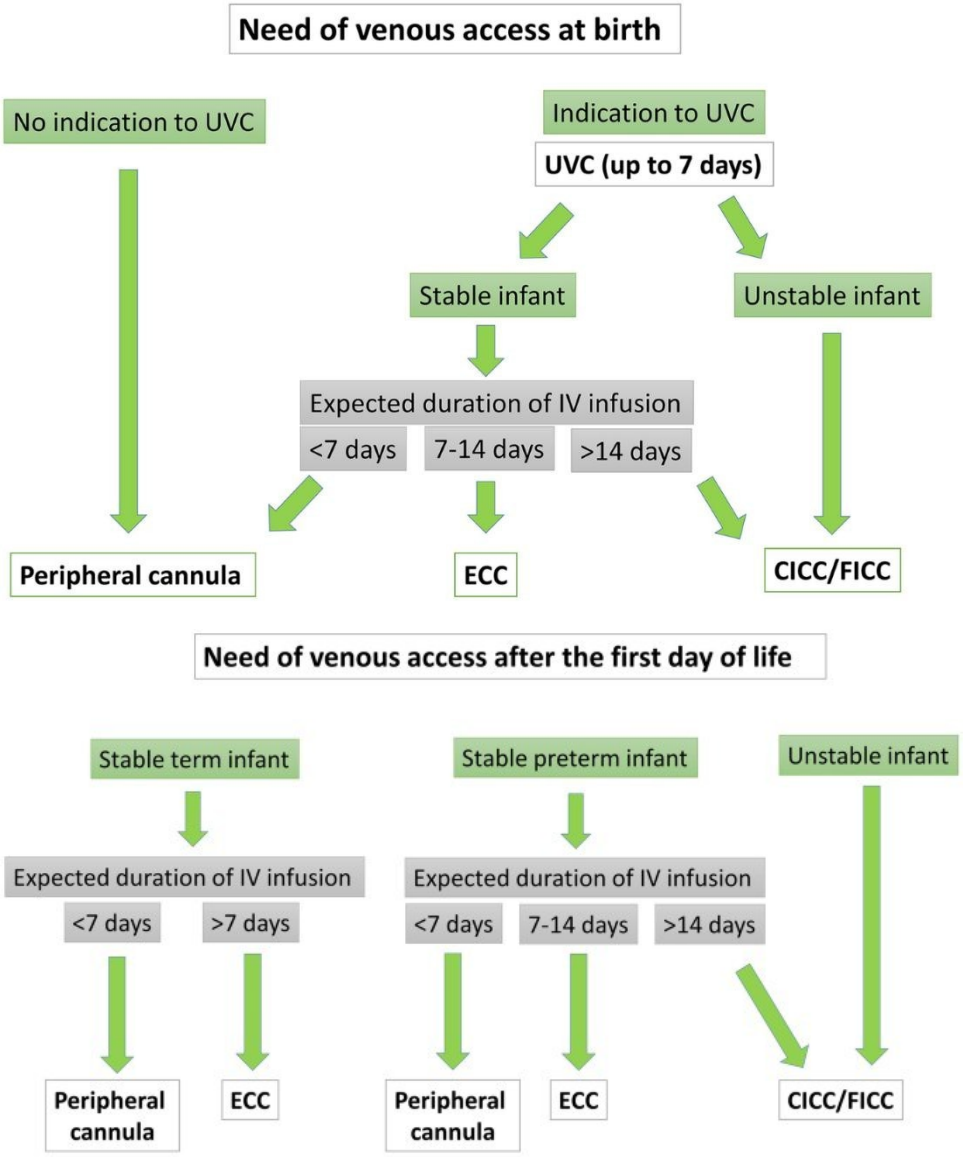
A CVC is therefore defined as a device with its tip located at the atriocaval junction. In neonates, various types of CVCs are used, including the umbilical venous catheter (UVC), which is used exclusively in this population, and the peripherally inserted central catheter (PICC), inserted through superficial veins of the limbs and also limited to neonates. ECCs (epicutaneo-caval catheters) are part of the PICCs. Other commonly used devices include the centrally inserted central catheter (CICC) and the femoral inserted central catheter (FICC).

CVCs can also be classified based on their duration of use, which may be short-, medium-, or long-term, as well as by the type of access—whether central or peripheral. The number of lumens further categorizes them and whether the device is tunneled or non-tunneled. Non-tunneled CVCs, including conventional CVCs and PICCs, are the focus of our study. Generally, a non-tunneled CVC is indicated for a treatment period of 2–3 weeks. PICCs typically last longer than a conventional CVC and are often used for treatments extending up to 3 months.[4]

1.2.2 Indications for use and device selection criteria

The primary indications for CVC use include administering intravenous drugs, providing parenteral nutrition, performing repeated blood sampling, and enabling continuous hemodynamic monitoring. Choosing the appropriate type of CVC depends on several factors: the intended purpose of the access, the type of drugs or solutions to be administered, the clinical setting (inpatient or outpatient), the expected duration of use, the patient's comorbidities, and the infection risk. It is recommended to follow the DAV expert algorithm, developed by the GAVeCeLT and GAVePed groups. This

algorithm helps clinicians select the most suitable central venous access device based on three main criteria: (a) the type of solution to be infused (such as irritant or vesicant drugs, hyperosmolar solutions, or parenteral nutrition); (b) the expected duration of intravenous therapy (short-, medium-, or long-term); and (c) the clinical setting (inpatient or outpatient). Using these factors, the algorithm recommends the most appropriate device among UVC, ECC, CICC, or FICC, balancing clinical efficacy and complication risk. This structured approach aims to standardize practice, enhance patient safety, and align with international guidelines (CDC, ESPNIC, GAVeCeLT)[5].



The UVCs, whether single- or double-lumen catheters, typically range from 2.5 to 5 Fr in size and are always made of polyurethane. They are considered particularly

useful and are frequently used for vascular access in newborns.[6] Considering the potential complications linked to UVC use—such as infections, thrombotic events, or secondary migration—the UVC should be removed as soon as it is no longer needed. However, it can be kept in place for up to 14 days if managed aseptically.[6] A review published in 2023 recommends that UVCs be preferably removed early (within 4–5 days) to reduce the risk of infectious and thrombotic complications.[5] Appropriate indications for UVC placement include (a) preterm infants born at or before 28 weeks of gestation; (b) neonates with severe respiratory distress (either intubated or on noninvasive ventilation with FiO2 > 40%), hemodynamic instability, or difficult peripheral venous access at birth; (c) neonates affected by asphyxia requiring therapeutic hypothermia. The use of UVC should also be considered in neonates needing parenteral nutrition (PN) at birth but who do not fall into the categories mentioned above, such as preterm infants with severe growth restriction and abnormal antenatal Doppler findings. Additionally, UVC placement may be indicated in neonates who will soon require the infusion of non-peripherally compatible solutions (such as IV solutions with pH < 5 or > 9, drugs with osmolarity > 600 mOsm/L, vesicant drugs, or drugs potentially causing endothelial damage). A longer dwelling time of UVC might be appropriate for babies with severe skin conditions, such as infants with collodion baby syndrome or harlequin ichthyosis.[5]

The diameter of an ECC ranges from 1 to 2.7 Fr. The size of the ECC should be determined after assessing the diameter of the veins. In this regard, the RaSuVA protocol[7] (rapid superficial vein assessment) involves a systematic examination of the superficial veins of the newborn, from the foot to the head, first on the right side and then on the left side. It evaluates seven sites where a superficial vein is most likely to be identified: (1) medial malleolus, (2) lateral malleolus, (3) retro popliteal area, (4) hand and wrist, (5) antecubital area, (6) preauricular zone, and (7) post-auricular zone. In infants with exhausted superficial veins (as indicated by RaSuVA) or in newborns where ECC insertion is difficult or impossible, the insertion of a CICC or FICC may be necessary.[5] ECCs are suitable for clinically stable preterm newborns requiring hydration and parenteral nutrition with an expected duration of more than 7 days. If PN is expected to last more than 14 days, a tunneled CICC or FICC should be preferred,

as retention of such devices beyond the second week increases the risk of infection and mechanical complications. ECCs should be made of polyurethane.[5]

In critically ill neonates admitted to the NICU, CVCs are generally preferred over peripheral venous catheters (PVCs) because they provide a more stable, safe, and durable venous access that meets the complex therapeutic needs of this vulnerable population. Central venous access is often necessary in the NICU for hemodynamic monitoring, repeated blood sampling, administration of large-volume fluids, or infusion of drugs and solutions incompatible with peripheral veins. In such cases, a large-bore (3–4 Fr) polyurethane catheter—preferably power-injectable—inserted into the brachiocephalic or internal jugular vein (CICC), or into the common femoral vein (FICC), may be a more appropriate option than ECC. Recent evidence increasingly supports the benefits of CICCs in preterm infants. Among the supra-clavicular sites, the brachiocephalic vein is generally considered the most accessible and safest target for ultrasound-guided puncture and cannulation in neonates. Ultrasound-guided CICC or FICC placement is indicated in several clinical situations: neonates of any gestational age with hemodynamic instability occurring after the first 24 hours of life—or earlier, when UVC placement is not possible or the catheter cannot be optimally positioned; infants who need or may need rapid fluid resuscitation in emergencies or before major surgeries; neonates with major congenital malformations requiring surgical intervention (such as large exomphalos or esophageal atresia); clinically stable infants for whom ECC placement has failed; patients needing repeated blood sampling or multiple transfusions; and preterm infants expected to need parenteral nutrition for more than two weeks, where CICC or FICC may be a safer and more durable option.[5]

1.3. Education and Training of Healthcare Professionals

1.3.1 Role of training in infection prevention

Reducing CLABSI requires well-designed training programs for healthcare providers and strong systems for monitoring and assessing care quality. Many studies consistently show that the risk of infection decreases when aseptic protocols are standardized[9], while insertion and management of intravascular catheters by

inadequately trained staff may lead to increased catheter colonization and a higher risk of CLABSI.[10] Additionally, infection risk increases when nurse staffing levels drop below critical thresholds.[11]

Healthcare facilities implementing CLABSI prevention efforts must ensure resources are available to provide proper education and training. Institutions are required to verify that all healthcare personnel involved in catheter insertion and maintenance complete a structured educational program on essential practices for CLABSI prevention before performing these procedures. Periodic retraining combined with competency assessments can offer additional benefits, and simulation-based training for correct catheter insertion and maintenance should be used whenever available. The quality of evidence supporting these last three measures is considered moderate, reflecting that only a limited number of studies exist, some with methodological limitations, variability in findings across studies, and/or wide confidence intervals around pooled estimates, but without major flaws. Additionally, hospitals should address both technical and socioadaptive aspects of CLABSI prevention. This includes providing formal training to healthcare personnel on device indications, placement, and maintenance, as well as conducting regular assessments of competencies to ensure ongoing adherence to best practices.[8]

In 2011, O'Grady et al. published the *Guidelines for the Prevention of Intravascular Catheter-related Infections*, which offer evidence-based recommendations aimed at decreasing the occurrence of these infections. A major focus of these guidelines is the education and training of healthcare personnel responsible for inserting and maintaining catheters. In the *Summary of Recommendations*, the section on *Education, Training, and Staffing* highlights three key elements, all classified as Category 1A—meaning they are strongly advised for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies. These elements include: educating healthcare personnel on the indications for intravascular catheter use, proper techniques for catheter insertion and care, and the necessary infection control measures to prevent intravascular catheterrelated infections; periodically evaluating both the knowledge of and adherence to the guidelines among all staff involved in inserting and managing

catheters; and ensuring that only trained personnel who can demonstrate competence are assigned to insert and care for both PVCs and CVCs.[6]

Audits are a key part of CLABSI prevention strategies in NICUs. Regularly reviewing clinical practices helps institutions evaluate how well they follow evidencebased guidelines for central line insertion, maintenance, and infection control. By consistently verifying compliance with aseptic protocols, hand hygiene, dressing changes, and line care, audits provide valuable feedback that helps spot gaps or deviations early. This ongoing process not only promotes accountability but also fosters a culture of safety and continuous improvement among healthcare staff. International guidelines, including those from the CDC, ESPNIC, and GAVeCeLT, emphasize the importance of audits in supporting education efforts, enhancing staff performance, and lowering CLABSI rates. In NICUs, where preterm and critically ill neonates are at high risk, audit-driven actions are especially effective in maintaining best practices, ensuring consistent care, and helping multidisciplinary teams uphold high standards of infection prevention.

Within our institution, surveillance of CLABSI incidence is conducted regularly to monitor care quality and identify potential critical issues by the dedicated CVC and infection control team. Additionally, systematic reviews of the literature are performed routinely to update existing protocols based on the latest international recommendations, organize internal training courses, and encourage participation in external educational programs to enhance professional skills.

1.4 Patient preparation and insertion procedures

1.4.1 Pre-procedural assessment

The recommended components of pre-procedural assessment for CVC placement in NICUs include: confirming evidence-based indications for CVC use to reduce unnecessary placements; verifying that all healthcare personnel involved have received education and demonstrated competency in CLABSI prevention; and ensuring adequate nurse staffing levels to support safe insertion and ongoing care. The Infectious Diseases Society of America recommends that facilities implement a

standardized checklist to document adherence to aseptic technique, with direct observation by a trained staff member empowered to halt the procedure if breaches occur. Hand hygiene must be performed before insertion, and the choice of insertion site should be tailored to each patient, considering infection risk and individual factors. These recommendations are supported by evidence showing that standardized protocols, thorough staff training, and proper staffing decrease catheter colonization and CLABSI rates in NICUs, as well as enhance overall patient safety and outcomes.[8]

Regarding indications for CVC use, before inserting a CVC, it is crucial to establish a clear clinical reason that justifies performing an invasive procedure, carefully weighing the risks of potential complications—including infectious, thrombotic, or mechanical issues—against the expected benefits. Several factors should guide the decision-making process, such as the patient's age, including gestational age and weight in neonates, the treatment plan, the availability of superficial venous access, the family's willingness to accept repeated venipuncture or central line placement, and the patient's hygienic needs, like the lack of sphincter control in newborns. In certain situations, such as prolonged fasting due to gastrointestinal immaturity or surgery, long-term therapies, or hemodynamic support in critically ill infants, the placement of a CVC becomes essential and cannot be delayed.

In neonatal and early pediatric patients who can be admitted to our NICU, specific clinical scenarios strongly support CVC insertion. These include stable preterm infants who require parenteral nutrition and prolonged intravenous therapy lasting more than 14 days, or those affected by gastrointestinal surgical pathologies such as necrotizing enterocolitis or intestinal perforation. It also applies to critically ill neonates and infants in need of aggressive fluid therapy during emergencies or before undergoing major surgical procedures, as well as those with severe congenital malformations requiring elective surgery, including congenital heart disease, esophageal atresia, omphalocele, or gastroschisis. Furthermore, neonates or infants with hemodynamic instability who require continuous infusion of vasoactive drugs and central venous pressure monitoring at any stage of life are clear candidates for central venous access. Additional indications include severe bronchopulmonary dysplasia requiring

mechanical ventilation at 36 weeks of postmenstrual age in infants dependent on intravenous therapy, as well as cases of exhausted superficial venous access, where scalp veins may represent the only remaining option after the depletion of venous sites in all four limbs.

In our unit, preparing a patient for CVC placement mainly involves obtaining written informed consent from the parents, in line with ethical and legal standards. Additionally, before the procedure, the infant's hygiene is carefully maintained by cleaning with sterile water to remove organic residues, and the newborn is then placed on clean, dry linens to reduce the risk of contamination. The catheter is usually inserted directly in the ward, either inside the incubator or on an open crib, based on the clinical condition and care setting. Pain prevention and management are key parts of the preprocedural assessment. For this reason, both non-pharmacological strategies and pharmacological sedoanalgesia are used according to the recommendations of the Italian Society of Neonatology (SIN) for preventing and treating neonatal pain. The specific pharmacological approach is customized to the patient's characteristics and the type of device being inserted, ensuring proper comfort and safety during the procedure.

As we mentioned, the choice of insertion site should be personalized. When selecting a site for CVC insertion, it is crucial to carefully assess the risks and benefits to choose a location that minimizes the risk of infectious complications. The insertion site greatly affects the risk of developing a CLABSI, as bacterial colonization of the skin varies by the anatomical region. In the intensive care setting, the subclavian vein is currently regarded as the preferred site for CVC insertion because it is associated with a lower risk of infectious complications. Earlier recommendations primarily focused on avoiding the femoral vein due to its higher risk of infection. While this advice remains valid, it has now been incorporated into a positive framing that explicitly highlights the subclavian vein as the optimal access point.[8] Moreover, the choice of access site should also consider the principle of venous preservation, especially in patients who may need long-term therapies such as total parenteral nutrition, short bowel syndrome management, chemotherapy, or renal replacement therapy.[12] Therefore, the decision must account for the patient's anatomy, the therapeutic goals, the expected duration of therapy—whether short term (20 days or

less) or long term (more than 20 days)—and the experience level of the operator performing the procedure.

1.4.2 Ultrasound-guided insertion techniques

Ultrasound-guided imaging during CVC placement significantly reduces the risk of inadvertent arterial puncture, catheter kinking, threading difficulties, and malpositioning, while also enhancing the overall safety of the procedure. Therefore, it is recommended that all CVC insertions in neonates and infants be performed under real-time ultrasound guidance. However, adequate simulation-based training remains essential to ensure correct use of this technique.[13] For CVCs inserted through deep veins, high-frequency linear probes are preferred because they provide optimal resolution for small vessels. Central line insertion can be performed with either a shortaxis ('out-of-plane') or long-axis ('in-plane') approach. Point-of-care ultrasound (POCUS) enables dynamic needle guidance during insertion and allows for real-time assessment and adjustment of the catheter tip position immediately after placement, reducing the need for confirmatory radiography. Evidence regarding catheter diameter, vessel size, and thrombosis risk indicates that maintaining the external catheter diameter within one-third of the internal vessel diameter may lower the incidence of thrombotic events. Ultrasound can be used prior to insertion to measure vessel diameter and select the most appropriate catheter size.[14] To date, only one randomized controlled trial has compared ultrasound with standard radiographic verification for tip confirmation, showing fewer manipulations after line placement and fewer radiographs needed.[15] The position of the UVC is most commonly evaluated using radiography; however, POCUS is superior and can be considered the gold standard for accurately locating the UVC tip and detecting catheter migration. This advantage is especially important in cases of abnormal anatomy, such as congenital diaphragmatic hernia, where radiographic evaluation is particularly challenging.[16,17]

1.4.3 Aseptic measures

Hand hygiene must always be a fundamental step in preventing CLABSIs. This can be achieved by washing hands with regular soap and water or using alcohol-based

hand rubs (ABHR). Hand hygiene should be performed before and after palpating catheter insertion sites, as well as before and after inserting, replacing, accessing, repairing, or dressing any CVC. Palpation of the insertion site should not occur after applying an antiseptic unless strict aseptic technique is maintained (Category IB—strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a solid theoretical rationale; or an accepted practice supported by limited evidence). In our unit, hand hygiene is carried out by washing with chlorhexidine-based soap and water for 1 minute before and after catheter insertion, as well as before and after any CVC management procedure. Alternatively, alcohol-based hand rub can be used.

Aseptic technique must always be maintained during both the insertion and ongoing care of CVCs (Category IB). For CVC insertion, sterile gloves are mandatory (Category IA), and new sterile gloves must always be used when handling a new catheter during guidewire exchanges (Category II - recommended for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale). When changing dressings on CVCs, either clean or sterile gloves may be worn (Category IC - required by state or federal regulations, rules, or standards).

Maximal sterile barrier precautions are necessary when inserting CVCs and during guidewire exchanges. These precautions include wearing a cap, mask, sterile gown, sterile gloves, and a sterile full-body drape (Category IB).

Skin preparation is another crucial element of infection prevention. The ideal antiseptic should have a biocidal effect, both destroying and inhibiting the growth of microorganisms on the skin for a sufficient duration, while being non- toxic and safe for the patient. At birth, the skin and mucous membranes of the newborn are quickly colonized by commensal bacteria. In preterm infants, coagulase- negative staphylococci dominate and make up about 80% of the total skin flora. The most heavily colonized areas include the umbilicus, skin folds, buttocks, and soles of the feet. The composition of neonatal skin flora varies depending on several factors, such as delivery method (vaginal or cesarean), type of care, gestational age, and feeding practices. In hospitalized preterm infants, skin flora is strongly influenced by the surrounding microbial ecosystem, making them highly vulnerable to colonization by

multidrug- resistant microorganisms. For CVC insertion and dressing changes, the preferred skin antisepsis solution contains more than 0.5% chlorhexidine with alcohol (Category IA).[19] In neonates, however, chlorhexidine use should be carefully evaluated based on clinical judgment and institutional protocols. If chlorhexidine is contraindicated, alternatives like povidone–iodine or alcohol may be used. In all cases, antiseptics must be allowed to dry completely according to the manufacturer's recommendations before catheter placement (Category IB). Unless contraindicated, alcohol- based antiseptic solutions are preferred. Our unit has decided to introduce 2% chlorhexidine in an alcohol- based solution applied with single-use applicators. The application of chlorhexidine should be done using a dabbing technique rather than scrubbing. In neonates below 26–27 weeks gestational age and weighing under 1000 g, some reactions have been reported in the literature. To reduce these reactions while maintaining the significant advantages of chlorhexidine, certain precautions should be taken, such as using single-dose containers, removing any excess chlorhexidine, rinsing with saline after application and drying, and avoiding scrubbing of the skin. Compared to other antiseptics, 2% chlorhexidine in 70% alcohol is the most effective disinfectant for preventing CLABSIs, combining the rapid disinfection and evaporation of alcohol with chlorhexidine's prolonged antimicrobial activity.[20]

Additionally, chlorhexidine has a broad-spectrum bactericidal effect, effective against Gram-positive and Gram-negative bacteria, facultative anaerobes, fungi, and viruses—including HIV—though it is not sporicidal, and it retains activity even in the presence of blood or serum, making it highly reliable in clinical practice.

Daily skin cleansing with a 2% chlorhexidine wash can further reduce the risk of CRBSI (Category II).

Overall, an effective strategy to prevent CRBSI should include three core components: comprehensive education for all healthcare personnel who insert and maintain catheters, strict adherence to maximum sterile barrier precautions during insertion, and the use of >0.5% chlorhexidine with alcohol for skin antisepsis (Category IA). Additional measures involve avoiding routine systemic antimicrobial prophylaxis before insertion or during catheter use (Category IB), while considering prophylactic antimicrobial lock solutions in patients with long-term catheters and

recurrent CRBSI despite strict aseptic protocols (Category II).[6,18] The most recommended lock solution currently is the 2% taurolidine lock, as it may significantly reduce CRBSI in pediatric patients. [21]

1.5. Management and Maintenance of CVCs

1.5.1 Dressing and site protection

There is strong agreement on the recommendation to use transparent bio-occlusive dressings to protect CVC insertion sites from infection, which therefore allow inspection of the exit site, are semipermeable, and highly breathable. Before applying the dressing, it is necessary to seal the exit site with cyanoacrylate glue, which stabilizes the CVC, reduces the risk of bleeding at the exit site, and lowers the risk of infection. Cyanoacrylate is a liquid tissue adhesive that creates a broad-spectrum antibacterial barrier, has a very short polymerization time (10–20 seconds), and provides adequate protection of the exit site. In neonates, the decision to use transparent or sponge dressings with chlorhexidine should be based on clinical judgment and institutional protocols. Whenever a chlorhexidine-containing dressing is applied, the site should be observed daily for any signs of irritation, allergic reaction, or necrosis.[18] It is indicated to replace the catheter site dressing if the dressing becomes damp, loosened, or visibly soiled (Category IB). Dressings on short-term CVC sites should be replaced at least every 7 days when transparent dressings are used, except for pediatric patients in whom the risk of catheter dislodgement may outweigh the benefits of a dressing change (Category IB). For tunneled or implanted CVCs, transparent dressings should be replaced no more than once per week—unless the dressing becomes soiled or loose—until the insertion site has fully healed (Category II). Catheter sites should be monitored regularly, either visually during dressing changes or by palpation through an intact dressing, with the frequency depending on the patient's clinical condition. If tenderness at the insertion site, fever of unclear origin, or other signs suggestive of a local or bloodstream infection occur, the dressing must be removed to allow a thorough inspection of the site (Category IB).[6]

1.5.2 Catheter securement

The use of sutureless securement devices is recommended (Category II) to reduce the risk of infection associated with CVCs. Catheter stabilization plays a crucial role in minimizing complications, such as phlebitis, catheter migration, and dislodgement, and is also considered beneficial in preventing CRBSIs. Since the pathogenesis of CRBSI is primarily linked to the migration of skin flora through the percutaneous entry site, sutureless devices offer an advantage by avoiding tissue disruption around the catheter insertion point and thereby limiting bacterial colonization.[22] In addition to lowering infection risk, these devices also enhance operator safety by eliminating the use of sutures, thus reducing the likelihood of sharps injuries and accidental needlestick exposure among healthcare providers. This dual benefit—improving both patient safety and staff protection—makes sutureless securement an effective and valuable practice in catheter management.[6]

1.5.3 Infusion line management

Proper management of CVCs is essential to prolong their dwell time and prevent complications.

At every nursing shift change, the CVC insertion site, catheter integrity, patency, dressing condition, infusion pump alarms, and the infusion set must be carefully inspected. The results of these checks should be documented in the patient's medical record. To avoid infusion pressures exceeding recommended levels, CVC infusions should be managed using pumps capable of measuring pressure values.

CVCs must be kept patent with sterile 0.9% saline flushes, administered before and after every drug infusion[23], preferably using the *start-and-stop technique*, and at least once every 7 days if the line is not in use. Flushing not only helps prevent occlusion but also contributes to reducing the risk of infection. In general, infection prevention requires minimizing unnecessary catheter access, disinfecting stopcocks with 2% chlorhexidine, administering only drugs and solutions prepared under sterile conditions, and replacing infusion sets every 72–96 hours—or every 24 hours when infusing parenteral nutrition (PN), lipid emulsions, or glucose solutions >10%.[6]

Contamination of the catheter hub or connector due to non-aseptic access techniques is a well-recognized risk factor for CLABSI development. One of the most effective strategies to reduce both CVC contamination and CLABSI incidence is the disinfection of catheter access ports with an appropriate antiseptic before each use, a practice internationally referred to as “scrub the hub.” Implementing targeted training programs for healthcare providers directly involved in CVC management (e.g., bedside nurses) is crucial to ensure adherence and compliance with this preventive measure.[6]

Every CVC access must therefore be preceded by manual scrubbing of the access port with sterile gauze soaked in 2% chlorhexidine in alcoholic solution, scrubbing for at least 15 seconds, and allowing the antiseptic to dry for 30 seconds. When povidone–iodine is used, a contact time of 2 minutes is required. As an alternative, disinfection can also be performed with port protectors (disinfectant caps) placed on needleless connectors.

Needleless connectors (needle-free connectors) with unidirectional valves and anti-reflux mechanisms offer significant advantages over perforable caps. They eliminate the risk of accidental needlestick injury for healthcare workers, reduce the risk of bloodborne pathogen transmission, allow direct connection with syringes and infusion sets, minimize blood reflux into the catheter lumen, and decrease the likelihood of occlusion and contamination.[24] These additional devices for intravenous therapy are sterile caps equipped with a valve that permits controlled access to the intravascular system. They are attached to the access ports of intravascular catheters, ensuring closure towards the external environment.

Needleless connectors must be designed to attach securely to the device or infusion line access port via a Luer-lock closure system, ensuring a safe and stable connection. However, it is essential to remember that needleless connectors also represent a potential route for intraluminal microbial contamination. Therefore, strict compliance with infection prevention recommendations is mandatory for their safe use.

1.5.4 Monitoring and daily evaluation

The prevention of CRBSI/CLABSI requires a daily assessment of the ongoing need for the catheter, with prompt removal as soon as it is no longer necessary. This process involves a continuous evaluation of the risk–benefit balance associated with maintaining the device in place. To support this goal, it is essential to perform a structured daily reassessment of the indication for CVC retention, using dedicated catheter monitoring charts. Moreover, the catheter insertion site must be evaluated daily, and the catheter sites must constantly be monitored when changing the dressing.[6]

1.6. Bundles for CLABSI Prevention

1.6.1 Definition of bundle

In large NICUs, the successful implementation of evidence-based changes can be achieved through continuous education and active engagement of bedside staff.[25] The CDC recommends that the management of all CVCs be carried out within the framework of a standardized care "bundle" (Category IB).[6] Bundles are operationally defined as a small set of behavioral recommendations and care practices, each individually evidence-based, which, when applied systematically and uniformly to a defined patient population, can have a statistically significant impact on improving the quality of a procedure in terms of safety, cost-effectiveness, and efficiency and are essential for delivering effective and safe care.[26] The use of bundles and checklists in the placement and management of CVCs has been associated with a substantial and sustained reduction in the incidence of CLABSI.[27] Starting from March 2023, following appropriate training of all medical and nursing staff, two specific groups of bundles have been introduced in our Unit for the insertion and management of CVCs.

1.6.2 Components of insertion and maintenance bundles

The two specific groups of bundles consist of an insertion bundle and a maintenance bundle.

The insertion bundle includes strict adherence to aseptic technique, consisting of proper hand hygiene, the use of maximal barrier precautions during catheter placement,

and skin disinfection with single-use 2% chlorhexidine alcohol-based solutions. The choice of the optimal venipuncture site is determined through systematic clinical or ultrasound assessment (RaCeVA or RaPeVA). Whenever possible, depending on the ongoing training and the competencies acquired by individual operators, intra-procedural verification of the central tip position should be performed in real time using ultrasound. Additional measures include protection of the exit site with cyanoacrylate glue, stabilization of the catheter using a sutureless securement device, and coverage with a transparent semipermeable membrane. A central line insertion care bundle can significantly reduce CLABSI rates. Although the effectiveness of individual bundles may vary, the use of maximal sterile barrier precautions during catheter insertion remains a fundamental component of any
insertion care bundle.[27]

The maintenance bundle emphasizes strict adherence to aseptic technique during all catheter-related procedures. This includes aseptic access and replacement of needleless connectors, as well as aseptic dressing changes and any maintenance interventions. Infusion line replacement must likewise be performed under aseptic conditions. Catheter patency is ensured by flushing with sterile saline using a pulsatile technique at every use, and by the consistent application of port protectors. Additionally, a structured daily reassessment of the necessity of maintaining the catheter in place is required, with prompt removal when it is no longer clinically indicated, thereby minimizing the risk of complications, such as CLABSI. A 2016 systematic review and meta-analysis including 2,370 ICUs demonstrated a significant association between the implementation of central line insertion and maintenance bundles and a reduced incidence of CLABSI across all ICU settings. [29]

1.6.3 Implementation in clinical practice

The implementation of NICU-specific CLABSI prevention bundles results in a significant reduction in infection rates and healthcare costs. This has been confirmed by a study published in June 2025, which was conducted in a tertiary university hospital with 2 NICUs. Following the implementation of NICU-specific CLABSI

prevention bundles, in NICU-1, CLABSI rates decreased from 29 to 4 per 1,000 central line days, while in NICU-2, they fell from 14.2 to 2.6 per 1,000 central line days. These reductions were accompanied by an approximate 80% decrease in the average healthcare cost per patient. The intervention integrated evidence-based practices, including rigorous aseptic techniques, standardized maintenance protocols, and enhanced hand hygiene, demonstrating the effectiveness of structured, multidisciplinary infection control strategies in improving neonatal outcomes and optimizing resource utilization. Although the implementation of bundles can initially increase the demand for human and material resources, this study confirmed that the reduction in CLABSI-associated costs far outweighs those expenses. Overall, the findings provide compelling evidence that adopting a structured CLABSI prevention bundle in the NICU setting significantly lowers infection rates and healthcare costs, thereby improving both patient safety and system efficiency.[30]

1.7. Complications and Risk Management

1.7.1 Infectious and mechanical complications

In neonates, CLABSI is the most frequently occurring life-threatening complication. Mechanical events, particularly occlusion, are common complications. Dislodgement, leakage, phlebitis, breakage, malposition, migration, retention, thrombosis, pericardial, and pleural effusion are relatively rare events according to literature reports.[31] A frequent complication of UVC placement is malposition of the catheter tip. If the tip is inadvertently positioned within the liver, it may lead to portal vein thrombosis and hepatic necrosis. When located too high in the right atrium, the tip can trigger arrhythmias or even cause cardiac perforation, with subsequent pericardial effusion and tamponade. In very low-birth-weight infants, progressive abdominal growth can significantly alter the catheter's position, resulting in UVC tip migration, which requires careful monitoring. Additional complications associated with prolonged UVC dwell time include sepsis and thrombosis. UVC-related thrombosis, in particular, may progress to thrombotic endocarditis or pulmonary hemorrhagic infarction.[32]

Regarding CLABSI symptoms, be alert for nonspecific signs and symptoms of systemic infection such as temperature instability, increased apnea, feeding intolerance, lethargy, and glucose intolerance. An unexplained rise or fall in the complete blood cell count, a new onset of thrombocytopenia, or an elevated C-reactive protein test result may indicate an indolent infection in an otherwise well infant.[31]

1.7.2 Management strategies

Recommended management strategies for CVCs in NICUs focus on the prevention and treatment of infectious complications (such as CLABSIs and local infections), as well as mechanical and thrombotic complications. The most effective approach is the implementation of evidence-based care bundles, which are structured sets of interventions performed collectively and reliably.

For infectious complications, bundles include strict hand hygiene, maximal sterile barrier precautions during insertion, skin antisepsis with alcoholic chlorhexidine (2% when feasible), use of transparent semipermeable dressings, daily site inspection, aseptic non-touch technique for all manipulations, disinfection of catheter hubs, prompt removal of unnecessary catheters, and regular staff education and audit. These measures have been shown to significantly reduce CLABSI rates, local infections, and associated morbidity and mortality in high-risk neonates.

Mechanical complications are minimized by using ultrasound guidance for insertion, selecting the optimal site and catheter type, ensuring operator competency, and employing checklists to standardize procedures. Thrombotic complications are addressed by choosing the smallest appropriate catheter, minimizing dwell time, and daily assessment for signs of thrombosis or malfunction.[33]

2. AIMS OF THE STUDY

The primary objective of this study was to determine if implementing a standardized, evidence-based bundle for CVC insertion and maintenance in the NICU reduces CLABSIs by comparing the periods before and after the intervention. Secondary objectives included examining the relationship between CVC type, birth weight, dwell time, and tip position control methods with infectious complications, and evaluating whether these links remain significant after adjusting for potential confounders using multivariable logistic regression models.

3. METHODS

3.1 Study Design, Population, and Study Period

This retrospective study was conducted in the Neonatal Intensive Care Unit (NICU) of the Policlinic of Modena. Since it was a retrospective study, informed consent was not required. The hospital ethics committee approved both the study protocol and data collection. The study included all catheters inserted and subsequently removed in the NICU between January 1, 2022, and December 31, 2024. CLABSI episodes were recorded and compared between the pre-intervention period (before the implementation of the new care bundle in the NICU), from January 1st, 2022, to February 28th, 2023, and the post-intervention period (after the implementation of the new care bundle in the NICU), from March 1st, 2023, to December 31st, 2024. Catheters placed or removed outside the Modena NICU and included in the dataset were excluded from the analysis. Since mechanical complications remained stable over the three years and are unaffected by care bundles, only infectious complications were included in the final statistical analysis. The study population was divided into two groups: very low birth weight (<1500 g) and non-very low birth weight (≥1500 g) neonates, to assess differences in infection risk.

3.2 Implementation of Bundles and Checklists

In March 2023, a new CVC insertion and maintenance bundle was introduced in our NICU, replacing two separate protocols previously dedicated to UVCs and PICCs. The new protocol provided a unified and standardized approach for managing all central lines in neonates. The updated protocol introduced several key changes. Continuous staff education and active infection surveillance, previously absent, were incorporated. Bundles and checklists were systematically applied in accordance with international recommendations (GAVeCeLT), with adherence monitored and quality indicators, such as catheter-related infections per 1,000 catheter days. Antiseptic practices were standardized with 2% chlorhexidine in alcoholic solution with monodose applicators as the first-choice agent, with specific precautions for extremely preterm infants or those weighing <1,000 g. Tip location, previously based on radiography, was replaced by POCUS or intracavitary electrocardiography (ECG), with radiography reserved for cases in which these methods were not feasible. Documentation of the final catheter tip position became mandatory in the patient's medical record.

Dwell time recommendations were also refined. While earlier guidelines were vague and generally advised against maintaining PICCs beyond 21 days, the new protocol set a maximum duration of 14 days for ECCs, recommending removal as soon as the line was no longer clinically necessary or when enteral feeding reached (among infants with ≥ 29 weeks of gestation) 100 mL/kg (Luca Maggio, Course of Parenteral Nutrition). Insertion site protection and securement were modernized with cyanoacrylate glue, sutureless securement devices, and transparent semipermeable dressings.

Post-insertion care was reinforced. Traditional continuous flushing with saline or heparin was replaced by pulsatile "start-and-stop" flushing with sterile saline. Additional measures included systematic disinfection of connectors ("scrub the hub") or the use of port protectors. Infusion pumps with pressure monitoring were recommended to ensure safe administration, and daily reassessment of the clinical need for the catheter was mandated.

3.3 Data Collection

Data were collected in May 2025 from medical record notes entered in the electronic sheet of the NICU (Metavision Electronic Medical Record, iMDsoft, Tel Aviv, Israel). For each catheter, the following data were collected: patient date of birth, birth weight, gestational age, weight and age at insertion, catheter type, date and site of insertion, whether insertion occurred before or after bundle implementation, catheter dwell time, reason for removal (elective or complication), removal site, type of complication (infective or mechanical), catheter day on which the complication occurred, microorganism identified in cases of CLABSI, antimicrobial therapy administered, method used for tip verification, and total catheter-days per patient. For baseline comparison, identical data were retrospectively collected for the period between January 1st, 2022, and December 31st, 2024.

3.4 Definitions

CLABSI

Central line–associated bloodstream infection, a primary BSI occurring in a patient who had a central line within the 48 hours preceding infection onset, in the absence of another identifiable source.

CVC

Central venous catheter, a device whose tip is positioned at the atriocaval junction.

UVC

Umbilical venous catheter, a central venous access device inserted through the umbilical vein, typically within the first hours of life, primarily used in the immediate neonatal period for the administration of fluids, parenteral nutrition, medications, and for blood sampling, particularly in critically ill or extremely preterm infants.

ECC

Epicutaneo-caval catheter, a peripherally inserted central catheter (PICC) placed through superficial veins of the upper or lower limbs or scalp, suitable for mediumterm use (generally 2–3 weeks) and indicated for hydration, parenteral nutrition, and administration of solutions not suitable for peripheral infusion.

CICC

Centrally Inserted Central Catheter, a central venous catheter inserted via direct cannulation of a central vein, such as the internal jugular, subclavian, brachiocephalic, or femoral vein, commonly used when reliable central access is needed urgently or when peripheral access is not feasible, and they are suitable for short- to medium-term use.

VLBW neonate

Very-low-birth-weight neonate, a neonate who at birth weighs less than 1500 g.

NVLBW neonate

Non-very-low-birth-weight neonate, a neonate with a birth weight of over 1500 g.

Bundle

A small set of behavioral recommendations and care practices, each individually evidence-based, which, when applied systematically and uniformly to a defined patient population, can have a significant impact on improving the quality of a procedure in terms of safety, cost-effectiveness, and efficiency, and are essential for delivering effective and safe care.

3.5. Statistical analysis

Mean, standard deviation, median, and interquartile range were calculated for continuous variables, while proportions were calculated for categorical variables. Chisquare test was used to assess the association between categorical variables. When the numbers were minimal, Fisher's exact test was used instead of the chi-square test. Mixed-effects models (for repeated measures) were used to evaluate the association between infectious complications and protocol modification, adjusting for age at birth, type of CVC, and CVC days.

A p-value lower than 0.05 was considered statistically significant. STATA software version 18 was used for the analyses.

4. RESULTS

Among 323 neonates with at least one CVC in place (gestational age ranging from 23 to 42 weeks; birth weight ranging from 430 to 4910 g), 109 (33.9%) had a birth weight < 1500g, and 213 (66.1%) had a birth weight ≥ 1500g. During study periods, a total of 556 CVCs were placed, of which 245 (44.1%) were UVCs, 224 (40.3%) were ECCs, and 87 (15.6%) were CICCs (Table 1 and Table 2).

Table 1. Demographics of the overall study population.

Variable	N	Median	IQR	Min	Max
Gestational age (weeks)	319 ¶	35	9	23	42
Birth weight (g)	322 ¶	2208.5	1980	430	4910
Total CVC days	323	6	9	0	151

CVC, Central Venous Catheter; IQR, Interquartile range.

¶ Information regarding gestational age and birth weight was lacking for 4 and 1 case, respectively

Table 2. Number of CVCs according to birth weight under or over 1500 g. Data are reported as number (percentage). Percent rates are calculated on the total number of each catheter type.

Catheter Type	All CVCs (n=556)	Birth weight <1500 g	Birth weight >1500g
UVC	245 (44.1%)	105 (42.9%)	140 (57.1%)
ECC	224 (40.3%)	172 (76.8%)	52 (23.2%)
CICC	87 (15.6%)	33 (37.9%)	54 (62.1%)

UVC, Umbilical Venous Catheter; ECC, Epicutaneo-caval Catheter; CICC, Centrally Inserted Central Catheter; CVC, Central Venous Catheter; IQR, Interquartile range

Table 3. Catheter dwell time according to each catheter type

Catheter Type	Median (days)	IQR	Min	Max
UVC	4	3	0	7
ECC	6	8	0	33
CICC	10	8	1	119
Total	5	5	0	119

UVC, Umbilical Venous Catheter; ECC, Epicutaneo-caval Catheter; CICC, Centrally Inserted Central Catheter; CVC, Central Venous Catheter; IQR, Interquartile range

Table 3 indicates that CICCs were associated with the longest median dwell times, followed by ECCs and UVCs.

Table 4. CVC complications according to birth weight under or over 1500 g. Data are reported as number (percentage).

Variable	All complications (n=552) ¶	Birth weight <1500 g	Birth weight ≥1500 g
Uncomplicated	413 (74.8%)	199 (70.3%)	214 (79.6%)
Mechanical complication	113 (20.5%)	66 (23.3%)	47 (17.5%)
CLABSIs	26 (4.7%)	18 (6.4%)	8 (3.0%)

CLABSI, Central Line Associated Blood Stream Infection

¶ Information was unavailable for 4 CVCs

The majority of catheters remained in place without complications throughout their dwell time and were removed electively. Mechanical complications were

approximately 20% of all complications (no further analysis is reported). CLABSIs were the goal of this study, and their rate was less than 5% of all complications.

Elective removal was more frequent in the NVLBW group, while removal due to mechanical or infectious issues was more common in the VLBW group (Table 4).

Table 5. Number of CVCs inserted in each neonate according to birth weight under or over 1500 g. Data are reported as number (percentage).

Number of CVCs	All (n=322)	<1500 g (n=109)	≥1500 g (n=213)
1	173 (53.7%)	27 (24.8%)	146 (68.5%)
2–4	124 (38.5%)	63 (57.8%)	61 (28.6%)
≥5	25 (7.8%)	19 (17.4%)	6 (2.8%)
Total	322 (100%)	109 (100%)	213 (100%)

CVC, Central Venous Catheter

Table 5 summarizes the distribution of the number of CVCs per patient, stratified by birth weight (<1500 g vs ≥1500 g). Patients with a birth weight <1500 g were more likely to require multiple CVCs compared to those ≥1500 g, with a higher proportion of cases receiving two or more catheters during hospitalization. This association between birth weight category and number of CVCs per patient was statistically significant, as demonstrated by Fisher's exact test ($p < 0.001$).

Table 6. Mode of assessing the correct position of the CVC tip according to the CVC type. Data are reported as number (percentage).

CVC Type	Ultrasound	X-ray	Both	Total
UVC	14 (6.0%)	216 (91.9%)	5 (2.1%)	235 (43.8%)
ECC	31 (14.0%)	185 (83.7%)	5 (2.3%)	221 (41.2%)
CICC	34 (42.0%)	36 (44.5%)	11 (13.6%)	81 (15.1%)
Total	79 (14.7%)	437 (81.4%)	21 (3.9%)	537 (100%)

UVC, Umbilical Venous Catheter; ECC, Epicutaneo-caval Catheter; CICC, Centrally Inserted Central Catheter; CVC, Central Venous Catheter

¶ information was unavailable for 19 CVCs

Table 6 summarizes tip methods to assess the tip position across different catheter types, revealing notable differences in practice. For UVCs and ECCs, X-ray was by far the most used method to confirm tip position, with ultrasound and combined approaches representing only a minority of cases. In contrast, CICCs were much more frequently verified with ultrasound, either alone or in combination with X-rays. There was a significant association between the catheter type and the method used to assess tip position ($p < 0.001$), confirming that the type of catheter strongly influences the choice of control method.

Table 7. CLABSIs according to catheter type. Data are reported as number (percentage).

Type of CVC	All	CLABSI
UVC	220 (100%)	3 (1.4%)
ECC	152 (100%)	14 (9.2%)
CICC	67 (100%)	9 (13.4%)
All CVCs	439 (100%)	26 (5.9%)

UVC, Umbilical Venous Catheter; ECC, Epicutaneo-caval Catheter; CICC, Centrally Inserted Central Catheter; CVC, Central Venous Catheter; CLABSI, Central Line Associated Blood Stream Infection

Table 7 summarizes the relation between catheter type and the presence of CLABSI, showing a clear association between the two variables. Infection rates differ significantly across the three CVC types, with ECCs and CICCs showing a higher proportion of infectious complications compared to UVCs. ($p < 0.001$), indicating that catheter type is an essential factor influencing the risk of CLABSI in this population.

Birth weight under 1500 g was associated with higher risks of CLABSI (18 out of 217 under 1500 g vs 8 out of 222 over 1500 g, $p=0.04$)

The comparison between the pre- and post-intervention periods showed a significant reduction in the incidence of infectious complications after the implementation of the new bundle (18 out of 186 vs 8 out of 252, $p < 0.01$), indicating that the intervention had a meaningful impact on lowering infection rates in the study.

Table 8. Incidence rates of infectious complications per 1000 CVC days

	Pre-intervention period	Post-intervention period	Total
CLABSIs, n	18	8	26
Total CVC days, n	1697	1811	3508
Incidence rate/1000 CVC days	10.61	4.42	7.41

CLABSI, Central Line Associated Blood Stream Infection; CVC, Central Venous Catheter

We calculated the incidence rates of infectious complications per 1000 CVC days, overall, before and after the bundle introduction (Table 8). Following the intervention, CLABSI rates decreased from 10.61 per 1,000 catheter days to 4.42 per 1,000 catheter days ($p = 0.04$).

Table 9. Mixed-effects logistic regression model for risk of infectious complications

Variable	OR	95% CI	P-value
Pre- vs post-intervention	0.3	0.1 – 0.9	0.028
Days of CVC	1.0	0.9 – 1.1	0.630
Birth Weight	1.0	1.0 – 1.1	0.204
Type of CVC (ECC vs UVC)	7.1	1.7 – 29.1	0.006
Type of CVC (CICC vs UVC)	18.7	3.6 – 97.3	0.0001

UVC, Umbilical Venous Catheter; ECC, Epicutaneo-caval Catheter; CICC, Centrally Inserted Central Catheter; CVC, Central Venous Catheter; OR, Odds Ratio; CI, Confidence Interval

After adjusting for potential confounders, the multivariable logistic regression analysis revealed that both the pre- and post-intervention periods, as well as the type of CVC (ECC vs. UVC; CICC vs. UVC), were predictors of infectious complications. Specifically, the analysis presented in Table 9 indicates that, with respect to ECCs, CICCs are more closely associated with CLABSI.

After adjusting for the mode of tip position control, the type of CVC was the only variable that remained associated with infectious complications.

The most common pathogens yielded in CLABSI episodes were *Staphylococcus epidermidis* (n = 13), *Staphylococcus aureus* (n = 3), *Klebsiella pneumoniae* (n = 3), and *Enterobacter cloacae* (n = 2). Less common organisms caused all other episodes, each occurring as a single case. These included *ESBL-producing Escherichia coli*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Streptococcus/Enterococcus spp*., *Klebsiella oxytoca*, and *Staphylococcus capitis*.

Figure 1. Pathogens isolated in CLABSI episodes during the pre-intervention period

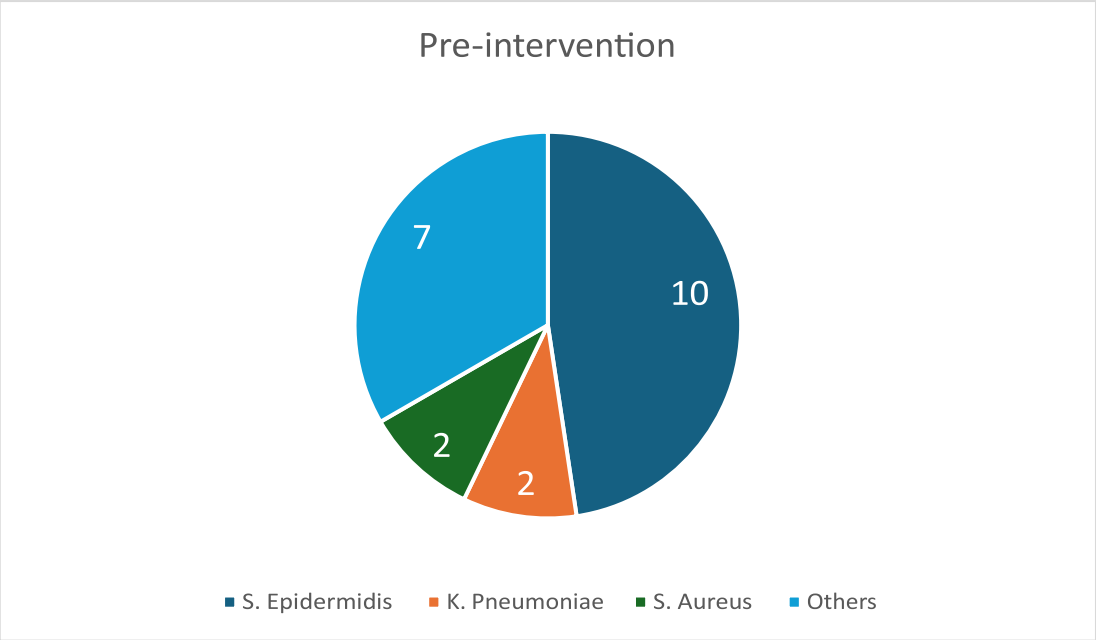
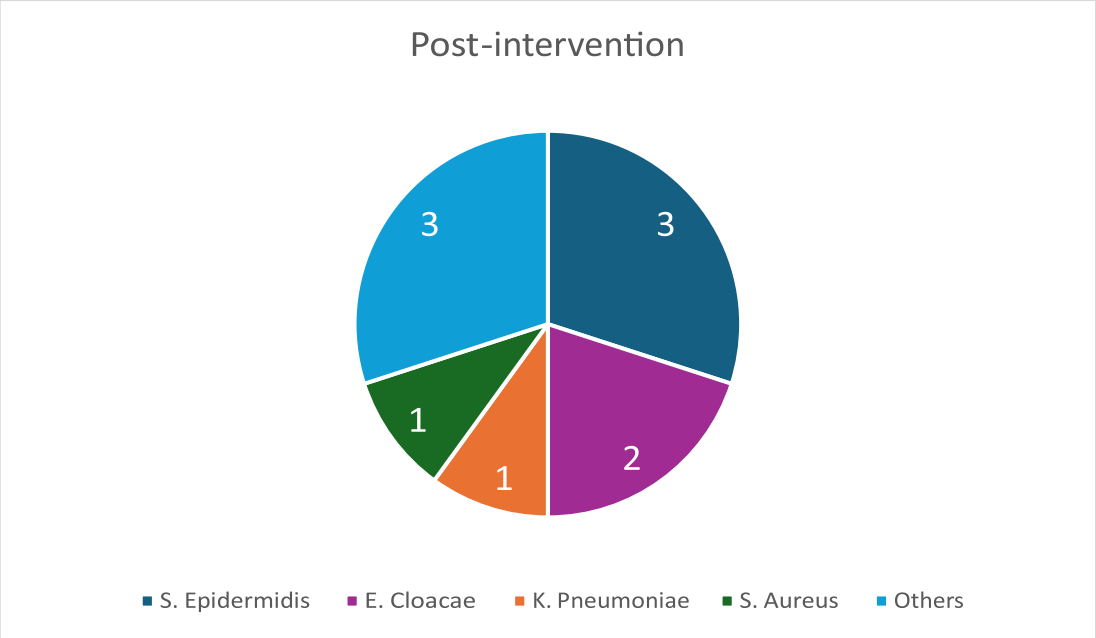


Figure 2. Pathogens isolated in CLABSI episodes during the post-intervention period



Figures 1 and 2 show the pathogens responsible for CLABSI episodes in the pre- versus post-intervention periods. In both periods, *Staphylococcus epidermidis* remained the most common organism. However, infections due to *Staphylococcus epidermidis* decreased after the intervention, indicating that the bundle implementation could have been especially effective against infections caused by coagulase-negative staphylococci. Other pathogens, such as *Klebsiella pneumoniae* and *Staphylococcus aureus*, showed relatively stable or slightly fluctuating proportions between the two periods, while rare isolates (e.g., *Enterococcus spp., Pseudomonas aeruginosa*) accounted for a small share of cases in both groups.

5. DISCUSSION

This study highlights that implementing the new bundle had a strong effect on reducing infection risk, with CLABSI rates decreasing by 70.16% in the postintervention period compared to the pre-intervention period. Such a significant reduction confirms the powerful clinical impact of the structured, evidence-based prevention strategies implemented in our NICU. This is supported by a 2011 study that reported applying standardized evidence-based central-line bundles and checklists in NICUs reduced CLABSI rates by 67%, a result very similar to what we currently observed.[35] Bundles' strength lies in their standardization (leading to reduced variability in clinical practice), with every step of catheter insertion and maintenance performed according to the highest standards of asepsis. Other previous studies and meta-analyses have also confirmed that central line bundles result in significant and sustained reductions in CLABSI rates across different settings. For example, Pronovost et al. reported that a five-element bundle in adult ICUs reduced CLABSI rates by more than 60%, maintaining these improvements over several years.[26] Studies carried out in neonates demonstrated that adherence to insertion and maintenance bundles could lower infection rates to near-zero levels, especially when combined with staff education and real-time feedback.[10, 37] Similar to our study, Holzmann-Pazgal (2012), demonstrated that a dedicated central-line maintenance team in a large NICU was associated with a 65% decrease in CLABSI rates.[38] Importantly, their results showed that this effect was sustained over time and across birth weight categories, emphasizing the importance of standardization and consistency in catheter care. Both interventions — whether through a dedicated line maintenance team or through standardized bundles — relied on rigorous adherence to evidence-based maintenance practices. The concordance between these results highlights that structured, multidisciplinary strategies are a cornerstone of infection prevention in high-risk neonatal populations.

We underscore the importance of not only implementing but also continuously reinforcing bundle adherence through regular staff training, simulation-based practice, and periodic audits of compliance and outcomes. Nevertheless, maintaining high adherence to bundle elements over time can be challenging. Studies have shown that compliance may decline without ongoing quality improvement efforts, leading to a

resurgence of infection rates.[39] To address this, our NICU has adopted a strategy of continuous education, regular auditing, and real-time feedback to staff, ensuring that the gains achieved with the bundle are sustained in the long term. Engaging multidisciplinary teams and fostering a culture of safety are also essential to promote ownership and accountability among all healthcare providers involved in central line care.

Furthermore, our findings highlight the higher infection risk associated with certain CVC types, especially CICCs, and emphasize the clinical importance of catheter choice in infection prevention strategies. In fact, our study shows that the type of CVC remains an independent risk factor for CLABSI, even after adjusting for confounders, and this result aligns with earlier research, including a 2020 study on risk factors for central venous catheter-related bloodstream infection in neonates.[36]

Therefore, it is crucial to customize the type of CVC for each patient, as recommended by international guidelines from GAVeCeLT.[5] These guidelines emphasize that vascular access should be individualized based on the patient's clinical condition, treatment duration, and infection risk, rather than focusing solely on technical factors. UVCs are generally preferred in the first days of life for early stabilization because they offer a quick and relatively safe central access route and are associated with lower infection rates, likely due to their short dwell time and placement soon after birth when colonization is minimal. However, extended use beyond the recommended period significantly increases the risk of infection.[40,41] This was also evident in our study, which shows that in our NICU, UVCs have a median dwell time of 4 days. Conversely, ECCs and CICCs are often necessary for medium or long-term intravenous therapy or parenteral nutrition and for critically ill neonates; however, they present a more invasive insertion technique and a higher risk of CLABSI, as confirmed by our findings, which show that CICCs had the highest proportional infection rates among all catheter types, in particular compared to ECCs. These results align with previous cohort and observational studies, which show that CICCs are more prone to microbial colonization and contamination caused by manipulation, and have a higher infection risk because of their longer dwell time, higher patient acuity, and complexity.[42]

Whenever possible, devices associated with a lower infection risk (i.e., ECCs) should be prioritized for use. In contrast, high-risk devices (i.e., CICCs) should be managed with strict infection prevention measures—including maximal sterile barrier precautions during insertion, standardized maintenance bundles, real-time tip position confirmation, and daily assessment of the ongoing need for the line. This tailored, riskbased approach aligns with international recommendations and is crucial for minimizing catheter exposure, reducing CLABSI rates, and improving overall neonatal outcomes. [42] The preference of ECCs' placement after UVCs also emerged from our study, where ECCs were placed more frequently than CICCs.

Although the method used to confirm the catheter tip position was not the main goal of this study, data were collected because it is an important factor in the overall safety of CVC management. The primary control method was X-ray for all types of CVCs. Ultrasound assessments were performed less frequently, likely because evaluating catheter tip position with this technique requires specifically trained and experienced operators, particularly because of the very small size of ECCs. [43,44]

Fewer skin commensals (such as S. epidermidis, typically associated with breaches in catheter care) were yielded from cultures after the bundle implementation. This finding is consistent to what reported by others; for example, Devrim et al. (2023) demonstrated a lower infection rate caused by skin commensals after bundles introduction, reflecting improved aseptic practices and septum disinfection. [45]

The persistence of Gram-negative infections (which are less likely to result from skin contamination and more often originate from intestinal translocation or hematogenous spread from other infection sites), emphasizes that not all CLABSIs can be prevented with bundles alone since the source of infection may not be the CVC. Additional targeted preventive strategies (such as antimicrobial stewardship, optimizing parenteral nutrition practices, and earlier transition to full enteral feeding) might be necessary to prevent Gram-negative and fungal infections. [46]

The strength of this study relies on the “before-and-after” design, enabling a direct comparison of the pre- and post-implementation periods. The study population was large and homogeneous, including all neonates admitted over a three-year span, with

at least one CVC in place, which helped minimize selection bias. Lastly, focusing on a clinically relevant outcome—the incidence of CLABSI—provides a globally recognized quality indicator directly connected to patient safety, highlighting the clinical significance of the results.

However, this study also has important limitations. Its single-center design, while ensuring consistency in protocols and patient management, may limit the generalizability of the results to other settings with different patient populations or clinical practices. The “before-and-after” design, although practical and well-suited for quality improvement interventions, is inherently vulnerable to temporal confounders, as other concurrent changes in care or patient characteristics may have influenced the observed outcomes. Furthermore, this study has a non-randomized design, which means that residual confounding variables cannot be entirely ruled out despite the use of multivariable and mixed-effects regression models. Additionally, some analyses may have been underpowered to detect minor but clinically relevant effects, especially when stratifying by catheter type or patient subgroup. Finally, the study relies on retrospective data collection, which could introduce risks of incomplete documentation or information bias; however, the systematic use of electronic medical records and standardized definitions helped mitigate these risks.

6. CONCLUSION

This study showed a significant and clinically meaningful decrease in CLABSIs after implementing a structured bundle for CVC insertion and maintenance in the NICU at the Policlinic of Modena, highlighting the substantial impact of standardized prevention strategies. The introduction of bundles is an independent predictor of infection, along with selecting the most appropriate CVC type, which is also a crucial aspect of infection prevention.

Using structured bundles, ongoing staff training, strict infection control measures, and careful aseptic techniques is essential for improving patient safety and reducing healthcare-associated infections. Special attention should be given to high-risk devices, such as CICCs, since enhanced preventive strategies and surveillance for these catheters could lead to a decrease in CLABSI rates.

Future research should aim to validate these findings through multicenter, prospective studies, evaluate the cost-effectiveness of bundle implementation, and explore additional methods to improve outcomes.

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