

Prognostic Value of Hyponatremia in Patients with Acute Coronary Syndrome

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ABSTRACT

Acute coronary syndrome (ACS) remains an important cause of morbidity and mortality, and simple laboratory markers that identify patients at increased risk may support early clinical risk stratification. Hyponatremia has been associated with neurohormonal activation and adverse outcomes in cardiovascular disease, but its prognostic relevance in patients with ACS requires evaluation in the clinical setting. This prospective single-centre study included 75 patients admitted with ACS to the intensive care unit of Government Royapettah Hospital, Chennai, between April and September 2016. Patients presenting within 12 hours of symptom onset with electrocardiographic evidence of ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, or unstable angina were enrolled. Patients with previous coronary artery disease, arrhythmias, cardiomyopathy or heart failure, previous diuretic use, cirrhosis, hypothyroidism, renal disease, marked renal dysfunction, or refusal to participate were excluded. Serum sodium was measured at admission, 48 hours, and discharge, with sodium <135 mmol/L defining hyponatremia. Patients were followed weekly for 30 days for morbidity and mortality. Nine patients (12.0%) were hyponatremic and 66 (88.0%) were normonatremic. Mean ejection fraction was lower in the hyponatremic group ($46.67 \pm 7.70\%$) than in the normonatremic group ($53.77 \pm 9.96\%$; $p=0.0436$), while serum sodium remained significantly lower at all three assessment points ($p<0.0001$ for each comparison). Killip class also differed significantly between groups ($p=0.0461$). Adverse in-hospital outcome occurred in 44.44% of hyponatremic patients compared with 10.61% of normonatremic patients ($p=0.0071$). Thirty-day mortality was 66.67% and 6.06%, respectively ($p<0.0001$). The reported logistic regression model identified admission, 48-hour, and discharge hyponatremia as significant predictors of mortality. In this cohort, hyponatremia was associated with lower ventricular systolic function, higher clinical severity, adverse in-hospital outcome, and substantially higher 30-day mortality. Serum sodium may therefore provide an accessible prognostic marker in ACS, although confirmation in larger multicentre cohorts is required.

Keywords: acute coronary syndrome, hyponatremia, myocardial infarction, serum sodium, mortality, prognosis

INTRODUCTION

Acute coronary syndrome (ACS) represents a spectrum of acute myocardial ischemic conditions comprising unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). ACS remains a major cause of hospital admission, morbidity, and premature mortality. The burden is particularly important in India, where coronary disease may occur at a comparatively younger age and where the clinical spectrum includes a substantial proportion of patients presenting with ST-elevation myocardial infarction. The CREATE registry, cited in the original study,

provided large-scale Indian data on treatment patterns and outcomes of ACS and highlighted the continuing importance of cardiovascular disease as a public-health problem in the country [1]. Other Indian and international studies have similarly emphasized the contribution of conventional risk factors, including diabetes mellitus, hypertension, smoking, dyslipidemia, and adverse metabolic profiles, to premature coronary events [2–4].

Risk stratification is an essential component of ACS management because patients who appear clinically similar at presentation may have substantially differ-

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ent short-term outcomes. Established clinical indicators include age, hemodynamic status, Killip class, ventricular function, electrocardiographic findings, cardiac biomarkers, and the extent of myocardial injury. In routine clinical practice, however, there is continued interest in inexpensive and readily available biochemical parameters that may provide additional prognostic information without requiring sophisticated technology. Serum sodium is routinely measured in patients admitted with acute cardiovascular illness and therefore represents a potentially useful candidate marker.

Hyponatremia is generally defined as a serum sodium concentration below 135 mmol/L. It may occur through several mechanisms, including loss of sodium, excess free-water retention, or a combination of these processes. In hospitalized patients with cardiovascular disease, reduced effective arterial blood volume can activate the sympathetic nervous system, renin–angiotensin–aldosterone system, and arginine vasopressin pathways. Increased arginine vasopressin activity promotes water retention, while neurohormonal activation may accompany impaired cardiac output and systemic circulatory stress. The resulting fall in serum sodium can therefore reflect the severity of the underlying physiological disturbance rather than being merely an isolated electrolyte abnormality [5–9].

The relationship between hyponatremia and adverse outcome has been most extensively studied in heart failure. Lower serum sodium has been associated with more advanced disease and increased mortality, and the pathophysiological interpretation is generally linked to neurohormonal activation and impaired effective arterial circulation. Similar mechanisms may operate after acute myocardial infarction, particularly when myocardial dysfunction produces reduced forward flow and compensatory neurohormonal responses. Earlier studies cited in the dissertation reported associations between hyponatremia and the severity or outcome of myocardial infarction. Flear and Hilton described the relationship between hyponatremia and myocardial infarction severity, while Goldberg and colleagues subsequently reported prognostic associations in patients with acute STEMI [10–12].

Goldberg et al. evaluated the prognostic importance of hyponatremia in acute STEMI and reported associations with subsequent heart failure and mortality

[10]. Their later work examined long-term mortality among survivors of acute STEMI and suggested that sodium concentration could retain prognostic significance beyond the initial hospitalization [12]. Other studies have examined admission sodium and in-hospital outcome in patients treated for STEMI, including patients undergoing primary angioplasty [13]. These observations support the concept that serum sodium may function as an indirect marker of disease severity and neurohormonal stress.

Despite these observations, the original study was designed specifically to examine the prognostic value of hyponatremia in a prospective cohort of patients with ACS and to assess its relationship with short-term outcomes. The study also considered clinical variables that could influence prognosis, including age, sex, diabetes mellitus, hypertension, smoking, ejection fraction, troponin T, cholesterol, urea, and Killip class. A further objective was to determine whether sodium concentration at admission, at 48 hours, and at discharge was associated with mortality during a 30-day follow-up period.

The rationale for the present analysis is therefore based on the clinical accessibility of serum sodium and the possibility that an abnormal value may identify patients with a greater burden of myocardial dysfunction or systemic circulatory stress. Importantly, an association between hyponatremia and mortality does not establish that hyponatremia itself causes adverse outcome, nor does it demonstrate that correction of serum sodium would improve survival. The value of the marker lies in its potential role in risk characterization when interpreted alongside established clinical and cardiac parameters.

OBJECTIVES

- To determine the prevalence of hyponatremia among patients presenting with acute coronary syndrome.
- To evaluate the prognostic significance of hyponatremia in patients with acute coronary syndrome.
- To assess the association between hyponatremia and short-term mortality during 30 days of follow-up.
- To examine the relationship of hyponatremia with selected clinical and cardiac variables, including ejection fraction, hypertension, diabetes mellitus,

smoking, Killip class, troponin T, and type of acute coronary syndrome.

MATERIALS AND METHODS

Study design and setting

This was a prospective, single-centre observational follow-up study conducted in the intensive care unit of Government Royapettah Hospital, Chennai, Tamil Nadu, India. The study period extended from April 2016 to September 2016. A total of 75 patients admitted with ACS during the study period were included for analysis. Ethical approval was obtained from the ethics committee of Kilpauk Medical College, and informed consent was obtained from participating patients before enrolment.

Participants and eligibility

Patients presenting within 12 hours of symptom onset and having electrocardiographic evidence consistent with STEMI, NSTEMI, or unstable angina were considered eligible. The diagnostic framework used in the original study incorporated the clinical presentation, ECG findings, and cardiac biomarkers. Patients with previous coronary artery disease were excluded because established coronary disease could alter baseline risk and the interpretation of a new acute event. Additional exclusion criteria were previous arrhythmia, cardiomyopathy or heart failure, previous diuretic therapy, cirrhosis, hypothyroidism, renal disease, serum creatinine greater than 2 mg/dL, blood urea greater than 60 mg/dL, and refusal to participate. These exclusions were intended to reduce major non-cardiac or pre-existing cardiovascular influences on serum sodium and prognosis.

Clinical and laboratory assessment

At enrolment, demographic and clinical information was recorded, including age, sex, diabetes mellitus, hypertension, smoking status, pulse rate, blood pressure, jugular venous pressure, and relevant cardiovascular and respiratory findings. A 12-lead electrocardiogram was obtained in all participants, with additional right-sided and posterior leads when clinically indicated. Routine laboratory investigations included blood glucose, renal function, electrolytes, and other investigations required for clinical care. Lipid profile and chest radiography were obtained before discharge as recorded in the original protocol.

Cardiac troponin T was assessed, and echocardiography was performed to document left ventricular ejection fraction and regional wall-motion abnormalities.

Serum sodium was measured by an ion-selective electrode method at three predefined time points: admission, 48 hours after admission, and discharge. Hyponatremia was defined as a serum sodium concentration below 135 mmol/L. Participants were classified according to the presence or absence of hyponatremia at the relevant assessment point. The admission value was used to characterize the initial biochemical status, whereas subsequent measurements allowed the persistence or resolution of hyponatremia to be observed during hospitalization.

Clinical severity and outcome assessment

Clinical severity was assessed using Killip classification. In-hospital outcomes were recorded during the index admission, and patients were subsequently followed weekly for 30 days. The follow-up assessment focused on morbidity and mortality. The principal short-term outcome examined in this analysis was death within 30 days of the ACS event. In-hospital adverse outcome was also compared between the hyponatremic and normonatremic groups.

Statistical analysis

Data were analyzed using SPSS version 16.0 and Microsoft Excel 2007 as reported in the original dissertation. Continuous variables were summarized using mean and standard deviation, while categorical variables were expressed as frequencies and percentages. Comparisons between hyponatremic and normonatremic participants were performed using the statistical procedures described in the original study. A p value below 0.05 was considered statistically significant. Logistic regression was used in the reported analysis to examine associations between selected clinical variables, sodium status, and mortality. Odds ratios (ORs), 95% confidence intervals (CIs), and p values were reported for the variables included in the model.

Ethical considerations

The study was conducted after institutional ethical approval, and informed consent was obtained from participants. The analysis used clinical and laboratory information collected as part of the prospective study. The present manuscript reports the findings of the

original dissertation without introducing additional participants or outcome measures.

RESULTS

Seventy-five patients with ACS were included in the analysis. Nine patients (12.0%) met the study definition of hyponatremia, while 66 patients (88.0%) were normonatremic. The relatively small number of hyponatremic participants should be considered when interpreting the estimates and particularly the width of the confidence intervals reported in the regression analysis.

The mean age of participants with hyponatremia was 54.44 ± 10.04 years compared with 48.95 ± 11.76 years among normonatremic participants; this difference was not statistically significant ($p=0.1863$). Men constituted 44.44% of the hyponatremic group and 66.67% of the normonatremic group ($p=0.1926$). Diabetes mellitus was present in 55.56% and 43.94%, respectively ($p=0.5114$), while hypertension was present in 55.56% and 34.85% ($p=0.2283$). Smoking was reported in 33.33% of the hyponatremic group and 42.42% of the normonatremic group ($p=0.6034$). Thus, none of these baseline characteristics showed a statistically significant difference between the two groups.

Left ventricular ejection fraction differed between groups. The mean ejection fraction was $46.67 \pm 7.70\%$ in patients with hyponatremia and $53.77 \pm 9.96\%$ in patients without hyponatremia, with a statistically significant difference ($p=0.0436$). This finding indicates that hyponatremic patients in this cohort had lower measured ventricular systolic function at the time of assessment.

Serum sodium concentrations were significantly different at each measurement point. Mean admission sodium was 131.11 ± 2.80 mmol/L in the hyponatremic group compared with 137.71 ± 1.48 mmol/L in the normonatremic group ($p<0.0001$). At 48 hours, the corresponding values were 132.67 ± 2.87 and 138.03 ± 2.64 mmol/L ($p<0.0001$). At discharge, mean sodium was 131.78 ± 3.56 mmol/L and 138.68 ± 2.68 mmol/L, respectively ($p<0.0001$).

All nine patients in the hyponatremic group had elevated troponin T, compared with 53 of 66 patients in the normonatremic group. The difference was not

statistically significant in the reported analysis ($p=0.1431$). Killip class, however, differed significantly between the groups ($p=0.0461$), indicating a relationship between hyponatremia and the clinical severity classification used in the study.

The distribution of ACS diagnoses did not show a statistically significant difference between the two sodium groups. Anterior wall myocardial infarction was the most frequently represented diagnosis in the cohort. The lack of a significant difference in diagnostic category suggests that the association of hyponatremia with outcome was not simply attributable to a statistically different distribution of the major ACS diagnostic groups.

Adverse in-hospital outcome occurred in 4 of 9 patients (44.44%) in the hyponatremic group compared with 7 of 66 patients (10.61%) in the normonatremic group. This difference was statistically significant ($p=0.0071$). During 30-day follow-up, 6 of 9 patients with hyponatremia died (66.67%), compared with 4 of 66 patients without hyponatremia (6.06%); the difference was highly statistically significant ($p<0.0001$).

The reported logistic regression analysis included demographic, clinical, cardiac, biochemical, and sodium-related variables. Age ≥ 65 years was associated with increased odds of mortality (OR 3.04, 95% CI 1.33–6.95; $p=0.0082$). Male sex, diabetes mellitus, hypertension, and smoking were not statistically significant in the reported model. Ejection fraction below 40% was associated with mortality (OR 3.62; $p=0.0001$). Admission hyponatremia showed an OR of 10.18 (95% CI 1.09–94.73; $p=0.0421$), 48-hour hyponatremia an OR of 3.04 (95% CI 1.33–6.95; $p=0.0182$), and discharge hyponatremia an OR of 4.29 (95% CI 1.12–16.52; $p=0.0397$). Elevated troponin T was also statistically significant in the reported model (OR 3.58; $p=0.0433$), while Killip class ≥ 2 had an OR of 4.81 ($p<0.0001$).

Because only nine patients were classified as hyponatremic, the regression estimates for sodium status have relatively wide confidence intervals. The results should therefore be interpreted as evidence of an association within this cohort rather than as precise estimates applicable to all patients with ACS.

Table I: Baseline Characteristics of Patients According to Sodium Status

Variable	Hyponatremia (n=9)	Normonatremia (n=66)	p value
Age, years	54.44 ± 10.04	48.95 ± 11.76	0.1863
Male sex	44.44%	66.67%	0.1926
Diabetes mellitus	55.56%	43.94%	0.5114
Hypertension	55.56%	34.85%	0.2283
Smoking	33.33%	42.42%	0.6034
Ejection fraction, %	46.67 ± 7.70	53.77 ± 9.96	0.0436
Elevated troponin T	100%	80.30%	0.1431
Killip class	Different distribution	—	0.0461

Table II: Serum Sodium Concentrations at Serial Assessment Points

Time point	Hyponatremia	Normonatremia	p value
Admission	131.11 ± 2.80	137.71 ± 1.48	<0.0001
48 hours	132.67 ± 2.87	138.03 ± 2.64	<0.0001
Discharge	131.78 ± 3.56	138.68 ± 2.68	<0.0001

Table III: Clinical Outcomes According to Sodium Status

Outcome	Hyponatremia (n=9)	Normonatremia (n=66)	p value
Adverse in-hospital outcome	44.44%	10.61%	0.0071
30-day mortality	66.67%	6.06%	<0.0001

DISCUSSION

The present prospective study examined the prognostic significance of hyponatremia in 75 patients with ACS and found that 12% of the cohort had sodium below 135 mmol/L. The principal observations were that hyponatremia was associated with lower left ventricular ejection fraction, a different distribution of Killip class, a greater frequency of adverse in-hospital outcome, and substantially higher 30-day mortality. The association remained present in the reported regression analysis for hyponatremia measured at admission, 48 hours, and discharge. These findings support the clinical relevance of serum sodium as a marker of risk in ACS, while the observational nature and small number of hyponatremic patients require cautious interpretation.

The prevalence of hyponatremia in this cohort was 12%. This finding is consistent with the concept that clinically meaningful sodium reduction occurs in a subset rather than the majority of patients with acute coronary events. The occurrence of hyponatremia in ACS can be understood in relation to the hemodynamic and neurohormonal changes accompanying acute myocardial injury. When myocardial performance falls, the effective arterial circulation may be perceived as inadequate despite total body sodium and

water status. Sympathetic activation, renin–angiotensin–aldosterone activation, and increased arginine vasopressin secretion can follow. Enhanced water retention may lower measured serum sodium and thereby provide an indirect biochemical signal of circulatory stress [5–9].

The significantly lower ejection fraction among hyponatremic participants is important because ventricular systolic function is itself a recognized determinant of outcome after myocardial infarction. In the present study, mean ejection fraction was approximately seven percentage points lower in the hyponatremic group. The coexistence of lower ejection fraction and hyponatremia is physiologically plausible: impaired ventricular function may reduce effective forward circulation and promote neurohormonal responses, while the resulting water retention contributes to dilutional hyponatremia. The observed association therefore supports the interpretation of hyponatremia as a marker accompanying more severe cardiovascular dysfunction rather than an isolated laboratory abnormality.

The significant difference in Killip class provides a complementary clinical measure of severity. Killip classification is based on the presence and severity of clinical heart failure following acute myocardial infarction. A higher Killip class indicates greater

hemodynamic compromise and is associated with poorer prognosis. The association between Killip class and hyponatremia observed in this study is consistent with the proposed pathophysiological relationship between circulatory stress, neurohormonal activation, water retention, and reduced serum sodium. The regression analysis also reported an OR of 4.81 for Killip class ≥ 2 , further emphasizing the prognostic importance of clinical severity.

The strongest clinical difference observed in the study was in short-term mortality. Thirty-day mortality was 66.67% among patients with hyponatremia compared with 6.06% among normonatremic patients. The difference was statistically significant at $p < 0.0001$. In addition, adverse in-hospital outcome occurred in 44.44% of hyponatremic patients compared with 10.61% of normonatremic patients. These results are directionally consistent with previous studies reporting increased adverse outcomes among patients with acute myocardial infarction and low serum sodium [10–14].

Goldberg et al. previously reported the prognostic importance of hyponatremia in acute STEMI and identified associations with subsequent heart failure and mortality [10]. Their later study of survivors also suggested an association with long-term mortality [12]. The present study differs in its prospective follow-up design and its inclusion of the broader ACS spectrum rather than restricting the cohort to STEMI alone. Nevertheless, the common finding is that a lower sodium concentration accompanies a higher-risk clinical phenotype. This consistency across studies strengthens the rationale for considering sodium as part of a broader risk assessment rather than treating it solely as an electrolyte measurement.

Other investigators have also examined admission sodium in relation to outcomes after acute myocardial infarction. Klotkowski et al. reported prognostic associations between sodium level on admission and in-hospital outcome in STEMI patients treated with primary angioplasty [13]. Aziz et al. similarly described in-hospital outcome in acute STEMI with hyponatremia [14]. These reports provide contextual support for the present findings, although differences in study population, treatment era, clinical definitions, and follow-up duration limit direct numerical comparison.

The absence of statistically significant differences in several conventional baseline characteristics is also relevant. Age, sex, diabetes mellitus, hypertension, and smoking did not differ significantly between the sodium groups in this cohort. This suggests that the observed association between hyponatremia and outcome cannot simply be described as a consequence of a statistically significant difference in these individual baseline characteristics. However, the sample was small, and absence of statistical significance should not be interpreted as proof that these factors had no influence on outcome.

Troponin T was elevated in all nine hyponatremic patients and in 53 of 66 normonatremic patients, but the difference did not reach statistical significance in the unadjusted comparison. In contrast, elevated troponin T was statistically significant in the reported logistic regression model. This apparent difference illustrates the importance of distinguishing between individual group comparisons and multivariable models. The regression model estimates the association of each variable within the set of variables included in the analysis and therefore should not be interpreted as equivalent to a simple comparison of proportions.

The regression findings are notable because admission hyponatremia was associated with an OR of 10.18 for mortality, while hyponatremia at 48 hours and discharge was associated with ORs of 3.04 and 4.29, respectively. However, the admission estimate had a very wide 95% CI of 1.09–94.73. This wide interval reflects the small number of events and the limited sample size and indicates considerable statistical uncertainty around the point estimate. The reported associations should therefore be viewed as hypothesis-generating rather than as precise estimates of the independent effect of hyponatremia.

An important conceptual point is that the study demonstrates association, not causation. Low sodium may be a consequence or marker of impaired cardiac function, neurohormonal activation, or more severe illness. The findings do not establish that hyponatremia directly causes death or that actively correcting serum sodium would reduce mortality. This distinction is clinically important because management of hyponatremia depends on its mechanism, severity, symptoms, fluid status, and the overall clinical condition of the patient.

The study also has practical implications. Serum sodium is inexpensive, routinely measured, and rapidly available in most hospitals. If the association observed in this cohort is confirmed in larger and contemporary ACS populations, sodium concentration could potentially contribute to early risk characterization alongside established variables such as Killip class, ejection fraction, ECG findings, and cardiac biomarkers. It should not be considered a substitute for established risk scores or clinical assessment, but it may provide an additional piece of information during the initial evaluation and subsequent inpatient monitoring.

Several limitations should be considered. First, the study was conducted at a single centre and included only 75 participants over a six-month recruitment period. Second, only nine participants were hyponatremic, which limits statistical power and results in wide confidence intervals for regression estimates. Third, the observational design prevents causal inference. Fourth, the study was conducted in a specific hospital setting and during a defined period, so the findings may not be directly generalizable to all contemporary ACS populations. Fifth, sodium concentration can be influenced by multiple clinical factors during hospitalization, some of which may not have been fully captured in the analysis. Finally, the follow-up period was limited to 30 days, and therefore the study does not establish the relationship between hyponatremia and longer-term outcomes in the broader ACS population.

Future studies should recruit larger, multicentre cohorts and include sufficient numbers of patients with hyponatremia to provide more stable multivariable estimates. Serial sodium measurements may be particularly useful because persistent or worsening hyponatremia could carry different prognostic information from a single low value at admission. Future research may also examine the relationship between sodium trajectories, ventricular function, heart failure development, revascularization strategy, and standardized risk scores. Such studies could determine whether adding sodium improves risk discrimination beyond established clinical predictors.

Finally, future studies should distinguish between mild, moderate, and severe hyponatremia and should record relevant measures of volume status and treatment exposure. Analysis of sodium trajectories could

determine whether persistent hyponatremia, new-onset hyponatremia, or correction during hospitalization has different prognostic meanings. Such work would help clarify whether serum sodium is primarily a marker of disease severity or whether specific sodium patterns identify distinct clinical phenotypes. The present findings provide a basis for this research but do not by themselves establish a treatment target.

Further research should also investigate whether the prognostic information provided by sodium remains significant after adjustment for established ACS risk scores and contemporary treatment strategies. The original cohort was recruited in 2016 and reflects the clinical environment and treatment practices of that period. Current ACS care may involve changes in reperfusion strategies, antiplatelet therapy, lipid-lowering treatment, heart-failure management, and intensive-care monitoring. A contemporary multicentre study could therefore determine whether the relationship between sodium and outcome remains present after accounting for current standards of care. It could also examine whether changes in sodium over time provide incremental prognostic information beyond the admission value.

From a practical standpoint, the main potential contribution of serum sodium is its accessibility. Unlike specialized biomarkers or advanced imaging, sodium is routinely included in basic biochemical assessment in patients admitted with suspected ACS. A low value can therefore be identified without additional specialized testing. If confirmed in larger studies, serial sodium assessment could be incorporated into broader clinical surveillance and may help identify patients who require closer observation. Such use would be complementary to, rather than a replacement for, established prognostic information derived from symptoms, ECG findings, biomarkers, ventricular function, hemodynamic status, and validated risk scores.

The study's prospective design is nevertheless useful because sodium measurements and follow-up were specified in advance and the participants were followed after the index admission. The use of repeated sodium measurements and a defined 30-day outcome also provides more information than a cross-sectional comparison of laboratory values. In addition, the study examined both clinical severity and objective cardiac function, allowing the sodium finding to be

considered alongside Killip class and ejection fraction. These features strengthen the clinical interpretability of the observed association, although they do not remove the limitations associated with sample size and single-centre recruitment.

The relatively high mortality observed among hyponatremic participants should also be interpreted in light of the absolute numbers. Six of nine hyponatremic patients died during 30-day follow-up, whereas four of 66 normonatremic patients died. The percentage difference is large, but the underlying number of hyponatremic participants is very small. A change in the outcome of only one or two patients would materially alter the percentage and the calculated effect estimates. This explains why the confidence interval around the admission hyponatremia odds ratio was broad. Larger cohorts are necessary to determine the stability and reproducibility of the observed association.

At the same time, the findings should not be interpreted as demonstrating that every patient with ACS and sodium below 135 mmol/L has the same degree of cardiac dysfunction or the same prognosis. Sodium concentration can be influenced by factors outside the myocardium, including fluid balance, renal function, endocrine disorders, medications, and the administration of intravenous fluids. Several of these potential influences were addressed through the exclusion criteria, particularly renal disease, hypothyroidism, cirrhosis, and previous diuretic use. Nevertheless, residual clinical influences cannot be completely excluded in an observational study. The distinction is important when translating the findings into clinical practice.

The relationship between hyponatremia and ventricular function also provides a clinically coherent explanation for the observed mortality difference. The hyponatremic group had a lower mean ejection fraction, and reduced ventricular performance can contribute to elevated filling pressures and neurohormonal activation. In a patient with acute myocardial injury, these changes may occur together with pulmonary or systemic congestion and a higher Killip class. The present results therefore fit a model in which hyponatremia is a readily measurable marker of a broader physiological state involving myocardial dysfunction and circulatory stress. This interpretation is more consistent with the available evidence than

considering serum sodium as an isolated determinant of outcome.

The timing of sodium assessment may have clinical relevance. An admission sodium value is available at the earliest stage of hospital evaluation and could potentially contribute to initial risk characterization. A 48-hour measurement may reflect the physiological response during the early course of myocardial injury and treatment, whereas the discharge value may summarize the patient's biochemical status after stabilization or continuing illness. The regression analysis reported significant associations at all three time points, although the estimates varied. These differences emphasize that a sodium value should be interpreted in temporal context rather than assuming that one measurement has identical meaning throughout the hospitalization.

The serial sodium observations deserve additional consideration because the study did not rely exclusively on a single admission measurement. Mean sodium remained substantially lower in the hyponatremic group at admission, 48 hours, and discharge. The persistence of the difference suggests that, in at least some patients, the abnormality was not simply a transient laboratory finding at presentation. At the same time, the mean values in the hyponatremic group remained within a relatively narrow range across the three measurements, and the study was not designed to distinguish the underlying mechanisms of hyponatremia, such as dilutional water retention, sodium loss, or treatment-related changes. Consequently, the serial measurements support the association with prognosis but cannot determine whether persistence of low sodium itself represents an independent biological mechanism.

CONCLUSION

In this prospective single-centre cohort of 75 patients with acute coronary syndrome, hyponatremia was present in 12% of patients and was associated with lower left ventricular ejection fraction, higher Killip class, adverse in-hospital outcome, and markedly higher 30-day mortality. Serum sodium remained significantly lower in the hyponatremic group at admission, 48 hours, and discharge. The reported regression analysis also demonstrated significant associations between hyponatremia at these time points and mortality. These findings indicate that serum sodium may serve as an accessible prognostic

marker that identifies a higher-risk clinical phenotype in ACS. Because the study involved a small number of hyponatremic patients and was conducted at a single centre, larger multicentre studies are required before the findings can be generalized or incorporated into formal prognostic models.

DECLARATIONS

Ethics approval and consent

Ethical approval was obtained from the ethics committee of Kilpauk Medical College. Informed consent was obtained from participants before enrolment, as reported in the original study.

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Conflict of interest

No conflict-of-interest statement was reported in the dissertation source. The authors should verify and update this declaration before journal submission.

Data availability

The manuscript is based on the dataset described in the original dissertation. A formal public data-sharing statement was not provided in the source document; this should be completed according to the requirements of the target journal.

Author contribution

The author contribution statement should be confirmed by the authors before submission and should accurately reflect study conception, data collection, analysis, interpretation, manuscript preparation, and approval of the final version.

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