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Original Article

General Medicine Section

Serum Uric Acid and Arterial pH in ICU Patients with Sepsis and their Correlation with SOFA Score: A Prospective Observational Study

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ABSTRACT

Introduction: Sepsis remains a critical medical emergency characterised by a dysregulated host response to infection, leading to life-threatening organ dysfunction. Early and accurate prediction of clinical outcomes in septic patients is essential for timely intervention. Common prognostic tools, such as the Sequential Organ Failure Assessment (SOFA) score, are widely used, but additional biochemical markers, such as Serum Uric Acid (SUA) and arterial blood pH, may enhance risk stratification.

Aim: To evaluate the role of SUA and arterial pH as prognostic markers in patients with sepsis admitted to the Intensive Care Unit (ICU) and to assess their correlation with SOFA scores.

Materials and Methods: A prospective observational study was conducted over a 12-month period in the Department of General Medicine at Dr. D. Y. Patil Medical College, Hospital, and Research Centre, Pimpri, Pune, Maharashtra, India. A total of 150 adult ICU patients diagnosed with sepsis were enrolled. SUA and arterial pH levels were measured on days 0, 1, 2, and 7, alongside serial SOFA scoring. Data were statistically analysed to determine trends and correlations between biomarkers and organ dysfunction severity.

Results: SUA levels and SOFA scores showed a statistically significant rising trend from day 0 to day 7 (p-value <0.001), while arterial pH progressively decreased, reflecting increasing metabolic acidosis. A strong positive correlation was observed between uric acid and SOFA scores (r-value=0.74) at day 7, whereas arterial pH showed an inverse correlation (r-value=-0.72). Both biomarkers demonstrated predictive utility for clinical deterioration in septic ICU patients.

Conclusion: SUA and arterial pH are valid and readily available biomarkers that are significantly correlated with the SOFA score. Their incorporation into SOFA scoring could enhance early prognostication and facilitate more accurate ICU management.

Keywords: Critical care, Immune dysregulation, Intensive care unit, Organ dysfunction, Prognostic biomarkers, Sequential organ failure assessment

INTRODUCTION

Sepsis is a fatal clinical syndrome involving a dysregulated host response to infection that causes generalised inflammation, organ failure, and extremely high mortality. It remains one of the greatest challenges in intensive care, adding a substantial amount of morbidity and ICU admissions globally [1]. Early detection of organ failure and timely identification of at-risk patients are vital objectives in the treatment of sepsis. The worldwide burden of sepsis is immense, affecting 49 million people every year and contributing to 11 million deaths, often due to delayed diagnosis and insufficient monitoring [2].

Historically, different scoring systems have been used to measure the severity of organ dysfunction in sepsis. Among these, the SOFA score has gained general acceptance as a prognostic indicator [3]. It includes physiological and laboratory markers to assess the degree of organ dysfunction and assists in guiding clinical management [4,5]. The SOFA score is a 24-point measure of organ dysfunction that evaluates six organ systems (renal, cardiovascular, pulmonary, hepatic, neurologic, haematologic), with 0-4 points assigned for each organ system. However, in many contexts, particularly in resource-poor settings, access to and timely use of SOFA scoring can be limited. This has led to increasing interest in assessing biochemical markers that are readily available and may provide similar or supplementary prognostic information [6].

The SUA, a metabolite of purine, has gained prominence as a surrogate marker of tissue damage and oxidative stress. Higher levels of SUA have been correlated with inflammatory states, endothelial dysfunction, and increased oxidative injury—all characteristics of sepsis pathophysiology [7]. Furthermore, uric acid acts both as an antioxidant and a pro-oxidant, depending on redox conditions, making it a marker of systemic metabolic distress in sepsis patients [8]. Similarly, arterial blood pH, derived from Arterial Blood Gas (ABG) analysis, serves as an important indicator of acid-base balance. A decrease in arterial pH typically reflects metabolic acidosis, a common and serious complication in sepsis due to tissue hypoperfusion, lactic acidosis, and renal dysfunction. Persistently low pH values have been associated with poor outcomes and increased mortality in critically ill patients [9,10].

The study aims to evaluate the role of SUA and arterial pH as prognostic indicators in sepsis and to determine their correlation with SOFA scores over time [1]. The formulation and implementation of the SOFA score have a long history, with repeated revisions of the sepsis definition over time. It is imperative to explore new modalities of clinical and laboratory assessments commonly available in ICUs. The addition of these modalities can improve the accuracy of the SOFA score and allow it to stand the test of time in this ever-evolving field of medicine. By analysing these parameters serially during the ICU stay, the study explores their dynamic relationship with the progression of organ dysfunction, thereby assessing their utility as adjunct markers in the early prediction of sepsis severity and outcomes.

The primary objective of the study was to evaluate the prognostic significance of SUA and arterial pH in sepsis. The secondary objective was to assess their correlation with SOFA scores and track the changes over time.

MATERIALS AND METHODS

This prospective observational study was conducted from April 2023 to April 2024 in the Department of General Medicine at Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pimpri,

Pune, Maharashtra, India. Ethics approval was obtained, with approval number IESC/PGS/2023/02.

Sample size calculation: With reference to the study conducted by Sukmawardhani I et al., in 2020, the correlation of SUA levels with the SOFA score on the first day was significant (r-value=0.4) [11]. Considering this value with a power of 80% and a 5% significance level, accounting for a 7% loss of subjects, the minimum sample size required was 51, using Winpepi version 11.38. However, 150 participants fulfilled the eligibility criteria and were included in the study.

A total of 150 adult patients admitted to the ICU with a diagnosis of sepsis were enrolled after obtaining approval from the Institutional Ethics Committee and written informed consent from the patients or their legal guardians.

Inclusion criteria: This encompassed patients aged 18 years and older who met the Sepsis-3 definition, characterised by suspected or documented infection along with an acute increase in the SOFA score of two or more points [1,7].

Exclusion criteria: This included patients with known malignancies, chronic kidney disease, pre-existing liver cirrhosis, autoimmune disorders, or those on immunosuppressive therapy, as these conditions could independently influence SUA levels and acid-base status [12].

Study Procedure

Detailed clinical history and examination findings were recorded at admission. Routine investigations were performed according to ICU protocol. SUA levels and ABG parameters were measured on day 0 (admission), day 1, day 2, and day 7 [12]. Arterial pH values were specifically recorded from ABG analysis. The SOFA score [5] was calculated on the same days using standard criteria, incorporating respiratory, cardiovascular, hepatic, coagulation, renal, and neurological parameters. All laboratory measurements were performed using standardised methods in the hospital's central laboratory.

STATISTICAL ANALYSIS

All collected data were entered into Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) version 20.0. Descriptive statistics such as mean and standard deviation were used for continuous variables, while categorical variables were expressed as frequencies and percentages. Pearson's correlation coefficient was applied to determine the relationship between SUA, arterial pH, and SOFA scores. Multivariate regression analysis was conducted to identify predictors of mortality. A p-value of less than 0.05 was considered statistically significant.

RESULTS

This study included 150 adult patients admitted to the ICU with a diagnosis of sepsis. The study population was assessed for trends in SUA, arterial blood pH, and SOFA scores over days 0, 1, 2, and 7. The goal was to examine temporal changes and establish prognostic correlations with organ dysfunction and patient outcomes. Among the study group, 107 patients survived, while 43 succumbed during their ICU stay.

The age-wise distribution of patients, with the highest representation in the 51-60 year age group 41 (27.3%), followed by the 41-50 year age group 34 (22.7%) were demonstrated in [Table/Fig-1]. Gender distribution revealed a male predominance, with 60.7% (n=91) of the patients being male [Table/Fig-2]. The distribution of primary sources of sepsis, with respiratory tract infections being the most common 56 (37.3%) is shown in [Table/Fig-3].

A progressive increase in mean SUA levels from 5.7±1.3 at day 0 to 7.5±1.6 on day 7 was noted. A corresponding decline in arterial blood pH values from 7.35±0.04 on day 0 to 7.25±0.07 over the same period was observed, indicating progression. Increasing SOFA scores from 6.2±2.1 on day 0 to 9.3±2.7 on day 7 reflected worsening organ dysfunction [Table/Fig-4].

Age group (years)	Number of patients (n,%)
18-30	18 (12.0)
31-40	26 (17.3)
41-50	34 (22.7)
51-60	41 (27.3)
>60	31 (20.7)

[Table/Fig-1]: Age distribution of study participants (N=150).

Gender	Number of patients (n,%)
Male	91 (60.7)
Female	59 (39.3)

[Table/Fig-2]: Gender distribution.

Source of infection	Number of patients (n,%)
Respiratory tract	56 (37.3)
Urinary tract	41 (27.3)
Abdominal sepsis	27 (18.0)
Skin/soft-tissue	16 (10.7)
Others	10 (6.7)

[Table/Fig-3]: Common sources of sepsis.

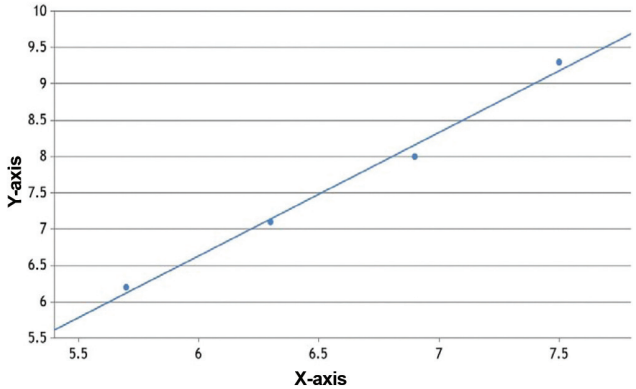
Day	Mean uric acid (mg/dL)	Standard deviation (±)	Mean arterial pH	Standard deviation (±)	Mean SOFA score	Standard deviation (±)
Day 0	5.7	1.3	7.35	0.04	6.2	2.1
Day 1	6.3	1.4	7.31	0.05	7.1	2.3
Day 2	6.9	1.5	7.28	0.06	8.0	2.4
Day 7	7.5	1.6	7.25	0.07	9.3	2.7

[Table/Fig-4]: Mean Serum Uric Acid (SUA), arterial pH and SOFA score levels over time.

A strong positive correlation was observed between SUA and SOFA score, with an r-value of 0.61 (p-value <0.01) on day 0 and 0.74 (p-value <0.01) on day 7 [Table/Fig-5,6]. A significant negative correlation between arterial pH and SOFA score over time, with a score on day 0 showing an r-value of -0.55 (p-value <0.01) and on day 7 an r-value of -0.72 (p-value <0.01) were demonstrated in [Table/Fig-7,8].

Day	Correlation coefficient (r-value)	p-value
Day 0	0.61	<0.001
Day 1	0.68	<0.001
Day 2	0.72	<0.001
Day 7	0.74	<0.001

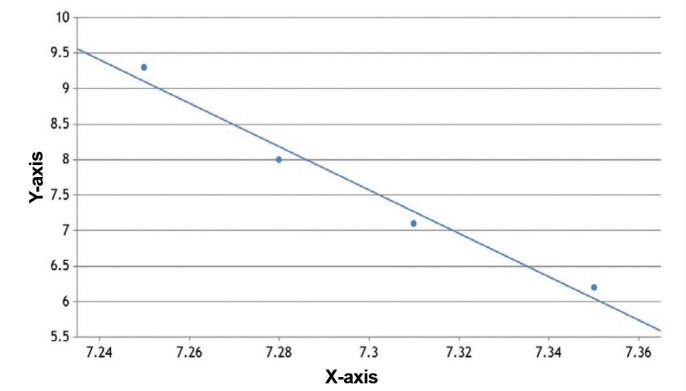
[Table/Fig-5]: Correlation of Serum Uric Acid (SUA) with SOFA score.



[Table/Fig-6]: Scatter plot between mean Serum Uric Acid (SUA) levels on X-axis and sofa score on Y-axis.
Mean Serum Uric Acid (SUA) (mg/dL)

Day	Correlation coefficient (r)	p-value
Day 0	-0.55	<0.001
Day 1	-0.62	<0.001
Day 2	-0.69	<0.001
Day 7	-0.72	<0.001

[Table/Fig-7]: Correlation of arterial pH with SOFA score.



[Table/Fig-8]: Scatter plot between mean arterial pH on X-axis and SOFA score on Y-axis.
SOFA score; Mean arterial pH

The values of SUA, arterial pH, and SOFA scores in survivors versus non survivors were compared in [Table/Fig-9]. It is evident that higher uric acid levels, significantly lower arterial pH, and markedly higher SOFA scores were present in non survivors compared to survivors (p-value <0.001). Based on the regression coefficients provided, SUA has a positive correlation with mortality (β=0.41, p-value=0.002). A positive coefficient indicates that higher SUA levels are independently associated with increased mortality, and this association was statistically significant.

Variables	Survivors (n=107)	Non survivors (n=43)	p-value
Mean uric acid±SD (mg/dL)	6.1±1.3	6.1±1.3	<0.001
Mean arterial pH±SD	7.31±0.04	7.21±0.06	<0.001
Mean SOFA score±SD	7.1±2.1	10.2±2.3	<0.001

[Table/Fig-9]: Serum Uric Acid (SUA), arterial pH and SOFA score levels - survivors vs non survivors. Wilcoxon Signed-Rank test of significance used.

In contrast, arterial pH shows a moderate negative correlation with SOFA score (β=-0.36, p-value=0.004), indicating that lower pH (greater acidosis) is associated with higher mortality. The analysis showed that elevated uric acid, worsening acidosis, and increased SOFA score are all independent significant predictors of mortality [Table/Fig-10].

Variables	Regression coefficient (β)	p-value
Serum Uric Acid (SUA)	0.41	0.002
Arterial pH	-0.36	0.004
SOFA score	0.49	<0.001

[Table/Fig-10]: Multivariate regression – predictors of mortality.

DISCUSSION

Sepsis is an intricate clinical syndrome that includes systemic inflammation, tissue hypoperfusion, and multiple organ dysfunction, requiring prompt diagnosis and risk stratification [13,14]. The aim of this study was to determine the prognostic significance of SUA and arterial blood pH levels in patients with sepsis admitted to the ICU, as well as their correlation with SOFA scores at different times. The data provide strong evidence that both biomarkers are dynamically correlated with the severity of the disease and can offer useful prognostic information in critically-ill patients.

The demographic profile of the 150 enrolled patients showed a majority of males (60.7%) and a greater incidence of sepsis among the 41-60 year age group. The most frequent cause of sepsis in this investigation was respiratory tract infections, followed by urinary and peritoneal infections. This aligns with earlier publications emphasising pneumonia and urosepsis as principal reasons for sepsis admissions to the ICU [15,16].

SUA levels were found to increase progressively from day 0 through day 7, and this trend was mirrored by rising SOFA scores. Uric acid is a known marker of oxidative stress and ischaemic injury and may reflect the extent of tissue hypoxia and systemic inflammation in sepsis [17]. The positive correlation observed between uric acid and SOFA scores across all days was statistically significant (r-value ranging from 0.61 to 0.74), indicating a strong correlation between metabolic stress and organ dysfunction. These findings are supported by earlier studies that linked hyperuricaemia to poor outcomes in critically-ill patients, reinforcing its role as a non invasive marker of disease severity [18-20].

Conversely, arterial pH values showed a consistent decline over the course of the ICU stay, suggesting progressive metabolic acidosis, a known prognostic marker in sepsis [21]. The study demonstrated a significant inverse correlation between arterial pH and SOFA scores, with the strength of the correlation increasing over time (r ranging from -0.55 to -0.72). Lower arterial pH values likely reflect cumulative lactic acidosis and renal dysfunction, both integral components of SOFA scoring. These findings are similar to the ABG analysis conducted in the study by Thorson SH et al., (1983) [22]. This emphasises the role of ABG parameters in complementing clinical assessments for sepsis progression [20].

A key observation was the significant difference in biomarker profiles between survivors and non survivors. Non survivors had substantially higher mean SUA levels and lower arterial pH, along with elevated SOFA scores, all of which reached statistical significance. Furthermore, multivariate regression analysis identified all three—uric acid, pH, and SOFA score—as independent predictors of mortality, reinforcing their clinical relevance in early risk stratification, as detailed in the studies by Sukmawardhani I et al., in 2020 and Pierrakos C et al., in 2010 [11,14].

The findings of this study hold substantial clinical implications. Since SUA and arterial pH are easily measurable and cost-effective tests, their integration into sepsis evaluation protocols could enhance bedside prognostication, especially in resource-limited settings where rapid access to scoring systems may not always be feasible. Critical care is a field that constantly requires revision and the use of novel tests and agents to enhance life-saving care. Its importance has become increasingly evident to the world during the recent pandemic crisis. The definitions of sepsis and the SOFA score will need a dynamic approach, especially with the global rise of antibiotic resistance and intrinsically resistant organisms [23]. The incorporation of novel biomarkers to improve accuracy in predicting the severity of patient outcomes must be a focus in the coming years. Subtle, albeit significant, additions to the six-parameter scoring system can enhance its usefulness in critical care management.

Limitation(s)

However, the study has its limitations. It was conducted in a single tertiary care center, which may limit the generalisability of the results. Additionally, the dynamic changes in biomarkers were assessed only up to day 7; extended follow-up could have provided more insight into late mortality or recovery patterns. Despite these limitations, the strength of the correlation and consistent trends across parameters affirm the potential utility of these markers.

CONCLUSION(S)

The prospective observational study clearly demonstrates that rising SUA levels are positively correlated with increasing SOFA scores, evidenced by a strong day 7 correlation of r≈0.74, signifying that higher SUA independently tracks with worsening organ dysfunction.

Conversely, arterial pH shows a strong negative correlation with SOFA (r≈-0.72 on Day 7), indicating that worsening acidosis is closely linked to an escalation in organ failure. Both biomarkers are statistically significant independent predictors of outcomes, underscoring their utility as cost-effective, dynamic indicators of sepsis severity. SUA levels and ABG pH measurements are simple and widely available; hence, their integration alongside SOFA scoring could greatly enhance early prognostication and risk stratification in ICU settings, particularly where resources are limited.

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