Bloodstream Infections: Diagnostic Utility of Blood Cultures, Contamination Challenges, and Emerging Antimicrobial Resistance – A Review

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***Abstract*—**Background: **Bloodstream infections (BSIs) are a significant cause of morbidity and mortality worldwide and require prompt diagnosis and appropriate antimicrobial therapy. Blood culture remains the gold standard for the detection of bacteremia; however, contamination and emerging antimicrobial resistance often limit its diagnostic and clinical utility. Objective: This review aims to summarize blood culture practices, contamination rates, etiological agents of bloodstream infections, and antimicrobial resistance patterns reported across different healthcare settings. Methods: A narrative review of observational studies, including retrospective, prospective, cross-sectional, and multicenter investigations, was conducted. Studies from tertiary care hospitals, emergency departments, neonatal intensive care units, and national surveillance programs were analyzed with respect to blood culture collection methods, microbial identification, definitions of contamination, and antimicrobial susceptibility testing. Results: Blood culture positivity and contamination rates varied widely across studies. Coagulase-negative staphylococci and other skin commensals were the most frequent contaminants. Staphylococcus aureus and Gram-negative organisms such as Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa were commonly identified as true bloodstream pathogens. A rising prevalence of multidrug-resistant organisms, including methicillin-resistant Staphylococcus aureus and extended-spectrum beta-lactamase-producing Gram-negative bacilli, was consistently reported. Conclusion: Blood culture contamination and antimicrobial resistance significantly impact the diagnosis and management of bloodstream infections. Strict adherence to aseptic collection techniques, continuous training of healthcare personnel, regular monitoring of contamination rates, and robust antimicrobial stewardship programs are essential to improve diagnostic accuracy and patient outcomes.**

***Index Terms*—Bloodstream infections; Blood culture; Contamination; Antimicrobial resistance; Bacteremia; Sepsis**

I. INTRODUCTION

Bloodstream infections (BSIs), including bacteremia and sepsis, continue to represent a significant global health challenge and are associated with considerable morbidity and mortality across all age groups [1]. Prompt identification of the causative pathogen and early initiation of appropriate antimicrobial therapy are critical determinants of patient survival, particularly in critically ill and septic patients [2]. Among available diagnostic investigations, blood culture remains the cornerstone for confirming BSIs and for enabling pathogen-directed antimicrobial treatment [3].

Despite its clinical importance, blood culture interpretation is often complicated by contamination during specimen collection. Contaminated blood cultures usually arise from the inadvertent introduction of commensal skin microorganisms, including coagulase-negative staphylococci, Corynebacterium species, Bacillus species, Micrococcus species, and Cutibacterium (Propionibacterium) acnes [4] [5]. Such false-positive results can mislead clinicians, resulting in unnecessary antimicrobial administration, repeated laboratory testing, increased hospital stay, and additional healthcare expenditure [6].

Differentiating true bacteremia from contamination requires a comprehensive assessment that integrates microbiological findings with the patient's clinical condition. Factors such as the identity of the isolated organism, number of positive blood culture sets, time

to culture positivity, and associated clinical and laboratory indicators such as fever, leukocytosis, and elevated inflammatory markers are crucial for accurate interpretation [1] [6]. Failure to appropriately distinguish contamination from genuine infection may lead to both overtreatment and delayed recognition of serious infections.

Blood culture contamination rates are widely used as a quality performance indicator in microbiology laboratories. International standards recommend that contamination rates should not exceed 3%, highlighting the importance of proper skin antisepsis, standardized collection techniques, and regular training of healthcare workers involved in blood sample collection [7][8][9]. Studies have consistently demonstrated that educational interventions, dedicated phlebotomy teams, and adherence to aseptic protocols significantly reduce contamination rates [10].

In parallel, the increasing prevalence of antimicrobial resistance among bloodstream pathogens has emerged as a major concern, complicating empirical therapy and limiting treatment options [11][12]. The distribution of causative organisms and their resistance profiles varies according to geographic location, patient population, and healthcare setting, emphasizing the need for continuous surveillance and periodic review of local and regional data [13].

Given the combined challenges of blood culture contamination and evolving antimicrobial resistance, a comprehensive synthesis of available evidence is essential. This review aims to critically examine the role of blood cultures in the diagnosis of bloodstream infections, explore the causes and consequences of blood culture contamination, and summarize reported trends in microbial etiology and antimicrobial susceptibility. Such an overview is intended to support improved diagnostic accuracy, rational antimicrobial use, and strengthened infection control practices.

II. METHODOLOGY

Study Design and Data Sources

This review is based on published observational studies, including retrospective, prospective, cross-sectional, and multicenter investigations that evaluated blood culture practices, bloodstream infections, contamination rates, and antimicrobial susceptibility patterns. The reviewed studies were conducted in tertiary care hospitals, emergency departments, neonatal intensive care units (NICUs), and national laboratory surveillance settings across different countries and healthcare systems [1][3].

Study Population and Eligibility Criteria

The included studies involved patients of various age groups adults, pediatric patients, and neonates with clinical suspicion of bacteremia or sepsis for whom blood cultures were performed as part of routine diagnostic evaluation. Neonatal studies primarily focused on early-onset sepsis occurring within the first week of life [14]. Common exclusion criteria across studies included patients with recent antibiotic exposure prior to blood collection, cases with suspected viral or parasitic infections, incomplete laboratory data, and cultures yielding mixed microbial growth suggestive of contamination [5].

Blood Sample Collection Procedures

Blood samples were collected using peripheral venipuncture or central venous access devices following strict aseptic techniques. Skin preparation typically involved cleansing with 70% isopropyl alcohol followed by iodine or chlorhexidine-based antiseptics, allowing sufficient drying time prior to venipuncture (Baron et al., 2013). Age-appropriate blood volumes were inoculated into aerobic and, when indicated, anaerobic blood culture bottles. In neonatal populations, smaller blood volumes were obtained to minimize iatrogenic blood loss (Polin, 2012).

Blood Culture Incubation and Monitoring

Blood culture bottles were promptly incubated in automated blood culture systems such as BD BACTEC or BacT/Alert, according to manufacturers' recommendations. Continuous monitoring was performed for a standard incubation period ranging from five to seven days. Cultures with no detectable microbial growth by the end of the incubation period were reported as negative [3][9].

Microbiological Identification of Isolates

Blood cultures flagged as positive underwent immediate Gram staining, and preliminary results were communicated to the treating clinicians. Positive samples were subcultured onto appropriate solid media, including blood agar, chocolate agar, and MacConkey agar, and incubated under suitable atmospheric conditions. Identification of isolates was

carried out using conventional biochemical tests or automated systems such as VITEK 2, depending on laboratory infrastructure [15].

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing (AST) was performed using standardized methods, most commonly the Kirby–Bauer disk diffusion technique or automated susceptibility platforms. Interpretation of results followed the Clinical and Laboratory Standards Institute (CLSI) guidelines applicable at the time of each study [7]. Specific phenotypic tests were used to detect resistance mechanisms, including cefoxitin disc testing for methicillin resistance in Staphylococcus species, confirmatory tests for extended-spectrum beta-lactamase (ESBL) production, and screening for carbapenem resistance among Gram-negative bacilli [16].

Definition of Blood Culture Contamination

Blood culture contamination was generally defined as the isolation of common skin commensals such as coagulase-negative Staphylococci, Corynebacterium species, Bacillus species (excluding Bacillus anthracis), Micrococcus species, and Cutibacterium acnes from a single blood culture set in the absence of compatible clinical features [4][5]. Cultures yielding multiple organisms were also considered contaminants unless clinical evidence supported true polymicrobial infection.

Data Extraction and Management

Data extracted from the reviewed studies included patient demographics, hospital location, source of blood culture collection, isolated microorganisms, antimicrobial susceptibility profiles, contamination rates, and clinical outcomes. Information was obtained from laboratory information systems, blood culture registers, and patient medical records, and was managed using electronic databases such as Microsoft Excel or REDCap [17].

Statistical Analysis

Most studies employed descriptive statistical methods to summarize findings. Categorical variables were expressed as frequencies and percentages, while continuous variables were reported as means with standard deviations. Blood culture contamination rates were calculated as the proportion of contaminated cultures relative to the total number of blood cultures processed. Comparative analyses between age groups, hospital units, or collection methods were performed using appropriate statistical tests, with a p-value of <0.05 considered statistically significant [10].

Ethical Considerations

All studies included in this review received approval from their respective institutional ethics committees or review boards. As the majority of studies were retrospective and involved analysis of routinely collected laboratory data, informed consent was waived in accordance with institutional and national ethical guidelines, and patient confidentiality was strictly maintained [18].

III. SYNTHESIS OF REVIEWED STUDIES

Across the reviewed studies, blood culture positivity rates varied widely depending on patient population, healthcare setting, and study design. Overall positivity ranged from approximately 10% to 30%, with higher yields reported among critically ill patients and neonates with suspected sepsis [1][3]. Gram-positive bacteria were frequently isolated, particularly Staphylococcus aureus and coagulase-negative Staphylococci, while Gram-negative organisms such as Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa predominated in several adult and neonatal studies [13].

Blood culture contamination rates showed considerable variation, ranging from less than 1% to over 6% in some settings. Contamination was most commonly attributed to skin commensals, with coagulase-negative staphylococci accounting for the majority of false-positive cultures [4][5]. Emergency departments and non-dedicated phlebotomy settings consistently reported higher contamination rates compared with wards using trained personnel or standardized collection protocols (Self et al., 2013).

Antimicrobial susceptibility patterns revealed increasing resistance among both Gram-positive and Gram-negative bloodstream isolates. Methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Gram-negative bacilli, including extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales and carbapenem-resistant organisms, were reported with notable frequency [16] [19]. Neonatal studies demonstrated emerging resistance to

traditionally recommended empirical agents such as ampicillin and gentamicin, particularly among Gram-negative pathogens [14].

IV. DISCUSSION

This review highlights the continued clinical importance of blood cultures in the diagnosis and management of bloodstream infections while underscoring persistent challenges related to contamination and antimicrobial resistance. Despite advances in automated culture systems and diagnostic technologies, blood culture contamination remains a significant problem that compromises diagnostic accuracy and contributes to inappropriate antimicrobial use [16].

The predominance of skin commensals as contaminants across studies emphasizes the critical role of proper collection techniques. Evidence consistently shows that inadequate skin antisepsis, improper venipuncture practices, and lack of trained personnel are major contributors to false-positive results [6]. High contamination rates not only increase laboratory workload but also expose patients to unnecessary antibiotics, thereby increasing the risk of adverse drug effects and promoting antimicrobial resistance.

The reviewed studies also demonstrate substantial geographic and population-based variation in the etiology of bloodstream infections. While Gram-positive organisms remain common, the rising burden of multidrug-resistant Gram-negative bacteria poses a serious threat, particularly in resource-limited settings and neonatal intensive care units [12][18]. These findings reinforce the importance of local and regional surveillance data to guide empirical therapy.

Furthermore, the increasing resistance to first-line empirical antibiotics observed in several studies raises concerns regarding current treatment protocols. Delayed administration of appropriate antimicrobial therapy has been strongly associated with increased mortality in septic patients, highlighting the need for timely culture results and rational antibiotic stewardship [2][13].

Overall, the findings suggest that reducing blood culture contamination through standardized protocols and strengthening antimicrobial stewardship programs are essential steps toward improving patient outcomes and optimizing healthcare resources.

V. CONCLUSION

Blood cultures remain the gold standard for the diagnosis of bloodstream infections and are indispensable for guiding targeted antimicrobial therapy. However, contamination of blood cultures continues to be a major challenge, leading to diagnostic uncertainty, unnecessary antibiotic use, and increased healthcare costs. The reviewed evidence demonstrates that adherence to strict aseptic collection techniques, ongoing staff training, and continuous monitoring of contamination rates are effective strategies to minimize false-positive results.

In parallel, the rising prevalence of antimicrobial resistance among bloodstream pathogens underscores the urgent need for regular surveillance of etiological agents and their susceptibility patterns. Integrating high-quality blood culture practices with robust antimicrobial stewardship programs is essential to ensure timely and appropriate therapy, reduce resistance, and improve patient outcomes. Future efforts should focus on standardizing blood culture procedures, enhancing laboratory–clinician communication, and strengthening infection control policies across healthcare settings.

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