

## Original Article

## Sodium Imbalance and In-Hospital Mortality in Patients Presenting with Sepsis at Tertiary Care Hospital

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### Abstract

**Objective:** To determine if presenting hyponatremia in septic patients is associated with higher in-hospital mortality.

**Methods:** This study was conducted at Aga Khan University Hospital Karachi, in the department of medicine for the duration of 6 months after ERC approval. Sample size of the study was 153 by taking prevalence of severe hyponatremia 15.8%, with margin of error = 6% and CI=95%. Those patients who were admitted with diagnosis of sepsis aged above 20 years were included in the study. Data was collected and recorded in computers, results were generated by using SPSS recent version and analysis was done by analyst.

**Results:** During the selected time frame for the study 153 patients were included in the study. Table-1 described the patient demographics, clinical characteristic and outcome of the patients included in the study, and comparison has been done amongst the two groups, with and without hyponatremia. Overall mortality in our study was found to be 39%, out of which 43.8% had hyponatremia, and 29.3% were with normal sodium levels. Females comprised of 51.2% of hyponatremic patients and 45.5% of normal serum sodium group. The SOFA score between these two groups did not show any significant difference. Patients with hyponatremia group had prolonged complicated hospital stay and required invasive ventilation (%) and had an increased mortality rate (43.8%) in comparison to patients who had normal sodium levels (29.3%).

**Conclusion:** Hyponatremia at presentation is not associated with higher in-hospital mortality in patients with sepsis.

**Keywords:** Hyponatremia, Sepsis, Sepsis-3, ICU

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### Introduction

Sepsis, the most devastating manifestation of infection is met with great trepidation and robust action by the medical teams in the Emergency Room (ER). Mortality due to sepsis ranges from 18-52%.<sup>1</sup> While its origin might be multivariate, the course and severity can be prognosticated by certain critical markers. Knowledge of these patterns is a powerful tool for diagnosis and management of critically ill patients and for predicting their outcome. One of these predictors is electrolyte disturbances at admission, particularly those of sodium,<sup>2</sup> which we decided to investigate in this study.

Sodium is the most abundant and osmotically active cation in the extracellular space responsible for regulating water shifts in the body.<sup>3</sup> During sepsis, most

homeostatic systems are compromised which may ultimately lead to sodium imbalances. When its levels are disturbed, the brain and the neuromuscular system are the ones most adversely affected. Hyponatremia may manifest as lethargy, disorientation and hyporeflexia. Hypernatremia on the other hand may present with overlapping symptoms of hyponatremia or can lead to hyperthermia, seizures and coma in severe cases.<sup>4</sup>

Studies have shown that irregular sodium levels affect a number of physiological functions and negatively impact prognosis for patients at admission or in the intensive care unit (ICU), irrespective of underlying comorbidities.<sup>5</sup> However, most of these studies focus on unselected patient groups from medical, cardiac or surgical ICUs. Our study is unique because our cross-section filtered just the patients who matched the criteria for sepsis at

admission. This single diagnosis was independent of the co-morbidities, which was prevalent in most patients. It reduced the generalizability of data gathered in dysnatremic patients at admission. While various scores and assessment tools exist to predict inpatient mortality, re-calibrating our diagnostic algorithms for septic patients according to sodium imbalances at the time of admission would lead to a more detailed appraisal of the situation. We hypothesized that initial deranged sodium levels, would be associated with higher in-hospital mortality among septic patients.

## Methods

The study was designed to be a cross sectional study conducted at The Aga Khan University, in the department of Medicine. The required sample size was calculated to be 153 patients; by assuming the prevalence of severe hyponatremia 15.8%, margin of error 6% and confidence level 'C.I.' 95%.<sup>6</sup> This sample size was calculated using the WHO software using the non-probability consecutive sampling.

Patients aged >20 years presenting with sepsis within 24 hours of admission according to sepsis-3 definition were included.<sup>7</sup> The patients were categorized into any one of the patterns of sodium imbalance; hyponatremia (<135 mmol/L) and normal serum sodium levels (>135 to <146 mmol/L). Sequential Organ Failure Assessment (SOFA) score, which describes the degree of organ dysfunction and predicts mortality in patients, was calculated for each septic patient.<sup>8</sup> The patients were categorized in to two groups; SOFA score > 10 and SOFA score <10. Each group was then assessed for hyponatremia at presentation.

The findings of qualitative variables (gender, residence status, hypertension, diabetes mellitus type II, dyslipidemia, smoking status, anemia, obesity status, occupational status, family monthly income, pattern of sodium imbalance (normal serum sodium levels and hyponatremia) and in-hospital mortality were entered in the proforma. Data was analyzed on SPSS Version 20. Frequencies and percentages were calculated for categorical variables like gender, residence status, hypertension, diabetes mellitus type II, and pattern of sodium imbalance (normal serum sodium levels or hyponatremia) and in-hospital mortality (yes/no). Post stratification chi-square test was applied taking p-value  $\leq 0.05$  as significant.

## Results

During the selected time frame for the study 153 patients were included in the study. Table-1 describes the patients' demographics, clinical characteristics, outcomes and comparison between those with and without hyponatremia. Overall mortality in our study was found to be

39%, out of which 43.8% had hyponatremia, and 29.3% were normonatremic. Female comprised of 51.2% of hyponatremia patients and 45.5% of normal serum sodium group.

The SOFA score between these two groups did not show any significant difference. Patients with hyponatremia group had prolonged complicated hospital stay and required invasive ventilation (54.5%) and had an increased mortality rate (43.8%) in comparison to patients who had normal sodium levels (29.3%).

**Table 1:** Demographic comparison of patients with and without hyponatremia

	Hyponatremia		P Value
	(Absent) n (%) n=41	(Present) n (%) n=112	
<b>Age (Years)</b>			
<50	8 (19.5%)	30 (26.8%)	0.36
>50	33 (80.5%)	82 (73.2%)	
<b>Gender</b>			
Male	20 (48.8%)	61 (54.5%)	0.53
Female	21 (51.2%)	51 (45.5%)	
<b>Comorbidities</b>			
Diabetes Mellitus	24 (58.5%)	54 (48.2%)	0.26
Hypertension	28 (68.3%)	68 (60.7%)	0.39
Chronic Kidney Disease	7 (17.1%)	17 (15.2%)	0.78
Chronic Liver Disease	5 (12.2%)	12 (10.7%)	0.80
<b>Ventilatory Support</b>			
No ventilatory support required.	7 (17.1%)	37 (33.0%)	0.13
Invasive	29 (70.7%)	61 (54.5%)	
Non-Invasive	5 (12.2%)	14 (12.5%)	
<b>Vasopressor</b>	16 (39.0%)	46 (41.1%)	0.82
<b>SOFA score</b>			
<10	27 (65.9%)	61 (54.5%)	
>10	14 (34.1%)	51 (45.5%)	
<b>Mortality</b>	12 (29.3%)	49 (43.8%)	0.11

## Discussion

Our analysis revealed that 73.20% of sepsis patients had hyponatremia, which is consistent with a recent Asian study that identified hyponatremia to occur in roughly 30–40% of all ICU admissions.<sup>9</sup> Similarly, another European study suggested around 40% of patients had hyponatremia on initial presentation to the emergency department<sup>10</sup>, making serum sodium levels an important aspect to consider in management of sepsis.

It is well established that hyponatremia linked to sepsis increases morbidity and death.<sup>9</sup> The death rate was found to be around 43.8% in patients with hyponatremia. Patients admitted for procedures involving the musculo-

skeletal system, metastatic cancer, and cardiovascular disease showed a strong correlation between hyponatremia and mortality as evident by study published in an American Journal.<sup>11</sup> Additionally, Whelan B.'s study found a substantial correlation between the likelihood of hospital mortality and hyponatremia, even after controlling for factors such as age, acute disease scores, sepsis criteria, ICU admission, and pre-transfusion needs—all of which were highly predictive of hospital death.<sup>12</sup> In contrast, those with normal serum sodium levels had a hospital death rate of 20% in Clayton's study, which included 108 patients with severe hyponatremia. It's interesting to note that, around two years later, patients with severe hyponatremia had a death rate of 45% as opposed to just 22% for patients with normal serum sodium levels.<sup>13</sup>

We observed that 73.2% of patients with sepsis and hyponatremia were older than 50 years of age. This extrapolates that age can be a risk factor for both hyponatremia and sepsis. In older adults, kidney function may be compromised causing retention of water leading to dilutional hyponatremia. Moreover, elderly are more susceptible to infections which increases their risk of developing sepsis.<sup>14</sup> Therefore, due to aforementioned reasons hyponatremia maybe related to a poor prognosis in elderly individuals with an increased associated mortality risk.<sup>3</sup>

The need for invasive respiratory support in hyponatremic patients was found to be 54.5%, compared to an Indian study where only 34% patients with low serum sodium levels required mechanical ventilation.<sup>12</sup> Furthermore, it was learned that patients who were admitted to intensive care unit with hyponatremia have increased length of stay and mortality rate along with higher dependence on invasive mechanical ventilation.<sup>15</sup>

Our study was limited by our inability to find an exact etiology of septic patients. As per the available literature, it may be related to dilution of the extracellular space with retained exogenous fluid.<sup>16</sup> This study was unique because we filtered and selected patients who met the criteria for sepsis at admission regardless of the comorbidities which reduced generalizability of dysnatremic patients.

No significant correlation was found between major comorbid conditions and hyponatremia. Out of 112 hyponatremic patients 54 pupils were diabetic compared to 24 out of 41 pupils in normonatremic group. This finding was contrary to one of the previous research which proved diabetes to be a risk factor for hyponatremia.<sup>3</sup> Similarly, we did not find any difference in patients with hypertension, chronic liver disease and chronic kidney disease. A second study linked the use of selective serotonin reuptake inhibitors (26%) and

thiazide diuretics (26%) to symptomatic hyponatremia (32.6%), congestive heart failure (HF) (26%) and SIADH (26%). The reason was multifactorial (congestive heart failure, SIADH, or medication use with volume depletion) in 21.7% of cases.<sup>17</sup>

Our study could not determine any gender prevalence, hyponatremia persisted in 54.5% male and 45.5% females with p value of 0.53; which in comparison to the past literature has been attributed females being more hyponatremic due to difference in muscles mass, hormones and various anatomical factors.<sup>9</sup>

## Conclusion

There was no significant difference in mortality between septic patients who initially presented with hyponatremia compared to those presenting with normal serum sodium levels.

**Conflict of Interest:** *None*

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