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**Original Article**

# Hyponatremia As A Prognostic Indicator in Acute Coronary Syndrome

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## ABSTRACT

**Background**: Hyponatremia, characterized by low serum sodium levels, has been identified as a potential prognostic marker in acute coronary syndrome (ACS). However, its precise relationship with ACS prognosis remains unclear, necessitating further investigation. **Aim**: This study aims to determine the incidence of hyponatremia in ACS patients and assess its role as a prognostic indicator. Additionally, the correlation between hyponatremia levels and left ventricular dysfunction (LVD) on 2D echocardiography will be evaluated. **Results**: The study included 40 ACS patients, predominantly middle-aged males with evidence of cardiac muscle damage and moderate LVD. The prevalence of hyponatremia varied among different ACS types, with higher rates observed in ST-elevation myocardial infarction (STEMI) subtypes. Significant associations were found between LVD and the presence of hyponatremia, as well as between hyponatremia and mortality in ACS patients. **Conclusion**: Hyponatremia appears to be prevalent in ACS patients and may serve as a poor prognostic indicator. Its association with LVD and increased mortality highlights the importance of monitoring and managing sodium levels in ACS patients. Further research is needed to explore potential interventions and strategies for improving outcomes in ACS patients with hyponatremia.

**Key Words**: *Hyponatremia, acute coronary syndrome, prognosis, left ventricular dysfunction, mortality*

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## INTRODUCTION:

Acute Coronary Syndrome is a serious condition that requires timely management to improve patient outcomes. Prognostic indicators are essential for assessing disease severity, guiding treatment decisions, and predicting outcomes[1]. Hyponatremia, characterized by low serum sodium levels, has emerged as a potential prognostic marker in various cardiovascular diseases[2]. However, the precise relationship between hyponatremia and Acute Coronary Syndrome prognosis is not fully understood, necessitating further investigation.

The pathophysiology of hyponatremia in Acute Coronary Syndrome involves complex mechanisms, including increased secretion of antidiuretic hormone (ADH), fluid shifts, and dilutional effects from fluid resuscitation[3,4]. Hyponatremia in Acute Coronary Syndrome is believed to reflect more severe myocardial injury and dysfunction and has been associated with an increased risk of arrhythmias[5], heart failure, and mortality

Despite the recognition of hyponatremia's significance in Acute Coronary Syndrome, limited evidence exists to guide its specific treatment in this context. However, correcting hyponatremia in a timely and safe manner is crucial, with treatment tailored to the severity of hyponatremia and the patient's clinical condition.

Further research is needed to establish a better understanding of the relationship between hyponatremia and Acute Coronary Syndrome prognosis. This study aims to address this knowledge gap through a comprehensive review of existing literature, analysis of available data, and investigation into the potential underlying mechanisms linking hyponatremia to adverse outcomes in Acute Coronary Syndrome. By improving our understanding of the prognostic significance of hyponatremia, this study may provide valuable insights for risk stratification, treatment decisions, and improved patient care in Acute Coronary Syndrome.

### Objective:

1. To determine the incidence of hyponatremia among patients with acute coronary syndrome.
2. To assess the correlation between levels of hyponatremia in patients presenting with ACS and LV dysfunction.

### Materials and Methods:

This prospective study was conducted at the Raichur Institute of Medical Sciences (RIMS) from March 2023 to

May 2023. A total of 40 patients with Acute Coronary Syndrome were enrolled from the General Medicine department's Outpatient Department (OPD) and Inpatient Department (IPD). Ethical approval was obtained, and informed consent was obtained from the participants. Baseline investigations, including serum sodium levels within 48 hours of presentation and 2D echocardiography within 5 days, were performed in accordance with guidelines and clinical indications throughout the study duration.

**Inclusion and Exclusion Criteria:**

The study included patients who met specific inclusion criteria, which consisted of individuals aged above 18 years and those diagnosed with acute coronary syndrome (ACS), including ST-elevation myocardial infarction (STEMI), non-STelevation myocardial infarction (NSTEMI), and unstable angina. However, several exclusion criteria were also applied. Patients with head trauma, postoperative patients, self-poisoning patients, and those with snake bites were excluded from the study. Additionally, patients who underwent percutaneous coronary intervention (PCI) during their hospital stay, including primary PCI, rescue PCI, or facilitated PCI, were not included. Patients with hypernatremia (serum sodium > 145 mg%) were excluded, along with those with endocrine disorders or those on medications known to cause hyponatremia. By applying these criteria, the study aimed to focus on a specific patient population to assess the incidence and prognostic implications of hyponatremia in acute ST elevation myocardial infarction patients.

**Baseline covariates:**

To minimize confounding effects and frailty bias, we collected and analysed baseline covariates including age, smoking status, sex, past medical history (hypertension, diabetes, transient ischemic attack, peripheral vascular disease, cancer, heart failure, myocardial infarction, chronic kidney disease), patients' acute coronary syndrome was followed up until discharge. They were categorized into two groups: the survived group and the mortality group. The survived group included patients who recovered from acute coronary syndrome, while the mortality group consisted of patients who passed away during their hospital stay. Additionally, within the survived group, further classification based on left ventricular ejection fraction (LVEF) was performed, dividing patients into mild, moderate, and severe LV dysfunction categories. The classification based on the severity of left ventricular (LV) dysfunction provided a more detailed analysis of the survival group. This comprehensive approach accounted for potential confounders, ensuring robust data analysis.

**Statistical Analysis:**

The data collected from the patients was subjected to statistical analysis. Quantitative variables were evaluated using t-test to determine their association and significance. Chi-square test was employed for qualitative variables. A significance level of $p < 0.05$ was considered to indicate a significant relationship between variables.

**Results:**

The study aimed to investigate the role of hyponatremia as a short-term prognostic indicator in acute coronary syndrome (ACS). A total of 40 patients with ACS participated in the study, with a mean age of 52.3 years (range: 30-77 years). Among the patients, 72.5% were male and 27.5% were female. The prevalence of risk factors in the patient population was 52.5% for smoking, 57.5% for hypertension, and 42.5% for diabetes mellitus (DM). The average serum sodium level was 131.6 mEq/L (range: 125.8-137.1 mEq/L). Notably, hyponatremia (serum sodium < 135 mEq/L) was observed in various ACS types, with percentages of 25% in STEMI IWMI, 27.5% in STEMI AWMI, 37.5% in NSTEMI, 7.5% in unstable angina, and 2.5% in STEMI. These findings suggest a significant prevalence of hyponatremia among ACS patients, particularly in the NSTEMI, STEMI IWMI, and STEMI AWMI subtypes. The high prevalence of risk factors, such as smoking, hypertension, and DM, underscores their association with ACS.

**Table 1**. Table Showing distribution of base line characteristics in the study population.

| INDICATORS | LEVEL | COUNT | TOTAL | PROPORTION | PVALUE |
|---|---|---|---|---|---|
| "AGEDISTRIBUTION" | 21-30 | 1 | 40 | 0.025 | < .001 |
| | 31-40 | 7 | 40 | 0.175 | < .001 |
| | 41-50 | 10 | 40 | 0.25 | 0.002 |
| | 51-60 | 11 | 40 | 0.275 | 0.006 |
| | 61-70 | 11 | 40 | 0.275 | 0.006 |
| SEX | MALE | 29 | 40 | 0.725 | 0.006 |
| | FEMALE | 11 | 40 | 0.275 | 0.006 |
| BMICLASSIFIED | NORMAL WEIGHT | 20 | 40 | 0.5 | 1 |
| | OVERWEIGHT | 16 | 40 | 0.4 | 0.268 |
| | OBESECLASS I | 2 | 40 | 0.05 | < .001 |

| | | | | | |
|---|---|---|---|---|---|
| | OBESECLASS II | 1 | 40 | 0.025 | < .001 |
| | OBESECLASS III | 1 | 40 | 0.025 | < .001 |
| HSTROPONINI | NORMAL | 6 | 40 | 0.15 | < .001 |
| | ELEVATED | 34 | 40 | 0.85 | < .001 |
| LVDYSFUNCTION | NORMAL LVFUNCTION | 12 | 40 | 0.3 | 0.017 |
| | MILDLV DYSFUNCTION | 12 | 40 | 0.3 | 0.017 |
| | MODERATELV DYSFUNCTION | 5 | 40 | 0.125 | < .001 |
| | SEVERE LVDYSFUNCTION | 10 | 40 | 0.28 | 0.002 |
| DEATH/SURVIVE | SURVIVE | 28 | 40 | 0.7 | 0.017 |
| | DEATH | 12 | 40 | 0.25 | < .001 |
| TYPESOFACS | STEMIIWMI | 10 | 40 | 0.25 | 0.002 |
| | STEMIAWMI | 11 | 40 | 0.275 | 0.006 |
| | NSTEMI | 15 | 40 | 0.375 | 0.154 |
| | UNSTABLE ANGINA | 3 | 40 | 0.075 | < .001 |
| HYPONATREMIA | NO | 12 | 40 | 0.3 | 0.017 |
| | YES | 28 | 40 | 0.7 | 0.017 |

Above table 1. shows that most patients were middle-aged males who were of normal weight. They had evidence of cardiac muscle damage and moderate LV dysfunction. Most patients survived, and those with STEMI IWMI or STEMI AWMI had a higher chance of survival than those with NSTEMI or unstable angina. Hyponatremia was also prevalent more among cases.

**Table 2**. Association between LV Dysfunction and Hyponatremia

| **LV Dysfunction** | **HYPONATREMIA** | | **Total** |
|---|---|---|---|
| | **Yes** | **No** | |
| NormalLV Function | 3 | 9 | 12 |
| MildLV Dysfunction | 11 | 1 | 12 |
| ModerateLV Dysfunction | 3 | 2 | 5 |
| SevereLV Dysfunction | 11 | 0 | 11 |
| Total | 28 | 12 | 40 |
| $\chi^2$19.2,df4 | | | |
| Pvalue<.001 | | | |

The table 2. demonstrates a strong association between LV Dysfunction and the presence of Hyponatremia in the study population. The findings suggest that as the severity of LV Dysfunction increases, the likelihood of having Hyponatremia also increases. These results highlight the potential relationship between these two factors and may have implications for understanding the underlying mechanisms and clinical management of patients with LV Dysfunction.

**Table 3**. Comparison of Hyponatremia and outcome in terms of mortality

| Outcome | HYPONATREMIA | | Total |
|---|---|---|---|
| | Yes | No | |
| Survived | 17 | 11 | 28 |
| Expired | 11 | 1 | 12 |
| Total | 28 | 12 | 40 |
| $\chi^2$3.83,df1 | | | |
| Pvalue0.05Significant | | | |

The above table 3. suggests a potential relationship between the outcome (survived or Expired) and the presence of Hyponatremia in the study population. The findings indicate that Hyponatremia may be associated with both survival and death, with a higher prevalence observed among patients who experienced death.

**Table 4**. Comparison of Hyponatremia and types of ACS

| TYPESOFACS | HYPONATREMIA | | TOTAL |
|---|---|---|---|
| | YES | NO | |
| STEMIIWMI | 8 | 3 | 11 |
| STEMIAWMI | 9 | 4 | 13 |
| NSTEMI | 10 | 3 | 13 |
| UNSTABLE ANGINA | 1 | 2 | 3 |
| TOTAL | 28 | 12 | 40 |
| $\chi^2$5.32,df2 | | | |
| Pvalue0.04Significant | | | |

The table 4. shows that the number of patients with ACS and hyponatremia was much higher than the number of patients with ACS who did not have hyponatremia. This difference was statistically significant, suggesting that there is a link between the two conditions. The findings of this study suggest that there is a strong association between ACS and hyponatremia. Patients with ACS should be monitored for signs and symptoms of hyponatremia, and treatment should be initiated promptly if hyponatremia is diagnosed.

**DISCUSSION:**

Hyponatremia, a common electrolyte disturbance, has been found to be associated with a poor prognosis in patients with acute heart failure. In our present study of 40 patients with acute coronary syndrome (ACS), the mean age was 52.3 years. Most cases fell within the age group of 51 to 60 years. Comparatively, the mean age of ACS patients in the study conducted by Saritha et al. was 57.28 years[5], while Goldberg's[6] study reported a mean age of 61 years. These findings indicate that Indians are more susceptible to experiencing myocardial infarction at a younger age compared to other populations.

The study by Mirza Md et al. found that the prevalence of risk factors in the patient population was 52% for hypertension, 49% for dyslipidemia, 46% for smoking, 39% for diabetes mellitus, and 24% for a family history of CAD[7]. These findings are similar to those of our study, which found that the prevalence of risk factors was 57.5% for hypertension, 52.5% for smoking, and 42.5% for diabetes mellitus. Both studies found that hypertension was the most common risk factor for acute coronary syndrome (ACS), followed by dyslipidemia, smoking, and diabetes mellitus. A family history of CAD was also a significant risk factor, but it was less common than the other factors. The findings of these studies suggest that hypertension, dys lipidemia, smoking, and diabetes mellitus are all important risk factors for ACS. These factors can lead to atherosclerosis, which is a build-up of plaque in the arteries. This build-up can narrow the arteries and restrict blood flow, which can lead to a heart attack or stroke.

The incidence of hyponatremia varies among different types of ACS. Patients with STEMI appear to have a higher risk of developing hyponatremia compared to those with NSTEMI or unstable angina. Hyponatremia in ACS patients is associated with potential complications such as heart failure and arrhythmias, but its full clinical significance requires further investigation. The meta-analysis and additional studies[8,9,10], confirm the increased risk of hyponatremia in ACS patients and its association with higher mortality rates, emphasizing the importance of monitoring and managing sodium levels in these individuals. Our study has revealed a significant finding regarding the relationship between left ventricular dysfunction (LVD) and hyponatremia. Patients with LVD exhibited hyponatremia in 70% of cases, while only 30% of patients without LVD had hyponatremia. This finding aligns with three other studies conducted by Filippatos et al (2013), McAuley et al. (2018), and Chua et al. (2019), which consistently demonstrate the association between LVD and hyponatremia.

Filippatos et al. found a 2.5-fold increased risk of hyponatremia in patients with LVD[11]. McAuley et al.

identified persistent hyponatremia as an independent predictor of adverse outcomes, including mortality and heart failure hospitalization[9]. Chua et al. reported a twofold increased risk of hyponatremia in patients with LVD admitted for heart failure[12]. These consistent findings across all four studies reinforce the validity of the association between LVD and hyponatremia. It is important to recognize and consider the risk of hyponatremia in patients with LVD, as it may serve as a potential indicator of poor prognosis in these individuals.

One of the most prevalent findings in cases of acute myocardial infarction is electrolyte disorder[13]. Among the various imbalances in electrolytes, serum sodium levels are particularly affected. Remarkably, 70% of the subjects in the study exhibited hyponatremia. Researchers have put forth the assertion that hyponatremia during the early stages of myocardial infarction could serve as an independent prognostic marker for the development of cardiac heart failure in hospitalized patients.

The findings from our study, which examined the association between hyponatremia and mortality in ACS patients, indicate a significant correlation between these factors. Among the ACS patients in our study, a substantial proportion (70%) were identified as having hyponatremia. Among those with hyponatremia, the survival rate was 61%, while 39% unfortunately expired. These results strongly suggest that the relationship between hyponatremia and mortality is not merely coincidental, but rather, hyponatremia is indeed associated with an elevated risk of mortality. This underscores the potential prognostic value of hyponatremia in this context.

Several other studies have also investigated the impact of hyponatremia on clinical outcomes in heart patients[13]. Tareen et al. stated that hyponatremia reflects poor clinical outcomes in heart patients, supporting the notion that low sodium levels are associated with adverse effects[14]. Similarly, Goldberg et al. found that hyponatremia plays a significant role in both short-term and long-term mortality in STEMI patients[6]. These studies align with our findings and provide further evidence for the association between hyponatremia and increased mortality risk.

However, it is worth noting that Lazzeri et al. reported contradictory results. Their study suggested that low sodium levels were not associated with mortality in patients whose baselines were managed[15]. These conflicting results raise the need for further investigation and exploration of potential factors that may contribute to the differing outcomes observed in different studies.

Despite the disparities, multiple researchers have demonstrated a positive association between low sodium levels and higher mortality rates compared to patients with normal sodium levels. These consistent findings across various studies suggest that hyponatremia may indeed serve as a significant risk factor for mortality in specific patient populations.

**CONCLUSION**:

The present study contributes to the growing body of evidence highlighting the prevalence and prognostic significance of hyponatremia in ACS patients. Recognizing and managing hyponatremia, particularly in patients with LVD, is crucial for improving patientoutcomes and identifying those at higher risk of mortality. Further research is needed to explore potential interventions and strategies to mitigate the adverse effects of hyponatremia in ACS patients.

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