Catheter-Related Bloodstream Infections: Epidemiology, Diagnostic Advances, Antimicrobial Resistance, and Prevention Strategies—A Comprehensive Review

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Abstract
Catheter-related bloodstream infections (CRBSIs) remain among the most significant healthcare-associated infections worldwide, contributing to substantial morbidity, mortality, prolonged hospitalization, and increased healthcare costs, particularly among critically ill patients requiring prolonged intravascular catheterization. These infections arise primarily through microbial colonization of catheter surfaces via extraluminal and intraluminal routes, with biofilm formation playing a central role in microbial persistence and therapeutic failure. The major causative pathogens include Gram-positive cocci, Gram-negative bacilli, and *Candida* species, many of which demonstrate multidrug resistance.Accurate diagnosis requires integration of clinical findings with microbiological evidence, including paired blood cultures, differential time to positivity, and catheter tip culture. Advances in rapid molecular diagnostics have improved early pathogen detection and resistance characterization, enabling more targeted therapeutic interventions. Effective management depends on prompt diagnosis, appropriate antimicrobial therapy, and timely decisions regarding catheter removal or salvage.Prevention remains the cornerstone of CRBSI control and relies on strict aseptic catheter insertion techniques, evidence-based maintenance bundles, surveillance systems, and antimicrobial stewardship programs. Emerging innovations, including antimicrobial-coated catheters, automated surveillance systems, and anti-biofilm strategies, offer promising opportunities for reducing infection burden.This review comprehensively summarizes the epidemiology, pathogenesis, diagnostic approaches, antimicrobial resistance mechanisms, management strategies, and prevention measures associated with CRBSIs, while highlighting recent advances and future directions aimed at improving clinical outcomes and strengthening infection prevention practices.

Keywords: Catheter-related bloodstream infection, CRBSI, central venous catheter, antimicrobial resistance, biofilm, nosocomial infection
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Introduction

Catheter-related bloodstream infections (CRBSIs) are among the most serious healthcare-associated infections and remain a major challenge for healthcare systems worldwide due to their association with increased morbidity, mortality, prolonged hospitalization, and higher healthcare costs [1]. The increasing use of intravascular catheters for hemodynamic monitoring, medication delivery, parenteral nutrition, and long-term vascular access has significantly improved patient care, but it has also increased the risk of bloodstream infections, particularly among critically ill patients in intensive care units (ICUs), oncology settings, and hemodialysis units.

CRBSIs develop when microorganisms gain entry into the bloodstream through contamination of the catheter insertion site, catheter hub colonization, intraluminal migration, or hematogenous spread from distant infection sites. A key factor in their pathogenesis is microbial biofilm formation on catheter surfaces, which protects pathogens from host immune responses and reduces susceptibility to antimicrobial therapy, resulting in persistent infections and therapeutic challenges [2].

The microbiological profile of CRBSIs includes Gram-positive bacteria, Gram-negative bacilli, and fungal pathogens. Although *Staphylococcus aureus* and coagulase-negative staphylococci remain the most frequently isolated organisms, recent reports indicate an increasing prevalence of Gram-negative pathogens such as *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*, along with *Candida* species, particularly in

immunocompromised patients [3]. The growing emergence of multidrug-resistant organisms further complicates treatment and contributes to poor clinical outcomes.

Accurate diagnosis remains challenging because clinical manifestations are often nonspecific. Conventional diagnostic methods, including differential time to positivity, quantitative blood cultures, and catheter tip cultures, remain essential, while molecular diagnostic tools have improved the speed and precision of pathogen detection[4]. However, variability in diagnostic practices continues to affect consistency in diagnosis.

Antimicrobial resistance has become a major obstacle in CRBSI management, with increasing reports of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and carbapenem-resistant Gram-negative pathogens [5]. Addressing CRBSIs also supports the **United Nations Sustainable Development Goal 3 (Good Health and Well-Being)** by promoting patient safety, reducing infectious disease burden, and strengthening healthcare quality. Effective infection prevention strategies, antimicrobial stewardship, and improved surveillance are therefore essential.This review provides a concise overview of the epidemiology, pathogenesis, diagnostic approaches, antimicrobial resistance patterns, and prevention strategies associated with CRBSIs, aiming to enhance understanding and support improved clinical management of these infections.

Literature Search Strategy

A structured literature search was conducted using PubMed, Scopus, Web of Science, and Google Scholar for studies published between January 2000 and March 2026. Search terms included "catheter-related bloodstream infection," "CRBSI," "central venous catheter infection," "biofilm," "antimicrobial resistance," and "device-associated bloodstream infection." Original research articles, systematic reviews, meta-analyses, clinical guidelines, and surveillance reports published in English were included. Studies lacking sufficient methodological detail or relevance were excluded.

1. Bloodstream Infections

Bloodstream infections (BSIs) are defined as the presence of pathogenic microorganisms, including bacteria and fungi, within the bloodstream, resulting in systemic infection that may progress to sepsis, septic shock, and multiple organ dysfunction if not diagnosed and treated promptly[6]. These infections are broadly classified as primary bloodstream infections, which originate directly within the vascular system without an identifiable source, and secondary bloodstream infections, which arise from established infections at distant anatomical sites such as the respiratory, urinary, or gastrointestinal tract[7]. The pathogenesis of BSIs involves microbial entry into the circulation through disruption of host defense barriers, invasive procedures, or dissemination from localized infections. Once microorganisms gain access to the bloodstream, they trigger systemic inflammatory responses that can lead to endothelial dysfunction, immune dysregulation, and widespread tissue injury [8]. Hospitalized and critically ill patients are particularly vulnerable due to frequent invasive interventions and prolonged vascular access**.**

2. Catheter-Related Bloodstream Infections

Catheter-related bloodstream infection (CRBSI) is a specific type of primary bloodstream infection that occurs in patients with an intravascular catheter, where microbiological evidence confirms the catheter as the source of infection[9]. Unlike central line-associated bloodstream infection (CLABSI), which is primarily a surveillance definition, CRBSI requires laboratory confirmation through catheter and peripheral blood cultures or differential time-to-positivity methods[10]. CRBSIs represent a major category of healthcare-associated infections and are associated with prolonged hospitalization, increased healthcare costs, and significant morbidity and mortality, particularly among critically ill patients requiring prolonged central venous access [11].

The pathogenesis of CRBSIs involves microbial colonization of catheter surfaces followed by bloodstream invasion through four principal routes, as illustrated in **Fig. 1**. The most common mechanism is extraluminal colonization, in which microorganisms originating from the patient's skin migrate along the external catheter surface from the insertion site toward the catheter tip[9]. Intraluminal contamination may occur through repeated manipulation of the catheter hub during medication administration or line access, allowing pathogens to colonize the internal lumen. Hematogenous seeding from distant infectious foci can result in secondary catheter colonization, while direct inoculation through contaminated intravenous fluids or infusates represents a less frequent but recognized route of infection [12].

A central event in CRBSI pathogenesis is biofilm formation. Following microbial adherence to catheter surfaces, pathogens produce an extracellular polymeric matrix that enhances attachment and provides protection against host immune defenses and antimicrobial agents [2]. This biofilm environment facilitates microbial persistence, promotes antimicrobial resistance, and contributes to recurrent or persistent infection. Common biofilm-forming pathogens include *Staphylococcus aureus*, coagulase-negative staphylococci, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Candida*

species. Their ability to survive within biofilms significantly complicates treatment and frequently necessitates catheter removal. As shown in **Fig. 1**, catheter colonization and subsequent bloodstream invasion occur through migration of skin flora along the external catheter surface, contamination of the internal lumen through the catheter hub, hematogenous seeding from distant infection sites, and direct inoculation through contaminated infusates.

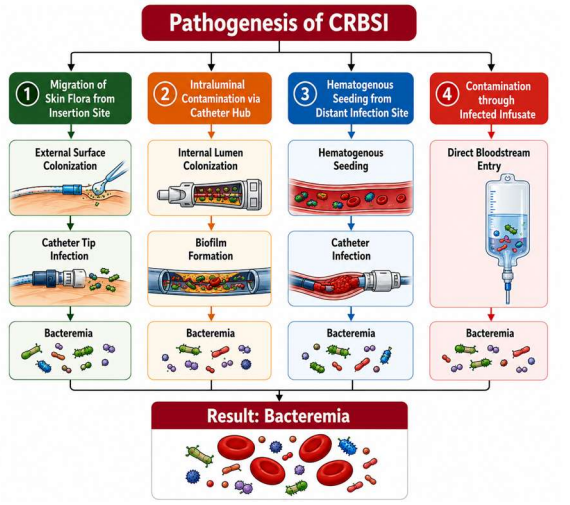

Figure 1. Pathogenesis of catheter-related bloodstream infection (CRBSI). Four distinct routes contribute to catheter colonization and subsequent bloodstream infection: (1) migration of skin flora along the external catheter surface from the insertion site; (2) intraluminal contamination through the catheter hub; (3) hematogenous seeding from a distant infectious focus; and (4) direct contamination through infected infusate. [Adapted from references 2, 9, and 12; original illustration by the authors].

3. Epidemiology of Catheter-Related Bloodstream Infections

CRBSIsconstitute a major proportion of HAIsworldwide and remain a significant cause of morbidity, mortality, and increased healthcare costs, particularly in ICUs where intravascular catheter use is common. The epidemiology of CRBSIs varies considerably across geographical regions, healthcare settings, and patient populations due to differences in infection prevention practices, healthcare infrastructure, patient comorbidities, and surveillance systems.

Globally, surveillance data have demonstrated substantial variation in CRBSI incidence across clinical settings. Early reports from the National Nosocomial Infections Surveillance (NNIS) system documented infection rates ranging from 2.1 to 30.2 per 1,000 catheter-days, with the highest rates observed in burn units and specialized critical care settings[13]. Subsequent surveillance data showed declining median infection rates, ranging from 1.8 to 5.2 per 1,000 catheter-days across various ICUs, reflecting improvements in infection control measures and implementation of evidence-based prevention bundles[14]. Studies from developed nations generally report lower CRBSI incidence compared with resource-limited settings. For instance, Lorente et al. (2005) reported an incidence of 2.79 infections per 1,000 catheter-days in adult ICU patients, whereas higher rates continue to be observed in neonatal and burn intensive care units due to prolonged catheter use, invasive interventions, and increased patient vulnerability[15, 16].BSIs are recognized as one of the leading causes of HAIs globally, with attributable mortality rates ranging from 12% to 25% [11]. In the United States, approximately 250,000 bloodstream infections are reported annually, with a significant proportion linked to intravascular catheter use[17]. In Europe, CRBSIs account for nearly 10%–20% of all HAIs and are associated with prolonged hospitalization, increased antimicrobial consumption, and elevated mortality[18]. Several studies have identified central venous catheters as a major independent risk factor, with infection risk increasing substantially with prolonged catheterization and repeated catheter manipulation [19].

In India, the burden of CRBSIs remains comparatively higher than that reported in developed countries, largely due to limited healthcare resources, overcrowding, inconsistent adherence to infection control practices, and variable surveillance systems. Reported incidence rates vary significantly across institutions and clinical settings. Singh et al. (2010) reported a relatively low incidence of 0.48 per 1,000 device-days in a rural teaching hospital, whereas Parameswaran et al. (2011)documented rates as high as 8.75 per 1,000 catheter-days in a tertiary care setting[20, 21]. Multicenter surveillance conducted by the International Nosocomial Infection Control Consortium (INICC) revealed CRBSI rates ranging from 7.6 to 9.1 per 1,000 catheter-days across Indian ICUs[22]. Similarly, Jaggi et al. (2012) reported infection rates ranging from 6 to 15 per 1,000 catheter-days across tertiary care hospitals, reflecting considerable inter-institutional variability[23].Additional Indian studies have consistently demonstrated elevated CRBSI rates. Datta et al. (2011) reported an incidence of 5.1 per 1,000 catheter-days, with Gram-negative pathogens predominating, while Sharma et al. (2014) documented rates of 7.92 per 1,000 catheter-days and identified prolonged catheterization and inadequate aseptic practices as major contributing factors[24, 25]. Kaur et al. (2015)and Mathur et al. (2014) similarly reported incidence rates exceeding 6 per 1,000 catheter-days among ICU patients[26, 27].

Encouragingly, intervention-based studies have shown that implementation of standardized catheter care bundles significantly reduces infection rates. Dudeja et al. (2017) demonstrated a reduction in CRBSI incidence from 9.4 to 3.2 per 1,000 catheter-days following strict adherence to evidence-based prevention protocols[28].Certain patient populations in India remain particularly vulnerable. Neonates in intensive care settings exhibit significantly higher infection rates, ranging from 10 to 22 per 1,000 catheter-days, largely due to immature immune defenses and prolonged vascular access requirements [29]. Pediatric ICU patients also demonstrate elevated susceptibility compared to adults. Similarly, patients undergoing hemodialysis represent another high-risk group, with reported CRBSI incidence ranging from 2.5 to 5.5 per 1,000 catheter-days, increasing with prolonged catheter dwell time [30, 31].

Overall, the epidemiological profile of CRBSIs demonstrates considerable global and regional variability, with a disproportionately higher burden observed in resource-limited settings such as India. These findings underscore the critical need for continuous surveillance, strict adherence to infection prevention bundles, antimicrobial stewardship, and strengthening of healthcare infrastructure to reduce CRBSI incidence and improve patient outcomes.

4. Diagnostic approach of Catheter-Related Bloodstream Infections (CRBSI)

Early and accurate diagnosis of CRBSI is essential for prompt therapeutic intervention and prevention of serious complications such as sepsis, metastatic infections, prolonged hospitalization, and increased mortality [10]. Diagnosis requires a systematic approach that integrates clinical evaluation with microbiological evidence to establish the catheter as the definitive source of bloodstream infection. Clinical suspicion should be raised in patients with indwelling intravascular catheters who develop signs of systemic infection without an identifiable alternative focus.

4.1 Clinical Diagnosis

The clinical presentation of CRBSI is often nonspecific and may vary according to the severity of infection and the patient's underlying condition. Common manifestations include fever, chills, rigors, and unexplained hypotension, which may occur intermittently or progress rapidly in severe cases [32, 33]. Early symptoms may include generalized malaise, fatigue, anorexia, and weakness, whereas advanced infection may present with high-grade fever, altered mental status, septic shock, and multiorgan dysfunction, particularly in critically ill or immunocompromised individuals[34].

Local signs of infection at the catheter insertion site, such as erythema, tenderness, induration, swelling, or purulent discharge, may indicate catheter involvement. However, the absence of these findings does not exclude CRBSI, especially in tunneled or long-term catheters where infection is often intraluminal and not externally apparent[10]. Persistent bacteremia may result in severe complications, including infective endocarditis, osteomyelitis, septic arthritis, spinal epidural abscess, and septic embolization [35].

4.2 Microbiological Diagnosis

Microbiological confirmation is essential for definitive diagnosis and remains the gold standard for CRBSI detection. Confirmation requires demonstration of the same pathogen in peripheral blood and catheter-related samples, along with exclusion of alternative infection sources [10].

- **Paired blood cultures** are the primary diagnostic method and involve simultaneous collection of blood samples from the catheter and a peripheral vein. Recovery of the same organism from both samples strongly suggests catheter-related infection. Quantitative paired blood culture enhances specificity by comparing microbial burden, with a colony count at least threefold greater in catheter-drawn blood indicating probable CRBSI [36].
- **Differential time to positivity (DTP)** is a widely accepted non-invasive diagnostic technique, particularly useful when catheter retention is preferred. It is based on the principle that blood drawn from an infected catheter contains a higher microbial load and therefore becomes positive earlier in automated culture systems. A positivity difference of at least two hours between catheter-drawn and peripheral blood cultures is considered strongly suggestive of CRBSI [37, 38]. This method is practical and avoids unnecessary catheter removal, although its reliability may be reduced in patients receiving prior antimicrobial therapy or in infections caused by slow-growing organisms.
- **Catheter tip culture** is performed when catheter removal is clinically indicated. The semiquantitative roll-plate technique remains the most commonly used method, with growth of ≥15 colony-forming units (CFU) considered indicative of significant catheter colonization [39]. Quantitative catheter tip culture, which identifies $\geq 10^2$–10^3CFU, offers greater sensitivity for detecting biofilm-associated infections[40]. Diagnostic confirmation is strengthened when identical organisms are isolated from both catheter tip and peripheral blood cultures, supported by matching antimicrobial susceptibility profiles[41].

The selection of diagnostic methods depends on catheter type, clinical stability of the patient, feasibility of catheter removal, and laboratory capabilities. Short-term catheters are often removed when infection is suspected, whereas long-term tunneled or implanted devices are typically preserved whenever possible, favoring non-removal diagnostic strategies such as DTP and paired blood cultures [42].Accurate diagnosis also requires proper specimen collection. Blood cultures should ideally be obtained before initiation of antimicrobial therapy and collected from all catheter lumens whenever feasible to maximize sensitivity. Careful interpretation is essential when common skin commensals such as coagulase-negative staphylococci are isolated, as contamination may mimic true infection [10].

Overall, an integrated diagnostic approach combining clinical suspicion with microbiological confirmation remains fundamental for reliable CRBSI detection. This strategy improves diagnostic precision, minimizes unnecessary catheter removal, and supports timely management, ultimately improving patient outcomes. A comparative summary of key diagnostic methods is presented in **Table 1**.

Table 1. Evidence-Based Diagnostic Approaches for Catheter-Related Bloodstream Infection (CRBSI) [Adapted from references 10, 41, and 43].

Method	Core Diagnostic Principle	Clinical Utility	Key Limitations	Sensitivity (%)	Specificity (%)
Simultaneous quantitative blood cultures	≥ 3-fold higher CFU in catheter vs peripheral blood	High specificity; guideline-supported	Technically demanding; costly	80–95	90–100
Differential Time to Positivity (DTP)	≥ 2-hour earlier positivity in catheter sample	Widely used; non-invasive	Variable sensitivity in certain infections	40–90	70–95
Catheter tip culture (semiquantitative)	≥ 15 CFU from catheter tip	Reference standard when catheter removed	Requires catheter removal	85–95	90–100
Catheter tip culture (quantitative)	≥ 10^2 – 10^3 CFU from catheter tip	Detects biofilm-associated infection	Requires specialized techniques	85–97	85–95
Paired qualitative blood cultures	Same organism in catheter and peripheral blood	Initial diagnostic approach	Limited specificity alone	High	Moderate
Acridine orange leukocyte cytospin	Direct visualization of microorganisms	Rapid adjunct test	Limited availability; operator dependent	75–90	~90
Endoluminal brush technique	≥ 100 CFU from catheter lumen	Enables diagnosis without removal	Procedural risks; rarely used	85–95	80–90

Abbreviations: CRBSI, catheter-related bloodstream infection; CFU, colony-forming unit; DTP, differential time to positivity; CLABSI, central line-associated bloodstream infection.

5. Risk Factors of Catheter-Related Bloodstream Infections

The development of CRBSIs is influenced by multiple interrelated factors involving catheter characteristics, patient-related conditions, and healthcare practices. Identification of these risk factors is essential for implementing targeted preventive strategies and reducing infection burden in clinical settings.

- **Catheter-Related Factors**

Catheter-related characteristics significantly contribute to CRBSI development. Prolonged catheter dwell time increases the risk of microbial colonization and biofilm formation on catheter surfaces, thereby facilitating bloodstream invasion [11,

[44]. Multilumen catheters are associated with greater infection risk than single-lumen devices because of increased manipulation and multiple access points. The insertion site also influences infection rates, with femoral vein catheterization generally associated with higher infection risk compared with subclavian or internal jugular access [45]. Repeated catheter manipulation and inadequate hub disinfection further enhance intraluminal contamination.

- **Patient-Related Factors**

Patient-related factors play a crucial role in determining susceptibility to CRBSIs. Immunocompromised states, including malignancy, neutropenia, and immunosuppressive therapy, predispose patients to infection[9]. Comorbidities such as diabetes mellitus, chronic kidney disease, and severe underlying illness further increase vulnerability. Prolonged intensive care unit stay, malnutrition, hypoalbuminemia, and advanced age are additional contributors associated with impaired host defense mechanisms and increased infection risk.

- **Healthcare-Related Factors**

Healthcare-associated practices significantly influence CRBSI incidence. Poor hand hygiene compliance, inadequate aseptic precautions during catheter insertion, inconsistent adherence to catheter care bundles, and insufficient staff training increase the likelihood of microbial contamination [46]. Overcrowding, staffing shortages, and inadequate infection surveillance systems further compromise infection prevention efforts, particularly in resource-limited healthcare settings.

- **Procedure-Related Factors**

Certain clinical interventions also increase CRBSI risk. Prolonged catheterization for total parenteral nutrition, chemotherapy, hemodialysis, and repeated vascular access procedures provide greater opportunity for microbial colonization and bloodstream invasion. Patients requiring frequent catheter access for therapeutic interventions are particularly susceptible.

In summary, CRBSIs result from a complex interaction of catheter-related, patient-related, procedural, and healthcare-associated factors. Effective prevention requires minimizing unnecessary catheter use, limiting catheter duration, ensuring strict adherence to aseptic protocols, and continuous surveillance of catheter care practices.

6. Antimicrobial Resistance in Catheter-Related Bloodstream Infections: Global and Indian Perspective

AMR has emerged as a major challenge in the management of CRBSIs worldwide. The widespread use of intravascular devices, prolonged hospitalization, extensive administration of broad-spectrum antibiotics, and increasing dependence on invasive procedures have collectively contributed to the emergence and dissemination of MDR pathogens in healthcare settings [7, 47]. The growing burden of antimicrobial-resistant CRBSI pathogens has significantly complicated treatment strategies, resulting in delayed therapeutic response, prolonged hospital stay, increased healthcare expenditure, and elevated mortality rates.

Globally, surveillance studies have shown that antimicrobial-resistant organisms account for a substantial proportion of CRBSI cases, particularly in ICUs. MRSA, methicillin-resistant coagulase-negative staphylococci,VRE, and carbapenem-resistant Gram-negative bacilli are among the most frequently reported resistant pathogens associated with catheter-related infections [48, 49]. Reports from the Centers for Disease Control and Prevention indicate that approximately 40–60% of *Staphylococcus aureus* isolates associated with device-related bloodstream infections demonstrate methicillin resistance, while resistance among Gram-negative pathogens continues to rise because of increasing production of ESBLs and carbapenemases[50]. Similarly, European surveillance data have documented increasing rates of carbapenem-resistant *K. pneumoniae* and *A. baumannii*, particularly among critically ill patients[51].

In low- and middle-income countries, including India, the burden of antimicrobial resistance in CRBSIs is substantially higher due to resource limitations, overcrowded healthcare facilities, inadequate infection control infrastructure, and inappropriate antimicrobial use. Indian studies have consistently documented a high prevalence of MDR Gram-negative bacilli among CRBSI isolates. Surveillance data from tertiary care hospitals indicate that ESBL-producing Enterobacterales account for approximately 40–70% of Gram-negative CRBSI isolates, whereas carbapenem resistance ranges from 20% to 50%, depending on geographical region and local antimicrobial practices [22, 24]. Studies from North India have identified carbapenem-resistant *K. pneumoniae* and *A. baumannii* as predominant pathogens, with resistance rates exceeding 50% in certain ICU settings [23, 24].

Regional variation in antimicrobial resistance patterns across India is considerable. Reports from South Indian tertiary care centers have documented a high prevalence of ESBL-producing *E. coli* and *K. pneumoniae*, whereas studies from Northern and Western India have highlighted increasing rates of metallo-β-lactamase-producing *P. aeruginosa* and *A. baumannii*[21, 28]. Neonatal and pediatric ICUs demonstrate a particularly high burden of resistant Gram-negative bacilli and methicillin-resistant

staphylococci, contributing significantly to morbidity and mortality [29]. Similarly, patients undergoing hemodialysis are at increased risk of CRBSIs caused by methicillin-resistant staphylococci and carbapenem-resistant Gram-negative pathogens, which further complicates management [27].

The mechanisms underlying antimicrobial resistance in CRBSI pathogens are multifactorial. In Gram-negative bacteria, resistance is predominantly mediated by β-lactamase production, including ESBLs and carbapenemases, which hydrolyze β-lactam antibiotics and compromise therapeutic efficacy [52]. The most frequently encountered ESBL genes include blaTEM, blaSHV, and blaCTX-M, while carbapenem resistance is commonly associated with blaNDM, blaKPC, blaOXA-48, blaVIM, and blaIMP. In Gram-positive organisms, methicillin resistance is primarily mediated by the mecA gene, which encodes the altered penicillin-binding protein PBP2a and confers reduced affinity for β-lactam antibiotics [53].

Given the increasing prevalence of MDR Gram-negative pathogens, fosfomycin has re-emerged as a promising therapeutic option. It exhibits activity against clinically important pathogens, including *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and carbapenem-resistant Enterobacterales. By inhibiting the MurA enzyme involved in peptidoglycan synthesis, fosfomycin acts through a unique mechanism that minimizes cross-resistance with other antimicrobial classes. In addition, its favorable tissue penetration and synergistic activity with other antimicrobial agents enhance its clinical utility. However, the emergence of plasmid-mediated resistance determinants, particularly *fosA* variants, highlights the need for continued surveillance and antimicrobial stewardship programs [70].

Table 2. Common Catheter-Related Bloodstream Infection Pathogens and Their Major Resistance Determinants

Pathogen	Common Resistance Genes	Clinical Significance
Staphylococcus aureus	mecA	Methicillin-resistant *S. aureus* (MRSA)
Enterococcus spp.	vanA, vanB	Vancomycin-resistant enterococci (VRE)
Klebsiella pneumoniae	blaNDM, blaOXA-48	Carbapenem resistance
Pseudomonas aeruginosa	blaVIM, blaIMP	Multidrug resistance
Acinetobacter baumannii	blaOXA-23, blaNDM	Extensive drug resistance
Candida spp.	ERG11 mutations	Azole resistance

Biofilm formation represents another critical mechanism contributing to antimicrobial resistance in CRBSIs. Microorganisms colonizing catheter surfaces produce extracellular polymeric substances that form a protective matrix, limiting antibiotic penetration and shielding embedded pathogens from host immune defenses [2]. Biofilm-associated organisms frequently exhibit reduced metabolic activity and phenotypic tolerance to antimicrobial agents, resulting in persistent infection, treatment failure, and recurrence. This explains why many CRBSIs fail to respond adequately to systemic antimicrobial therapy alone and often require catheter removal.

The clinical consequences of antimicrobial resistance in CRBSIs are substantial. Infections caused by resistant organisms are associated with delayed initiation of effective therapy, recurrent bacteremia, prolonged ICU stay, septic shock, and significantly increased mortality compared with infections caused by susceptible isolates[7]. Indian studies have reported mortality rates exceeding 30% among patients with carbapenem-resistant CRBSIs, particularly in critically ill populations [25].

Molecular characterization has significantly improved understanding of resistance epidemiology by enabling precise identification of resistance-associated genes and transmission pathways. While phenotypic susceptibility testing remains essential for determining antimicrobial profiles, molecular methods provide rapid detection of specific resistance determinants, thereby supporting early therapeutic decision-making and surveillance efforts [55]. Studies from Indian tertiary care centers have frequently identified blaNDM and blaOXA-48 as dominant carbapenemase genes among catheter-associated Gram-negative isolates, reflecting the increasing burden of carbapenem resistance in ICU settings. In Gram-positive pathogens, the mecA gene remains the principal determinant of methicillin resistance, while vanA and vanB contribute to vancomycin resistance in enterococci.

Molecular diagnostic techniques such as PCR, multiplex PCR, and whole-genome sequencing (WGS) have become increasingly valuable for detecting resistance genes and tracking clonal dissemination of resistant strains within healthcare environments[54]. The integration of molecular surveillance into routine CRBSI monitoring is particularly important in high-burden settings such as India, where rapid identification of resistance determinants can guide targeted therapy and strengthen antimicrobial stewardship programs.

Effective control of AMR in CRBSIs requires a comprehensive and multidisciplinary approach, including strict adherence to catheter care bundles, implementation of antimicrobial stewardship programs, early microbiological diagnosis, molecular resistance monitoring, and continuous surveillance. These strategies are essential for limiting the spread of resistant pathogens, reducing infection burden, and improving clinical outcomes in both global and regional healthcare settings [7, 46].

7. Management of Catheter-Related Bloodstream Infections

The management of CRBSIs requires a multidisciplinary and evidence-based approach involving intensivists, infectious disease specialists, clinical microbiologists, and infection prevention teams. Early recognition and timely intervention are essential to reduce morbidity, mortality, and healthcare-associated complications. Effective management depends on accurate clinical assessment, prompt microbiological diagnosis, appropriate antimicrobial therapy, and timely decisions regarding catheter removal or salvage [7, 10].

Initial management begins with careful clinical assessment to identify signs of systemic infection and determine the severity of illness. Patients presenting with fever, chills, hypotension, or unexplained sepsis in the presence of an intravascular catheter should be evaluated promptly for CRBSI. Diagnostic workup includes detailed clinical examination, evaluation of catheter insertion sites, hematological and biochemical investigations, and microbiological confirmation through paired blood cultures or catheter tip cultures when indicated [38]. Early communication of blood culture results and antimicrobial susceptibility data is critical for guiding therapeutic decisions.

Systemic antimicrobial therapy remains the cornerstone of CRBSI management. Empirical treatment should be initiated promptly after obtaining blood cultures and should provide broad coverage against likely pathogens based on patient risk factors, severity of illness, local epidemiology, and institutional antimicrobial resistance patterns. Coverage for Gram-positive organisms, particularly MRSA, is commonly achieved using vancomycin as first-line therapy, while daptomycin may be preferred in cases of elevated vancomycin minimum inhibitory concentration or treatment failure [55]. Gram-negative coverage should be guided by local resistance trends and may include fourth-generation cephalosporins, carbapenems, or β-lactam/β-lactamase inhibitor combinations, with aminoglycosides considered in critically ill patients[44]. In patients at high risk for fungal infection, especially those with prolonged catheterization or severe immunosuppression, empirical antifungal therapy with echinocandins may be considered [56].

The decision to remove or retain the catheter is a critical component of CRBSI management. Immediate catheter removal is generally recommended in patients with severe sepsis, hemodynamic instability, persistent bacteremia, tunnel infection, or infections caused by highly virulent organisms such as *S. aureus*, *P. aeruginosa*, fungi, or MDR pathogens [10]. Catheter retention may be considered in selected patients with uncomplicated infections when maintaining vascular access is essential, provided close clinical monitoring is ensured.

Antibiotic lock therapy (ALT) has emerged as an important adjunctive strategy for catheter salvage, particularly in long-term vascular access devices. This technique involves instillation of highly concentrated antimicrobial solutions into the catheter lumen for a defined dwell time to eradicate intraluminal biofilm-associated microorganisms. ALT is most effective when used in combination with systemic antimicrobial therapy and has demonstrated favorable outcomes in infections caused by less virulent organisms such as coagulase-negative staphylococci. However, its efficacy is limited in infections caused by *Staphylococcus aureus*, Gram-negative bacilli, and fungal pathogens[57].

Biofilm formation remains a major challenge in CRBSI management because it impairs antimicrobial penetration and promotes microbial persistence. Biofilm-associated organisms exhibit increased tolerance to antimicrobial agents, often resulting in treatment failure and recurrent infection. This frequently necessitates catheter removal despite systemic therapy[2].

Successful management also depends on strict adherence to infection prevention and control measures. Continuous surveillance of CRBSI rates, antimicrobial stewardship programs, regular clinical audits, and multidisciplinary review of infection trends are essential for optimizing therapeutic outcomes and minimizing recurrence. Timely diagnosis, appropriate antimicrobial selection, and individualized catheter management strategies remain central to improving patient prognosis.

8. Prevention and Control of Catheter-Related Bloodstream Infections

Prevention of catheter-related bloodstream infections remains a major priority in modern healthcare, particularly in intensive care units where intravascular devices are extensively used. Evidence indicates that a substantial proportion of CRBSIs are preventable through strict adherence to evidence-based infection prevention strategies. These

interventions aim to minimize microbial colonization of catheters, interrupt transmission pathways, and reduce the risk of bloodstream invasion [46, 59].

Appropriate catheter insertion practices form the foundation of CRBSI prevention. Strict hand hygiene, maximal sterile barrier precautions, use of chlorhexidine-based skin antisepsis, and selection of optimal catheter insertion sites significantly reduce infection risk. The subclavian vein is generally preferred over the femoral site because of its lower infection risk, provided there are no contraindications [46].

Catheter maintenance practices are equally important for preventing infection. Proper disinfection of catheter hubs and needleless connectors before each access is critical because these sites represent major portals for microbial entry. The "scrub the hub" technique using alcohol-based antiseptics has been shown to significantly reduce contamination and subsequent bloodstream infection [60]. Routine flushing and locking protocols also contribute to maintaining catheter patency and reducing intraluminal microbial colonization[61].

Preventive interventions can be broadly classified into active and passive strategies. Active strategies include manual disinfection, catheter flushing, and antimicrobial lock therapy, whereas passive strategies involve adjunctive technologies such as antiseptic barrier caps and antimicrobial-impregnated catheters. Passive disinfection devices have demonstrated promising results by providing continuous antimicrobial activity while reducing dependence on healthcare worker compliance[62,63].

The implementation of bundled prevention strategies has proven highly effective in reducing CRBSI incidence. Catheter care bundles combine multiple evidence-based interventions, including hand hygiene, chlorhexidine skin preparation, maximal sterile barrier precautions, optimal catheter site selection, and daily review of catheter necessity. Studies have reported reductions in CRBSI rates ranging from 40% to 80% following bundle implementation [64, 65]. Regular audits, feedback mechanisms, and compliance monitoring are essential to sustain these improvements.

Healthcare worker education and adherence to standardized protocols are critical determinants of successful prevention. Inconsistent compliance with catheter maintenance practices remains a significant challenge in many healthcare settings, particularly in resource-limited institutions. Contributing factors include inadequate training, high workload, staffing shortages, and limited availability of infection prevention resources[66, 67].

Recent advances in CRBSI prevention include the use of innovative disinfection technologies, antimicrobial-coated catheters, and automated compliance-monitoring systems. These emerging strategies have shown potential to further reduce infection risk, although their cost-effectiveness and long-term clinical impact require further evaluation [68].Global healthcare disruptions, including the COVID-19 pandemic, have highlighted the vulnerability of infection prevention programs. Increased patient burden, staffing limitations, and disruption of routine surveillance activities have been associated with increased rates of healthcare-associated infections, including CRBSIs [59, 69,70].

This cross-sectional study was conducted at Rama Medical College Hospital and Research Centre, Kanpur, on 100 patients clinically diagnosed with osteomyelitis. The aim was to determine the microbiological profile of osteomyelitis and evaluate the antibiotic resistance patterns of bacterial isolates, with special emphasis on multidrug-resistant (MDR) organisms. Of the 100 samples, 76% were culture positive**.** Staphylococcus species (47.4%) were the most common isolates, followed by Escherichia coli (14.4%)**,** Klebsiella spp. (11.8%)**,** Pseudomonas spp. (9.2%)**,** and Proteus spp. (5.2%)**.** Among the *Staphylococcus aureus* isolates, 44.4% were methicillin-resistant (MRSA)**,** and all MRSA isolates were sensitive to linezolid**.** Among Gram-negative bacilli, ESBL producers accounted for 50%**,** AmpC producers for 17.6%**,** and MBL producers for 14.7%**,** with these resistant isolates remaining susceptible to colistin and polymyxin B**.** The study concluded that MDR organisms are common in osteomyelitis and emphasized the importance of culture-guided antibiotic therapy, infection control practices, and antimicrobial stewardship to reduce resistance[70].

Overall, effective prevention and control of CRBSIs require sustained institutional commitment, multidisciplinary collaboration, adherence to evidence-based guidelines, and continuous surveillance. Strengthening infection prevention programs remains essential for reducing CRBSI burden and improving patient safety across healthcare settings.

9. Conclusion

CRBSIs remain a major healthcare concern because of their significant impact on patient morbidity, mortality, prolonged hospitalization, and increased healthcare costs. The persistence of MDR pathogens and biofilm-associated antimicrobial tolerance continues to complicate diagnosis and management, particularly in critical care and resource-limited settings.Recent advances in rapid molecular diagnostics, MALDI-TOF MS, whole-genome sequencing, antimicrobial-coated catheters, and automated surveillance systems have improved early detection and infection control practices. Emerging

innovations, including artificial intelligence-assisted surveillance and nanotechnology-based antimicrobial coatings, offer promising opportunities for enhanced prevention and management. Future research should focus on developing cost-effective rapid diagnostic tools, novel anti-biofilm strategies, and multicenter surveillance studies to monitor evolving resistance trends and optimize region-specific therapeutic approaches. Greater integration of molecular resistance monitoring and innovative catheter technologies will be essential for improving patient outcomes and reducing CRBSI burden.

To reduce the burden of CRBSIs, the following recommendations are essential:

- Strict adherence to evidence-based catheter insertion and maintenance bundles
- Continuous healthcare worker education and competency assessment
- Routine microbiological surveillance and antimicrobial resistance monitoring
- Strengthening antimicrobial stewardship programs
- Early adoption of rapid molecular diagnostic techniques
- Regular auditing of catheter care practices and compliance monitoring
- Development of institution-specific infection prevention protocols
- Investment in advanced catheter technologies and automated surveillance systems

The integration of rapid diagnostics, antimicrobial stewardship, molecular surveillance, and evidence-based catheter care bundles remains central to reducing CRBSI burden and improving patient safety globally, particularly in resource-limited healthcare settings.

Declarations

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