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**Positive Blood Culture Results Predominantly Unrevealed among Adults Patients with Sepsis**

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**Abstract**

Sepsis is increasing every year and can be life-threatening. In the diagnosis of sepsis, it is challenging to identify the causative agent of infection. This research aims to determine the proportion of positive blood culture in sepsis patients at Hasanuddin University Hospital, Makassar. Blood cultures were collected from 98 adult patients with sepsis manifestations. This research design is cross-sectional with a descriptive observation approach. The data analysed in descriptive statistics were utilised to summarise patient demographics, treatments, and outcomes. Thirteen of 98 samples were positive for microbial pathogens (13.26%). The elderly group had the highest percentage (76.5%); eighty-seven patients (88.77%) were treated with antibiotic therapy prior to blood culture collection. Cephalosporins are the most administered antibiotics (72.4%). Administration of empirical therapy prior to blood culture collection may decrease the sensitivity of culture results. The culture of the infectious focus should be done to assist in the consideration of antimicrobial treatment.

**Keyword**: Blood Culture, Sepsis, Infection

**Abstrak**

Sepsis meningkat setiap tahun dan dapat mengancam jiwa. Diagnosis sepsis merupakan tantangan untuk mengidentifikasi agen penyebab infeksi. Penelitian ini bertujuan untuk mengetahui proporsi kultur darah positif pada pasien sepsis di Rumah Sakit Universitas Hasanuddin, Makassar. Kultur darah dikumpulkan dari 98 pasien dewasa dengan manifestasi sepsis. Studi *cross-sectional* dengan metode observasional deskriptif. Data yang telah diolah dalam statistik deskriptif digunakan untuk merangkum demografi pasien, perawatan, dan hasil. Analisis dilakukan dengan menggunakan IBM® SPSS Statistics 22.Tiga belas dari Sembilan puluh delapan sampel positif ditemukan mikroba patogen (13.26%). Kelompok lanjut usia memiliki persentase tertinggi (76.6%), delapan puluh tujuh pasien (88.77%) sudah diobati dengan antibiotik sebelum pengambilan kultur darah. Golongan cephalosporin merupakan antibiotik yang paling banyak diberikan sebanyak 72,4%. Pemberian terapi empiris sebelum pengambilan kultur darah dapat menurunkan sensitivitas hasil kultur. Kultur dari fokus infeksi perlu dilakukan untuk membantu dalam pertimbangan pengobatan antimikroba.

**Kata kunci**: Kultur Darah, Sepsis, Infeksi

**Introduction**

Sepsis is increasing every year and can be life-threatening. A life-threatening condition that arises when the body's response to infection causes injury to tissues and organs in the host.1 In the diagnosis of sepsis, it is challenging to identify the causative agent of infection. Sepsis can be caused by bacterial, viral, or fungal infections. It requires prompt and appropriate monitoring and administration of antimicrobials.2,3,4

Risk factors for sepsis include immunosuppression, renal disease, cancer or malignancy, diabetes mellitus, chronic lung disease, congestive heart failure, and alcohol use.5 Risk factors for sepsis in patients admitted to surgical, neurological, trauma, and ICU care. Age, especially in neonates or the elderly, gender, and comorbidities are non-modifiable risk factors. Critical care interventions and surgery-related factors are modifiable factors and suggest that improving surgical patient care and effective management of critical care interventions may play an important role in reducing the occurrence of sepsis in patients admitted to the ICU.6

Sepsis is most caused by bacteria, but in recent years the incidence of sepsis has increased in fungal infections, especially *Candida* species. Mortality from sepsis caused by *Candida* species is higher than infection with *Pseudomonas aeruginosa, Staphylococcus aureus* or *Escherichia coli*. Improper management of sepsis leads to sepsis shock, multiple organ failure and death. Severe sepsis and septic shock cause mortality in intensive care units globally, ranging from 30-50%.7 As many as 8-10% of causes of septic shock are caused by *Candida* infection. Septic shock with candidemia causes a high mortality of 54-66%. Abdominal infection is one of the sources of sepsis and septic shock in Candidemia.8 Blood culture sensitivity is decreased in sepsis patients receiving empirical antimicrobial therapy.1 The foundation of sepsis management continues with early antimicrobial administration, control of the source of infection, and supportive care.1 Rapid detection of sepsis can help in providing better management.9 Molecular detection has the potential to identify microorganisms and provide relevant antibiotic resistance information in less time than is currently required for blood cultures. Tests using nucleic acid amplification technology (NAAT) rapidly makes copies of DNA or RNA derived from pathogens or host cells through biochemical reactions, amplifying nucleic acid sequences to detectable levels. The sequences are then used to identify the causative agent of infection or immune response. The use of NAAT for sepsis diagnosis is associated with challenges in reliably capturing and amplifying pathogen nucleic acids from complex samples such as blood, where the causative agent of infection is in low amounts or polymicrobial in the human DNA.10

**Methods**

This study was conducted using the descriptive observational method with a cross-sectional approach using primary data. This study aims to determine the positive blood cultures identified by the BacT/Alert automatic (bioMérieux, Marcy-I’Étoile, France) detection method in sepsis patients treated at Hasanuddin University Hospital Makassar. Identification of microorganisms causing bloodstream infections was carried out at the Microbiology Laboratory of Hasanuddin University Hospital Makassar.

This study was approved by the Health Research Ethics Committee of Hasanuddin University with protocol number uH22070400 and letter number 775/UN4.6.4.5.31/PP36/2022. Data from medical record has been processed in descriptive statistics were utilized to summarize patient demographics, treatments, and outcomes. The mean, frequency distribution, and percentage were calculated for categorical variables. Analysis was conducted using the IBM® SPSS Statistics 22 (IBM Corp., New York, NY, USA).

Adult patients (≥19 years old), Quick Sequential Organ Failure Assessment (qSOFA)/ SOFA score screening in suspected sepsis for consideration of culture collection. Initial qSOFA assessment with a score of 2 is at high risk for sepsis, qSOFA criteria: 1) Respiratory rate ≥22/min, 2) Glasgow Coma Scale <15, and 3) Systolic blood pressure ≤100 mmHg. SOFA score includes the respiratory system, coagulation system, liver function, cardiovascular system, central nervous system, and renal function. Scores ranged from 0 to 24 points, with a score of 7 points meaning organ dysfunction. Ninety-eight adult patients attended the Hasanuddin University Hospital, Makassar, during the period from January 2022 to August 2023.

Blood cultures were collected from two peripheral sites. The collection area was disinfected with 70% isopropyl alcohol before blood collection. 8-10 mL of blood was drawn and inoculated into BacT/ALERT® aerobic culture bottles (bioMérieux, Marcy-I’Étoile, France). After blood collection, the sample is immediately taken to the laboratory and incubated in an automated BacT/ALERT® system. Positive blood cultures were Gram-stained. Gram stain usually takes less time, and ideally, the Gram stain results should be communicated to the doctor in a timely manner. Positive blood culture were inoculated onto Blood Agar, Chocolate agar and MacConkey media. Identified using the Vitek® 2 ID system (bioMérieux, Marcy-I’Étoile, France).

**Results**

Data were collected from 98 patients; the percentage of female patients was 51.0%. Most patients were treated in the ward (59.18%). Based on this study, the elderly group had the highest percentage (76.5%). Positive blood cultures were found in 13.2% of patients, as shown in Table 1.

The results of this study showed that most of the blood cultures were negative in 85 patients (86.7%). Seven blood cultures were positive for Gram-positive bacteria (*Staphylococcus aureus* and Coagulase-negative *Staphylococci*); there were five Gram-negative bacteria identified (*Escherichia coli, Acinetobacter baumannii*, and *Burkholderia cepacia*); and 2 yeasts identified as *Candida* species.

Most patients (88.77%) had received antibiotic therapy prior to blood culture collection, with the most prescribed antibiotics being cephalosporins (72.4%) followed by quinolones. Eleven patients died during treatment, six of whom were admitted to the ICU with positive blood culture results.

**Table 1. Patient Demographic Data, Identified Microorganisms, and Types of Antibiotics used During Treatment**

|  |  |
| --- | --- |
| **Demographic Variables (n=98)** | **Mean/Freq (%)** |
| **Sex** |  |
|  | Male | 48 (49.0) |
| Female | 50 (51.0) |
| **High Risk for Sepsis** |   |
|  | Malignancy | 24 (24.5) |
| Parenteral Nutrition | 35 (35.7) |
| Chronic Kidney Injury | 38 (38.8) |
| Diabetes Mellitus | 32 (32.7) |
| Hypertension | 26 (26.5) |
| Liver Disease  | 6 (6.1) |
| CVC | 24 (24.5) |
| **Room** |   |
|  | ICU | 40 (40.8) |
| Ward | 58 (59.2) |
| **Identified Microorganism** |
|   | *Staphylococcus aureus* | 5 (5.1) |
| *Coagulase-negative Staphylococci* | 2 (2.0) |
| *Escherichia coli* | 2 (2.0) |
| *Acinetobacter baumannii* | 1 (1.0) |
| *Burkholderia cepacia* | 1 (1.0) |
| *Candida species* | 2 (2.0) |
| **Antimicrobial** |
|   | Cephalosporine | 71 (72.4) |
| Quinolone | 24 (24.5) |
| Carbapenem | 11 (11.2) |
| Penicillin | 1 (1.0) |
| Metronidazole | 19 (19.4) |
| Others | 15 (15.3) |

*\*Note: CVC: Central Venous Catheter, ICU: Intensive Care Unit*

**Discussion**

Blood culture is an important diagnostic tool for the identifying of the causative agent of infection in patients with sepsis, sepsis shock, and infective endocarditis.11 An unknown source of infection is associated with a poor prognosis. Delayed control of the source of infection may increase mortality.

Negative blood cultures can be caused by previous antibiotic administration or other causes other than bacterial infections, such as fungi or viruses.7 Empirical antibiotics are often given for long periods of time for suspected sepsis, even in the absence of clinical signs of infection, while waiting for blood culture results.12 Previous studies have shown that about 28–50% of sepsis patients have negative blood culture. Delayed, effective antibiotic administration every hour in patients with septic shock will result in death. Interventional laboratory tests should be done to consider continuing, narrowing, or stopping antibiotics to found non-infectious causes if blood culture results are negative.13 In early sepsis, collection of blood cultures after administration of empirical antibiotic therapy decreases sensitivity.1,14 It is necessary to perform molecular identification to detect microorganisms in negative blood culture results.15

The combination of infection biomarkers shows accurate results for the identification of causative agents of infections in the body, such as bloodstream infections.2,3 Infection control practices must be implemented when managing patients to prevent sepsis. With the increased risk of sepsis in hospitals, it is necessary to provide appropriate diagnostic services and administer appropriate and adequate antibiotics.16 Optimal administration of antibiotics is important to ensure their effectiveness, reduce the cost burden of antibiotic use and prevent antibiotic resistance.17,18

Contamination occurred when a single positive blood culture bottle was found and the bacteria identified as coagulase-negative *Staphylococcus, Bacillus, Propionibacterium acnes*, or *Corynebacterium* species.19 All positive blood culture cases in this study were monomicrobial. Gram-positive bacteria were most common than Gram-negative bacteria in this study. This is consistent with other studies. Gram-positive organisms as causative agents of infection in sepsis cases are associated with invasive procedures in severely ill patients.16

Six sepsis patients admitted to the ICU with positive culture died during treatment. This is consistent with previous studies in which patients with positive culture results had a higher in-hospital mortality rate.20 Selection of appropriate culture from the focus of infection prior to antibiotic administration, respiratory culture where appropriate, MRSA (Methicillin-Resistant *Staphylococcus aureus*) swabs, ASP (Antibiotic Stewardship program), and rapid diagnostic testing can help reduce antibiotic administration and more quickly choose the right antimicrobial.18 Antibiotic therapy, even for multiple doses, can lead to unnecessary costs, substantial toxicity, clinically important changes in microbial flora, and increased drug resistance. Hospital policy in developing rapid identification of sepsis patients for treatment consideration using antimicrobial regimens broad enough to cover all infection-causing pathogens.21

The limitations of this study are that in some patients, it was difficult to draw blood with the appropriate amount of blood volume, not during the febrile phase, and patients had received antibiotic therapy before. This study was limited to single-hospital, so it cannot be generalized. Infection control programs in hospitals should continue to be implemented to reduce the risk of infection, control the inappropriate use of antimicrobials, and prevent increasing resistance.

**Conclusion**

Administration of empirical therapy prior to blood culture collection may decrease the sensitivity of culture results. Consideration should be given to culture of the focus of infection to assist in the consideration of antimicrobial treatment. Care interventions and the use of medical devices in treated patients, especially those receiving surgery, need to be carried out to reduce the incidence of sepsis in patients in the ICU.

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