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A Clinical Evaluation Of Hyponatremia As A Prognostic Indicator In Patients Hospitalized With Sepsis

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Abstract
Introduction:
Hyponatremia is frequently observed in critically ill patients, including those with sepsis. Its prognostic value in sepsis, however, remains unclear.
Objective:
To assess the prevalence and prognostic implications of hyponatremia in patients admitted with sepsis.
Methods:
A prospective cohort study was conducted on 95 patients diagnosed with sepsis and grouped as normonatremic (Group A, n = 37) and hyponatremic (Group B, n = 58). Clinical parameters including age, gender, serum sodium levels, total leukocyte count (TLC), heart rate, hospital stay duration, ventilator requirement, and mortality were analyzed using chi-square and t-tests. A p-value < 0.05 was considered statistically significant.
Results:
Hyponatremia was observed in 61.05% of septic patients (p = 0.031). Most hyponatremic cases were aged 31–70 years (p = 0.023), with no significant gender difference (p = 0.115). Mean sodium levels were significantly lower in Group B (129.17 mmol/L) compared to Group A (140.29 mmol/L) (p < 0.0001). Hyponatremic patients had higher TLC (p = 0.0131) and longer hospital stays (mean 5.45 vs. 4.08 days, p = 0.0013). Interestingly, normonatremic patients exhibited higher heart rates (p < 0.0001). Although more hyponatremic patients required ventilator support (30/58 vs. 14/37), the difference was not statistically significant (p = 0.186). Mortality was significantly higher in Group B (26 vs. 9 deaths; p = 0.043), but sodium levels did not independently predict mortality within groups. Subgroup analysis revealed no significant associations between hyponatremia severity and mortality (p = 0.768) or ventilator requirement (p = 0.870). Survivors across both groups showed significantly different heart rates (p = 0.00006). In Group B, non-survivors had significantly higher TLC (p = 0.03769), but leukocytosis did not vary significantly with hyponatremia severity (p > 0.05).
Conclusion:
Hyponatremia is prevalent in sepsis and associated with prolonged hospital stay and increased mortality. However, its severity does not significantly influence ventilator requirements or mortality, suggesting that while hyponatremia reflects disease severity, it may not independently determine clinical outcomes in sepsis.
Keywords: *Hyponatremia, Sepsis, Prognostic indicator, Mortality, Hospital stay, Ventilator requirement, Inflammatory markers, Sodium levels, Total leukocyte count (TLC)*

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I. Introduction

Hyponatremia, defined as a serum sodium concentration below 135 mEq/L, is a common electrolyte disturbance frequently observed in critically ill patients. In the context of sepsis—a life-threatening condition marked by a dysregulated immune response to infection—hyponatremia is particularly significant due to its association with increased morbidity, prolonged hospital stay, and higher mortality, especially in septic shock where mortality can reach 50% [1,2].

Sepsis induces widespread inflammation, endothelial dysfunction, and multiorgan failure, disrupting fluid and electrolyte balance. Inflammatory cytokines such as IL-6 and TNF-α promote non-osmotic ADH release, leading to dilutional hyponatremia. Sepsis-induced hypovolemia and increased vascular permeability further stimulate ADH through baroreceptor mechanisms, compounding sodium imbalance [3–7]. The classification of hyponatremia based on osmolality and volume status—hypovolemic, euvolemic, or hypervolemic—guides diagnosis and therapy. In sepsis, hyponatremia is often hypovolemic or euvolemic, with SIADH playing a central role. Contributing factors include hypotonic IV fluids and renal dysfunction [8–10].

Clinical manifestations vary from mild symptoms (fatigue, nausea) to severe neurological complications (seizures, coma, cerebral edema), particularly in acute cases. Chronic hyponatremia may cause cognitive decline and worsen outcomes [11,12]. Management is challenging; acute cases may require rapid correction, while chronic hyponatremia mandates gradual sodium normalization to prevent osmotic demyelination syndrome (ODS). Guidelines recommend limiting correction to 8–10 mEq/L in 24 hours [13,14].

Treatment depends on the underlying cause. SIADH-related hyponatremia is managed with fluid restriction and sometimes hypertonic saline or vasopressin antagonists. Hypovolemic hyponatremia is treated with isotonic fluids, while hypervolemic cases may require diuretics or renal replacement therapy [15].

Hyponatremia has been associated with adverse outcomes in sepsis, including prolonged ICU stay, mechanical ventilation, and higher mortality [16–18]. It may act as both a marker of illness severity and a contributor to immune and hemodynamic instability [19,20]. The fluctuating nature of sepsis necessitates frequent reassessment and individualized fluid management. Emerging tools like bedside ultrasound may help optimize therapy [21,22].

Given its high prevalence and potential prognostic implications, the present study aims to investigate the clinical outcomes associated with hyponatremia in patients diagnosed with sepsis [23,24]. The specific objectives are to assess the prevalence of hyponatremia, evaluate its effect on the duration of hospital stay, and analyze the association between the severity of hyponatremia and key clinical outcomes, including in-hospital mortality and the requirement for ventilatory support.

II. Materials And Methods

This prospective cohort study was conducted in the Department of General Medicine, G.R. Medical College, Gwalior (M.P.), from May 2023 to September 2024. A total of 95 patients meeting the inclusion criteria were enrolled. Eligible participants were adults (≥18 years) presenting with sepsis, defined by the presence of at least two SIRS criteria and serum sodium levels ≤135 mEq/L. Patients were excluded if they had received prior treatment for sepsis, were pregnant or lactating, had hypernatremia (Na^+ >145 mEq/L), or refused consent. All participants were evaluated for demographic details, comorbidities, and clinical parameters. Based on serum sodium levels, patients were categorized into eunatremic and hyponatremic groups. Outcomes including duration of hospital stay, need for ventilatory support, and in-hospital mortality were assessed. Follow-up was conducted over a 14-day period, with patients classified as survivors or non-survivors based on discharge status. Data were collected using a structured proforma, and statistical analysis was performed using SPSS software, with p-values <0.05 considered significant. Ethical clearance was obtained from the Institutional Ethics Committee. Informed consent was acquired from all participants, ensuring privacy and confidentiality. The limitations of the study include a relatively small sample size, a single-center design, a lack of long-term follow-up, the absence of serial sodium measurements, and no differentiation of hyponatremia etiology.

III. Result

In this study, hyponatremia was present in 61.05% of sepsis patients, significantly higher than the expected 50% ($\chi^2(1) = 4.64$, $p = 0.031$) in Figure 1. This highlights its clinical relevance and supports the role of serum sodium as a key parameter in the assessment and risk stratification of septic patients.

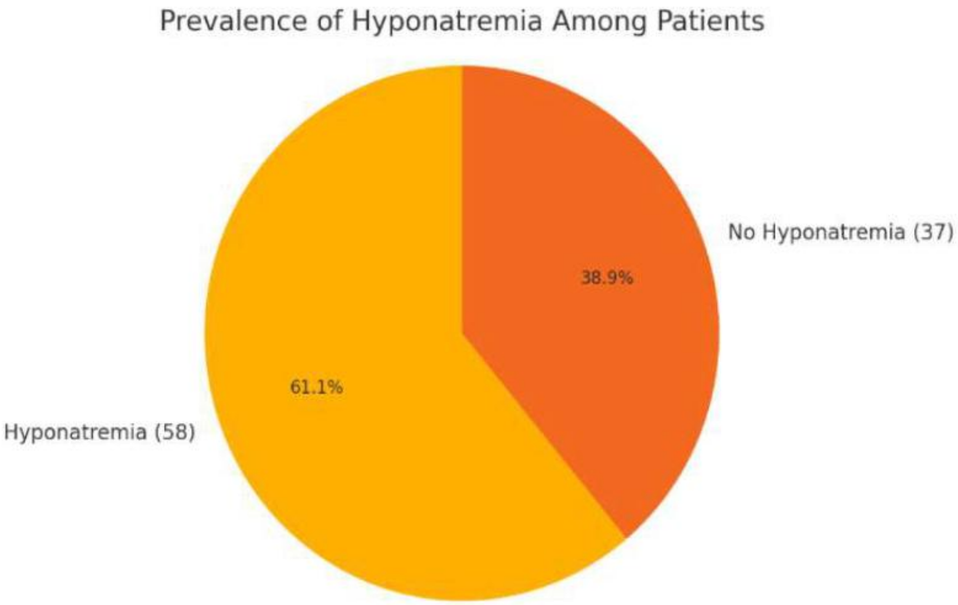

Figure 1: Prevalence of hyponatremia among the patients admitted with sepsis

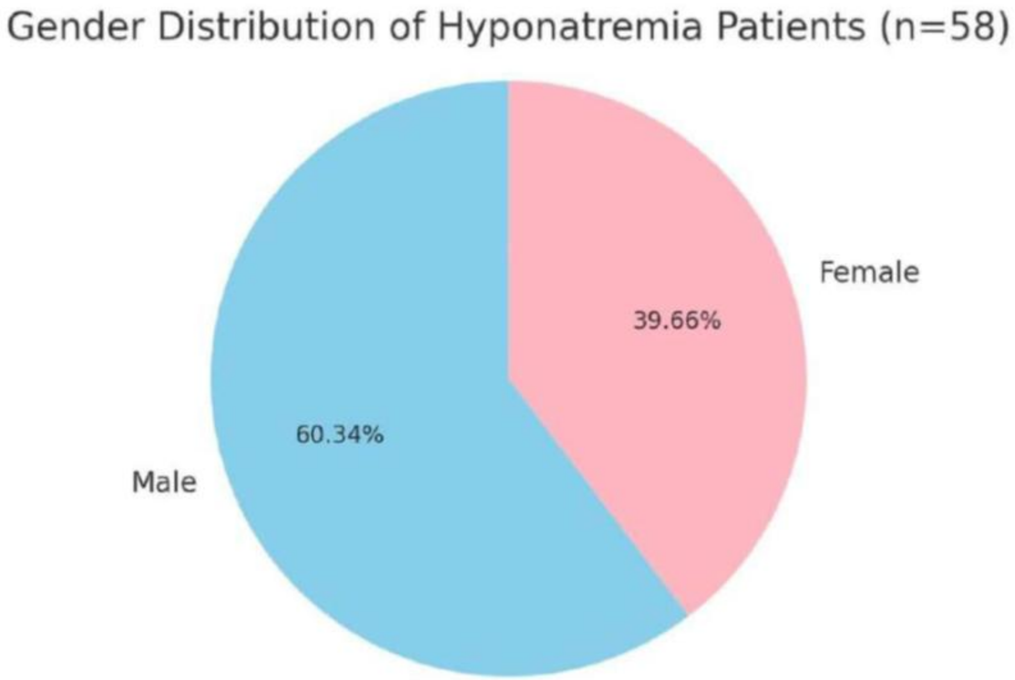

Figure 2: Gender distribution of hyponatremia patients

A chi-square goodness-of-fit test ($\chi^2(1) = 2.48$, $p = 0.115$) showed no significant deviation from equal gender distribution in Figure 2, indicating that hyponatremia affected males and females similarly in this sepsis cohort.

Table 1: Age distribution of hyponatremia patients

Age (yrs)	patient count	Percentage %
18 to 30	5	8.6%
31-50	21	36%
51-70	22	37.9%
>70	10	17.2%
Total	58	
chi-square statistic 14.448, p value:0.023		

A Chi-square goodness-of-fit test was performed to examine whether patients were evenly distributed across age groups (18–30, 31–50, 51–70, >70 years). The test yielded a significant result ($\chi^2 = 14.41$, $p = 0.0024$), indicating a non-uniform distribution mentioned in Table 1. Specifically, individuals aged 31–70 years were overrepresented, while the 18–30 age group was underrepresented. This uneven distribution may reflect age-related variations in sepsis incidence or healthcare-seeking behavior.

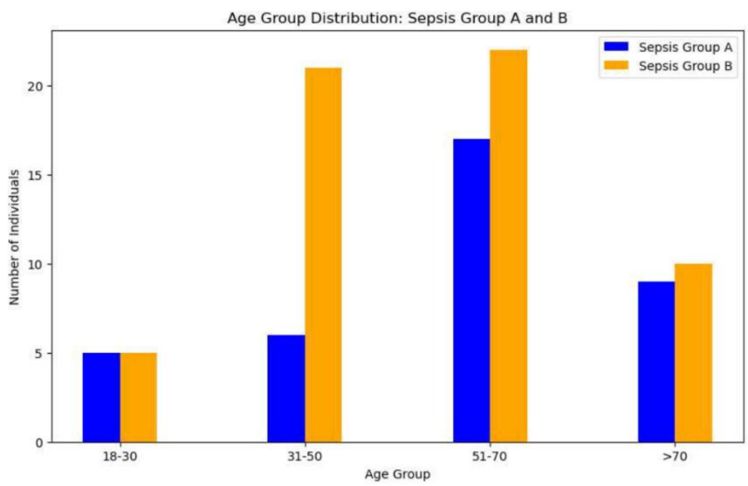

Figure 3: Age Group Distribution among sepsis groups

Since the p-value (0.2255) is greater than the conventional threshold of 0.05, the analysis indicates no statistically significant association between patient age and sepsis group classification in Figure 3. This suggests that the distribution of patients across different age groups does not differ meaningfully between the groups being compared. Therefore, age does not appear to be a determining factor in distinguishing between the sepsis groups in this study population.

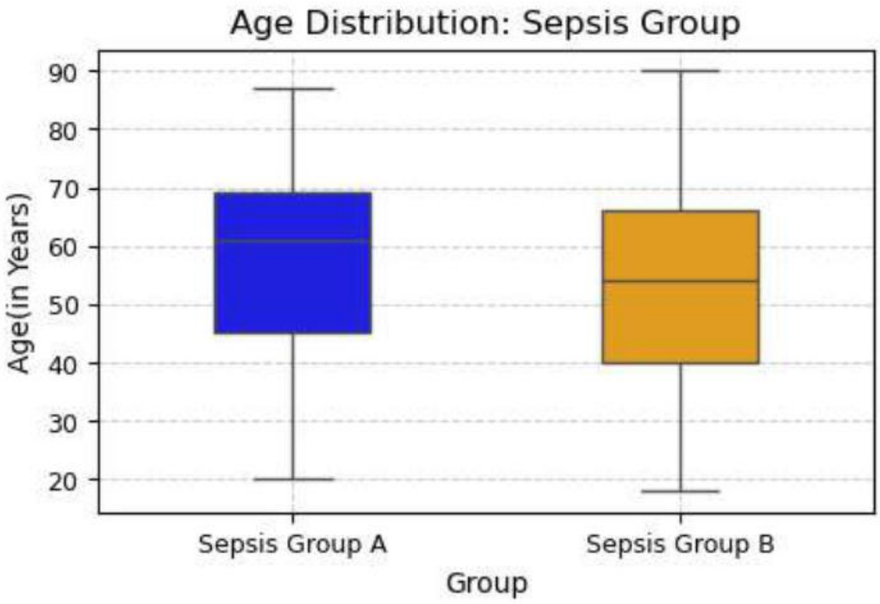

Figure 4: Age Distribution Comparison between sepsis groups

Since the p-value (0.6947) exceeds 0.05, there is no statistically significant association between gender and sepsis group classification, suggesting gender does not influence group distribution or outcomes in Figure 4.

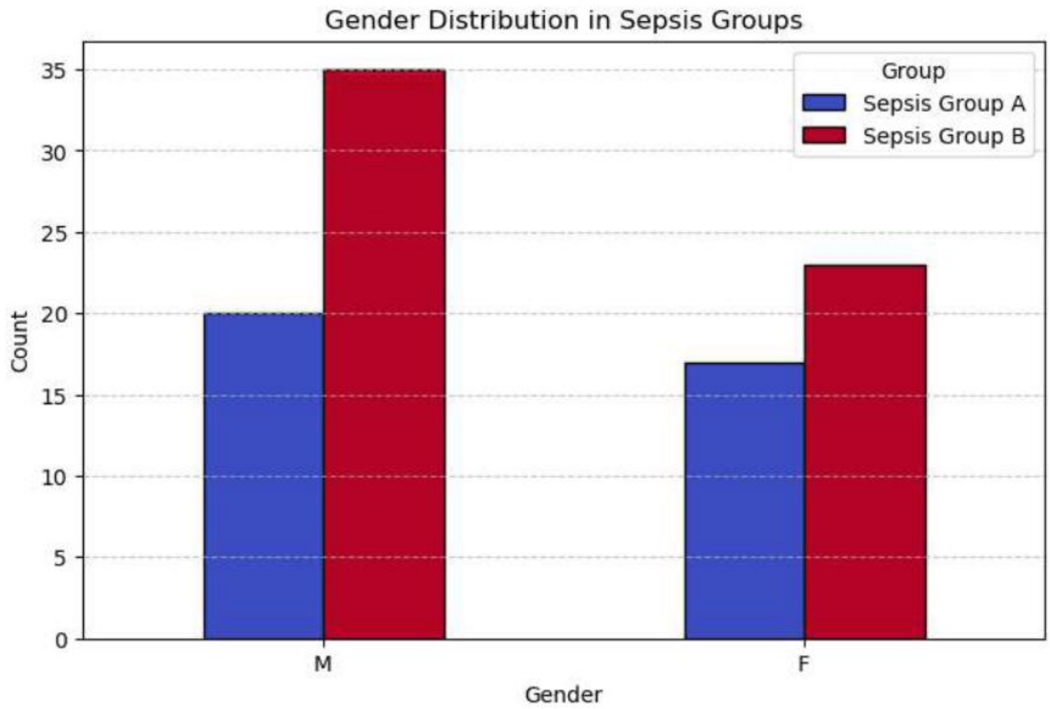

Figure 5: Gender Distribution Comparison between sepsis groups

Since the p-value (0.6947) is greater than 0.05, we conclude that there is not statistically significant association of Gender between Sepsis Groups in Figure 5.

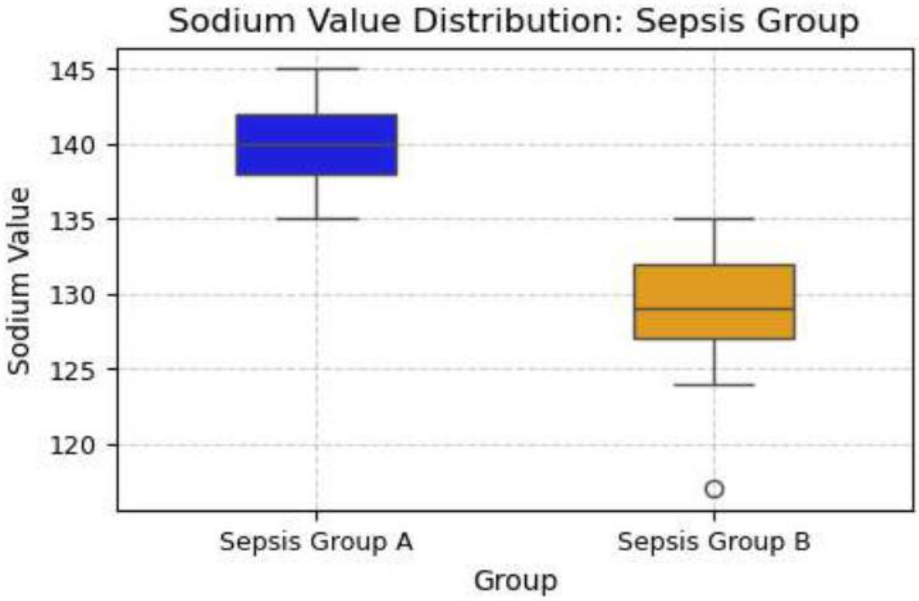

Figure 6: Sodium Value Distribution

Since the p-value (0.0000) is below the 0.05 threshold, there is a statistically significant association between sodium levels and sepsis group classification in Figure 6.

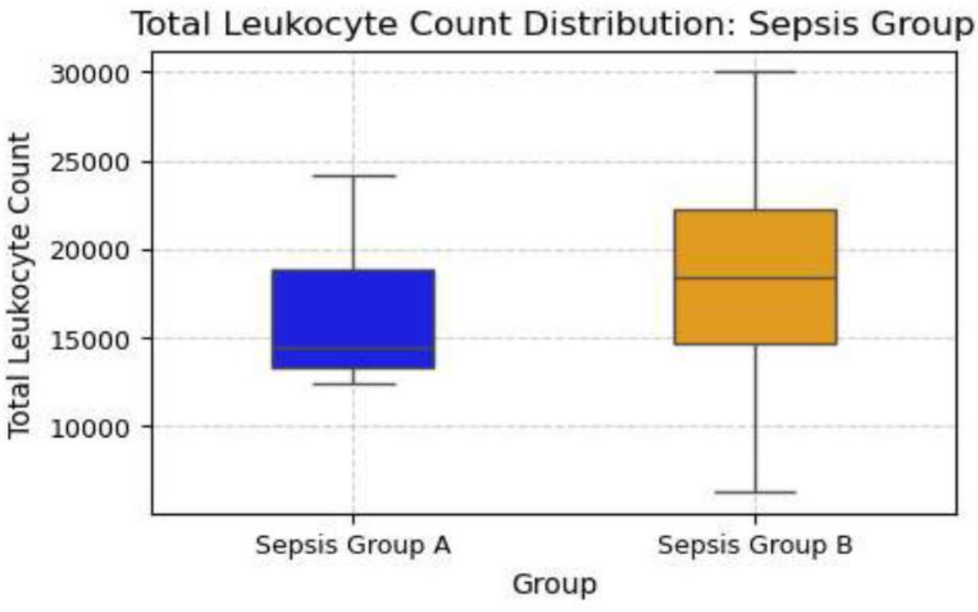

Figure 7: Total Leukocyte Count Distribution

Since the p-value (0.0131) is below the 0.05 threshold, there is a statistically significant association between total leukocyte count and sepsis group classification in Figure 7.

Table 2: Heart Rate Distribution Comparison

Heart Rate	Sepsis Group A	Sepsis Group B
Count	37	58
Mean	109.92	99.78
Std	11.43	5.32
Min	92	90
25%	100	96
50%	109	98
75%	120	102
Max	135	110

T-test Statistic: 5.8522 P-value: 0.0000

Since the p-value (0.0000) is below 0.05, heart rate is significantly associated with sepsis groups. The T-test (t = 4.9421, p = 0.0000) confirms this difference. Group A showed a broader heart rate range (92–135 bpm) than Group B (96–110 bpm), suggesting a stronger physiological response, possibly due to more severe infection or inflammation.

Table 2 illustrates the comparison of heart rate between Sepsis Groups A and B. Group A shows a significantly higher mean heart rate (109.92 bpm) than Group B (99.78 bpm), along with greater variability (standard deviation: 11.43 vs. 5.32)

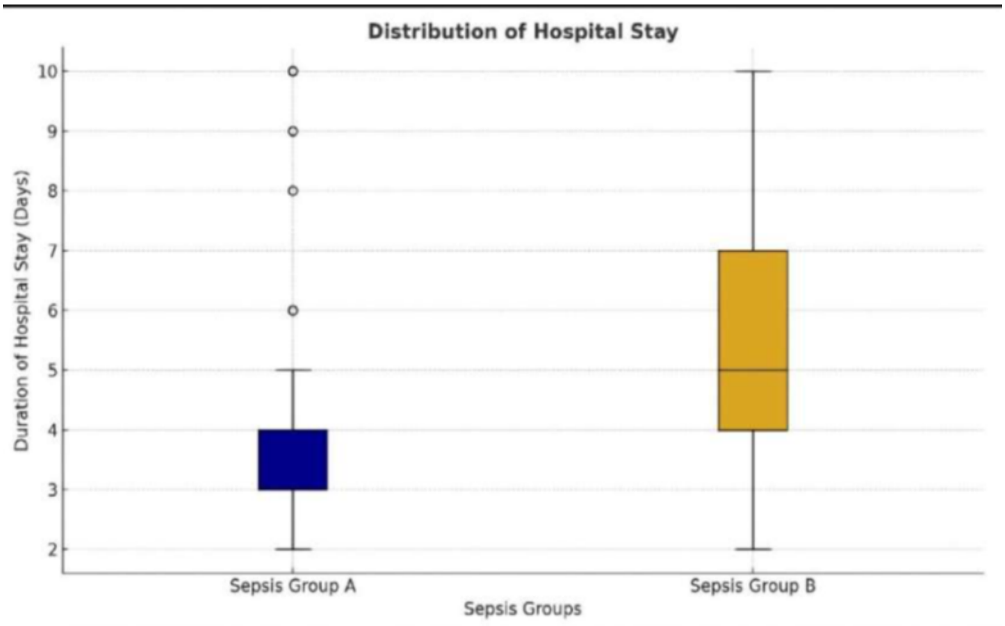

Fig 8: Duration of Hospital Stay Distribution Comparison

Since the p-value (0.0013) is less than 0.05, there is a statistically significant difference in hospital stay between the sepsis groups in **Figure 8**.

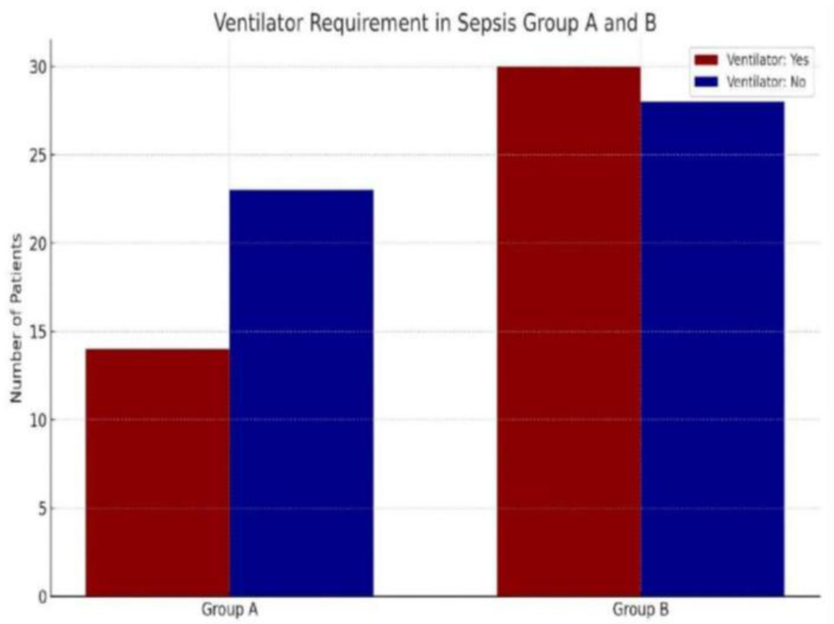

Figure 9: Ventilator Requirement Distribution Comparison

Since the p-value (0.186) is greater than 0.05, there is no statistically significant association between ventilator requirement and sepsis group classification in **Figure 9**.

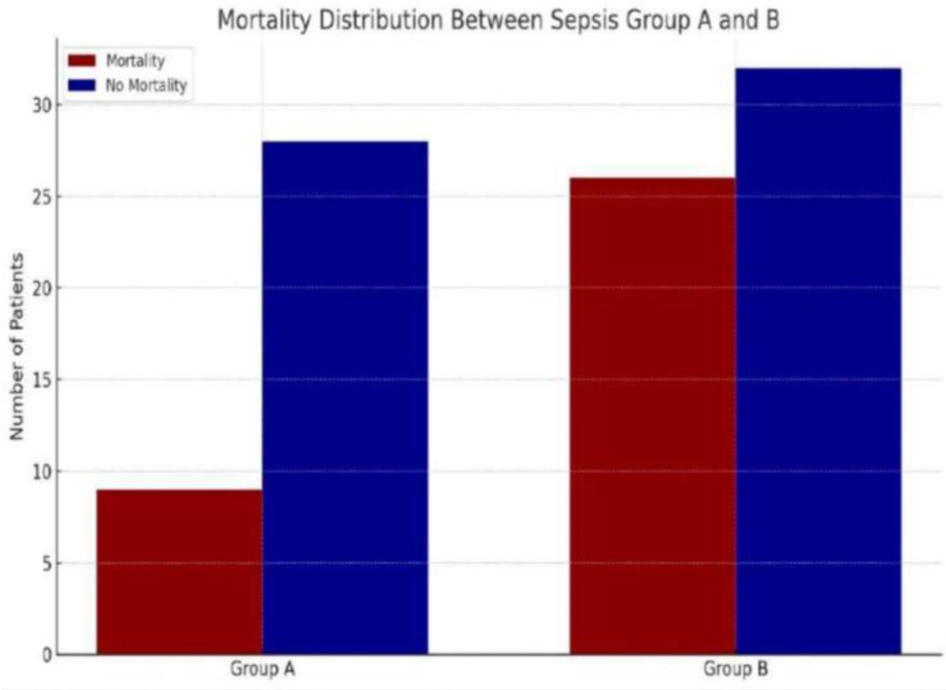

Figure 10: Mortality Distribution Comparison

Since the p-value (0.043) is less than 0.05, we conclude that there is a statistically significant association between mortality and sepsis group classification in **Figure 10**.

Table 3: Correlation between sodium value and mortality in Sepsis Groups

Sodium Count	Mortality		P value
	Yes	No	
Sepsis Group A	140.15 ±3.08 (n=9)	140.38 ±2.48 (n=28)	0.821
Sepsis Group B	129.53 ±3.39 (n=26)	128.59 ±3.39 (n=32)	0.293
P- value	0.0000	0.0000	

Although Group B (hyponatremic patients) had significantly lower sodium levels than Group A ($p < 0.001$), sodium concentration did not predict mortality in either group (Group A: $p = 0.821$; Group B: $p = 0.293$) in Table 3, suggesting hyponatremia may be a secondary marker rather than a direct predictor of sepsis-related mortality.

Table 4: Correlation between Sodium Value and Ventilation Requirement in Sepsis Groups

Sodium Count	Ventilation Requirement		P value
	Yes	No	
Sepsis Group A	139.88 ± 2.96 (n=14)	140.65 ±2.41 (n=23)	0.376
Sepsis Group B	129.03 ± 3.82 9 (n=30)	129.41 ±2.61 (n=28)	0.654
P- value	0.0000	0.0000	

Although Group B had significantly lower sodium levels ($p < 0.001$), sodium concentration did not predict ventilation needs in either group (Group A: $p = 0.376$; Group B: $p = 0.654$) in Table 4, suggesting hyponatremia may not independently drive mechanical ventilation in sepsis.

Table 5: Correlation between Heart Rate and mortality in between Sepsis Groups

Heart Rate	Mortality		P value
	Yes	No	
Sepsis Group A	106.85 ±11.19 (n=9)	111.58 ±11.44 (n=28)	0.2646
Sepsis Group B	100.36 ±5.72 (n=26)	99.82 ±4.53 (n=32)	0.6723
P- value	0.0649	0.00006	

The heart rate did not significantly predict mortality within either group (Group A: p = 0.2646; Group B: p = 0.6723) in Table 5, though the significant inter-group difference among survivors (p = 0.00006) suggests sepsis severity may influence cardiovascular response.

Table 6: Correlation between TLC and mortality in Sepsis

TLC	Mortality		P value
	Yes	No	
Sepsis Group A	17729.23±3899.97 (n=9)	15787.5 ±3534.69 (n=28)	**0.17910**
Sepsis Group B	19311.39 ±5032.18 (n=26)	18313.64 ±5302.41 (n=32)	**0.44229**
P- value	**0.38769**	**0.03769**	

TLC was not linked to mortality in Group A (p = 0.38769), but was significantly higher in non-survivors of Group B (p = 0.03769) in Table 6, suggesting leukocytosis may indicate severity in certain sepsis phenotypes.

Table 7: Correlation of the Severity of hyponatremia with mortality in Sepsis Group B.

TLC	Mortality	
	Yes	No
Mild	13	13
Moderate	10	15
Severe	3	4
Chi-square Statistic: 0.5278, p-value: 0.7680		

In Sepsis Group B, hyponatremia severity was not significantly associated with mortality ($\chi^2 = 0.5278$, $p = 0.7680$) in Table 7, suggesting sodium imbalance is more a secondary marker than an independent predictor of sepsis mortality.

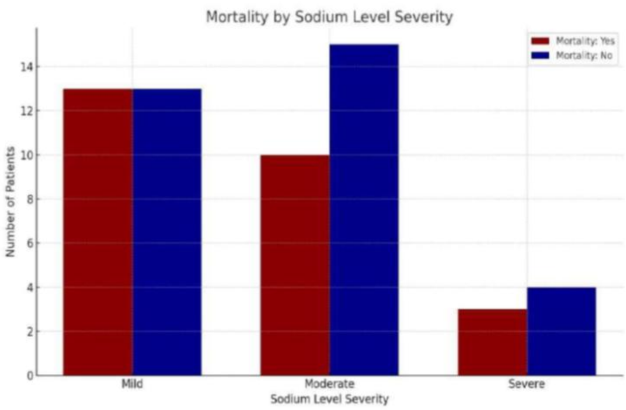

Figure 11: Correlation of Severity of hyponatremia with mortality in between Sepsis Group B.

In Sepsis Group B, sodium level severity showed no significant association with ventilator need ($\chi^2 = 0.278$, $p = 0.870$) in Figure 11, suggesting hyponatremia may not independently drive respiratory failure in sepsis.

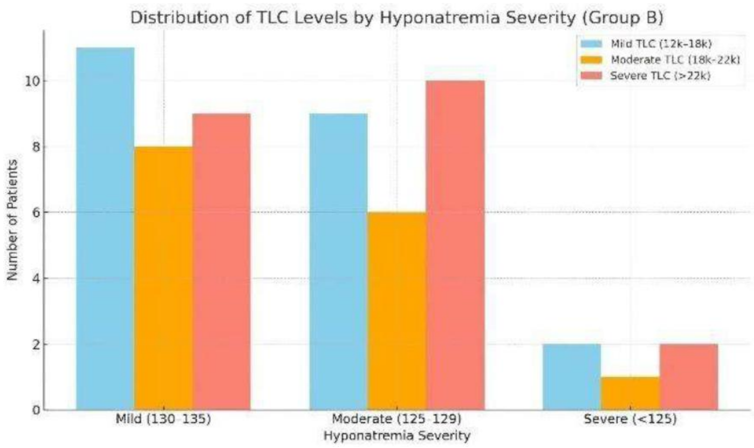

Figure: 12 Correlation of Severity of hyponatremia with Severity of leucocytosis in Sepsis Group B

The findings indicate no statistically significant link between hyponatremia severity and leukocytosis ($p > 0.05$) in Figure 12, suggesting that total leukocyte counts remain consistent across varying degrees of sodium imbalance.

IV. Discussion

The present study provides a detailed and multidimensional evaluation of hyponatremia and its clinical implications in patients admitted with sepsis, emphasizing not only the prevalence of electrolyte imbalances but also their correlation with key clinical outcomes such as duration of hospital stay, ventilatory support, and mortality. This analysis integrates demographic variables, clinical parameters, and laboratory values to offer a clearer understanding of how hyponatremia fits into the broader pathophysiology of sepsis.

The prevalence of hyponatremia among the sepsis cohort was found to be 61.05% (58 out of 95 patients), which is consistent with global literature that estimates the prevalence to lie between 30–50% in sepsis patients, as highlighted by Jansch et al. This high prevalence was further supported by findings from Sandeep Kumar and Kumari Pratima, who reported a similar rate of 69.47%, underscoring the commonality of this electrolyte disturbance in the septic population. The most affected age groups in the current study were 31–70 years, aligning with findings by Ronak Prakashkumar Shah et al., who reported a mean age of 50.74 years, indicating a higher burden of hyponatremia in middle-aged to elderly patients, potentially due to diminished physiological reserve or underlying comorbidities.

Gender distribution showed a higher prevalence of males in both sepsis groups (Group A: 54%, Group B: 60%), though without statistical significance, aligning with studies such as Shah et al., where 62.32% of participants were male, possibly reflecting broader epidemiological trends in sepsis incidence across genders.

A statistically significant difference in Total Leukocyte Count (TLC) between the sepsis groups was observed, with Group B non-survivors displaying significantly elevated TLC ($p = 0.03769$). This supports the role of leukocytosis as a potential marker of sepsis severity, particularly in hyponatremic phenotypes. Similarly, heart rate was notably higher and more variable in Group A, which may indicate a stronger physiological stress response due to systemic inflammation or cardiovascular compensation. These differences suggest potential hemodynamic or inflammatory phenotypes within sepsis, which merit further investigation for personalized risk stratification.

The duration of hospital stay was significantly longer in Group B (mean 5.45 days) compared to Group A (mean 4.08 days), suggesting greater illness severity and/or prolonged recovery in hyponatremic patients. Although ventilator requirements were higher in Group B, this difference was not statistically significant, implying that factors beyond sodium levels—such as respiratory function, underlying comorbidities, or infection source may more directly influence the need for mechanical ventilation.

A stark difference in mortality rates was observed, with Group B accounting for nearly 74.7% of total deaths, showing a statistically significant association between mortality and sepsis group classification. These results are echoed by studies from Yichen Wang and Nishant Sharma, who reported higher in-hospital mortality in patients with serum sodium ≤135 mEq/L, and by Dr. S. Muthulakshmi and Dr. M. Muralidharan, who documented a strong correlation between sodium derangements and mortality. However, despite Group B's lower sodium levels, the severity of hyponatremia (mild, moderate, severe) did not independently predict mortality or ventilation need within either group. This finding is critical, as it suggests that while hyponatremia is common and clinically relevant, it may serve more as a surrogate marker for underlying systemic dysfunction rather than a direct prognostic determinant.

This study underscores the complex and multifactorial nature of sepsis outcomes, where individual parameters like sodium levels, leukocytosis, and heart rate must be interpreted in a clinical context rather than in isolation. While hyponatremia is highly prevalent and associated with markers of severity and mortality, its role appears to be correlative rather than causative. These findings support a comprehensive, patient-centered approach to sepsis management, highlighting the need for holistic clinical evaluation rather than dependence on isolated biochemical markers.

V. Conclusion

This study underscores the high prevalence of hyponatremia (61.05%) among sepsis patients and its association with important clinical outcomes. Patients with hyponatremia had notably longer hospital stays, and a higher mortality rate (44.8%) compared to those with normal sodium levels (24.3%), suggesting its value as an indicator of disease severity. Despite these associations, neither sodium concentration nor the severity of hyponatremia independently predicted mortality or the need for ventilatory support. Although the heart rate was found to be lower in the hyponatremic group, its clinical significance remains uncertain. Furthermore, no meaningful link was observed between the severity of hyponatremia and leukocytosis. Overall, the findings suggest that while hyponatremia may not directly determine outcomes, it serves as a valuable clinical marker for identifying patients with potentially more severe illness, supporting its role in the routine assessment and management of sepsis.

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