RESEARCH ARTICLE DOI: 10.53555/q5h4h045

COMPARATIVE ANALYSIS OF BASELINE CHARACTERISTICS AND CLINICAL OUTCOMES IN SIRS AND SEPSIS PATIENTS: A PROSPECTIVE STUDY

Dr. Erum Amir^{1*}, Dr. Shazia Fahmi², Dr. Javeria Maqsood³, Dr. Amtul Quddos Latif⁴, Dr. Rabia Arshad⁵, Nuzhat Firdous⁶

^{1*}MBBS, MPhil, CHPE, Assistant Professor, Department of Pathology, Karachi Metropolitan University, Pakistan

²MBBS, MPhil, CHPE, Assistant Professor, Department of Anatomy, Karachi Metropolitan University, Pakistan

 MBBS, FCPS, Cardiologist, Senior Registrar, National Medical Centre, Karachi Pakistan
 MBBS, MCPS, MPhil, CHPE, Associate Professor and HOD, Main Clinical and Diagnostic Laboratory, JPMC, Karachi Pakistan

⁵Professor, Department of Pharmacology, Dow International Dental College, Dow University of Health Sciences, Karachi Pakistan

⁶Principal College of Nursing, CMH, Institute of Medical Sciences(CIMS), Bahawalpur

*Corresponding Author: Dr. Erum Amir

*MBBS, MPhil, CHPE, Assistant Professor, Pathology Department Karachi Metropolitan University, Pakistan Email: erumamir09@gmail.com

Abstract

Background:

Sepsis is a life-threatening condition characterized by organ dysfunction due to a dysregulated immune response to infection. It is a major cause of morbidity and mortality globally, particularly in low- and middle-income countries (LMICs). The Sequential Organ Failure Assessment (SOFA) score and Glasgow Coma Scale (GCS) are critical markers for predicting sepsis outcomes.

Objective:

This study aims to compare the baseline characteristics and clinical outcomes of patients diagnosed with Systemic Inflammatory Response Syndrome (SIRS) and sepsis in a resource-limited setting, focusing on the role of clinical diagnostic parameters like SOFA, GCS, and other vital signs.

Methods:

A prospective cohort observational study was conducted at Jinnah Postgraduate Medical Centre (JPMC), Karachi, from June 2023 to June 2024. A total of 200 patients, including 79 with SIRS and 121 with sepsis, were included. Baseline characteristics, clinical parameters (SOFA, GCS, blood pressure, respiratory rate), and outcomes (mortality, ICU stay) were assessed. Data were analyzed using SPSS, and statistical significance was set at p < 0.05.

Results:

Sepsis patients were older, with a significantly higher mortality rate (58.3% vs. 13.9% in SIRS, p < 0.01). SOFA and GCS scores were significantly worse in sepsis patients compared to those with SIRS, both on Day 1 and Day 3 (p < 0.01). Culture positivity was significantly higher in sepsis patients

(29.8% vs. 6.3% in SIRS, p = 0.01). The study also revealed significant hemodynamic and neurological deterioration in sepsis patients.

Conclusion:

Sepsis patients exhibit significantly higher organ dysfunction and mortality compared to SIRS patients. The SOFA and GCS scores proved valuable in predicting clinical outcomes. The findings highlight the urgent need for improved sepsis management, early diagnosis, and better healthcare resources in LMICs to reduce the high mortality associated with sepsis.

Keywords: Sepsis, Systemic Inflammatory Response Syndrome (SIRS), SOFA score, Glasgow Coma Scale, mortality, low- and middle-income countries (LMICs), ICU

Introduction

Sepsis, as defined by the Sepsis-3 guidelines, is a life-threatening condition characterized by organ dysfunction due to a dysregulated immune response to infection (Nedeva, 2021; Wayland et al., 2024). It represents a critical syndrome where the body's defense mechanisms, meant to eliminate infection, lead to tissue damage and organ failure. The evolution of sepsis definitions reflects its complex pathophysiology, as earlier criteria were insufficient in identifying the delicate balance between pathogenic virulence factors and host immune responses (Joosten et al., 2024). These guidelines, formulated by the Surviving Sepsis Campaign (SSC), introduced clinical criteria for diagnosing sepsis, highlighting organ dysfunction as a predictor of disease severity (Arora et al., 2023). Septic shock, the more severe form, is identified when sepsis induces persistent hypotension requiring vasopressors and results in elevated lactate levels despite adequate fluid resuscitation (Cinel et al., 2020).

The systemic inflammatory response syndrome (SIRS) criteria, once used to identify sepsis, were eliminated in Sepsis-3 due to their nonspecific nature and lack of clinical efficacy in distinguishing infectious from non-infectious systemic inflammation (He et al., 2024). While the syndrome manifests through infection and the immune response, sepsis occurs when this immune reaction becomes maladaptive, causing harm to the body itself (Mun et al., 2024). The sources of infection leading to sepsis are diverse, including the respiratory tract, abdomen, musculoskeletal system, central nervous system, and genitourinary system (Chou et al., 2020)

Global and Local Burden of Sepsis

Sepsis presents a significant global health challenge, affecting around 31 million individuals annually and leading to approximately six million deaths worldwide (Cassini et al., 2020). The Centers for Disease Control and Prevention (CDC) estimates that in the United States alone, 1.7 million cases of sepsis occur each year, resulting in 270,000 deaths—accounting for one in three hospital-related fatalities (Belden, 2023). The burden of sepsis extends globally, impacting both neonates and children, with an estimated 3 million neonates and 1.2 million children affected annually, contributing to 30% of neonatal deaths (Muzammil et al., 2024; Qin, 2024; Thomson, 2022). In lower-income countries the mortality rate ranges between 60% to 80% for sepsis cases, significantly higher than in high-income countries, where the rate is around 15% for severe sepsis and up to 50% for septic shock (La Via et al., 2024; Machado et al., 2023). The true global epidemiological burden of sepsis remains elusive due to incomplete data, especially from low- and middle-income countries (Barroso, 2023). The majority of studies focus on high-income countries, leaving a gap in understanding the disease's true impact in resource-limited settings.

Clinical Outcomes of Sepsis

Sepsis is associated with high morbidity and mortality, particularly in older patients and those with comorbidities such as diabetes, cardiovascular disease, and autoimmune disorders (Stenberg et al., 2023). Mortality rates in sepsis patients vary widely, from 34.5% in the United States to 37.5% in Australia and New Zealand (Madkour et al., 2022). In addition to short-term mortality, sepsis

survivors face significant long-term complications. Studies show that up to 59% of severe sepsis patients die within five years of the initial episode, and many survivors suffer from cognitive impairments and physical disabilities (Cavaillon et al., 2020). Post-sepsis syndrome, a collection of physical and psychological impairments, is increasingly recognized, affecting survivors' quality of life through muscular weakness, neurocognitive impairments such as anxiety, dementia, and even post-traumatic stress disorder (Taylor et al., 2020).

Sepsis remains a leading cause of mortality and long-term health complications, necessitating ongoing care for survivors, many of whom are re-hospitalized within a year due to complications such as cardiac failure, respiratory distress, and acute renal failure (Nguyen et al., 2006). The complex and heterogeneous nature of sepsis, with its variable clinical outcomes and unpredictable disease trajectory, continues to challenge healthcare systems globally.

Diagnosis of Sepsis

Diagnosing sepsis remains a challenge, as conventional diagnostic methods, such as blood cultures, often fail to identify pathogens in septic patients. Microbial culture has long been considered the gold standard for sepsis diagnosis. However, it is increasingly recognized that conventional blood cultures are often ineffective, especially in critically ill sepsis patients. One study revealed that conventional methods could not identify pathogens in nearly 70% of severe sepsis cases (Heming et al., 2021; Wang et al., 2020)

Polymerase Chain Reaction (PCR) has emerged as a promising diagnostic tool, enabling rapid detection of bacterial DNA in blood samples. Despite its advantages, PCR results remain positive in only 34.7% of severe sepsis cases (Teoh, 2022). One of the major limitations of molecular methods like PCR is their inability to distinguish between colonization and true pathogenic infections. This issue is largely due to the increased sensitivity of PCR, which may detect bacterial DNA even in the absence of an active infection (Deusenbery et al., 2021).

Several reasons account for the failure of cultures in sepsis patients. First, organ failure may occur before the initiation of antibiotic treatment. Second, inappropriate culture techniques or insufficient sample volumes can result in negative results (Martínez et al., 2020). Third, certain resistant or atypical microorganisms are undetectable by traditional cultures, further complicating diagnosis. Lastly, some patients may suffer from non-infectious conditions that mimic sepsis (Chahin & Opal, 2020).

All these challenges highlight significant knowledge gaps in the current understanding of sepsis diagnosis and treatment. While microbial cultures remain the standard diagnostic tool, their limitations necessitate the exploration of other biomarkers and clinical parameters to ensure a timely and accurate diagnosis.

Diagnostic Variables and Biomarkers

In our study we emphasize the role of clinical parameters like sofa and Glasgow coma scale. Procalcitonin and hs crp are also widely used markers for sepsis diagnosis but these are expensive. Although these markers have shown promise in identifying sepsis, they are often expensive and not always accessible, particularly in public healthcare settings like Jinnah Postgraduate Medical Centre (JPMC), where our study was conducted. Given the high patient load and limited resources at such hospitals, finding cost-effective and accessible diagnostic options is essential.

Procalcitonin, for example, is typically secreted only by thyroid C cells in healthy individuals and is cleaved rapidly into calcitonin, with levels below 0.1 ng/ml (Censi et al., 2023). However, during sepsis, proinflammatory factors such as bacterial lipopolysaccharides stimulate the release of procalcitonin from all parenchymal cells in the body. This leads to a significant increase in procalcitonin levels, particularly in patients with bacteremia and multiple organ failure, where levels can exceed 100 ng/ml, making it an effective marker of disease severity (Lee et al., 2022).

Research has also shown that elevated procalcitonin levels are associated with higher mortality rates in sepsis patients. In particular, non-survivors tend to have significantly higher procalcitonin levels

compared to survivors, further supporting its role as a mortality marker in critically ill patients (de Guadiana-Romualdo et al., 2024).

Role of SOFA Score and Clinical Parameters

In addition to biochemical markers, clinical diagnostic tools such as the Sequential Organ Failure Assessment (SOFA) score play a crucial role in predicting sepsis outcomes. The SOFA score assesses the severity of organ dysfunction by evaluating six organ systems: the respiratory, cardiovascular, hepatic, renal, coagulation, and central nervous systems (Kashyap et al., 2021). A higher SOFA score correlates with increased mortality risk and poorer outcomes in ICU patients.

The SOFA score is particularly valuable in resource-limited settings, where it can help stratify patients based on their risk of fatal outcomes. In some ICUs, geriatric patients are often given lower priority than younger patients. However, the SOFA score provides an objective assessment that can guide decision-making, even in low-resource settings (Anireddy, 2024).

Despite its advantages, the SOFA score is difficult to apply in emergency or ward settings, where critical patients may not have immediate access to biochemical tests. Recognizing this limitation, the Sepsis-3 guidelines introduced the quick SOFA (qSOFA) score, which simplifies the SOFA score into three clinical parameters: low blood pressure (systolic BP <100 mmHg), respiratory rate (>22 breaths/min), and altered mental status (Glasgow Coma Scale <15) (Lahiri et al., 2022). This bedside tool allows for rapid assessment and identification of patients at risk of poor outcomes, particularly outside the ICU.

Operational Definitions

Systemic Inflammatory Response Syndrome (SIRS):

SIRS is a severe condition related to systemic inflammation, organ dysfunction, and failure, with or without an infectious cause. To diagnose SIRS, at least two of the following criteria must be met:

Temperature >38°C or <36°C

Respiratory rate >22 breaths per minute or PaCO2 <32 mmHg

Heart rate >90 beats per minute

White blood cell count >12,000/mm³ or <4,000/mm³ (Aliu-Bejta, 2021).

Sepsis:

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated immune response to infection (Cao et al., 2023).

SOFA Score:

The SOFA score evaluates the performance of six organ systems, with higher scores indicating greater organ dysfunction and a higher likelihood of mortality (Liengswangwong et al., 2024).

Quick SOFA (qSOFA):

qSOFA is a bedside assessment tool that identifies patients with suspected infections at risk for poor outcomes. It includes three variables:

Systolic blood pressure <100 mmHg

Respiratory rate >22 breaths per minute

Altered mental status (Glasgow Coma Scale <15) (Singer et al., 2019).

Aims and Objectives of the Study

To evaluate the baseline characteristics of SIRS and sepsis patients using clinical markers, including the Glasgow Coma Scale and SOFA scores.

To analyze and compare clinical outcomes, such as mortality rates and hospital stays, between patients diagnosed with SIRS and sepsis.

Rationale of the Study

The rationale for this study is to address the clinical challenge of differentiating between SIRS and sepsis, two conditions with overlapping features but differing prognoses and treatment strategies. As SIRS has been excluded from the sepsis continuum due to its low clinical specificity, a detailed comparison of baseline characteristics and clinical outcomes between SIRS and sepsis patients is essential. This study aims to provide insights into key clinical markers, such as the Glasgow Coma Scale and Sequential Organ Failure Assessment score, to better predict outcomes and guide treatment decisions, ultimately improving patient care and resource allocation in critical care settings

METHODOLOGY

Study Design

The present study was designed as a prospective cohort observational, hospital-based study. The primary aim was to evaluate and compare the baseline characteristics and clinical outcomes of patients diagnosed with Systemic Inflammatory Response Syndrome (SIRS) and sepsis using clinical and biochemical markers.

Study Setting

The research was conducted in the Department of Clinical Pathology, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi, in collaboration with the following departments:

Intensive Care Unit (ICU), Medical Unit-4, JPMC, Karachi

Surgical Intensive Care Unit, Department of Anesthesiology, JPMC, Karachi

Study Duration:

The study was conducted over a one-year period from June 2023 to June 2024.

Study Population:

The study population consisted of patients admitted to the Medical and Surgical Intensive Care Units (ICUs) of JPMC, Karachi. Patients were assessed for SIRS based on the SIRS criteria, while sepsis was diagnosed according to the Sepsis-3 criteria, as recommended by the Surviving Sepsis Campaign (SSC) guidelines.

Ethical Considerations:

Written informed consent was obtained from all patients or their next of kin before participation in the study. All data were handled confidentially, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Selection of Patients

A total of 200 consecutive adult patients, irrespective of sex, aged 18 years and above, who were admitted to the Medical and Surgical ICUs of JPMC, Karachi, were included in the study. Patients were selected based on predefined inclusion and exclusion criteria.

Inclusion Criteria:

Patients diagnosed with SIRS based on the presence of at least two of the following clinical criteria: Temperature >38°C or <36°CRespiratory rate >22 breaths per minute or PaCO2 <32 mmHgHeart rate >90 beats per minute White blood cell count >12,000/mm³ or <4,000/mm³

Patients diagnosed with sepsis according to the Sepsis-3 criteria, defined as life-threatening organ dysfunction caused by a deregulated host response to infection. Patients admitted to the Medical and Surgical ICUs.

Exclusion Criteria:

Patients below 18 years of age.Pregnant women. Patients with chronic immunosuppressive conditions, including HIV/AIDS, or those receiving long-term steroid therapy. Patients admitted with non-infectious conditions mimicking sepsis.

Data Collection

Upon inclusion in the study, each patient or their next of kin was thoroughly interviewed to gather clinical details related to the illness. The following data were recorded:

Demographic Information: Age, sex, medical history, and comorbidities. **Clinical Data:** Vital signs (e.g., temperature, blood pressure, heart rate, respiratory rate), Glasgow Coma Scale (GCS) score, Sequential Organ Failure Assessment (SOFA) score, **Laboratory Investigations:** White blood cell count, platelet count, serum bilirubin, creatinine levels, , and other relevant biochemical markers.

Outcomes Data: Hospital stay duration, ICU stay, and mortality.

Statistical Analysis

All data were entered into SPSS (Version 23.0) for statistical analysis. Descriptive statistics were used to summarize baseline characteristics. Continuous variables were presented as mean \pm standard deviation (SD) and compared using the t-test or Mann-Whitney U test as appropriate. Categorical variables were presented as frequencies and percentages, and compared using the chi-square test. A p-value of less than 0.05 was considered statistically significant.

The following analyses were performed:

Comparison of Clinical Parameters: The baseline characteristics, including GCS, SOFA, were compared between SIRS and sepsis patients.

Clinical Outcomes: Mortality rates and hospital stay durations were compared between the two groups.

Predictive Value of Clincal Markers: The relationship between SOFA scores, and mortality in sepsis patients was evaluated.

This methodology allowed for a comprehensive assessment of clinical parameters and outcomes in patients with SIRS and sepsis, providing valuable insights into their management in critical care settings.

Results

Baseline Characteristics

A total of 200 patients were included in the study, with 79 diagnosed with Systemic Inflammatory Response Syndrome (SIRS) and 121 diagnosed with sepsis. The baseline characteristics, including demographics, length of hospital, culture results, and mortality rates, are presented in **Table 1**.

Table 1: Baseline Characteristics of SIRS and Sepsis Patients

Characteristics	SIRS $(n = 79)$	Sepsis (n = 121)	p-value
Gender			
Male	41 (51.9%)	58 (47.9%)	0.58
Female	38 (48.1%)	63 (52.1%)	
Age Group			
18-25 years	19 (24.1%)	14 (11.6%)	
26-35 years	13 (16.5%)	8 (6.6%)	
36-45 years	13 (16.5%)	21 (17.4%)	
46-55 years	7 (8.9%)	14 (11.6%)	
56-65 years	11 (13.9%)	21 (17.4%)	0.02*
66-75 years	9 (11.4%)	16 (13.2%)	

>75 years	7 (8.9%)	27 (22.3%)		
Mean \pm SD	45.24 ± 20.2	55.14 ± 19.9		
Ward				
Surgical	9 (11.4%)	18 (14.9%)	0.48	
Medicine	70 (88.6%)	103 (85.1%)		
Culture				
Positive	5 (6.3%)	36 (29.8%)	0.01*	
Negative	74 (93.7%)	85 (70.2%)		
Mortality				
No	68 (86.1%)	50 (41.7%)	<0.01*	
Yes	11 (13.9%)	70 (58.3%)		
Average Length of ICU Stay (Days)	12.36 ± 7.34	15.43 ± 7.46		

The results show significant differences between the SIRS and sepsis groups. Sepsis patients were generally older, with a higher percentage of individuals over 75 years old (22.3% in sepsis vs. 8.9% in SIRS, p = 0.02). Additionally, culture positivity was significantly more common among sepsis patients (29.8% vs. 6.3%, p = 0.01), and the mortality rate was substantially higher in the sepsis group (58.3% vs. 13.9%, p < 0.01).

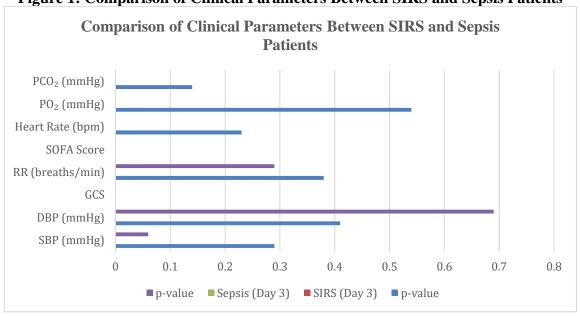
Comparison of Clinical Parameters

Key clinical parameters, such as the Sequential Organ Failure Assessment (SOFA) score, Glasgow Coma Scale (GCS), and other vital signs, were recorded on Day 1 and Day 3. These results are displayed in **Table 4**.

 Table 4: Comparison of Clinical Parameters Between SIRS and Sepsis Patients

Parameters	SIRS (Day 1)	Sepsis (Day 1)	p-value	SIRS (Day 3)	Sepsis (Day 3)	p-value
SBP (mmHg)	90 (25)	90 (20)	0.29	90 (30)	90 (20)	0.06
DBP (mmHg)	60 (20)	50 (20)	0.41	50 (20)	50 (25)	0.69
GCS	14 (5)	7 (7)	<0.01*	15 (5)	7 (8)	<0.01*
RR (breaths/min)	24 (7)	25 (6)	0.38	24 (7)	24 (7)	0.29
SOFA Score	4 (5)	12 (8)	<0.01*	4 (5)	13 (10)	<0.01*
Heart Rate (bpm)	100 (22)	98 (25)	0.23			
PO ₂ (mmHg)	109.5 (45.05)	111 (44.17)	0.54			
PCO ₂ (mmHg)	37.08 (13)	39.72 (13)	0.14			

Figure 1: Comparison of Clinical Parameters Between SIRS and Sepsis Patients



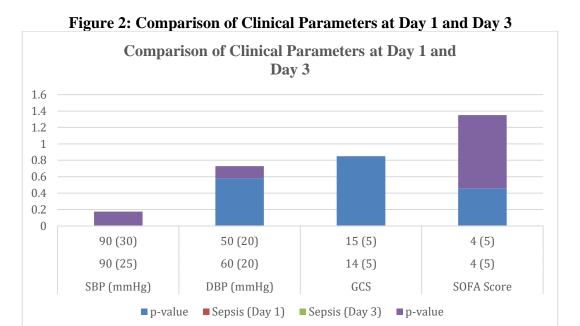
There were significant differences in the SOFA and GCS scores between the two groups at both time points. The sepsis group had significantly higher SOFA scores, indicating greater organ dysfunction (p < 0.01). Additionally, the GCS scores were significantly lower in sepsis patients, reflecting more severe neurological impairment (p < 0.01).

Clinical Outcomes

A comparison of clinical parameters within the SIRS and sepsis groups at Day 1 and Day 3 is shown in **Table 5**.

Table 5: Comparison of Clinical Parameters at Day 1 and Day 3

Parameters	SIRS	(Day	SIRS	(Day	p-	Sepsis	(Day	Sepsis	(Day	p-
	1)		3)		value	1)		3)		value
SBP (mmHg)	90 (25))	90 (30))	0.006*	90 (20)		90 (20)		0.175
DBP (mmHg)	60 (20))	50 (20))	0.58	50 (20)		50 (25)		0.148
GCS	14 (5)		15 (5)		0.85	7 (7)		7 (8)		0.04*
SOFA Score	4 (5)		4 (5)		0.46	12 (8)		13 (10)		0.89



Within the sepsis group, there was a significant change in GCS score from Day 1 to Day 3 (p = 0.04), indicating progressive neurological deterioration. In contrast, the SIRS group showed a significant decrease in systolic blood pressure (SBP) between Day 1 and Day 3 (p = 0.006), suggesting worsening hemodynamic status.

Discussion

The results of our prospective study provide a comprehensive comparative analysis of the baseline characteristics and clinical outcomes of patients diagnosed with Systemic Inflammatory Response Syndrome (SIRS) and sepsis in a resource-limited setting. The findings highlight the significant disparities between these two conditions, particularly in terms of mortality, organ dysfunction, and the utility of clinical markers such as the Sequential Organ Failure Assessment (SOFA) score and Glasgow Coma Scale (GCS).

A key observation from our study is the stark difference in the age distribution and mortality rates between SIRS and sepsis patients. Sepsis patients were significantly older, which aligns with the existing literature, suggesting that advanced age is a critical risk factor for sepsis due to declining immune function and higher prevalence of comorbidities such as cardiovascular disease, diabetes, and chronic kidney disease. In contrast, SIRS patients were generally younger, and their condition was less severe, as evidenced by lower SOFA scores and better GCS ratings. The higher mortality rate in sepsis patients (58.3%) compared to SIRS patients (13.9%) is consistent with global data that show sepsis as a leading cause of death, particularly in older populations with existing health conditions.

The study clearly demonstrates that sepsis is associated with significantly higher levels of organ dysfunction, as indicated by both Day 1 and Day 3 SOFA scores. This result is consistent with previous studies, which have established SOFA as a robust predictor of sepsis outcomes. In this study, the mean SOFA scores for sepsis patients were substantially higher than those for SIRS patients, underlining the utility of this score in stratifying patients by the severity of their illness . The correlation between higher SOFA scores and increased mortality in sepsis patients further validates its use as a diagnostic and prognostic tool, especially in settings where more advanced diagnostic techniques may not be readily available .

Interestingly, our study also observed that SIRS patients had relatively stable SOFA scores over the course of their ICU stay, whereas sepsis patients experienced worsening scores, reflecting ongoing organ dysfunction despite medical intervention. This highlights the more progressive and damaging nature of sepsis compared to SIRS, underscoring the importance of early recognition and aggressive treatment of sepsis to mitigate worsening outcomes .

The deterioration in both hemodynamic and neurological function in sepsis patients, as evidenced by lower blood pressure and higher respiratory rates, is another critical finding. Sepsis-induced hypotension is a well-recognized marker of disease severity, often necessitating vasopressor support, as seen in many of our sepsis patients. These hemodynamic alterations are indicative of septic shock, which, when untreated, leads to multi-organ failure and significantly increases the risk of death .

Neurologically, sepsis patients also presented with lower GCS scores compared to SIRS patients, suggesting that sepsis has a more profound impact on consciousness and cognitive function. This finding supports previous reports that altered mental status is a key feature of sepsis and septic shock, often associated with the development of sepsis-associated encephalopathy (SAE). GCS scores, along with SOFA, proved valuable not only for initial patient assessment but also for monitoring clinical progression .

Another important outcome from this study is the significantly higher rate of culture positivity in sepsis patients (29.8%) compared to SIRS patients (6.3%). The presence of a positive microbial culture provides definitive evidence of infection, which distinguishes sepsis from SIRS—a condition that can occur due to non-infectious causes such as trauma or pancreatitis. This result reinforces the Sepsis-3 definition of sepsis as an infection-driven syndrome of organ dysfunction, while also highlighting the limitations of culture-based diagnostics in resource-limited settings like Jinnah Postgraduate Medical Centre (JPMC). A relatively low rate of culture positivity in sepsis patients (less than one-third) mirrors global trends where conventional blood cultures fail to identify pathogens in up to 70% of severe sepsis cases. This gap in diagnostics underscores the need for rapid, reliable, and affordable molecular diagnostics, such as PCR, particularly in low- and middle-income countries (LMICs).

The findings from our study have profound implications for clinical practice, especially in LMICs where healthcare infrastructure may be inadequate to manage complex conditions like sepsis. The high mortality rate observed in sepsis patients points to the need for early diagnosis and prompt intervention, which are critical for improving outcomes in such settings. The utility of the SOFA and GCS scores as predictive tools is particularly valuable in resource-limited hospitals like JPMC, where access to advanced diagnostics is often constrained.

Furthermore, the study highlights the need for improved infection control measures and the development of cost-effective diagnostic strategies to reduce the burden of sepsis in LMICs. This includes strengthening the capacity for microbiological testing, expanding access to affordable biomarkers such as procalcitonin, and improving sepsis management protocols, which may help reduce the unacceptably high mortality rate associated with this condition.

Limitations of the Study

While the study provides valuable insights into the differences between SIRS and sepsis, there are several limitations that must be acknowledged. First, the relatively small sample size may limit the generalizability of our findings to other populations, particularly in different geographic regions or healthcare settings. Second, the reliance on culture-based diagnostics in a resource-limited setting may have underestimated the true burden of infection in sepsis patients. Future studies should incorporate more advanced molecular diagnostics to overcome these limitations.

Conclusion

This study provides valuable insights into the clinical differences between SIRS and sepsis patients, emphasizing the critical role of diagnostic markers such as the SOFA score and Glasgow Coma Scale in predicting patient outcomes. The high mortality rate observed in sepsis patients (58.3%) reflects the severe impact of sepsis in resource-limited settings like JPMC, Karachi, where delayed diagnosis and limited access to advanced care significantly contribute to poorer outcomes.

Our findings highlight the need for rapid, cost-effective diagnostic tools and timely interventions, especially in low- and middle-income countries, where the burden of sepsis is disproportionately high. The significant differences in organ dysfunction, as indicated by higher SOFA scores and lower GCS scores in sepsis patients, underscore the complexity of sepsis and the need for improved clinical management strategies.

In conclusion, this study reinforces the importance of early recognition and targeted treatment in sepsis management. Efforts should focus on enhancing diagnostic capabilities, improving critical care resources, and developing tailored strategies to reduce sepsis-related mortality in resource-constrained environments. Further research is essential to address the challenges in sepsis diagnosis and treatment, particularly in low-income settings, to ultimately improve patient survival and outcomes.

References

- 1. Aliu-Bejta, A. (2021). *Prognostic impact of increased serum presepsin concentrations on sepsis outcome* University of Zagreb. School of Medicine].
- 2. Anireddy, D. (2024). ENHANCING CLINICAL DECISION-MAKING IN LOW-RESOURCE SETTINGS: COMPARING MORTALITY RISK SCORES FOR ADULT CRITICAL CARE PATIENTS IN LESOTHO DURING THE COVID-19 PANDEMIC Johns Hopkins University].
- 3. Arora, J., Mendelson, A. A., & Fox-Robichaud, A. (2023). Sepsis: network pathophysiology and implications for early diagnosis. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 324(5), R613-R624.
- 4. Barroso, J. M. L. A. (2023). Sepsis endotypes and phenotypes: biomarkers and clinical phenotypes upon ICU admission: a systematic review.
- 5. Belden, B. (2023). *The Impact of Sepsis Screening Integration in the Outpatient Setting*. Oklahoma City University.
- 6. Cao, M., Wang, G., & Xie, J. (2023). Immune dysregulation in sepsis: experiences, lessons and perspectives. *Cell Death Discovery*, *9*(1), 465.
- 7. Cassini, A., Allegranzi, B., Fleischmann-Struzek, C., Kortz, T., Markwart, R., Saito, H., Bonet, M., Brizuela, V., Mehrtash, H., & Tuncalp Mingard, Ö. (2020). Global Report on the epidemiology and burden on sepsis: current evidence, identifying gaps and future directions. Global Report on the epidemiology and burden on sepsis: current evidence, identifying gaps and future directions.
- 8. Cavaillon, J. M., Singer, M., & Skirecki, T. (2020). Sepsis therapies: learning from 30 years of failure of translational research to propose new leads. *EMBO molecular medicine*, *12*(4), e10128.
- 9. Censi, S., Manso, J., & Mian, C. (2023). Other markers of medullary thyroid cancer, not only calcitonin. *European Journal of Endocrinology*, *188*(1), R1-R13.

- 10. Chahin, A., & Opal, S. M. (2020). The Clinical Approach to Sepsis and Its Mimics in the Critical Care Unit. In *Infectious Diseases and Antimicrobial Stewardship in Critical Care Medicine* (pp. 147-154). CRC Press.
- 11. Chou, E. H., Mann, S., Hsu, T.-C., Hsu, W.-T., Liu, C. C.-Y., Bhakta, T., Hassani, D. M., & Lee, C.-C. (2020). Incidence, trends, and outcomes of infection sites among hospitalizations of sepsis: a nationwide study. *PloS one*, *15*(1), e0227752.
- 12. Cinel, I., Kasapoglu, U. S., Gul, F., & Dellinger, R. P. (2020). The initial resuscitation of septic shock. *Journal of Critical Care*, *57*, 108-117.
- 13. de Guadiana-Romualdo, L. G., Botella, L. A., Rojas, C. R., Candel, A. P., Sánchez, R. J., Zamora, P. C., Albaladejo-Otón, M. D., & Allegue-Gallego, J. M. (2024). Mortality prediction model from combined serial lactate, procalcitonin and calprotectin levels in critically ill patients with sepsis: A retrospective study according to Sepsis-3 definition. *Medicina Intensiva (English Edition)*.
- 14. Deusenbery, C., Wang, Y., & Shukla, A. (2021). Recent innovations in bacterial infection detection and treatment. *ACS Infectious Diseases*, 7(4), 695-720.
- 15. He, R.-R., Yue, G.-L., Dong, M.-L., Wang, J.-Q., & Cheng, C. (2024). Sepsis Biomarkers: Advancements and Clinical Applications—A Narrative Review. *International Journal of Molecular Sciences*, 25(16), 9010.
- 16. Heming, N., Azabou, E., Cazaumayou, X., Moine, P., & Annane, D. (2021). Sepsis in the critically ill patient: current and emerging management strategies. *Expert Review of Anti-Infective Therapy*, 19(5), 635-647.
- 17. Joosten, S. C., Wiersinga, W. J., & van der Poll, T. (2024). Dysregulation of Host–Pathogen Interactions in Sepsis: Host-Related Factors. Seminars in Respiratory and Critical Care Medicine,
- 18. Kashyap, R., Sherani, K. M., Dutt, T., Gnanapandithan, K., Sagar, M., Vallabhajosyula, S., Vakil, A. P., & Surani, S. (2021). Current utility of sequential organ failure assessment score: a literature review and future directions. *The Open Respiratory Medicine Journal*, 15, 1.
- 19. La Via, L., Sangiorgio, G., Stefani, S., Marino, A., Nunnari, G., Cocuzza, S., La Mantia, I., Cacopardo, B., Stracquadanio, S., & Spampinato, S. (2024). The Global Burden of Sepsis and Septic Shock. *Epidemiologia*, *5*(3), 456-478.
- 20. Lahiri, R., Rehan, M., Banerjee, S., Gadre, S., Paul, P., & Gupta, S. (2022). The Utility of SOFA Score and Acute Physiology and Chronic Health Evaluation (APACHE II) Score in Analysing Patients with Multiple Organ Dysfunction Syndrome and Sepsis. *International Journal of Medical and All Body Health Research*, *3*(04), 18-47.
- 21. Lee, S., Song, J., Park, D. W., Seok, H., Ahn, S., Kim, J., Park, J., Cho, H.-j., & Moon, S. (2022). Diagnostic and prognostic value of presepsin and procalcitonin in non-infectious organ failure, sepsis, and septic shock: a prospective observational study according to the Sepsis-3 definitions. *BMC infectious diseases*, 22(1), 8.
- 22. Liengswangwong, W., Siriwannabhorn, R., Leela-Amornsin, S., Yuksen, C., Sanguanwit, P., Duangsri, C., Kusonkhum, N., & Saelim, P. (2024). Comparison of Modified Early Warning Score (MEWS), Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation II (APACHE II) for early prediction of septic shock in diabetic patients in Emergency Departments. *BMC Emergency Medicine*, 24(1), 161.
- 23. Machado, F. R., Cavalcanti, A. B., Braga, M. A., Tallo, F. S., Bossa, A., Souza, J. L., Ferreira, J. F., Pizzol, F. d., Monteiro, M. B., & Angus, D. C. (2023). Sepsis in Brazilian emergency departments: a prospective multicenter observational study. *Internal and Emergency Medicine*, 18(2), 409-421.
- 24. Madkour, A. M., ELMaraghy, A. A., & Elsayed, M. M. (2022). Prevalence and outcome of sepsis in respiratory intensive care unit. *The Egyptian Journal of Bronchology*, *16*(1), 29.
- 25. Martínez, M. L., Plata-Menchaca, E. P., Ruiz-Rodríguez, J. C., & Ferrer, R. (2020). An approach to antibiotic treatment in patients with sepsis. *Journal of thoracic disease*, *12*(3), 1007.

- 26. Mun, S.-J., Cho, E., Kim, H. K., Gil, W. J., & Yang, C.-S. (2024). Enhancing acute inflammatory and sepsis treatment: superiority of membrane receptor blockade. *Frontiers in Immunology*, *15*, 1424768.
- 27. Muzammil, M. M., Mohiuddin, M. F., Arif, A., & Qurram, S. M. N. (2024). MICROBIOLOGICAL PROFILE OF NEONATAL SEPSIS IN NICU OF TERTIARY CARE HOSPITAL. *Int J Acad Med Pharm*, *6*(2), 824-828.
- 28. Nedeva, C. (2021). Inflammation and cell death of the innate and adaptive immune system during sepsis. *Biomolecules*, 11(7), 1011.
- 29. Nguyen, H. B., Rivers, E. P., Abrahamian, F. M., Moran, G. J., Abraham, E., Trzeciak, S., Huang, D. T., Osborn, T., Stevens, D., & Talan, D. A. (2006). Severe sepsis and septic shock: review of the literature and emergency department management guidelines. *Annals of emergency medicine*, 48(1), 54. e51.
- 30. Qin, Y. (2024). *Deriving Biological Meaning and Clinical Application for Pediatric Sepsis with Data-driven Analysis* University of Pittsburgh].
- 31. Stenberg, H., Li, X., Pello-Esso, W., Lönn, S. L., Thønnings, S., Khoshnood, A., Knudsen, J. D., Sundquist, K., & Jansåker, F. (2023). The effects of sociodemographic factors and comorbidities on sepsis: A nationwide Swedish cohort study. *Preventive medicine reports*, *35*, 102326.
- 32. Taylor, S. P., Chou, S.-H., Sierra, M. F., Shuman, T. P., McWilliams, A. D., Taylor, B. T., Russo, M., Evans, S. L., Rossman, W., & Murphy, S. (2020). Association between adherence to recommended care and outcomes for adult survivors of sepsis. *Annals of the American Thoracic Society*, *17*(1), 89-97.
- 33. Teoh, T. K. (2022). The role and impact of molecular diagnostics in modern clinical microbiology University of Limerick].
- 34. Thomson, K. (2022). Assessment of antibiotic resistance in pathogens causing neonatal sepsis, associated mortality and recommended treatment options in low-and middle-income countries Cardiff University].
- 35. Wang, M., Jiang, L., Zhu, B., Li, W., Du, B., Kang, Y., Weng, L., Qin, T., Ma, X., & Zhu, D. (2020). The prevalence, risk factors, and outcomes of sepsis in critically ill patients in China: a multicenter prospective cohort study. *Frontiers in Medicine*, 7, 593808.
- 36. Wayland, J., Teixeira, J. P., & Nielsen, N. D. (2024). Sepsis in 2024: A Review. *Anaesthesia & Intensive Care Medicine*.