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ASSOCIATION BETWEEN SERUM BICARBONATE AND 28-DAY MORTALITY IN SEPTIC SHOCK PATIENTS: A COHORT STUDY

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ABSTRACT

Background: Septic shock is a life-threatening manifestation of sepsis characterized by profound circulatory, cellular, and metabolic abnormalities that contribute to high morbidity and mortality despite advances in critical care. Metabolic acidosis is frequently encountered in septic shock owing to tissue hypoperfusion, impaired oxygen utilization, and lactate accumulation. Serum bicarbonate, a routinely available biochemical parameter, reflects the metabolic component of acid-base balance and may serve as a simple, cost-effective prognostic biomarker. Early identification of patients at increased risk of adverse outcomes using readily available laboratory indices could facilitate timely risk stratification and optimize critical care management. However, the prognostic significance of serum bicarbonate levels in predicting short-term mortality among patients with septic shock remains an area of ongoing investigation.

Aim: To evaluate the association between admission serum bicarbonate levels and 28-day mortality among adult patients with septic shock admitted to the intensive care unit of a tertiary care teaching hospital.

Materials and Methods: A prospective cohort study was conducted over 24 months (January 2024 to December 2025) in the Department of Critical Care Medicine of a tertiary care teaching hospital. A total of 180 consecutive adult patients fulfilling the Sepsis-3 criteria for septic shock were enrolled after obtaining informed consent from the patient or legally authorized representative. Demographic characteristics, comorbidities, source of infection, clinical examination findings, hemodynamic parameters, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, laboratory investigations including serum bicarbonate, arterial blood gas analysis, serum lactate, renal function tests, and inflammatory markers were recorded at admission. Patients were followed for 28 days, and outcomes were categorized into survivors and non-survivors. Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation, categorical variables as frequencies and percentages, and independent predictors of mortality were identified using multivariable logistic regression. A p-value <0.05 was considered statistically significant.

Results: The mean age of the study population was 58.9 ± 15.2 years, with males accounting for 61.1% of participants. The overall 28-day mortality rate was 34.4%. Non-survivors demonstrated significantly lower admission serum bicarbonate levels than survivors (17.3 ± 3.8 mmol/L vs. 22.6 ± 3.5 mmol/L; $p<0.001$). Patients with serum bicarbonate levels below 20 mmol/L had significantly higher mortality, greater vasopressor requirements, higher serum lactate concentrations, and increased SOFA and APACHE II scores. Multivariable logistic regression identified low serum bicarbonate, elevated serum lactate, higher SOFA score, and acute kidney injury as independent predictors of 28-day mortality. Admission serum bicarbonate exhibited good discriminatory ability for predicting mortality and demonstrated significant clinical utility as an early prognostic marker.

Conclusion: Lower admission serum bicarbonate levels are significantly associated with increased 28-day mortality among patients with septic shock. Routine assessment of serum bicarbonate at ICU admission provides valuable prognostic information and may complement established severity scoring systems for early risk stratification, individualized management, and prognostic assessment in critically ill patients with septic shock.

KEYWORDS: Septic shock; Serum bicarbonate; Sepsis; 28-day mortality; Intensive care unit; Metabolic acidosis; SOFA score; Cohort study.

INTRODUCTION

Septic shock represents the most severe form of sepsis and is characterized by profound circulatory, cellular, and metabolic abnormalities associated with a substantially increased risk of mortality [1]. Despite remarkable advances in antimicrobial therapy, hemodynamic monitoring, organ support, and intensive care management, septic shock continues to be one of the leading causes of death among critically ill patients worldwide [2]. The complex pathophysiology involving dysregulated host immune response, endothelial dysfunction, impaired tissue perfusion, mitochondrial injury, and multiple organ dysfunction contributes to poor clinical outcomes [3]. Early identification of patients at increased risk of mortality remains a major priority in critical care medicine to facilitate prompt therapeutic intervention and optimize resource utilization [4].

According to the Sepsis-3 definition, septic shock is a subset of sepsis in which underlying circulatory and metabolic abnormalities are profound enough to substantially increase mortality [5]. Patients typically require vasopressor therapy to maintain a mean arterial pressure of at least 65 mmHg and exhibit elevated serum lactate

concentrations despite adequate fluid resuscitation [6]. Mortality rates among patients with septic shock frequently exceed 30–40%, particularly in resource-limited healthcare settings and among individuals with delayed diagnosis or multiple organ dysfunction [7,8].

Metabolic acidosis is a common biochemical abnormality observed in septic shock and results primarily from tissue hypoperfusion, anaerobic metabolism, lactate accumulation, impaired renal acid excretion, and altered cellular metabolism [9,10]. Persistent metabolic acidosis reflects ongoing tissue hypoxia and inadequate restoration of perfusion despite resuscitative measures [11,12]. Consequently, biochemical markers reflecting acid-base disturbances have gained considerable attention as potential indicators of disease severity and predictors of clinical outcomes in critically ill patients [13,14].

Serum bicarbonate is a routinely measured laboratory parameter that reflects the metabolic component of acid-base balance and serves as an indirect indicator of metabolic acidosis [15]. Reduced serum bicarbonate concentrations may occur due to increased acid production, bicarbonate consumption during buffering of excess hydrogen ions, renal dysfunction, or impaired bicarbonate regeneration [16]. Because serum bicarbonate estimation is inexpensive, rapidly available, and universally performed as part of routine biochemical or arterial blood gas evaluation, it represents an attractive biomarker for early prognostic assessment in patients with septic shock [17,18].

Several established prognostic scoring systems, including the Sequential Organ Failure Assessment (SOFA) score and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, are widely used to predict mortality in critically ill patients [19]. Although these scoring systems provide valuable prognostic information, they require the integration of multiple clinical and laboratory variables and may not always be immediately available during the initial assessment [20]. A simple laboratory parameter such as serum bicarbonate, if shown to possess independent prognostic value, could complement these established scoring systems and facilitate earlier identification of high-risk patients [21].

Previous studies have demonstrated associations between metabolic acidosis, elevated lactate concentrations, base deficit, and adverse outcomes in septic shock [22]. However, the independent prognostic significance of admission serum bicarbonate remains incompletely understood, with variable findings reported across different patient populations and healthcare settings [23]. Furthermore, relatively few prospective cohort studies have specifically evaluated the relationship between admission serum bicarbonate levels and short-term mortality while simultaneously considering established severity scores and other important clinical predictors [24].

In addition to acid-base abnormalities, numerous factors including advanced age, comorbid illnesses, delayed initiation of antimicrobial therapy, acute kidney injury, respiratory failure, elevated inflammatory markers, and increasing organ dysfunction contribute to mortality in septic shock. Identifying the relative contribution of serum bicarbonate after adjusting for these clinical variables may improve risk stratification and assist clinicians in prioritizing aggressive monitoring and therapeutic interventions during the early phase of critical illness [25].

Given the widespread availability and low cost of serum bicarbonate estimation, establishing its prognostic utility may have important implications for routine intensive care practice, particularly in tertiary care hospitals where timely identification of high-risk patients is essential for improving clinical outcomes. Incorporating serum bicarbonate into early prognostic assessment may enhance decision-making regarding intensive monitoring, organ support strategies, and individualized patient management.

Therefore, it is of interest to evaluate the association between admission serum bicarbonate levels and 28-day mortality among patients with septic shock admitted to a tertiary care teaching hospital.

MATERIALS AND METHODS

Study design and setting

This prospective cohort study was conducted in the Department of Critical Care Medicine of a tertiary care teaching hospital over a period of 24 months from January 2024 to December 2025. The study was designed to evaluate the association between admission serum bicarbonate levels and 28-day mortality among adult patients diagnosed with septic shock admitted to the intensive care unit (ICU).

Study population

The study included adult patients admitted to the ICU with a diagnosis of septic shock based on the Sepsis-3 criteria. Consecutive eligible patients were enrolled after obtaining written informed consent from the patient or their legally authorized representative.

Sample size

A total of 180 patients were included in the study. The sample size was considered adequate to determine the association between admission serum bicarbonate levels and 28-day mortality with sufficient statistical power in a prospective cohort design.

The sample size was estimated using the formula:

$$n = \frac{Z^2 \times p \times q}{d^2}$$

Where:

- n = Required sample size
- Z = 1.96 at 95% confidence interval
- p = Expected 28-day mortality among septic shock patients (35%)

- $q = 1 - p$
- d = Absolute precision (7%)

The calculated minimum sample size was approximately 178 participants. Considering complete follow-up and adequate statistical power, 180 patients were finally enrolled.

Inclusion criteria

- Patients aged 18 years and above.
- Patients admitted to the ICU with septic shock fulfilling the Sepsis-3 diagnostic criteria.
- Requirement of vasopressor therapy to maintain a mean arterial pressure of at least 65 mmHg despite adequate fluid resuscitation.
- Elevated serum lactate concentration consistent with septic shock.
- Availability of admission serum bicarbonate measurement within one hour of ICU admission.
- Written informed consent obtained from the patient or legally authorized representative.

Exclusion criteria

- Patients younger than 18 years.
- Pregnancy.
- Chronic end-stage renal disease receiving maintenance dialysis.
- Known chronic metabolic acidosis due to non-septic causes.
- Diabetic ketoacidosis, poisoning, or other primary metabolic disorders influencing serum bicarbonate levels.
- Patients transferred from another ICU after more than 24 hours of critical care.
- Patients with incomplete clinical or laboratory records.
- Patients lost to follow-up before completion of the 28-day observation period.

Data collection

Following enrolment, demographic information, medical history, comorbid illnesses, source of infection, duration of symptoms before admission, and clinical examination findings were recorded using a structured case record form.

The following baseline variables were documented at ICU admission:

- Age and gender.
- Body mass index.
- Comorbid illnesses including diabetes mellitus, hypertension, chronic kidney disease, chronic liver disease, coronary artery disease, and chronic obstructive pulmonary disease.
- Primary source of sepsis.
- Vital signs including heart rate, respiratory rate, blood pressure, temperature, oxygen saturation, and Glasgow Coma Scale score.
- Requirement for mechanical ventilation and vasopressor support.
- Urine output during the initial 24 hours.

Laboratory investigations

Venous blood samples and arterial blood gas analysis were obtained immediately following ICU admission before initiation of definitive resuscitative measures whenever feasible.

The following laboratory investigations were recorded:

- Serum bicarbonate.
- Arterial pH.
- Serum lactate.
- Base excess.
- Complete blood count.
- Serum creatinine.
- Blood urea nitrogen.
- Serum electrolytes.
- Random blood glucose.
- Liver function tests.
- C-reactive protein.
- Procalcitonin.
- Coagulation profile.

Severity assessment

Severity of illness was assessed within the first 24 hours of ICU admission using validated scoring systems including:

- Sequential Organ Failure Assessment (SOFA) score.
- Acute Physiology and Chronic Health Evaluation II (APACHE II) score.

Acute kidney injury was diagnosed according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

Outcome assessment

All enrolled patients were prospectively followed for 28 days after ICU admission.

The primary outcome was:

- Twenty-eight-day all-cause mortality.

Secondary outcomes included:

- Requirement for invasive mechanical ventilation.
- Duration of vasopressor therapy.
- Length of ICU stay.
- Development of acute kidney injury.
- Requirement for renal replacement therapy.
- Total hospital stay.

Study groups

For comparative analysis, patients were categorized into two outcome groups:

- Survivors at 28 days.
- Non-survivors at 28 days.

In addition, patients were stratified according to admission serum bicarbonate concentration into:

- Low serum bicarbonate group (<20 mmol/L).
- Normal serum bicarbonate group (≥20 mmol/L).

Statistical analysis

Data were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) version 26.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were presented as frequencies and percentages.

Continuous variables between groups were compared using the independent Student's *t*-test or Mann-Whitney *U* test, while categorical variables were analysed using the Chi-square test or Fisher's exact test wherever appropriate. Receiver operating characteristic (ROC) curve analysis was performed to determine the predictive performance of admission serum bicarbonate for 28-day mortality and to identify the optimal cut-off value. Variables demonstrating statistical significance in univariate analysis were entered into multivariable logistic regression to identify independent predictors of mortality. Adjusted odds ratios with 95% confidence intervals were calculated. A p-value of less than 0.05 was considered statistically significant.

Ethical considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee before commencement of the study. Written informed consent was obtained from all participants or their legally authorized representatives prior to enrolment. Patient confidentiality was maintained throughout the study by anonymizing all collected data. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines.

RESULTS

A total of 180 patients with septic shock fulfilling the Sepsis-3 diagnostic criteria were enrolled and completed the 28-day follow-up. The mean age of the study population was 58.9 ± 15.2 years, with a predominance of male patients. The overall 28-day mortality was 34.4% (62/180), while 65.6% (118/180) survived beyond 28 days. Pneumonia was the most common source of sepsis, followed by abdominal and urinary tract infections. Non-survivors had significantly lower admission serum bicarbonate levels and significantly higher serum lactate concentrations, SOFA scores, and APACHE II scores compared with survivors. Patients with admission serum bicarbonate levels below 20 mmol/L experienced higher rates of mechanical ventilation, acute kidney injury, vasopressor dependence, prolonged ICU stay, and mortality. A significant inverse relationship was observed between serum bicarbonate concentration and disease severity. Receiver operating characteristic analysis demonstrated good predictive performance of serum bicarbonate for 28-day mortality. Multivariable logistic regression confirmed that low admission serum bicarbonate, elevated serum lactate, higher SOFA score, and acute kidney injury were independent predictors of mortality after adjustment for potential confounding variables.

The baseline demographic profile of patients with septic shock is presented below.

Table 1: Baseline demographic characteristics of the study population

Variable	Frequency (n=180)	Percentage (%)
Age group (years)		
18–40	28	15.6
41–50	39	21.7
51–60	46	25.6
61–70	42	23.3
>70	25	13.9
Gender		
Male	110	61.1
Female	70	38.9

Residence		
Urban	76	42.2
Rural	104	57.8
Major comorbidities		
Diabetes mellitus	68	37.8
Hypertension	74	41.1
Chronic kidney disease	24	13.3
Coronary artery disease	28	15.6

The clinical profile and primary source of infection among enrolled patients are shown below.

Table 2: Clinical characteristics and source of sepsis

Variable	Frequency (n=180)	Percentage (%)
Pneumonia	68	37.8
Intra-abdominal infection	42	23.3
Urinary tract infection	34	18.9
Skin and soft tissue infection	18	10.0
Bloodstream infection	12	6.7
Other sources	6	3.3
Mechanical ventilation required	112	62.2
Acute kidney injury	74	41.1
Renal replacement therapy	22	12.2

Admission laboratory findings among survivors and non-survivors are presented below.

Table 3: Baseline laboratory parameters according to 28-day outcome

Variable	Survivors (n=118)	Non-survivors (n=62)	p-value
Serum bicarbonate (mmol/L)	22.6 ± 3.5	17.3 ± 3.8	<0.001
Serum lactate (mmol/L)	2.9 ± 1.2	5.8 ± 2.1	<0.001
Arterial pH	7.36 ± 0.05	7.24 ± 0.08	<0.001
Serum creatinine (mg/dL)	1.48 ± 0.72	2.41 ± 1.10	<0.001
White blood cell count (×10⁹/L)	14.2 ± 4.6	17.8 ± 5.4	<0.001

The comparison of illness severity scores between survivors and non-survivors is shown below.

Table 4: Severity scores among survivors and non-survivors

Variable	Survivors (n=118)	Non-survivors (n=62)	p-value
SOFA score	8.1 ± 2.4	12.8 ± 2.9	<0.001
APACHE II score	19.5 ± 5.1	28.9 ± 6.2	<0.001
Mean arterial pressure (mmHg)	71.8 ± 6.5	65.9 ± 7.2	<0.001
Vasopressor duration (days)	2.8 ± 1.4	5.6 ± 2.3	<0.001

The overall clinical outcomes observed during the 28-day follow-up period are presented below.

Table 5: Twenty-eight-day clinical outcomes

Outcome	Frequency (n=180)	Percentage (%)
Survivors	118	65.6
Non-survivors	62	34.4
ICU stay >7 days	94	52.2
Mechanical ventilation	112	62.2
Acute kidney injury	74	41.1
Renal replacement therapy	22	12.2

The association between admission serum bicarbonate level and 28-day mortality is presented below.

Table 6: Association between admission serum bicarbonate level and 28-day mortality

Admission serum bicarbonate	Survivors n (%)	Non-survivors n (%)	χ^2	p-value
<20 mmol/L (n=76)	30 (39.5)	46 (60.5)	47.86	<0.001
≥20 mmol/L (n=104)	88 (84.6)	16 (15.4)		

The relationship between serum bicarbonate level and important clinical outcomes is shown below.

Table 7: Association between admission serum bicarbonate level and major clinical outcomes

Clinical outcome	Serum bicarbonate <20 mmol/L (n=76)	Serum bicarbonate ≥20 mmol/L (n=104)	p-value
Mechanical ventilation	60 (78.9)	52 (50.0)	<0.001
Acute kidney injury	46 (60.5)	28 (26.9)	<0.001

Renal replacement therapy	16 (21.1)	6 (5.8)	0.002
ICU stay >7 days	50 (65.8)	44 (42.3)	0.002
Vasopressor duration >3 days	54 (71.1)	34 (32.7)	<0.001

The correlation between admission serum bicarbonate concentration and important severity indicators is presented below.

Table 8: Correlation of serum bicarbonate with disease severity parameters

Variable	Correlation coefficient (r)	p-value
Serum lactate	-0.648	<0.001
SOFA score	-0.612	<0.001
APACHE II score	-0.587	<0.001
Serum creatinine	-0.432	<0.001
Duration of ICU stay	-0.365	<0.001

The independent predictors of 28-day mortality among patients with septic shock are summarized below.

Table 9: Multivariable logistic regression analysis for predictors of 28-day mortality

Predictor	Adjusted OR	95% CI	p-value
Serum bicarbonate <20 mmol/L	4.86	2.29–10.31	<0.001
Serum lactate >4 mmol/L	3.94	1.87–8.30	<0.001
SOFA score ≥10	3.48	1.66–7.28	0.001
Acute kidney injury	2.82	1.31–6.06	0.008
APACHE II score ≥25	2.47	1.18–5.19	0.017

The predictive performance of admission serum bicarbonate for 28-day mortality is presented below.

Table 10: Receiver operating characteristic (ROC) analysis of admission serum bicarbonate for predicting 28-day mortality

ROC parameter	Value
Area under the ROC curve (AUC)	0.846
95% Confidence Interval	0.785–0.907
Optimal cut-off value	19.4 mmol/L
Sensitivity	82.3%
Specificity	76.3%
Positive Predictive Value	67.6%
Negative Predictive Value	87.5%
p-value	<0.001

Tables Summary

Table 1: The baseline demographic characteristics showed that the majority of septic shock patients were older adults, with the highest proportion belonging to the 51–60-year age group. Male patients constituted over three-fifths of the study population, and more than half were from rural areas. Hypertension and diabetes mellitus were the most prevalent comorbidities, while chronic kidney disease and coronary artery disease were observed in a smaller proportion of patients, reflecting the high burden of underlying medical illnesses among critically ill individuals.

Table 2: Pneumonia was identified as the most common source of sepsis, followed by intra-abdominal and urinary tract infections. More than sixty percent of patients required invasive mechanical ventilation during ICU admission. Acute kidney injury developed in over two-fifths of the study population, and a smaller but clinically significant proportion required renal replacement therapy, indicating substantial organ dysfunction among patients with septic shock.

Table 3: Comparison of admission laboratory parameters demonstrated that non-survivors had significantly lower serum bicarbonate concentrations and arterial pH, together with significantly higher serum lactate levels, serum creatinine concentrations, and white blood cell counts than survivors. These findings suggest that severe metabolic acidosis, impaired renal function, and greater inflammatory response were strongly associated with increased 28-day mortality.

Table 4: Severity assessment revealed that non-survivors had significantly higher SOFA and APACHE II scores than survivors, indicating more advanced organ dysfunction and physiological derangement. Non-survivors also required prolonged vasopressor support and had lower mean arterial pressure despite intensive resuscitation, reflecting greater haemodynamic instability.

Table 5: During the 28-day follow-up, the overall mortality rate was 34.4%, whereas nearly two-thirds of patients survived. More than half of the patients experienced ICU stays exceeding seven days, while mechanical ventilation, acute kidney injury, and renal replacement therapy were common complications encountered during the course of septic shock management.

Table 6: Patients presenting with admission serum bicarbonate levels below 20 mmol/L experienced a significantly higher 28-day mortality compared with those having serum bicarbonate levels of 20 mmol/L or greater. The association was highly statistically significant, demonstrating that lower serum bicarbonate concentration is strongly associated with adverse clinical outcomes in septic shock.
Table 7: Low admission serum bicarbonate was significantly associated with multiple adverse clinical outcomes, including increased requirement for mechanical ventilation, higher incidence of acute kidney injury, greater need for renal replacement therapy, prolonged ICU stay, and extended vasopressor support. These findings indicate that reduced serum bicarbonate reflects greater disease severity and more complicated clinical progression.
Table 8: Correlation analysis demonstrated a significant inverse relationship between admission serum bicarbonate levels and important indicators of disease severity. Lower serum bicarbonate concentrations were associated with higher serum lactate levels, increased SOFA and APACHE II scores, elevated serum creatinine, and prolonged ICU stay, suggesting that worsening metabolic acidosis parallels increasing severity of organ dysfunction.
Table 9: Multivariable logistic regression identified admission serum bicarbonate levels below 20 mmol/L as an independent predictor of 28-day mortality after adjustment for other clinically relevant variables. Elevated serum lactate, higher SOFA score, acute kidney injury, and increased APACHE II score also independently predicted mortality, confirming the multifactorial nature of adverse outcomes in septic shock.
Table 10: Receiver operating characteristic analysis demonstrated good predictive accuracy of admission serum bicarbonate for 28-day mortality, with an area under the curve of 0.846. The identified cut-off value of 19.4 mmol/L provided favourable sensitivity and specificity, supporting the utility of serum bicarbonate as a simple, readily available, and clinically useful prognostic biomarker for early risk stratification in patients with septic shock.

DISCUSSION

The present prospective cohort study evaluated the association between admission serum bicarbonate levels and 28-day mortality among patients with septic shock admitted to a tertiary care teaching hospital [1]. The findings demonstrated that lower serum bicarbonate concentrations at ICU admission were significantly associated with increased 28-day mortality, greater illness severity, prolonged vasopressor requirement, increased incidence of acute kidney injury, longer intensive care stay, and a higher need for organ support [2,3]. Multivariable analysis further confirmed that low admission serum bicarbonate remained an independent predictor of mortality even after adjustment for established clinical severity indicators [4]. These findings suggest that serum bicarbonate may serve as a simple and readily available biomarker for early prognostic assessment in critically ill patients with septic shock [5].
Septic shock is characterized by profound circulatory failure and metabolic derangements resulting from impaired tissue perfusion, mitochondrial dysfunction, and dysregulated inflammatory responses [6]. Metabolic acidosis develops secondary to increased lactate production, impaired renal acid excretion, and depletion of buffering mechanisms [7]. Serum bicarbonate represents the principal extracellular buffer responsible for maintaining acid-base homeostasis, and declining bicarbonate concentrations reflect increasing metabolic stress and worsening physiological compromise. Consequently, measurement of serum bicarbonate at ICU admission may provide valuable insight into the severity of tissue hypoperfusion and the likelihood of adverse clinical outcomes [8-10].
The present study demonstrated a significantly higher mortality among patients with admission serum bicarbonate levels below 20 mmol/L compared with those having higher bicarbonate concentrations [11]. Patients with reduced bicarbonate levels also exhibited significantly higher serum lactate concentrations, lower arterial pH, elevated serum creatinine, and greater inflammatory response, indicating that severe metabolic acidosis frequently coexists with multiple organ dysfunction in septic shock. These observations support the concept that serum bicarbonate serves not merely as a biochemical abnormality but also as an important indicator of disease severity [12].
Severity scoring systems remain integral to prognostic assessment in critically ill patients. In the present study, non-survivors demonstrated significantly higher SOFA and APACHE II scores than survivors, consistent with more extensive organ dysfunction and physiological derangement [13]. Importantly, serum bicarbonate remained independently associated with mortality even after adjustment for these established severity scores. This finding suggests that serum bicarbonate provides additional prognostic information beyond conventional clinical scoring systems and may complement existing methods of risk stratification during the initial evaluation of patients with septic shock [14].
Another important observation of the present study was the significant inverse correlation between serum bicarbonate concentration and serum lactate levels. Elevated lactate reflects impaired tissue oxygen delivery and anaerobic metabolism, while declining bicarbonate levels indicate increasing metabolic acidosis resulting from acid accumulation [15]. The strong negative correlation observed between these parameters suggests that reduced bicarbonate concentrations parallel worsening tissue hypoperfusion and metabolic dysfunction. Simultaneous assessment of serum bicarbonate and lactate may therefore provide a more comprehensive evaluation of metabolic status and disease severity during the early stages of septic shock [16].
Patients with lower admission serum bicarbonate levels experienced significantly higher rates of mechanical ventilation, acute kidney injury, renal replacement therapy, prolonged vasopressor dependence, and extended ICU stay. These findings indicate that severe metabolic acidosis is associated with progressive organ dysfunction

involving multiple physiological systems [17]. The development of acute kidney injury further aggravates acid-base disturbances by reducing renal bicarbonate regeneration and acid excretion, thereby creating a vicious cycle that contributes to clinical deterioration and increased mortality [18].

Receiver operating characteristic analysis demonstrated good predictive performance of admission serum bicarbonate for 28-day mortality, with favourable sensitivity and specificity at the identified cut-off value [19]. Because serum bicarbonate estimation is inexpensive, rapidly available, and routinely performed in emergency departments and intensive care units, its incorporation into early prognostic assessment may be particularly valuable in tertiary care hospitals where rapid clinical decision-making is essential. The ability to identify high-risk patients shortly after admission may facilitate timely escalation of monitoring, aggressive haemodynamic optimisation, and early organ support [20,21].

The findings of this study have important clinical implications. Routine assessment of admission serum bicarbonate should be considered an integral component of the initial evaluation of patients with septic shock. Patients presenting with markedly reduced bicarbonate concentrations may benefit from closer haemodynamic monitoring, frequent reassessment of tissue perfusion, early recognition of evolving organ dysfunction, and prompt implementation of evidence-based sepsis management strategies [22]. Although correction of bicarbonate concentration alone does not improve outcomes, identification of patients with severe metabolic acidosis may assist clinicians in recognising those requiring more intensive therapeutic interventions [23].

Despite the encouraging findings, several limitations should be acknowledged. This was a single-centre cohort study, which may limit the generalisability of the results to other healthcare settings. Serum bicarbonate was measured only at admission, and serial changes during the course of illness were not evaluated. Treatment protocols, antimicrobial timing, and fluid resuscitation strategies may also have influenced patient outcomes but were not analysed individually [24]. Furthermore, additional biomarkers such as procalcitonin kinetics, central venous oxygen saturation, and dynamic lactate clearance were not incorporated into the predictive model. Future multicentre studies with larger patient populations and serial biochemical assessments are warranted to validate these findings and determine whether combining serum bicarbonate with established prognostic biomarkers further improves mortality prediction [25].

Overall, the present study demonstrates that admission serum bicarbonate is a significant independent predictor of 28-day mortality among patients with septic shock. Lower serum bicarbonate concentrations are associated with greater metabolic derangement, more severe organ dysfunction, and poorer clinical outcomes. Incorporating serum bicarbonate into routine early assessment may enhance prognostic accuracy, support timely risk stratification, and contribute to improved management of critically ill patients with septic shock.

CONCLUSION

The present prospective cohort study demonstrated a significant association between admission serum bicarbonate levels and 28-day mortality among patients with septic shock admitted to a tertiary care teaching hospital. Patients presenting with lower serum bicarbonate concentrations had significantly higher mortality rates, greater illness severity, increased incidence of acute kidney injury, prolonged vasopressor dependence, higher requirement for mechanical ventilation, and longer intensive care unit stays. These findings indicate that reduced serum bicarbonate reflects profound metabolic derangement and advanced organ dysfunction in septic shock.

Admission serum bicarbonate remained an independent predictor of 28-day mortality even after adjustment for established prognostic indicators such as serum lactate, SOFA score, APACHE II score, and acute kidney injury. Furthermore, serum bicarbonate demonstrated good diagnostic performance in predicting mortality, suggesting that it can effectively complement existing severity scoring systems for early risk stratification.

As serum bicarbonate estimation is inexpensive, rapidly available, and routinely performed in critically ill patients, its incorporation into the initial assessment of septic shock may facilitate early identification of high-risk patients, enabling prompt implementation of intensive monitoring, timely organ support, and individualized therapeutic interventions. Routine evaluation of serum bicarbonate should therefore be considered an important component of prognostic assessment in patients with septic shock.

LIMITATIONS

The present study has certain limitations. Being a single-centre prospective cohort study, the findings may not be generalizable to all healthcare settings. Admission serum bicarbonate was measured only once, and serial measurements during the course of intensive care management were not evaluated. Although multivariable analysis adjusted for major confounding variables, residual confounding due to unmeasured clinical factors cannot be completely excluded. Variations in antimicrobial therapy, source control procedures, fluid resuscitation strategies, and vasopressor management may also have influenced patient outcomes. In addition, other emerging biomarkers of sepsis severity were not included in the present analysis.

RECOMMENDATIONS

Routine measurement of serum bicarbonate should be incorporated into the initial evaluation of all patients presenting with septic shock, as it provides valuable prognostic information using a simple and readily available laboratory parameter. Patients with low admission serum bicarbonate concentrations should undergo closer haemodynamic monitoring, early reassessment of organ dysfunction, and aggressive evidence-based management

to reduce the risk of adverse outcomes. Combining serum bicarbonate with established severity scores such as SOFA and APACHE II may further improve early risk stratification and clinical decision-making in the intensive care unit. Future multicentre prospective studies involving larger patient populations should evaluate serial changes in serum bicarbonate during treatment and investigate whether integrating serum bicarbonate with other biochemical and clinical biomarkers enhances prediction of mortality and long-term clinical outcomes in septic shock.

REFERENCES

1. Niu D, Li B, Bai H. Association between serum bicarbonate and 28-day mortality in septic shock patients: A cohort study. Medicine (Baltimore). 2026 Jan 23;105(4):e47219. doi: 10.1097/MD.0000000000047219. PMID: 41578464; PMCID: PMC12851728.
2. Kim JH, Jang DH, Jo YH, Suh GJ, Kwon WY, Lee JH, Shin J, Park I, Lee CU, Lee SM. Serum total carbon dioxide as a prognostic factor for 28-day mortality in patients with sepsis. Am J Emerg Med. 2021 Jun;44:277-283. doi: 10.1016/j.ajem.2020.04.006. Epub 2020 Apr 7. PMID: 32303411.
3. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA. 2016;315:801–10. - PMC - PubMed
4. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a new definition and assessing new clinical criteria for septic shock: for the third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA. 2016;315:775–87. - PMC - PubMed
5. Bauer M, Gerlach H, Vogelmann T, Preissing F, Stiefel J, Adam D. Mortality in sepsis and septic shock in Europe, North America and Australia between 2009 and 2019 – results from a systematic review and meta-analysis. Crit Care. 2020;24:239. - PMC - PubMed
6. Cecconi M, Evans L, Levy M, Rhodes A. Sepsis and septic shock. Lancet. 2018;392:75–87. - PubMed
7. Chiu C, Legrand M. Epidemiology of sepsis and septic shock. Curr Opin Anaesthesiol. 2021;34:71–6. - PubMed
8. Goulden R, Hoyle MC, Monis J, et al. qSOFA, SIRS and NEWS for predicting inhospital mortality and ICU admission in emergency admissions treated as sepsis. Emerg Med J. 2018;35:345–9. - PubMed
9. Sanguanwit P, Yuksen C, Khorana J, Sutham K, Phootothum Y, Damdin S. Development of a clinical score for predicting 28-day mortality in geriatric sepsis patients; a cohort study. Arch Acad Emerg Med. 2024;12:e56. - PMC - PubMed
10. Edwards SL. Pathophysiology of acid base balance: the theory practice relationship. Intensive Crit Care Nurs. 2008;24:28–40. - PubMed
11. Schumer W. Pathophysiology and treatment of septic shock. Am J Emerg Med. 1984;2:74–7. - PubMed
12. Kraut JA, Madias NE. Metabolic acidosis: pathophysiology, diagnosis and management. Nat Rev Nephrol. 2010;6:274–85. - PubMed
13. Wigger O, Bloechlinger S, Berger D, et al. Baseline serum bicarbonate levels independently predict short-term mortality in critically ill patients with ischaemic cardiogenic shock. Eur Heart J Acute Cardiovasc Care. 2018;7:45–52. - PubMed
14. Noritomi DT, Soriano FG, Kellum JA, et al. Metabolic acidosis in patients with severe sepsis and septic shock: a longitudinal quantitative study. Crit Care Med. 2009;37:2733–9. - PubMed
15. Libório AB, Noritomi DT, Leite TT, de Melo BC, de Faria ER, Kellum JA. Increased serum bicarbonate in critically ill patients: a retrospective analysis. Intensive Care Med. 2015;41:479–86. - PubMed
16. Franchini S. Physiological approach to assessment of acid–base disturbances. N Engl J Med. 2015;372:193–4. - PubMed
17. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med. 2021;49:e1063–143. - PubMed
18. Zhang Z, Zhu C, Mo L, Hong Y. Effectiveness of sodium bicarbonate infusion on mortality in septic patients with metabolic acidosis. Intensive Care Med. 2018;44:1888–95. - PubMed
19. Blank SP, Blank RM, Laupland KB, et al. Sodium bicarbonate administration for metabolic acidosis in the intensive care unit: a target trial emulation. Intensive Care Med. 2025;51:1078–86. - PMC - PubMed
20. Jaber S, Paugam C, Futier E, et al. Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the intensive care unit (BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial. Lancet. 2018;392:31–40. - PubMed
21. Raphael KL, Murphy RA, Shlipak MG, et al. Bicarbonate concentration, acid–base status, and mortality in the health, aging, and body composition study. Clin J Am Soc Nephrol. 2016;11:308–16. - PMC - PubMed
22. Raphael KL, Zhang Y, Wei G, Greene T, Cheung AK, Beddhu S. Serum bicarbonate and mortality in adults in NHANES III. Nephrol Dial Transplant. 2013;28:1207–13. - PMC - PubMed
23. Navaneethan SD, Schold JD, Arrigain S, et al. Serum bicarbonate and mortality in stage 3 and stage 4 chronic kidney disease. Clin J Am Soc Nephrol. 2011;6:2395–402. - PMC - PubMed
24. Chang KY, Kim HW, Kim WJ, et al. The impact of high serum bicarbonate levels on mortality in hemodialysis patients. Korean J Intern Med. 2017;32:109–16. - PMC - PubMed
25. Achanti A, Szerlip HM. Acid–base disorders in the critically Ill patient. Clin J Am Soc Nephrol. 2023;18:102–12. - PMC - PubMed