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A study on prognostic significance of hyponatremia in acute: St-elevation myocardial infarction

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Abstract
Short- and long-term prognostic value of hyponatremia in acute coronary syndrome concluded that, hyponatremia has a significant prognostic value for short- and long-term adverse events in patients with acute coronary syndrome. Thus, the dynamic monitoring of serum sodium levels may help to identify and risk stratify for optimal management. The study population consists of 100 consecutive patients presenting with acute ST elevation myocardial infarction admitted in Tertiary care Hospital for a period of 12 months. Detailed history was taken and complete physical examination was done. Patients with hyponatremia on admission had lightly higher percentage (23%) that is 3 deaths in 13 patients and patients with hyponatremia within 72 h had 2 deaths among 14 patients (14.28%). Our study showed 25.9% of mortality in hyponatremia associated acute ST -elevation patients. Goldberg *et al*. in their study found 24% mortality.

Keywords: Hyponatremia, acute St-elevation, myocardial infarction

Introduction
Hyponatremia is defined as a serum sodium level <135mmol/. The severity of hyponatremia was defined as mild (131-135mEq/L) and moderate (125-135mEq/L) and severe (<125mmol/L). Hyponatremia is the most frequently encountered electrolyte abnormality in clinical practice and has a poor prognosis in both STEMI and heart failure (HF)patients [1]. It exacerbates both short- and long-term mortality, rehospitalization rates, as well as the average length of stay in the hospital [2]. Although it is still a mystery whether hyponatremia is just a marker of iller patients or the core of poor prognosis in patients with STEMI and HF, one thing is certain: timely recognition of patients at risk for developing hyponatremia could help to commence early treatment.
Short- and long-term prognostic value of hyponatremia in acute coronary syndrome concluded that, hyponatremia has a significant prognostic value for short- and long-term adverse events in patients with acute coronary syndrome. Thus, the dynamic monitoring of serum sodium levels may help to identify and risk stratify for optimal management. And also, in certain cases treating of hyponatremia may achieve improved survival of the patients. This study has been undertaken to evaluate the prognostic importance of hyponatremia in acute ST elevation myocardial infarction and to study its importance in determining the mortality rate in acute ST elevation myocardial infarction and short-term survival.
Treating hyponatremia in acute settings resulted in reducing long term mortality as a result hyponatremia acts as a very important marker not only in determining the prognosis in acute MI, but also treating hyponatremia in acute settings gives long term mortality benefits.

Materials and Methods
Study place and study duration
This study was carried out in the Tertiary care hospital for a period of 12 months.

Study design: This is a prospective observational study.

Study Sample: The study population consists of 100 consecutive patients presenting with acute ST elevation myocardial infarction admitted in Tertiary care Hospital for a period of 12 months. Detailed history was taken and complete physical examination was done.

Inclusion criteria

1. All the patients who were willing to participate in the study were included in the study after taking informed consent.
2. All patients with definite diagnosis of acute ST elevation myocardial infarction, Based on

A. Symptoms of acute myocardial infarction - retrosternal compressive chest pain lasting for greater than 30 minutes and not relieved by rest or nitrates,
B. New electrocardiographic changes of acute ST elevation myocardial infarction
   a. ST elevation of greater than 0.1mv in all leads (with two contiguous leads) except V2-V3 where ST elevation is greater than 0.2mv.
   b. Development of pathological Qwaves
C. Detection of elevation of cardiac troponin levels > 0.04
D. Imaging evidence of new loss of viable myocardium or new regional wall motional abnormality.

Exclusion Criteria

Patient with

1. Acute and chronic renal failure
2. Acute and chronic liver failure
3. Acute gastroenteritis
4. Malignancy
5. Previous myocardial infarction or heart failure
6. Acute or chronic cerebro vascular accident
7. Hypertension patient on diuretics
8. Acute or chronic pulmonary embolism
9. Hypothyroidism, hyperthyroidism

Sample Size

Sample size of 100 was taken after calculating according to the prevalence rate of previous studies 25% and allowable standard error of 10% by using the formula

Sample size $n = 4pq/l^2$

Where

P-prevalence rate
q- 1-p
l^2 – permissible error

Outcomes

Primary outcome -The primary outcome was all-cause mortality within 30 days of hospital admission.
Secondary outcome – The secondary outcomes were the time until discharge from the hospital and among these patient's subsequent death within 30 days of hospital admission.

Data Collection

This study was approved by the Ethical Committee of our institute. Patients were selected for the study according to the inclusion and exclusion criteria, mentioned above. Detailed history regarding symptoms, smoking, diabetes mellitus, hypertension, Chronic kidney disease, Ischemic or hemorrhagic stroke, drug intake was enquired. Vital signs, waist/Hip ratio, 15 lead-ECG, 2D echo finding, Troponin levels, Blood sugar levels, serum creatinine, BUN and serum electrolytes were noted.
Plasma sodium concentrations are obtained on admission and at 24, 48, and 72 hours thereafter. And hyponatremia is defined as mean serum sodium levels less than 135 meq/L during first 72 hours of hospitalization. After revascularization by various methods like thrombolysis, percutaneous intervention and stenting, Coronary artery bypass graft, patients were followed up till they leave the hospital. During the hospital stay they were closely monitored for development of complications like Heart failure, Cardiogenic shock, Arrhythmias, thromboembolism and sudden cardiac death. After hospital discharge, clinical endpoint information was acquired by reviewing the national death registry, contacting each patient individually, and independently reviewing the hospital course for major clinical events if the patient had been re hospitalized.

Variables recorded during the study

1) Complete history and physical examination

a. Chest pain onset, type, duration associated symptoms like sweating palpitations, dyspnea.
b. Past history of cardiac disease, diabetes, CKD, malignancy and past medical history of diuretics.

2) Ecg, 2d Echo, Troponin I Levels

a. site of infarction - anterior, inferior, lateral, septal, posterior, antero lateral, right ventricular
b. site of regional wall motion abnormality
c. value of troponin I levels

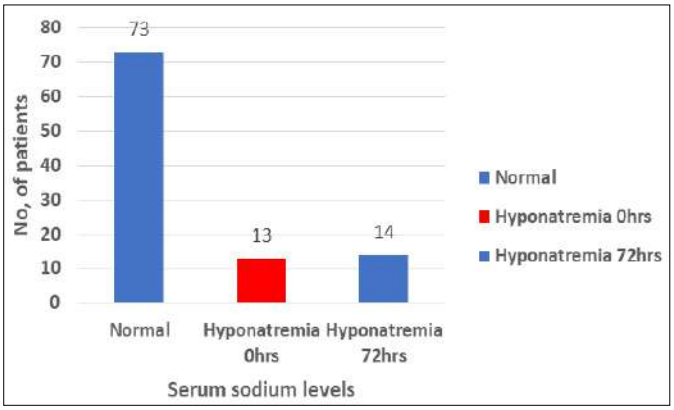
3) Laboratory investigations

a. Complete blood count
b. Serum creatinine, Blood Urea Nitrogen
c. Blood sugar d) Serum electrolytes including sodium

Statistical Analysis

Continuous variables are expressed as mean (±standard deviation), and categorical variables are expressed as numbers and percentages. Baseline characteristics between the groups were compared using Student *t* test for continuous variables and Pearson chi-square test or Fisher exact for categorical variables. And multivariate analysis is used to check the significance of baseline characteristics in relation to hyponatremia for continuous variables and for categorical variables chi-square test was used. The variables were considered statistically significant with confidence interval of 95 and P value 0f less than 0.05. The variables included in the analyses were age, gender, risk factors (hypertension, diabetes mellitus, smoking status), Killip classification, LVEF, diagnosis (STEMI vs NSTEMI), myocardial infarction site. These baseline characteristics were compared with normal sodium levels, hyponatremia at admission and hyponatremia by72 hours. And hyponatremia and multiple variables including age, gender, hypertension, diabetes, smoking, infarction site, Killip class were analysed using multivariate logistic analysis with respect to outcomes that is survivors and non survivors. Odds ratio is used to check the relative risk of hyponatremia in comparison to normal sodium levels with respect to mortality. Statistical analysis was performed using the Statistical Package for Social Sciences software, version 27.

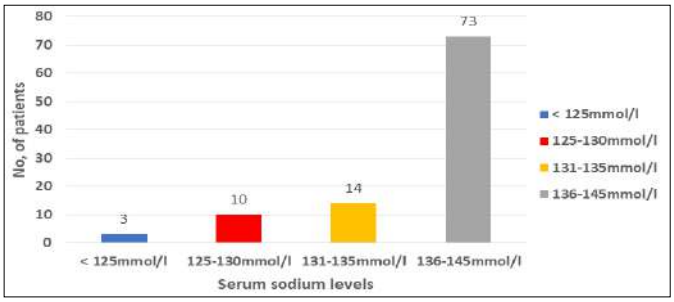
Observation and Results: Distribution of Serum Sodium Levels At O Hours And At 72 Hours



Graph 1: Show the patients of serum and sodium levels

Among 100 patients 73 had normal sodium levels, while 13 patients developed hyponatremia at 0hours and 14 patients by 72 hours of presentation.

Severity of hyponatremia in acute ST elevation MI patients



Graph 2: Show the patients of hyponatremia

27 Patients had hyponatremia. Hyponatremia was found to be distributed more between 131-135 = 14(mild hyponatremia) between 125-130 were 10 patients (moderate hyponatremia) 3 Patients had sodium levels less than 125 (severe hyponatremia).

Table 1: Showing Baseline Characteristics

Characteristics	Normal Sodium Levels	Hyponatremia on Admission	Hyponatremia in 72 hours	T or x^2	P value
Age	54.04+/- 12.371	59.92+/- 10.226	63.36+/-12.667	4.176	0.018
Gender Male Female	49 24	9 4	10 4	0.033	0.743
Diabetes	14	7	2	4.325	0.016
Smoking	21	9	7	6.067	0.003
Hypertension	17	5	8	3.606	0.031
Infarction Anterior Inferior	38 20	7 5	9 2	0.242	0.786
Killip Cla Ss ½ Killip class 3/4	72 1	9 4	11 3	9.897	<0.001
Ejection Fraction	45.66 +/-6.939	37.69 +/- 8.179	40.00 +/- 7.716	9.029	<0.001

Note: Results are expressed as Mean +/-SD, probability $P< 0.05$ is considered statistically significant

Table 2: Effect of serum sodium levels and its outcome

Sodium levels	Total	Recovered	Death
Normal	73	71 (97.2%)	2 (2.7%)
Hyponatremia 0hrs	13	10 (77%)	3 (23%)
Hyponatremia 72hrs	14	12 (85.7%)	2 (14.2%)
Total	100	93	7

As compared to normal sodium levels mortality rate was higher in hyponatremia group that is 5 patients died out of 27patients with hyponatremia and acute ST elevation Myocardial Infarction.

Table 3: Severity of hyponatremia and its outcome in terms of mortality

Sodium levels	Total	Recovered	Death
<125mmol/l	3	1 (33%)	2 (66.6)
125-130mmol/l	10	9 (90%)	1 (10%)
131-135mmol/l	14	12 (85.7%)	2 (14%)
136-145mmol/l	73	71 (97.2)	2 (2.73%)
Total	100	93	7

2 deaths occurred when sodium was <125, and 3 deaths when sodium levels less than 130.

Results

Total subjects were divided into three groups; those with normal sodium levels, hyponatremia on admission and at 72 h. These groups were analysed with regard to age, sex, risk factors, type of infarction, ejection fraction and Killip class with multivariate analysis and Chi Square tests as required. We got statistically significant results for hyponatraemic group with Killip class, and ejection fraction (<0.0001), diabetes (*P* - 0.016), smoking (P – 0.003), hypertension (P – 0.031). Patients who presented with hyponatremia had higher incidence of anterior infarction (54%), lower ejection fraction (38.845), compared to patients with normal sodium levels. Mean ejection fraction was Among the patients

presented with normal sodium levels, non survivors at the endpoint were 2 patients, when compared to 3 deaths which occurred in hyponatremia group at the time of admission and total of 5 patients who died, who had hyponatremia by the end of 72hrs. Out of 7 patients who died, 5 were males and 2 were females. In terms of percentage of non survivors in each group at the end of 30 days patients in the group of decreased sodium levels had a significantly high percentage (18.51%) when compared to patients with normal sodium levels (2.73%). Patients with hyponatremia on admission had lightly higher percentage (23%) that is 3 deaths in 13 patients and patients with hyponatremia within 72 h had 2 deaths among 14 patients (14.28%). Our study showed 25.9% of mortality in hyponatremia associated acute ST - elevation patients. Goldberg *et al*. in their study found 24% mortality. Chiara Lazzri *et al*. in their study found11.3% were ventilated, 9% were on NIV support, Hashmi *et al*. their study found 12% mortality among hyponatraemic patients.

45.66 +/-6.939in normal sodium group, 37.69 +/- 8.179 in hyponatremia on admission group 40.00 +/- 7.716 in hyponatremia within 72-h group. The mean Killip class were 1.01 in normal sodium group, 1.31 in hyponatremia on admission and 1.21 in hyponatremia within 72hrs. Patients with hyponatremia on admission were older, it was statistically significant (P = 0.021). But there was also no significant predilection towards either sex (P = 0.743).

Discussion

In the present study, hyponatremia was present in 27 patients out of 100 patients who presented with acute ST elevation myocardial infarction. In the previous studies prevalence of hyponatremia was found to be up to 23.2% which was studied by systemic review and meta-analysis by Qiang-Qiang ma *et al*. in acute ST elevation MI patients.

Hyponatremia with sodium levels less than 125mmol/l was considered to be severe hyponatremia and between 126-130 as moderate and 131-135 as mild hyponatremia. 3 patients had severe hyponatremia, 10 patients moderate and 14 patients had mild hyponatremia. (refer graph 2)

Hyponatremia occurring in myocardial infarction is because of non-osmotic release of vasopressin and neuro hormonal activation. And severity of hyponatremia is directly proportional to the degree of myocardial injury.

Previous studies have shown the prevalence of hyponatremia in patients suffering from STEMI ranges between 12.5% - 25% [3]. And patients presenting with hyponatremia and myocardial infarction have increase in 30 days mortality rate and long-term mortality rate compared to normal sodium levels with myocardial infarction [2].

Following Acute Myocardial Infraction there occurs complex neuro hormonal activation involving non osmotic release of vasopressin and activation of sympathetic nervous system, Renin angiotensin activating system. This complex neuro hormonal activation is associated with hyponatremia [4, 5].

The magnitude of neuro hormonal change is related to the severity of myocardial damage which in turn is reflected in severity of hyponatremia.

From table 1, it is found that Patients with risk factors, diabetes, hypertension, and smoking had significant hyponatremia, and patients also had more than 1 risk factors who presented with hyponatremia. Among 37 smokers 16 (43%) had hyponatremia. In 30 hypertensive patients 13 (43%) had hyponatremia and in 23 diabetics 9 (39%) had hyponatremia.29.62% of patients with anterior myocardial infarction had hyponatremia and among 8 patients with KILLIP CLASS 3 OR 4, 7 patients had hyponatremia.

In the previous studies of Goldberg *et al*. demonstrated that the prevalence of hyponatremia was 12.5% - 23.2%. And 32% of hyponatraemic subjects to be diabetic, 40% to be smokers and hypertensive.

Goldberg *et al*. in their study had 55% anterior infarction in hyponatraemic group, with mean ejection fraction of 42, mean Killip class of 1.6. They got significant base line characteristics for age, diabetes, Killip class, ejection fraction and anterior infarction. But in our study, we couldn't get significant anterior infarction may be due to smaller sample size. Thus, our study had similar results pertaining to hyponatremia and base line characteristics. (Refer table 8)

Detailed analysis of hyponatremia group with respect to our study end points that is death or survival till 30days from the date of admission was done. Also, the analysis was done with respect to diabetes, hypertension, smoking, age, gender, anterior infarction, Killip class with study endpoint.

Patients outcome was also correlated well with severity of hyponatremia. A total of 3 patients had sodium levels less than 125mmol/l and 2 patients died in 3 patients. 1 death among 10 patients with sodium levels between 126–130 mmol/l and 2 deaths in 14 patients with sodium levels between 131-135. 2 deaths occurred in 73 patients who had normal sodium levels.

Odds ratio for 30 DAYS mortality was found to be 10.650 for hyponatremia on admission which had significant P value 0.015 but hyponatremia within 72 hours had odds ratio of 5.917 with P value of 0.090.

Outcomes were analysed in terms of variables. The mean age for the patients who died was 66.57 which was older than who recovered 56.11 with P value 0.021 statistically significant.

Mean serum sodium value was 131.89 in the patients who died but 137.30 who recovered. Mean ejection fraction was 37.57 in the patients who died (P< 0.001) and 44.30 in who recovered and 3 out of 8 patients with Killip class 3/4 occurred death.

In 2004 Alexander Goldberg *et al*, conducted study to show that prevalence of hyponatremia in acute myocardial infarction patients and prognostic implications of hyponatremia in acute MI patients wherein they were able to find that hyponatremia on admission or early development of hyponatremia in patients with acute ST Elevation MI was an independent predictor for 30-day mortality [2].

In 2006 Goldberg *et al.* showed hyponatremia in acute MI was also a predictor for long term mortality and readmission of Myocardial Infarction patients with heart failure after hospital discharge [6].

In 2013, Waqar Qureshi *et al*, published that corrected and persistent hyponatremia in patients presenting with acute myocardial infarction is all cause mortality and major adverse cardiac events, heart failure related 30 days of rehospitalization and in certain cases treating of hyponatremia may achieve improved survival of the patients reducing long term mortality [7].

Statistical analysis turned out be significant for diabetes (P = 0.001), hypertension (P = 0.013), hyponatremia (P = <0.001), ejection fraction (P = <0.001) and Killip class (<0.001). Smoking had p value of 0.051 All the variables

with P value < 0.05 were included in the multivariate logistic regression analysis. Hyponatremia remained a significant independent predictor of 30 days mortality with *P* value of <0.001. This is in concordance to a similar study conducted by Qiang – Qiang *et al*. who found hyponatremia (*P* < 0.001) as significant factor in determining the short-term mortality rate 30days. Goldberg *et al*. in their study also found that hyponatremia was independently associated with 30-day mortality.

Conclusion

From our study we can conclude that hyponatremia at the time of admission and within 72 hours is a significant and independent predictor of mortality in acute ST elevation myocardial infarction patients. Hence measuring plasma sodium levels aids in management of the myocardial infarction patients by timely intervening and to reduce mortality rate. Further studies are required to establish whether hyponatremia alone or hyponatremia with neurohormonal activation in combination will result in increased mortality rate in acute ST elevation myocardial infarction patients by measuring serum AVP values, plasma renin activity, catecholamine levels, ANP, plasma osmolality in relation to hyponatremia.

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