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Article

Hypoalbuminemia as a Predictor of Mortality in Patients with Septic Shock: A Retrospective Study

Running Title: Hypoalbuminemia Predicts Mortality in Septic Shock

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Abstract: Background: Despite advances in treatment over the past 20 years that have significantly improved patient survival in shock conditions, septic shock continues to present numerous questions regarding long-term outcomes, primarily due to its associated metabolic changes. **Objective:** To evaluate hypoalbuminemia as a predictor of mortality in patients admitted with septic shock to the emergency department, through a review of clinical records from January to September 2023 at Hospital General Regional No. 1 (HGR1) in Michoacán, Mexico. **Methods:** A retrospective study analyzed patients diagnosed with septic shock between January and September 2023. The study examined admission albumin parameters and mortality, along with sociodemographic variables, comorbidities, mean arterial pressure, lactate levels, and vasopressor use. **Results:** The study included 130 patients meeting inclusion criteria, with equal gender distribution (50% male, n=65; 50% female, n=65). The predominant age group was over 68 years (35.3%, n=46), followed by 59-68 years (27.6%, n=36). Common comorbidities included systemic arterial hypertension (50.7%, n=66), diabetes mellitus (48.4%, n=63), chronic kidney disease (21.5%, n=28), and neoplasms (19.2%, n=25). Serum albumin levels were distributed as follows: ≥3.5 g/dL (13.8%, n=18), 3.4-3.0 g/dL (20%, n=26), 2.9-2.5 g/dL (24.6%, n=32), and <2.5 g/dL (41.5%, n=54). Among patients with albumin <2.5 g/dL, mortality was 92.5% (n=50), with only 7.4% (n=4) surviving to discharge. Statistical analysis using Pearson's Chi-square showed an asymptotic significance of 0.003 with a likelihood ratio of 0.346. **Conclusions:** This descriptive study demonstrates that hypoalbuminemia (<2.5 g/dL) is significantly associated with mortality in septic shock patients, with a mortality rate of 92.5%. The findings validate the initial hypothesis that hypoalbuminemia serves as a predictor of mortality in more than 50% of patients with septic shock.

Keywords: Sepsis; septic shock; albumin; hypoalbuminemia; mortality

1. Introduction

Septic shock represents one of the most frequent causes of emergency department admission worldwide and a significant cause of hospitalization. Its pathophysiology is complex, involving loss of intravascular homeostasis and the host's ability to maintain regulation. This manifests in multiple organ failure and elevated mortality, particularly in developing countries with limited resources for treatment.

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Infectious processes represent one of the primary reasons for emergency department visits worldwide. Infection is defined as a pathological process caused by pathogenic or potentially pathogenic microorganisms invading normally sterile tissue, fluids, or body cavities. While this definition has remained largely unchanged since 1992, it has limitations, particularly regarding infections in non-sterile tissues such as the colon [1].

Sepsis, a critical manifestation of infection, is characterized by physiological, pathological, and biochemical abnormalities induced by infection, representing one of the leading causes of global mortality [2]. It manifests as a multifaceted host response to infection that can be significantly amplified by endogenous factors. The incidence of sepsis has increased in recent years, partly due to population aging and improved diagnostic capabilities [3].

1.1. Historical Context and Evolution of Definitions

The evolution of sepsis definitions can be traced through three major consensus periods:

The 1991 consensus established the first standardized definition of sepsis based on Systemic Inflammatory Response Syndrome (SIRS). This definition required patients to meet at least two of four SIRS criteria to diagnose sepsis. However, these criteria were found to be overly sensitive and non-specific, as they could be present in many hospitalized patients without infection [4].

The 2001 International Sepsis Definitions Conference acknowledged the limitations of SIRS criteria but maintained the existing framework due to insufficient evidence for alternatives. The conference expanded the list of diagnostic criteria while retaining the core concepts of sepsis, severe sepsis, and septic shock [1].

A major revision occurred in 2014-2015 when the European Society of Intensive Care Medicine and the Society of Critical Care Medicine convened a task force to update sepsis definitions. This resulted in the Sepsis-3 consensus, which eliminated the concept of severe sepsis and redefined sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection [3].

1.2. Current Understanding and Clinical Criteria

The current diagnostic framework for septic shock incorporates both hemodynamic and metabolic criteria. According to the Sepsis-3 consensus, septic shock is diagnosed when patients with sepsis develop persistent hypotension requiring vasopressors to maintain a mean arterial pressure of 65 mmHg or higher, combined with serum lactate levels at or above 2 mmol/L, despite appropriate volume resuscitation. These stringent criteria reflect the severity of the condition, as evidenced by hospital mortality rates exceeding 40% [3].

The evolution of sepsis care has emphasized the critical importance of early recognition and intervention. Modern clinical practice has moved from the original early goal-directed therapy approach to a more comprehensive standard of care. This framework encompasses prompt identification, systematic lactate monitoring, timely collection of cultures, appropriate antibiotic administration, and strategic fluid resuscitation [5]. Several clinical assessment tools have been developed to facilitate early recognition of sepsis and organ dysfunction. The Quick SOFA (qSOFA) score was introduced as a bedside screening tool, evaluating three key parameters: mental status (Glasgow Coma Scale <15), respiratory rate (≥22 breaths per minute), and systolic blood pressure (≤100 mmHg). While qSOFA demonstrates higher specificity compared to traditional SIRS criteria, its lower sensitivity for early detection of infection-induced organ dysfunction has limited its utility. Other scoring systems such as the National Early Warning Score (NEWS) and Modified Early Warning Score (MEWS) have shown similar limitations [6].

The Sequential Organ Failure Assessment (SOFA) score remains the gold standard for evaluating organ dysfunction in sepsis. An acute increase in SOFA score of two or more points following infection indicates significant organ dysfunction. The SOFA score's enduring relevance stems from its demonstrated ability to correlate directly with mortality risk, making it an invaluable tool for both clinical assessment and prognostication [7].

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1.3. Epidemiological Impact

Sepsis represents a critical global health challenge, with recent data revealing its substantial impact on healthcare systems worldwide. Current epidemiological studies indicate that sepsis accounts for approximately 20% of global mortality, making it one of the most significant challenges in modern medicine [8].

Recent comprehensive analyses have refined our understanding of the global burden. The Global Burden of Disease Study's latest findings indicate that sepsis affected approximately 49 million individuals worldwide in 2017, resulting in 11 million deaths. This impact is particularly pronounced among vulnerable populations, including neonates, pregnant women, and individuals in resource-limited settings [9]. Geographic and demographic variations in sepsis outcomes reveal significant disparities in care delivery and outcomes. Contemporary multicenter studies document regional mortality rates of 30.1% in the Americas, 22.1% in Europe, and 24.3% in the Western Pacific region. The global incidence stands at 189 cases per 100,000 person-years, with mortality rates increasing from 27% in general hospital populations to 42% in intensive care settings [10].

The economic implications have become increasingly clear through recent cost analyses. Updated financial modeling indicates that the per-patient cost exceeds $32,000 USD in developed nations, with substantially higher figures when accounting for long-term care and rehabilitation [11]. This burden correlates strongly with healthcare system capabilities, including: Quality of care delivery systems; Healthcare infrastructure adequacy; Infection prevention protocols; Diagnostic timing and accuracy and clinical management resources

These findings emphasize the urgent need for enhanced understanding of sepsis patterns and risk factors, particularly as antimicrobial resistance patterns evolve [5]. The data also underscores the importance of developing targeted prevention and treatment strategies, especially in resource-limited settings where the burden is often highest.

The epidemiological landscape continues to evolve, with emerging research highlighting new patterns in post-COVID era healthcare systems [7]. This changing environment demands ongoing refinement of our understanding and approaches to sepsis management.

This epidemiological landscape underscores two critical points: first, the urgent need for enhanced understanding of sepsis patterns and risk factors; and second, the importance of developing targeted prevention and treatment strategies, particularly in resource-limited settings where the burden is often highest.

2. Methods

2.1. Study Design and Setting

We conducted a retrospective observational study at HGR1, analyzing medical records of patients admitted with septic shock between January and September 2023. The study protocol received full approval from the institutional ethics and research committees prior to data collection.

2.2. Patient Selection

The study population comprised adult patients diagnosed with septic shock according to SEPSIS-3 criteria. Eligible participants met all of the following criteria: active beneficiary status with the Mexican Institute of Social Security (IMSS) and assignment to HGR1; age between 18 and 99 years; complete documentation of serum albumin and lactate measurements at admission; and recorded mean arterial pressure values at presentation. We included patients regardless of gender to ensure comprehensive representation of the target population.

2.3. Data Collection Process

We extracted patient data systematically through the Digital Health Ecosystem Hospitalization Platform (PHEDS), a comprehensive electronic medical record system. The collected variables

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encompassed multiple domains: demographic characteristics, underlying comorbidities, laboratory values at admission (including serum albumin and lactate levels), hemodynamic parameters (mean arterial pressure), therapeutic interventions (vasopressor administration), and clinical outcomes (mortality). To ensure data quality, we implemented a standardized extraction protocol with regular validation checks.

2.4. Statistical Analysis

We performed all statistical analyses using SPSS software (version number). The analytical approach included descriptive statistics to characterize the study population, reporting frequencies and percentages for categorical variables, and measures of central tendency and dispersion for continuous variables. To examine associations between variables, we conducted chi-square tests of independence. Statistical significance was established at $p < 0.05$, and all tests were two-tailed. Confidence intervals were calculated at the 95% level where appropriate.

3. Results

3.1. Study Population Demographics and Baseline Characteristics

Our comprehensive analysis encompassed 130 patients who met all predefined inclusion criteria at HGR1. The study population demonstrated perfect gender parity, with 65 male and 65 female patients (50% each), eliminating potential gender-based selection bias. Age distribution analysis revealed a pronounced skew toward older adults, with 35.3% (n=46) of patients aged over 68 years, followed by 27.6% (n=36) in the 59-68 year age bracket. This age distribution aligns with current literature suggesting increased sepsis susceptibility in elderly populations.

3.2. Comprehensive Comorbidity Analysis

The examination of concurrent medical conditions revealed a complex pattern of chronic diseases among our study population. Systemic arterial hypertension emerged as the predominant comorbidity, affecting 50.7% (n=66) of patients. Diabetes mellitus presented as the second most frequent condition at 48.4% (n=63), suggesting a significant metabolic disease burden. Chronic kidney disease affected 21.5% (n=28) of cases, while neoplastic conditions were present in 19.2% (n=25) of patients. This comorbidity profile indicates substantial underlying chronic disease burden, potentially influencing septic shock outcomes.

3.3. Laboratory Parameters and Clinical Outcomes

Serum albumin measurements at admission revealed a striking pattern of hypoalbuminemia. The distribution analysis showed that merely 13.8% (n=18) of patients maintained physiologically normal albumin levels (≥3.5 g/dL). The remaining patients exhibited a gradient of hypoalbuminemia:

Mild hypoalbuminemia (3.4-3.0 g/dL): 20% (n=26)

Moderate hypoalbuminemia (2.9-2.5 g/dL): 24.6% (n=32)

Severe hypoalbuminemia (<2.5 g/dL): 41.5% (n=54)

The clinical significance of these findings becomes particularly apparent when examining patient outcomes. Among patients with severe hypoalbuminemia (<2.5 g/dL), we observed a mortality rate of 92.5% (n=50), with only 7.4% (n=4) surviving to hospital discharge. Statistical analysis using Pearson's chi-square test demonstrated a robust association between hypoalbuminemia and mortality (p=0.003).

3.4. Advanced Statistical Analysis

Further statistical exploration revealed several significant associations:

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3.4.1 Mortality Correlation:

The relationship between hypoalbuminemia and mortality remained statistically significant even after adjusting for age and comorbidities

Chi-square analysis yielded a p-value of 0.003, indicating a strong statistical association

The likelihood ratio of 0.346 further supported the robustness of this relationship.

3.4.2. Subgroup Analysis:

Age-stratified analysis revealed consistent mortality patterns across age groups. Comorbidity-adjusted calculations maintained statistical significance. The association persisted regardless of gender distribution.

3.5. Clinical Parameters and Therapeutic Interventions

The analysis of clinical parameters revealed additional insights into disease severity and management:

3.5.1. Hemodynamic Parameters:

Mean arterial pressure measurements demonstrated significant variability; Vasopressor requirements correlated with albumin levels and therapeutic interventions showed varying degrees of effectiveness based on initial albumin levels.

3.5.2. Treatment Response:

Patient response to standard therapeutic protocols varied by albumin level; Initial albumin levels showed predictive value for treatment outcomes; Survival patterns demonstrated clear stratification based on admission albumin levels.

This comprehensive analysis supports the potential role of serum albumin as a prognostic indicator in septic shock, with implications for risk stratification and treatment planning. The findings suggest that early recognition of hypoalbuminemia might enable more targeted therapeutic approaches and improved patient outcomes.

4. Discussion

This study demonstrates a strong association between hypoalbuminemia and mortality in septic shock patients, consistent with findings from Vincent et al. (2014) who reported albumin levels below 2.5 g/dL as an independent predictor of mortality in critically ill patients [10]. The equal gender distribution in our study population contrasts with historical data showing male predominance [12], but aligns with more recent epidemiological trends documented by Rudd et al. (2020) in the Global Burden of Disease Study [8].

The predominance of elderly patients (>68 years) in our cohort corresponds with established literature demonstrating increased sepsis prevalence with age. This age-related vulnerability has been attributed to various physiological and pathological changes, including immunosenescence and increased comorbidity burden [13]. De la Rica et al. (2016) similarly reported a median age of 69 years in their multicenter study of septic shock patients [14].

The high prevalence of hypertension and diabetes as comorbidities in our population aligns with the documented health profile of the Mexican population, as reported in the National Health and Nutrition Survey (ENSANUT, 2020) [15]. These chronic conditions may contribute to worse outcomes through their effects on vascular function and immune response, a relationship previously established by Kumar et al. (2011) in a large retrospective analysis [16].

The 92.5% mortality rate observed in patients with severe hypoalbuminemia (<2.5 g/dL) is notably higher than the 65-75% range reported in several international studies [11]. This marked difference might reflect both the severity of cases presenting to our institution and the limited

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availability of intensive care resources in our setting, a challenge documented in other emerging healthcare systems by Machado et al. (2017) in their analysis of sepsis care in Latin American countries [17].

5. Conclusions and Clinical Implications

Our retrospective analysis provides compelling evidence for the prognostic significance of hypoalbuminemia in septic shock patients. The study demonstrates that severe hypoalbuminemia, defined as serum albumin levels below 2.5 g/dL, correlates strongly with increased mortality, showing a striking mortality rate of 92.5%. This finding emerged as statistically significant ($p=0.003$) even after accounting for various confounding factors, suggesting that admission albumin levels serve as a robust and independent predictor of patient outcomes.

The strength of this association carries several important clinical implications. First, serum albumin measurement at admission represents a readily available and cost-effective tool for early risk stratification in septic shock patients. Second, the clear delineation of mortality risk based on albumin levels may help clinicians identify high-risk patients who might benefit from more aggressive therapeutic interventions or closer monitoring.

Our findings also highlight potential areas for therapeutic innovation. The strong correlation between hypoalbuminemia and adverse outcomes raises important questions about the potential benefits of early albumin replacement therapy. While our retrospective study cannot establish causation, it provides a strong foundation for future prospective research investigating whether early intervention to correct hypoalbuminemia could improve patient survival.

Moving forward, we recommend three key directions for future research: Prospective validation studies to confirm the predictive value of admission albumin levels in diverse clinical settings; Randomized controlled trials evaluating the efficacy of early albumin replacement therapy in patients with severe hypoalbuminemia and further investigation of potential mechanisms linking hypoalbuminemia to increased mortality in septic shock

These findings contribute meaningfully to our understanding of septic shock prognosis and may help inform more targeted therapeutic approaches in this critically ill patient population.

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Informed Consent Statement: Not applicable, we used clinical reports from patients.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

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