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Impact of blood culture positivity on clinical outcomes in sepsis: a prospective observational study

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SUMMARY

Background: Bacteremia is usually considered a marker for severe infection, yet the correlation between blood culture positivity and mortality in sepsis remains uncertain. This study aimed to evaluate whether blood culture positivity is associated with adverse clinical outcomes in patients with sepsis.
Methods: This prospective observational study included adult patients with sepsis admitted to a tertiary care hospital. Patients were classified into culture-positive and culture-negative groups based on blood culture results. Clinical outcomes including 30-day mortality, length of hospital stay, and vasopressor requirement were compared. Multivariable logistic and Cox regression models were used to assess the independent association of bacteremia with mortality, adjusting for age, and comorbidities.
Results: Of 633 patients, 41.9% (n=265) were blood culture-positive. Although culture-positive patients had higher SOFA, SAPS II scores, and procalcitonin levels, 30-day mortality was similar between groups (20.8% vs. 26.1%; p=0.12). Length of hospital stay was comparable (median 14 vs. 16 days; p=0.374), as was ICU stay duration (p=0.693). On multivariable analysis, bacteremia was not independently associated with 30-day mortality (adjusted OR 0.62, 95% CI:0.28-1.37, p=0.236). Kaplan-Meier analysis showed a non-significant trend toward higher survival in the culture-positive group (HR 1.30, 95% CI: 0.80-2.10, p=0.293).
Conclusions: Although blood culture-positive sepsis was associated with higher disease severity at presentation, it did not result in increased 30-day mortality. These findings suggest that bacteremia alone does not determine sepsis outcomes, and culture-negative sepsis should be managed with equal clinical urgency.

Keywords: Sepsis, Culture-positive, Culture-negative, mortality, outcome.

INTRODUCTION

Sepsis is a leading cause of mortality and morbidity causing significant impact on health burden. The estimated mortality in sepsis ranges from 10% to 40%, particularly in patients with septic shock [1, 2]. Timely identification of the causative pathogen is critical in guiding appropriate antimicrobial therapy and improving outcomes. Blood cultures remain the gold standard for diagnosing bloodstream infections and play a pivotal role in the management of sepsis. Culture positivity not only enables pathogen-specific treatment but is also considered a surrogate marker for higher bacterial load and systemic dissemination of infection [3, 4]. Despite being the gold standard for pathogen identification, blood cultures can remain negative in a substantial proportion of cases, ranging from 30% to 50% in various studies [5, 6]. This culture negativity is attributed to several factors such as prior antibiotic exposure, fastidious or

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slow-growing organisms, low microbial burden, and inadequate sampling volume [6]. The lack of pathogen identification can complicate clinical decision-making, due to diagnostic uncertainty and inability to optimize therapy based on a specific pathogen.

It is often assumed that blood culture-negative sepsis represents a less severe form of illness due to the absence of bacteremia; however, this hypothesis may be misleading. There is a considerable gap in the literature and ongoing debate regarding whether the presence of bacteremia independently correlates with worse clinical outcomes. Available studies have reported conflicting results: some suggest that culture-positive sepsis is associated with higher mortality due to increased microbial burden, while others have found no significant difference or even worse outcomes in culture-negative patients, possibly due to delays in targeted therapy [7-9]. Due to persistent discrepancies, we conducted this study to compare the clinical outcomes of blood culture-positive and culture-negative sepsis and to better understand the prognostic significance of blood culture status in sepsis.

METHODS AND MATERIALS

Study Design

This was a prospective cohort study conducted in a tertiary care centre in Western India. We included all adult patients (≥18 years) who were admitted to the medical wards and ICU with sepsis between January 2023 to December 2024. Sepsis was defined as according to The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) [1]. All patients with viral, fungal, parasitic, and tubercular sepsis were excluded. Patients with polymicrobial bloodstream infections were excluded to reduce heterogeneity and allow clearer comparison of clinical outcomes between monomicrobial culture-positive and culture-negative sepsis. Patients who had received antibiotics for 48 hours or more prior to blood culture collection, and contaminant positive cultures were also excluded.

Data collection

All adult patients diagnosed with sepsis were prospectively enrolled during the study period after meeting predefined inclusion criteria. Clinical and demographic data were recorded at the time of enrolment, including age, gender, comorbidities, suspected source of infection, vital signs, laboratory parameters, and severity scores: Sequential Organ Failure Assessment (SOFA), and Simplified Acute Physiology Score II (SAPS II). Blood cultures were obtained prior to initiation of antimicrobial therapy. Patients were then followed for 30 days to assess clinical outcomes, including mortality, requirement of vasopressor support, and ICU admission. Only the first episode of sepsis per patient was documented. In patients with negative blood cultures, the source of infection was determined based on clinico-radiological findings, and microbiological evidence from non-blood specimens (e.g., urine, sputum, body fluids).

Data definition

Sepsis was defined according to the Sepsis-3 criteria as life-threatening organ dysfunction with a SOFA score ≥2 from baseline [1]. Culture-positive sepsis included patients with bacterial growth in blood cultures after ruling out contamination. Culture-negative sepsis referred to those with clinical features of sepsis but no bacterial growth in blood. Septic Shock was defined as the requirement for vasopressors to maintain a mean arterial pressure ≥65 mmHg despite fluid resuscitation [1]. The source of infection was determined based on a combination of clinical presentation, imaging findings, and microbiological data, and was categorized according to modified CDC/NHSN surveillance definitions for site-specific infections where applicable (e.g., urinary tract, respiratory, intra-abdominal, skin and soft tissue,). In cases where multiple potential sources were present, the predominant clinical source was determined by treating physicians and recorded. Laboratory parameters, including hematological, renal, hepatic, and inflammatory markers, were recorded on the day of clinical diagnosis of sepsis and blood culture collection, irrespective of subsequent culture positivity or negativity. The primary outcome was 30-day mortality. Secondary outcomes included length of hospital stay, ICU stay, and vasopressor requirement. This study was approved by the Institutional Ethics Committee, (AIIMS/IEC/2023/4484).

Statistical Analysis

Data were analyzed using SPSS version 21 and DATAtab software. Continuous variables were

summarized as mean ± standard deviation or median (interquartile range), and categorical variables as frequencies and percentages. Comparisons between culture-positive and culture-negative sepsis groups were made using the Chi-square test. The association between blood culture positivity and 30-day mortality was assessed using both unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Adjustment was performed using multivariable logistic regression, incorporating covariates with known prognostic relevance (age, Charlson comorbidity index, and SOFA score). Kaplan-Meier survival analysis was performed to estimate 30-day survival, and differences between groups were assessed using the log-rank test. A p-value <0.05 was considered statistically significant.

RESULTS

Clinical characteristics

A total of 633 patients with sepsis were enrolled in this study, of whom 265 (41.9%) had blood culture-positive sepsis and 368 (58.1%) had culture-negative sepsis. The median age of the cohort was 53 years (IQR: 35-65), and 59.2% were male. The prevalence of common comorbidities included diabetes mellitus (35.2%), chronic kidney disease (22%), chronic liver disease (5.5%), cardiac disease (15.3%), and immunosuppression (10.9%). Except for chronic kidney disease, which was found significantly higher among culture-negative group, other comorbidities did not differ significantly between the two groups (Table 1).

Baseline laboratory parameters demonstrated some significant differences. The median leukocyte counts were higher in the culture-negative group (p<0.001, Table 1). Inflammatory markers such as C-reactive protein (267 vs. 190 mg/L; p <0.001) and ferritin (1149 vs. 612 ng/mL; p=0.001) were higher in culture-negative patients. There was a trend for higher procalcitonin (PCT) levels in culture positive sepsis, though it was statistically insignificant (p=0.394). Notably, the median SOFA score was higher in the culture-positive group [12 (IQR: 5-8)] compared to culture-negative sepsis [8 (IQR: 5-7); p=0.005], indicating greater severity of illness. Similarly, SAPS II scores were

Table 1 - Comparison of clinical and laboratory characteristics of Blood culture-positive and Culture-negative sepsis.

Variables	*Blood culture positive (n=265), (%)*	*Blood culture negative (n=368), (%)*	*P value*
Age (Year), Median (IQR)	53 (35-65)	54 (36-60)	0.291
Gender (Male)	157 (59.2)	219 (59.5)	0.956
Comorbidities			
Diabetes	85 (32.1)	138 (37.6)	0.315
CKD	37 (13.9)	102 (27.7)	0.002
Cardiac	38 (14.3)	54 (14.7)	0.828
Immunodeficiency	36 (13.6)	33 (8.9)	0.219
CLD	21 (7.9)	14 (3.8)	0.179
Hb (g/dL)	10 (8.2-11.2)	9.8 (8.6-11.6)	0.499
TLC (cells/µL)	16340 (10700-23560)	22000 (17400-26000)	<0.001
PLT (cells/µL)	173000 (106000-276000)	178000 (100250-243950)	0.356
Creatinine (mg/dL)	1.67 (0.91-3.1)	2.56 (1.9-4.6)	<0.001
Albumin (g/dL)	2.8 (2.4-3.3)	3.1 (2.8-3.4)	0.012
NLR	9 (5-15)	7 (4.1-10.8)	0.001
LDH (U/L)	201 (171-288)	248 (212-370)	0.005
Lactate (mmol/L)	3.3 (2.7-4.5	3.5 (1.5-2.9)	0.148
Ferritin (ng/mL)	612 (453-1144)	1149 (622-1593)	0.001
CRP (mg/L)	190 (142.3-250)	267 (218-321)	0.001
PCT (ng/L)	3.4 (1.8-11.5)	2.8 (2.2-5.8)	0.394
SOFA	12 (5-8)	8 (5-7)	0.005
SAPS II	66 (50-75)	60 (50-73)	0.525

All laboratory values are presented as Median (IQR). Abbreviations: CKD = chronic kidney disease, CLD = chronic liver disease, TLC = total leukocyte count, PLT = platelet count, NLR = neutrophil-to-lymphocyte ratio, LDH = lactate dehydrogenase, CRP = C-reactive protein, PCT = procalcitonin, SOFA = Sequential Organ Failure Assessment, SAPS II = Simplified Acute Physiology Score II.

also numerically higher in the culture-positive group but did not reach statistical significance (Median SAPS II: 66 vs 60, p=0.525).

Site of infection and etiology

The most common site of infection in the overall cohort was the urinary tract (27%), followed by respiratory tract (19.3%), abdomen (10.7%), skin and soft tissues (6.2%) and CNS (3.2%). Urinary tract infections were distributed similarly between the blood culture-positive and culture-negative groups (Table 2). Respiratory infections were significantly more frequent in the culture-negative group (23.1% vs. 14.0%; p=0.004), while abdominal infections were more common in the culture-positive group (14.3% vs. 8.2%; p=0.013). Central nervous system infections were also more prevalent in culture-negative patients (4.9% vs. 0.8%; p=0.003). Among patients with positive blood cultures, the predominant organisms were *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* (Figure 1), comprising the majority of bloodstream infections. In the culture-negative group, the presumed source of infection was determined based on clin-

Table 2 - Comparison of Blood culture-positive and Culture-negative sepsis based on site of infection (in culture negative sepsis, site of infection is determined by clinico-radiological findings and isolation of pathogen from local source).

Primary infection Site	*Blood culture-positive (n=265), (%)*	*Blood culture-negative (n=368), (%)*	*P value*
Urinary tract	73 (27.5)	98 (26.6)	0.797
Respiratory	37 (14)	85 (23.1)	0.004
Abdomen	38 (14.3)	30 (8.2)	0.013
Skin & Soft tissues	12 (4.5)	27 (7.3)	0.147
Central nervous system	2 (0.8)	18 (4.9)	0.003
Bone/Joints	13 (4.9)	11 (3)	0.213
Others[a]	20 (7.5)	9 (2.4)	0.002
Unknown	70 (26.5)	90 (24.5)	0.576

a = other sites are endocarditis (8) and catheter related infection (21).

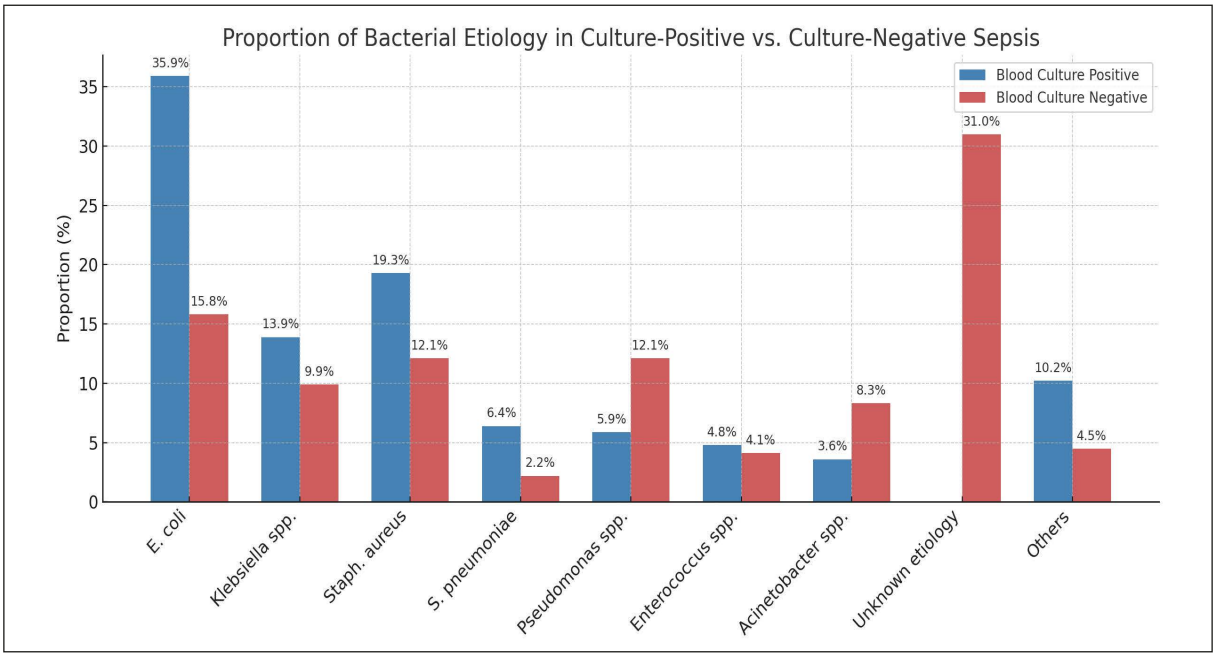

Figure 1 - Distribution of Bacterial Etiology in Blood Culture-Positive and Culture-Negative Sepsis (In the blood culture-negative group, etiology was identified based on clinical judgment, response to empirical therapy, and supportive evidence from non-blood microbiological samples).

ico-radiologic evidence, and cultures from non-blood specimens where available. We also compared the empirical antibiotic regimens between the two groups and observed that broad-spectrum agents were more frequently used in the culture-negative group; however, this difference was not statistically significant (p=0.09).

Primary and secondary outcomes

The overall 30-day mortality in this study cohort was 23.9% (151/633). Mortality was higher in the blood culture-negative group compared to the culture-positive group (26.1% vs. 20.8%, p=0.12), although this difference was not statistically significant. Patients with culture-negative sepsis had a significantly higher incidence of septic shock (61.4% vs. 40%, p<0.001, Table 3). However, the median duration of vasopressor support was slightly shorter in culture-negative patients (3 days vs. 4 days, p=0.024). No significant difference were found between the two groups in length of hospital stay (median 16 vs. 14 days, p=0.374), duration of ICU stay (median 2 vs. 0 days, p=0.693), and incidence of acute kidney injury (51.3% vs. 54.7%, p=0.403).

We performed both unadjusted and multivariable logistic regression analyses to evaluate the association between bacteremia and 30-day mortality, adjusting for key clinical covariates. Unadjusted logistic regression showed that blood culture positivity was not associated with increased 30-day mortality (OR: 0.76, 95% CI: 0.44-1.31, p=0.324). This finding remained consistent after adjustment for age, SOFA score, and Charlson Comorbidity Index (adjusted OR: 0.62, 95% CI: 0.28-1.37, p=0.236, Table 4). Kaplan–Meier survival analysis showed a non-significant trend toward worse survival (30 days mortality) in culture-negative sepsis (adjusted HR: 1.30, 95% CI: 0.80-2.10, p=0.293, Figure 2).

Multivariate analysis of clinical predictors (Figure 3) revealed that increasing age and higher SOFA scores were significantly associated with an increased risk of 30-day mortality. In contrast, blood culture status (positivity or negativity) was not independently associated with mortality. Additionally, inflammatory sepsis biomarkers including CRP, lactate, and PCT showed no significant association with 30-day mortality in this cohort (Figure 3). We also evaluated the association of mortality with site of infection. The highest mortality rate was observed among patients with CNS infections (80%), compared to those with LRTI (18.9%) and UTI (12.9%) (p<0.001). Furthermore, in multivariable logistic regression, CNS infection was independently associated with increased mortality (adjusted odds ratio: 1.9; 95% CI: 1.2–2.8; p=0.009), compared to other infection sources.

Table 3 - Comparison of Clinical outcomes in Blood culture-positive and Blood culture-negative sepsis.

Variables	*Overall (n=633), (%)*	*Blood culture-positive (n=265), (%)*	*Blood culture-negative (n=368), (%)*	*P value*
Mortality (30 days)	151 (23.9)	55 (20.8)	96 (26.1)	0.120
LOS[a] (Hospital)	15 (10-20)	14 (10-21)	16 (10-18)	0.374
LOS (ICU)	2 (0-7)	0 (0-10)	2 (0-6)	0.693
Septic shock	232 (36.7)	106 (40)	226 (61.4)	<0.001
Duration of inotropes	4 (0-6)	4 (2-6)	3 (0-6)	0.024
AKI	334 (52.8)	145 (54.7)	189 (51.3)	0.403

a= Length of stay in days, LOS and duration of inotropes in Median with IQR, AKI = acute kidney injury.

Table 4 - The association of Bacteremia with 30 days mortality (Compare with non-bacteremic sepsis, Odds ratio is adjusted for age, Charlson comorbidity index, and SOFA score).

Covariable		*Odds ratio*	*Confidence Interval (95%)*	*P value*
Bacteremia	Unadjusted	0.76	0.44 - 1.31	0.324
	Adjusted	0.62	0.28 - 1.37	0.236

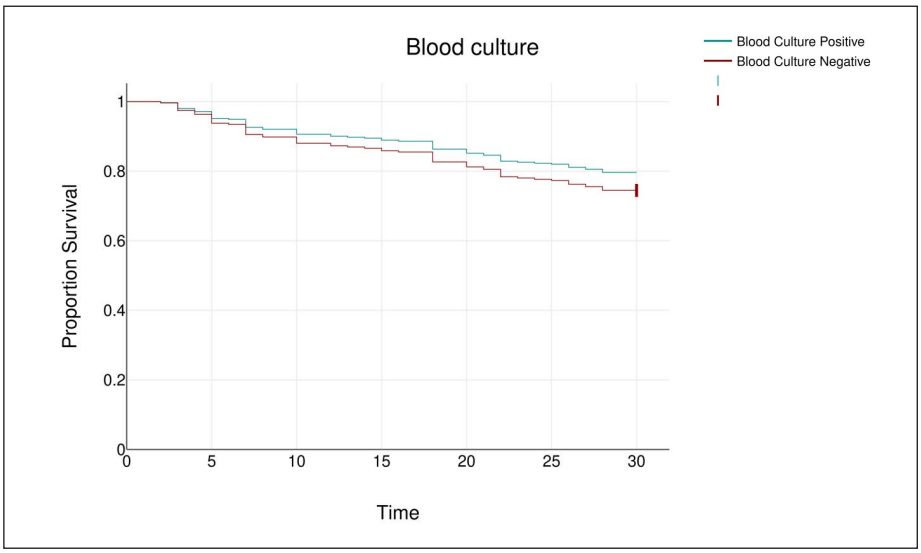

Figure 2
Adjusted Kaplan–Meier survival curves comparing culture-positive and culture-negative sepsis (Survival estimates were derived from a Cox proportional hazards model adjusted for age and SOFA score. The analysis demonstrated a non-significant trend toward higher mortality in culture-negative sepsis (Hazard Ratio: 1.30; 95% Confidence Interval: 0.80-2.10; p=0.293).

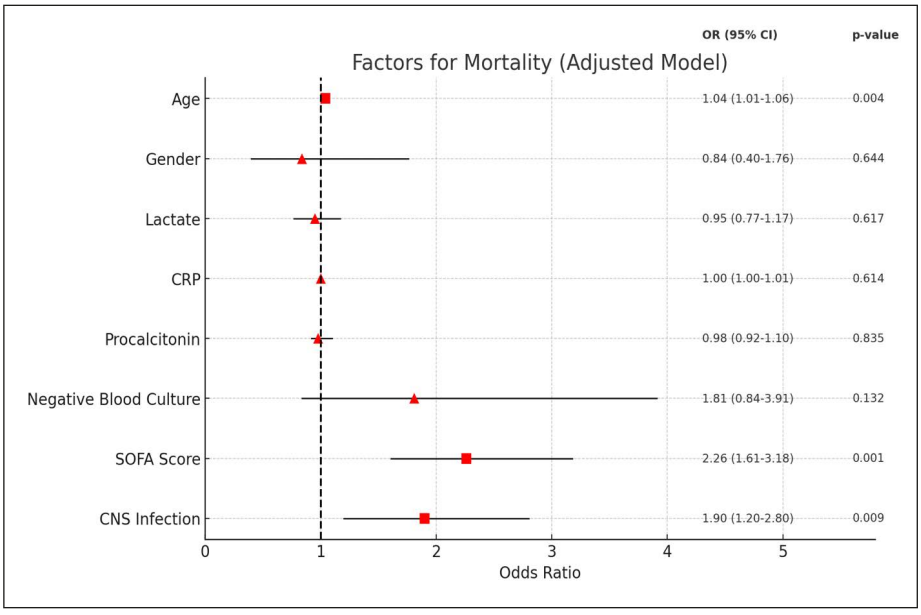

Figure 3
Adjusted Odds Ratios for Predictors of 30 days Mortality in Sepsis.

DISCUSSION

In the absence of microbiological confirmation, clinicians are often unable to optimize therapy based on pathogen-specific susceptibilities, which may contribute to poorer outcomes compared to culture-positive sepsis. To evaluate the impact of blood culture negativity on clinical outcomes, we conducted a prospective cohort study of adult patients with sepsis. In our study, we found that culture-negative sepsis accounted for a substantial proportion of cases (58.1%). The high rate of culture negativity in our cohort may be explained by several factors, including prior antibiotic exposure, inadequate sampling, or infections caused by fastidious pathogens. Blood culture positivity was associated with greater illness severity, as evidenced by higher SOFA and SAPS II scores. Nev-

ertheless, Despite having more severe disease spectrum at presentation, blood culture positivity was not independently associated with increased 30-day mortality after adjusting for key clinical variables including age, comorbidity burden, and organ dysfunction.

Our findings are consistent with previous literature that challenges the assumption that culture-negative sepsis represents a milder phenotype. Several studies have examined the prognostic significance of blood culture status in patients with sepsis, although the results remain heterogeneous. Mellhammar *et al.* reported significantly higher 90-day mortality in culture-positive patients (47%) compared to culture-negative patients (36%) in a propensity-matched cohort, suggesting that bacteremia may reflect more severe disease or suboptimal early therapy [10]. Similarly, a retrospective cohort study from China observed increased late mortality and prolonged hospital stay among bacteremic patients, despite comparable early outcomes [11].

In contrast, studies by Sigakis *et al.* and Nejtek *et al.* found no statistically significant differences in mortality between culture-positive and culture-negative groups after adjusting for severity of illness, although bacteremic patients tended to require more intensive care support [12, 13]. Similarly, a report from a pediatric septic shock cohort documented comparable mortality across both groups, despite higher inflammatory markers in culture-positive cases [14]. In our study, patients with culture-positive sepsis had significantly higher SOFA scores and showed a trend toward increased SAPS II scores and PCT levels at presentation, suggesting greater physiological derangement and a heightened inflammatory response. This likely reflects a higher microbial burden or a more invasive infection in bacteremic patients. A large multicenter study (FORECAST) by Komori *et al*. also reported greater organ dysfunction in bacteremic patients, but no significant difference in in-hospital mortality findings that are consistent with our results [15]. These mixed findings are further supported by a meta-analysis by Li *et al*., which pooled data from over 22,000 sepsis patients and found that culture positivity was not significantly associated with overall mortality (OR: 0.95; 95% CI: 0.88-1.01) [16]. However, bacteremic patients had longer hospital stays and required prolonged mechanical ventilation. Our study supports this broader evidence, reinforcing that blood culture status alone is not an independent predictor of mortality.

This inconsistency in the literature highlights the heterogeneity of the sepsis syndrome and suggests that host response and illness severity may be more important determinants of outcome than microbiological confirmation alone. Previous studies have highlighted that immune dysregulation, rather than pathogen burden, plays a central role in the pathogenesis of poor outcomes in sepsis [17-19]. In the current study, there was a trend toward higher PCT levels among culture-positive patients; however, the mortality rates remained similar across groups. This suggests that while PCT may reflect disease severity, it does not independently predict clinical outcomes. Therefore, relying on PCT alone for risk stratification may be insufficient in the management of sepsis [20-24]. Our findings support the growing recognition that sepsis is a highly heterogeneous condition. Clinical decision-making should be guided by patient-specific factors such as illness severity, comorbidities, and host immune status, rather than microbiological confirmation alone. While culture status remains important for antimicrobial selection, it may not adequately reflect disease course or prognosis. A precision medicine approach that integrates clinical severity, comorbidities, biomarkers, and potentially genomic or immunologic profiles could facilitate more tailored and effective sepsis management. Such stratification has been shown to identify distinct sepsis phenotypes that differ in their clinical outcomes and responses to treatment [25, 26]. This approach may ultimately enhance prognostication and support more efficient use of healthcare resources.

This study has some important limitations. First, although patients were prospectively enrolled, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings. Second, while we adjusted for key clinical variables in the multivariate analysis, the possibility of residual confounding cannot be excluded. Third, we excluded polymicrobial and fungal bloodstream infections to maintain a homogeneous cohort, which may reduce the broader applicability of our results. Although we excluded patients who had received prolonged antibiotic therapy (antibiotic initiation >48 hours prior to blood culture collection), undocumented early antibiotic

exposure may still have influenced patient outcomes by altering the disease course and its severity. We also did not assess long-term outcomes beyond 30 days or patient-centered endpoints such as post-discharge functional status, which are important areas for future research. We were unable to include antimicrobial resistance profiles in the analysis due to incomplete susceptibility data across all culture-positive cases, which may have influenced mortality outcomes. Lastly, polymicrobial bloodstream infections were not included in this analysis, which may limit the generalizability of our findings to patients with mixed-organism sepsis.

In summary, blood culture-positive sepsis was associated with higher disease severity at presentation, reflected by significantly elevated SOFA scores. However, 30-day mortality remained similar between the two groups. These findings suggest that the presence or absence of bacteremia does not independently influence short-term outcomes in sepsis. This study contributes to the limited prospective data on this subject, particularly from low and middle-income settings, and highlights the importance of early severity assessment and timely antibiotic initiation over microbiological confirmation alone.

Ethical compliance statement

The study was conducted in accordance with 1964 Helsinki Declaration. The research did not involve any procedures that violated national or international laws concerning human, animal, or environmental rights.

Conflict of interest

The authors declare that there are no conflicts of interest related to the content of this manuscript.

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REFERENCES

[1] Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016; 315: 801-810.

[2] Vincent JL, Jones G, David S, Olariu E, Cadwell KK. Frequency and mortality of septic shock in Europe and North America: a systematic review and meta-analysis. *Crit Care*. 2019; 23: 196.

[3] Christaki E, Giamarellos-Bourboulis EJ. The complex pathogenesis of bacteremia: from antimicrobial clearance mechanisms to the genetic background of the host. *Virulence*. 2014; 5: 57-65.

[4] Holmes CL, Anderson MT, Mobley HLT, Bachman MA. Pathogenesis of Gram-Negative Bacteremia. *Clin Microbiol Rev*. 2021; 34: e00234-20.

[5] Kethireddy S, Bilgili B, Sees A, et al; Cooperative Antimicrobial Therapy of Septic Shock (CATSS) Database Research Group. Culture-Negative Septic Shock Compared With Culture-Positive Septic Shock: A Retrospective Cohort Study. *Crit Care Med*. 2018; 46: 506-512.

[6] Bast J, Scheer C, Rehberg S, et al. Mortality of blood-culture-positive vs. blood-culture-negative patients with severe sepsis and septic shock. *Infection*. 2015; 43: S58-S59.

[7] Nannan Panday RS, Lammers EMJ, Alam N, Nanayakkara PWB. An overview of positive cultures and clinical outcomes in septic patients: a sub-analysis of the Prehospital Antibiotics Against Sepsis (PHANTASi) trial. *Crit Care*. 2019; 23: 182.

[8] Phua J, Ngerng W, See K, et al. Characteristics and outcomes of culture-negative versus culture-positive severe sepsis. *Crit Care*. 2013; 17: R202

[9] Gupta S, Sakhuja A, Kumar G, McGrath E, Nanchal RS, Kashani KB. Culture-Negative Severe Sepsis: Nationwide Trends and Outcomes. *Chest*. 2016; 150: 1251-1259.

[10] Mellhammar L, Kahn F, Whitlow C, Kander T, Christensson B, Linder A. Bacteremic sepsis leads to higher mortality when adjusting for confounders with propensity score matching. *Sci Rep*. 2021; 11: 6972.

[11] Yang L, Lin Y, Wang J, Song J, Wei B, Zhang X, et al. Comparison of Clinical Characteristics and Outcomes Between Positive and Negative Blood Culture Septic Patients: A Retrospective Cohort Study. *Infect Drug Resist*. 2021; 14: 4191-4205.

[12] Sigakis MJG, Jewell E, Maile MD, Cinti SK, Bateman BT, Engoren M. Culture-Negative and Culture-Positive Sepsis: A Comparison of Characteristics and Outcomes. *Anesth Analg*. 2019; 129: 1300-1309.

[13] Nejtek T, Müller M, Moravec M, Průcha M, Zazula R. Bacteremia in Patients with Sepsis in the ICU: Does It Make a Difference? *Microorganisms*. 2023; 11: 2357.

[14] Huang H, Chen J, Dang H, Liu C, Fu YQ. Comparing outcomes between culture-positive and culture-negative septic shock in a PICU: A retrospective cohort study. *Front Pediatr*. 2022; 10: 1001565.

[15] Komori A, Abe T, Kushimoto S, et al; JAAM FORECAST group. Characteristics and outcomes of bacteremia among ICU-admitted patients with severe sepsis. *Sci Rep*. 2020; 10: 2983.

[16] Li Y, Guo J, Yang H, Li H, Shen Y, Zhang D. Comparison of culture-negative and culture-positive sepsis or septic shock: a systematic review and meta-analysis. *Crit Care*. 2021; 25: 167.

[17] Delano MJ, Ward PA. The immune system's role in

sepsis progression, resolution, and long-term outcome. *Immunol Rev*. 2016; 274: 330-353.
[18] Shankar-Hari M, Fear D, Lavender P, Mare T, Beale R, Swanson C, et al. Activation-Associated Accelerated Apoptosis of Memory B Cells in Critically Ill Patients With Sepsis. *Crit Care Med*. 2017; 45: 875-882.
[19] van der Poll T, van de Veerdonk FL, Scicluna BP, Netea MG. The immunopathology of sepsis and potential therapeutic targets. *Nat Rev Immunol*. 2017; 17: 407-420.
[20] Durrance RJ, Ullah T, Patel H, et al. Marked Elevation in Serum Procalcitonin Levels Do Not Correlate With Severity of Disease or Mortality in Hospitalized Patients: A Retrospective Study. *Biomark Insights.* 2020; 15: 1177271920917941.
[21] Schupp T, Weidner K, Rusnak J, Jawhar S, Forner J, Dulatahu F, et al. C-reactive protein and procalcitonin during course of sepsis and septic shock. *Ir J Med Sci*. 2024; 193: 457-468.
[22] Molano-Franco D, Arevalo-Rodriguez I, Muriel A, et al; SEPSIS-BIOMARKERS Collaborators. Basal procalcitonin, C-reactive protein, interleukin-6, and presepsin for prediction of mortality in critically ill septic patients: a systematic review and meta-analysis. *Diagn Progn Res*. 2023; 7: 15.
[23] Varela-Patiño M, López-Izquierdo R, Velayos-García P, et al. Usefulness of infection biomarkers for diagnosing bacteremia in patients with a sepsis code in the emergency department. *Infez Med*. 2020; 28(1): 29-36.
[24] Robati Anaraki M, Nouri-Vaskeh M, Abdoli Oskouie S. Effectiveness of procalcitonin-guided antibiotic therapy to shorten treatment duration in critically-ill patients with bloodstream infections: a systematic review and meta-analysis. *Infez Med*. 2020; 28(1): 37-47.
[25] Ruiz-Rodriguez JC, Plata-Menchaca EP, Chiscano-Camón L, et al. Precision medicine in sepsis and septic shock: From omics to clinical tools. *World J Crit Care Med*. 2022; 11: 1-21.
[26] Lazăr A, Georgescu AM, Vitin A, Azamfirei L. Precision Medicine and its Role in the Treatment of Sepsis: A Personalised View. *J Crit Care Med*. (Targu Mures). 2019; 5: 90-96.