

# Hyponatremia among Sepsis Patients in the Critical Care Unit and its Association with the SOFA Score: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Hyponatremia is a frequent electrolyte imbalance observed in critically-ill patients. The Sequential Organ Failure Assessment (SOFA) score is a tool used in sepsis management to assess the severity of organ dysfunction and predict mortality in critically-ill patients. Thus, establishing an association between hyponatremia and the SOFA score aids in triaging patients at high risk of mortality and enhancing management strategies.

**Aim:** To estimate the prevalence of hyponatremia in sepsis patients hospitalised in the critical care unit and analyse its association with SOFA scores.

**Materials and Methods:** The prospective observational cross-sectional study was carried out at the Critical Care Unit of Smt. B. K. Shah Medical Institute and Research Centre, Sumandeep Vidyapeeth Deemed to be University, Piparia, Waghodia, Gujarat, India over a one-month duration in November 2024 on 88 sepsis patients aged over 18 years. Following informed consent, routine investigations such as Arterial Blood Gas (ABG), serum bilirubin, platelet count, creatinine, and sodium levels were performed. SOFA scores were calculated at the time of admission, and the severity of hyponatremia was assessed. Statistical tests for prevalence and associations within the data were applied, and the Chi-square test with a p-value of less than 0.05 was considered statistically significant.

**Results:** The mean age of study patients with hyponatremia was 50.74 years, with a standard deviation of 16.49 years. The majority of study participants were male, comprising 62.32%, while females accounted for 37.68%. Hyponatremia was observed in 78.4% of sepsis patients, with 39.8% exhibiting mild hyponatremia, 25% moderate hyponatremia, and 13.6% severe hyponatremia. A SOFA score of 2 was most frequent in 19 patients (27.5%), and the mean SOFA score was 4.42, with a standard deviation of 2.34. The three most common aetiological diagnoses for hyponatremia were lower respiratory tract infection, followed by decompensated Chronic Liver Disease (CLD) and acute ischaemic stroke with aspiration pneumonia. The association between the SOFA score and the severity of hyponatremia was statistically significant, as indicated by the Chi-square test ( $p < 0.05$ ). Additionally, a statistically significant association was observed between the severity of hyponatremia and specific components of the SOFA score, namely platelet count and serum creatinine.

**Conclusion:** Hyponatremia is highly prevalent in critically-ill sepsis patients. The association between hyponatremia and SOFA scores highlights the need for timely diagnosis and management of hyponatremia to reduce morbidity and mortality.

**Keywords:** Decompensated chronic liver disease, Ischaemic stroke, Lower respiratory tract infection, Sequential organ failure assessment

## INTRODUCTION

Sepsis is a grave condition characterised by organ dysfunction resulting from an excessive immune response to infection. It is a global health concern, affecting millions annually and ranking as one of the principal causes of critical illness, morbidity, and mortality [1]. The study by Hammond NE et al., estimated the prevalence of sepsis in an Intensive Care Unit (ICU) setting. The study included 680 patients from 35 ICUs across various Indian states. The prevalence of sepsis was found to be 46.2% according to the Sepsis-2 definition, 33.2% according to the Sepsis-3 definition, and 56.4% using either definition [2].

Critically-ill sepsis patients often experience hyponatremia, which occurs in 30-40% of cases [3]. Hyponatremia in sepsis patients increases morbidity and mortality, especially in those with co-morbid illnesses [4]. Therefore, early and accurate diagnosis, along with appropriate management, is essential. In a cohort study by Wald R et al., increased mortality was observed in hospitalised patients with hyponatremia [5].

The SOFA score is a vital tool in critical care for evaluating organ dysfunction. It assesses the kidneys, liver, lungs, heart, coagulation, and neurological status. The score helps evaluate disease and sepsis severity and predict outcomes and survival for sepsis patients in the Intensive Care Unit (ICU). High degrees of organ dysfunction and mortality are observed in patients with high SOFA scores [6].

The available data on hyponatremia associated with increased morbidity and mortality, as assessed by the SOFA score in sepsis patients within Indian ICU settings, is limited [7,8]. Therefore, the present study evaluates the presence of hyponatremia and examines its potential association with SOFA scores in sepsis patients admitted to the ICU.

## MATERIALS AND METHODS

The prospective observational cross-sectional study was carried out at the Critical Care Unit of Shri Bhikhbai Kanjibhai Shah Medical Institute and Research Hospital, Piparia, Waghodia, Gujarat, over a one-month duration in November 2024. Ethical approval was obtained from the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC/ON/Medi/RP/OCT/24/25). The study adhered to the ethical standards outlined in the Declaration of Helsinki and the Indian Council of Medical Research.

### Sample size calculation:

$$n = Z^2 \times p \times q / e^2$$

$Z = 1.96$  at a 95% Confidence Interval (CI)

$p$ =prevalence of hyponatremia in sepsis patients admitted to the Critical Care Department, taken as 30% (0.3). The prevalence of hyponatremia in sepsis patients in the ICU, as observed by DeVita MV et al., is around 30-40% [3].

$q = 1 - p = 0.7$   $e = \text{margin of error} = 10\%$ .

The calculated sample size is 80, and by adding a 10% non response rate, the total sample size is 88.

**Inclusion criteria:** Sepsis patients aged over 18 years admitted to the critical care unit who met the Sepsis-3 guidelines were included [9].

**Exclusion criteria:** Patients with hyperlipidemia, paraproteinemia, hyperglycemia, hypernatremia, or those receiving mannitol or radiographic contrast agents were excluded.

## Study Procedure

The study included 88 patients who were admitted to the critical care unit over a one-month period and met the Sepsis-3 guidelines. Participants were selected based on the inclusion and exclusion criteria, and written informed consent was obtained. A standard protocol of history-taking and clinical examination was conducted. Blood samples for routine tests were collected upon admission. Investigations necessary for the study, including ABG analysis ( $\text{PaO}_2/\text{FiO}_2$ ), serum bilirubin, platelet count, serum creatinine, and serum sodium, were performed as part of standard procedures. The SOFA score was calculated upon admission to the critical care unit, and the risk of mortality was predicted [Table/Fig-1] [10,11].

SOFA score	Predicted mortality %
0-1	0
2-3	6.4
4-5	20.2
6-7	21.5
8-9	33.3
10-11	50
12-14	95.2
>14	95.2

[Table/Fig-1]: Predicted mortality according to the original SOFA score [10,11].

Hyponatremia: Sodium level is equal to or less than 135 mmol/L.

Mild hyponatremia: 130-135 mmol/L

Moderate hyponatremia: 125-129 mmol/L

Severe hyponatremia: <125 mmol/L [4,12].

## STATISTICAL ANALYSIS

The appropriate statistical tests were applied to determine the prevalence and associations within the data. A Chi-square test with a p-value of less than 0.05 was considered statistically significant.

## RESULTS

The average age of study patients with hyponatremia was 50.74 years, with a standard deviation of 16.49 years, indicating a moderately wide age distribution among the participants. The gender-wise distribution of the study subjects with hyponatremia (n=69) revealed that the majority were male, comprising 43 (62.32%) participants, while females accounted for 26 (37.68%) participants [Table/Fig-2]. This indicates a higher representation of males in the study population with hyponatremia.

Parameters	Mean $\pm$ SD
Age (years)	50.74 $\pm$ 16.49
Gender	Number of participants (%)
Female	26 (37.68)
Male	43 (62.32)

[Table/Fig-2]: Demographic profile of study participants with hyponatremia (n=69).

Among the study participants (n=88), 19 (21.6%) patients had normal sodium levels. The prevalence of hyponatremia was notably high, with 78.4% exhibiting varying degrees of the condition [Table/Fig-3]. These findings highlight the significant burden of hyponatremia among patients admitted to the critical care Department.

Hyponatremia	Frequency n (%)	Prevalence (%)
No hyponatremia	19	21.6
Mild	35	39.8
Moderate	22	25.0
Severe	12	13.6

[Table/Fig-3]: Prevalence of hyponatremia in study subjects (N=88).

The most common aetiological diagnoses in participants with hyponatremia were as follows: lower respiratory tract infection, which was the most frequent, affecting 23% of cases (16 patients). This was followed by decompensated CLD in 6 (9%) cases, ischaemic stroke with aspiration pneumonia in 4 (6%) patients, and urosepsis in 4 (6%) patients [Table/Fig-4]. Other significant etiological causes of hyponatremia in the remaining cases included acute haemorrhagic stroke in 4 (5.5%) patients, acute cardiogenic shock in 4 (5.5%) patients, decompensated heart failure in 3 (5%) patients, acute encephalitis in 3 (5%) patients, acute kidney injury on chronic kidney disease in 3 (5%) patients, and Central Nervous System (CNS) malignancy in 3 (4%) patients. The other causes include acute gastroenteritis, viral fever, Chronic Obstructive Pulmonary Disease (COPD) exacerbation, Guillain-Barré syndrome, and cerebral venous thrombosis. These findings highlight the various underlying conditions contributing to hyponatremia in critically-ill sepsis patients.

Diagnosis	Frequency n (%)	Percentage (%)
Lower Respiratory Tract Infection (LRTI)	16	23
Decompensated Chronic Liver Disease (CLD)	6	9
Acute ischaemic stroke with aspiration pneumonia	4	6
Urosepsis	4	6

[Table/Fig-4]: Most common aetiological diagnosis in participants with hyponatremia.

The most frequent SOFA score in hyponatremic patients was two, observed in 19 (27.5%) patients. Higher SOFA scores were less common, with 6 (6.8%) patients having scores of 8 and 5 (7.2%) patients with a score of nine. The mean SOFA score among 69 patients with hyponatremia was 4.42, with a standard deviation of 2.34. These findings illustrate that the majority of patients had lower SOFA scores, reflecting milder organ dysfunction, although a significant proportion had moderate to severe scores, correlating with higher mortality risks.

The analysis of the association between SOFA scores and the severity of hyponatremia revealed a statistically significant relationship, as indicated by the Chi-square test result ( $p<0.05$ ) [Table/Fig-5].

SOFA score	Hyponatremia				Chi-square test (p-value)
	No hyponatremia	Mild hyponatremia	Moderate hyponatremia	Severe hyponatremia	
2	7	10	4	5	32.03 (<0.05)
3	1	3	7	4	
4	1	6	3	0	
5	6	3	2	0	
6	0	5	1	0	
7	3	2	2	1	
8	0	2	2	2	
9	1	4	1	0	

[Table/Fig-5]: Distribution of hyponatremia severity across different SOFA scores and its statistical association.

A significant association was found between platelet count and serum creatinine with hyponatremia severity, as evidenced by a Chi-square test (p-value of 0.03 and p-value <0.05, respectively). Patients with normal platelet counts showed higher frequencies of normal sodium levels (16) and mild hyponatremia (22), while those with abnormal platelet counts had fewer severe cases. Abnormal

serum creatinine levels were more common in participants with severe hyponatremia, suggesting a link between kidney function and sodium disturbances [Table/Fig-6].

hyponatremia was found to negatively impact stroke outcomes, highlighting the importance of closely monitoring serum sodium levels to prevent mortality [18].

Components of SOFA score		Hyponatremia			Chi-square test (p-value)	
		No	Mild hyponatremia	Moderate hyponatremia		
PaO <sub>2</sub> /FiO <sub>2</sub>	*Normal	8	20	9	10	6.87 (0.07)
	Abnormal	11	15	13	2	
Platelet count (lac/cumm)	Normal	16	22	18	12	8.45 (0.03)
	Abnormal	3	13	4	0	
S. bilirubin (mg/dL)	Normal	12	12	8	7	5.68 (0.12)
	Abnormal	7	23	14	5	
Mean arterial pressure (mmHg)	Normal	19	35	21	11	3.75 (0.28)
	Abnormal	0	0	1	1	
GCS	Normal	13	18	13	11	6.57 (0.08)
	Abnormal	6	17	9	1	
S. creatinine (mg%)	Normal	7	11	16	0	19.13 (<0.05)
	Abnormal	12	24	6	12	

**[Table/Fig-6]:** Association between components of SOFA score and hyponatremia severity.

(\*Normal values: PaO<sub>2</sub>/FiO<sub>2</sub> ≥400; Platelet count ≥1.5 lac/cumm; serum bilirubin ≥1.2 mg/dL; serum creatinine ≥1.2 mg/dL; GCS: Glasgow coma score-15; MAP: Mean arterial pressure ≥70 mm of Hg)

## DISCUSSION

Sepsis, a dysregulated host reaction to an infection, is a major cause of hospitalisation and Intensive Care Unit (ICU) mortality [13]. In the Intensive Care across Nations (ICON) audit, 10,069 patients older than 16 years who were hospitalised in the ICU were prospectively included from Europe (54.1%), Asia (19.2%), America (17.1%), and other continents (9.6%). The incidence of sepsis ranged from 13.6 to 39.3%, and the mortality rate in intensive care was 25.8% [14].

The average age of study patients with hyponatremia was 50.74 years, with a standard deviation of 16.49 years [Table/Fig-2]. This was higher than the average age reported in the study by Kumar S et al., which was 44 years [7]. Among the study subjects with hyponatremia, 62.32% were male, and 37.68% were female. This contrasts with the findings of the study by Padhi R et al., where 56.5% of hyponatremic patients were female and 43.5% were male [8]. In present study, the prevalence of hyponatremia was notably high at 78.4%, with 39.8% classified as mild, 25% as moderate, and 13.6% as severe [Table/Fig-3]. In contrast, the study by Parajuli S et al., reported a significantly lower prevalence of hyponatremia, observed in 20.59% of their 102 patients [15].

In present study, the most common causes of hyponatremia were lower respiratory tract infections (18.2%), followed by decompensated liver disease (6.8%), ischaemic stroke with aspiration pneumonia as a complication (4.5%), and urosepsis (4.5%) [Table/Fig-4]. In contrast, the study by Padhi R et al., reported that the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) due to pneumonia (36.25%) was the most frequent cause, followed by severe sepsis (21.51%) and trauma (21.11%) [8]. Similar results were observed in the study by Nair V et al., which found that pneumonia is frequently associated with hyponatremia at the time of admission, leading to severe illness, prolonged hospitalisation, and increased mortality [16].

In present study, decompensated liver disease was the second most common cause of hyponatremia, observed in 6.8% of hyponatremic patients. This is significantly lower compared to the findings of a study by Bhandari A and Chaudhary A, where a high prevalence of hyponatremia (41.22%) was reported among patients with CLD. In their study of 114 patients, 47 were found to have hyponatremia, with a 95% confidence interval ranging from 32.18% to 50.25% [17].

In present study, ischaemic stroke accounted for 4.5% of hyponatremia cases, which is considerably lower than the 35% reported in the study by Saleem S et al., [18]. In their study, the most common causes of hyponatremia in stroke patients were identified as SIADH and Cerebral Salt Wasting syndrome (CSW). Overall,

The SOFA score assesses the severity of illness using straightforward measurements of major organ function based on routine tests. It requires only six variables, enabling quick evaluation. The scores are calculated 24 hours after ICU admission and subsequently every 48 hours. This scoring system has been validated in both medical and surgical ICUs, demonstrating that higher SOFA scores are associated with lower survival rates [19].

In present study, the most frequent SOFA score observed in sepsis patients with hyponatremia was two, recorded in 19 patients (27.5%). Higher SOFA scores were less frequent, with six patients (6.8%) having scores of eight and five patients having a score of nine. The mean SOFA score was 4.42, with a standard deviation of 2.34. This contrasts with the study by Jones AE et al., where the average SOFA score at admission to the Emergency Department was  $7.1 \pm 3.6$  points [6]. Similarly, in the study by Kumar S et al., the mean SOFA score at the time of admission was  $6.18 \pm 2.38$  points, which is also higher than present findings [7].

In present study, the association between SOFA scores and the severity of hyponatremia showed a statistically significant result, as demonstrated by the Chi-square test ( $p < 0.05$ ) [Table/Fig-5]. This suggests that the predicted mortality risk based on the SOFA score is higher in sepsis patients with hyponatremia, indicating they are at an increased risk of mortality [Table/Fig-1]. Thus, the SOFA score is a valuable tool for triaging patients and prioritising treatment.

Similar results supporting the findings of present study have been reported in the following studies. A retrospective study by Nzerue CM et al., which included 168 patients with severe hyponatremia, found that 89 patients (52.9%) displayed symptoms, with a significant mortality rate of 20.2% (34 patients) [20]. In line with this, the study by Padhi R et al., showed that patients with hyponatremia experienced longer ICU stays, prolonged mechanical ventilation, and a higher mortality rate [8]. Like-wise, Shakhe J et al., observed greater mortality, prolonged ICU stays, and higher ventilator usage in ICU patients with hyponatremia [21]. Additionally, Funk GC et al., conducted a large retrospective study involving 151,486 adults across 77 ICUs in Austria over a 10-year period, finding that all forms and severities of dysnatremia were linked to higher mortality rates [22].

In contrast to present study, Kumar S et al., found no significant association between the overall SOFA score for sepsis and the severity or presence of hyponatremia, suggesting differing findings in terms of the predictive value of SOFA scores in their study [7].

The present study found a significant association between platelet count and the severity of hyponatremia, as demonstrated by a

Chi-square test (p-value of 0.03) [Table/Fig-6]. Patients with normal platelet counts exhibited a higher frequency of normal sodium levels and mild hyponatremia, whereas those with abnormal platelet counts had a lower frequency of normal sodium levels and a higher occurrence of mild and moderate hyponatremia.

In present study, the association between serum creatinine levels and the severity of hyponatremia was statistically significant, as evidenced by the Chi-square test (p-value of <0.05) [Table/Fig-6]. Abnormal serum creatinine levels were more common among participants with severe hyponatremia, suggesting a link between kidney function and sodium disturbances. The present study results contrast with those observed in the study conducted by Kumar S et al., where no correlation was found between the individual components of the SOFA score and hyponatremia [7].

### Limitation(s)

The study is conducted at a single institution, which may limit generalisability to other populations or settings. Additionally, the study does not include the endpoint of mortality in sepsis patients; therefore, only the predicted mortality rate is considered to evaluate the prognosis.

### CONCLUSION(S)

The association between hyponatremia and the SOFA score in sepsis patients holds significant clinical relevance. Hyponatremia, a frequent electrolyte imbalance in critically-ill individuals, reflects illness severity and may exacerbate organ dysfunction. It aids in risk stratification, guides targeted interventions, and helps predict mortality risk in sepsis patients. This relationship facilitates early intervention, minimises complications, and improves patient outcomes in sepsis management.

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