



HYPONATREMIA SERVING AS A MORTALITY INDICATOR FOR ACUTE ST ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT **INTRODUCTION:** Acute ST-elevation myocardial infarction (STEMI) is a clinical syndrome involving myocardial ischemia, ECG changes and chest pain. In the developed world, the incidence and prevalence of coronary artery disease has decreased significantly over the last three decades whereas it has increased in the developing world. Hyponatremia, defined as a serum sodium concentration of less than 135 mmol/l, has prevalence ranging from 12.5% to 23.2% in patients with STEMI⁷ and around 25 % in patients with heart failure⁸. Hyponatremia is common after MI, though may not be a complication, is associated with adverse outcome in hospitalized patients. The plasma sodium concentrations rise, once the clinical improvement sets in. **AIM:** To find prognostic importance of hyponatremia in acute ST elevation myocardial infarction. **MATERIALS& METHODS:** 94 cases of Acute ST-elevation myocardial infarction (STEMI) fulfilling inclusion and exclusion criteria were enrolled in present study. After an overnight fasting, blood was taken for general routine investigations and lipid profile. Serum sodium levels were obtained on admission(day0), on day1, day2 and day3 along with 2D echocardiography findings on admission. **RESULTS:** In survivors' group have mean age of 51.0±12.44, 21% were females and 79% were males, 22% with hyponatremia, 44% were smokers, 23% were diabetics, 17% were hypertensives, 79% were in Killip class I 19% were in Killip class II, 1% in Killip class III and 1% in Killip class IV and mean ejection fraction was 43.23±3.35 as compared to non-survivors' group. Odd's ratio for 30day mortality is higher in groups with hyponatremia i.e., Group2 (6.88) and Group3 (4.00) when compared to Group1 i.e., (0.06) suggesting increased risk of mortality with hyponatremia. **CONCLUSION:** Hyponatremia on admission or early development of hyponatremia in acute-STEMI patients can be used as an independent predictor of 30day mortality.

KEYWORDS : Hyponatremia, STEMI, Killip class.

INTRODUCTION:

Acute ST-elevation myocardial infarction (STEMI) is a clinical syndrome involving myocardial ischemia, ECG changes and chest pain. Myocardial infarction (MI) definition includes confirmation of myocardial ischemic injury with abnormal cardiac biomarkers¹. Major risk factors are dyslipidemia, diabetes mellitus, hypertension, smoking and family history²³. Cardiovascular disorders, particularly STEMI and heart failure, are estimated to affect 17.3 million people worldwide every year^{4,5,6}. Hyponatremia is a common electrolyte disorder in hospitalized patients especially in heart failure, nephrotic syndrome, or cirrhosis.

Complications of myocardial infarction include ventricular free wall rupture, interventricular septum rupture and acute mitral regurgitation, ventricular tachycardias, apical aneurysms, etc.. Hyponatremia is common after MI, though may not be a complication, is associated with adverse outcome in hospitalized patients. The plasma sodium concentrations rise, once the clinical improvement sets in. In acute STEMI, baroreceptor activation leads to activation of sympathetic nervous system which releases hormones like vasopressin and activate renin angiotensin system (RAS). Magnitude of these neuro-hormonal changes is related to severity of myocardial damage. The neurohormonal activation that accompanies acute myocardial infarction is similar to that which accompanies heart failure. Hyponatremia is considered as a marker of these hormonal changes and may serve as a simple, easily available and cost-effective marker to identify patients at high risk, has also been identified as an independent predictor of short- term mortality, long- term mortality, and re-hospitalizations because of heart failure^{7,8,9}. Whether hyponatremia in the acute phase of ST segment elevation myocardial infarction is just a marker of adverse patients or it is able to exert a direct adverse effect on the cardiovascular system is still unknown.

With this perspective present study was undertaken to determine the prognostic importance of hyponatremia in major adverse cardiac events.

MATERIALS AND METHODS:

94 cases of Acute ST-elevation myocardial infarction (STEMI) fulfilling inclusion and exclusion criteria were enrolled in present study after approval of institutional ethics committee. The study was undertaken in the Department of Medicine, MGM Medical College & Hospital, Aurangabad, a tertiary care hospital conducted from November 2020 to November 2022.

Thorough detailed history with details of family, personal and past history of comorbidities and detailed cardiac as well as physical examination was performed. Serum sodium levels were obtained on admission(day0), on day1, day2 and day3. Ion selective electrode auto analyser (VITROS-5600) was used for determining plasma sodium concentrations. 2D echocardiography findings were also recorded on admission. On the basis of serum sodium status, total 94 cases were divided into three groups as follows-

- A. Group 1(N=68):** patients with normal sodium levels.
- B. Group2 (N=10):** hyponatremia on admission.
- C. Group3 (N=16):** hyponatremia within 72 hours of admission.

Regular follow up was done till 30 days for observing the prognostic importance of hyponatremia in the setup of STEMI.

INCLUSION CRITERIA:

1. Anginal chest pain lasting more than 20 minutes with STEMI on ECG and elevated CKMB and Troponin levels are taken.

EXCLUSION CRITERIA:

1. Individuals of age < 18 years
2. Conditions causing hyponatremia eg: head injury, syndrome of inappropriate anti diuretic hormone (SIADH), etc.,
3. Patients on drugs causing hyponatremia eg: Thiazide diuretics.
4. All patients diagnosed as acute cardiac event other than STEMI.
5. Patients who are not willing for participation.

STATISTICAL ANALYSIS:

Data collected compiled in MS EXCEL Sheet 2018. Analysis of Data

is done by SPSS Software Version 2.0. Qualitative data tabulated in the frequency and percentage form. Quantitative data tabulated in the form of Mean, Median, Mode, Standard deviation. Both Qualitative and Quantitative data represented in the form of visual impression like Bar Diagram. Microsoft word and Excel have been used to generate graphs, tables etc.

OBSERVATIONS AND RESULTS:

TABLE:1 Distribution of cases according to age

Age group Years	Frequency cases
< 40	16 (17 %)
40 to 60	51 (55 %)
> 60	27 (28 %)
Total	94 (100 %)

Table:1 shows maximum number of patients were in the age group between 40-60 years i.e., 55% followed by age group >60years i.e., 28%.

TABLE:2 Baseline characteristics of 94 patients

Characteristics	Normal sodium level(n=68)	Hyponatremia Admission (n=10)	Hyponatremia within 72 hrs (n=16)	P value
MEAN ±SD, NUMBER (%) OR MEDIAN				
AGE(YRS)	51.47±11.9	60.6±17.55	51.56±12.04	F=2.39 P=0.09
MALE SEX	53(78 %)	8(80 %)	12(75 %)	χ ² =0.099 p=0.951
DIABETES	16(24 %)	5(50 %)	5(31 %)	χ ² =3.17 p=0.204
SMOKING	26(38 %)	6(60 %)	11(69 %)	χ ² =5.77 p=0.05
HYPERTENSION	14(21 %)	2(20 %)	3(19 %)	χ ² =0.02 p=0.986
KILLIP CLASS	1.25±0.46	1.8±1.03	1.5±0.96	F=3.63 p=0.03
EJECTION FRACTION (%)	44.23±3.10	40.42±1.03	39.70±1.35	F=22.9 p=<0.00001

TABLE: 3 Distribution of cases in terms of mortality in patients with severity of hyponatremia.

Range of Sodium levels in hyponatremia patients	No. of patients	Mortality
<130	9	6(67%)
130-134	17	2(12%)
P value=0.007		

Table:3 shows maximum mortality is found in patients with severe hyponatremia (<130) i.e., 67%.

TABLE:4 Odds ratio for 30day mortality in all groups

	Survivors	Non survivors	Odds ratio	P value
Group1	66	2	0.06	-
Group2	6	4	6.88	0.01
Group3	12	4	4.00	0.05

Table:4 shows high odds ratio was observed in groups with hyponatremia i.e., Group2 i.e., hyponatremia on admission (6.88) and Group3 i.e., hyponatremia within 72 hours of admission (4.00).

Table:5 Distribution of baseline characteristics in survivors and non-survivors

	Survivors (N=84)	Non-survivors (N=10)	T or χ ²	P value
Age(yrs) (Mean±SD)	51.0±12.44	66.28±6.79	2.71	0.007
Sex- Males-Females	66(79%) 18(21%)	7 (70%) 3(30%)	0.37	0.53
Hyponatremia (Mean ±SD)	18(22%)	8(80%)	15.32	0.00009
Smoking	37(44%)	6(60%)	0.91	0.33

Diabetes	19(23%)	7(70%)	10.02	0.001
Hypertension	14(17%)	5(50%)	6.15	0.01
Killip class I	66(79%)	3(30%)	24.09	0.00002
II	16(19%)	3(30%)		
III	1(1%)	3(30%)		
IV	1(1%)	1(10%)		
EF (%) (mean±SD)	43.23±3.35	41.54±2.72	-1.53	0.12

Table:6 Variables showing independent association with 30day mortality.

Variable	p value
Age	0.007
Sex	0.53
Smoking	0.33
Hypertension	0.01
Diabetes	0.001
Killip class	0.00002
Hyponatremia	0.00009
Ejection fraction	0.12

So, multivariate regression analysis showed that along with other risk factors, hyponatremia was the significant independent predictor of 30day mortality.

DISCUSSION

In our study maximum number of patients were in the age group 40-60 years which is 51(55%) of the cases and next highest number of patients were found in the age group >60 i.e., 27 (28%). The mean age in cases with hyponatremia on admission was 60.617.55years.

In a similar study by Vikas et al. (2018)¹⁰, maximum number of cases were in the age group of 41-60 years i.e., 106(53%). However, the mean age in cases with hyponatremia on admission was 64.719.46 years, higher than the other cases. However no statistical significance was found in determining older age as a risk factor for hyponatremia.

In present study, history of smoking was associated with 26 patients (38%) in Group1, 6 patients (60%) in Group2 and 11 patients (69%) in Group3 respectively. Diabetics were 16(24%) in Group1, 5(50%) in Group2 and 5(31%) in Group3 respectively with a p value of 0.204. Hypertensives were 14(21%) in Group1, 2(20%) in Group2 and 3(19%) in Group3 patients respectively. In a similar survey by Vikas et al. (2018)¹⁰, it was observed that smoking was found to be in 80 patients (62 %), 18 patients (13.9 %) and 31 patients (24 %) with a p value of 0.148 at normal sodium level, hyponatremia upon admission, and hyponatremia within 72 hours respectively. The presence of diabetes in 27 patients (54 %) at normal sodium levels, 8 patients (16 %) with hyponatremia on admission, and 15 patients (30 %) with hyponatremia within 72 hours, with a p value of 0.083. Hypertension was found to be in 5 (26.3 %) patients with normal sodium levels, in 8 (42.1 %) patients with hyponatremia on admission, and in 6 (31.5 %) patients with hyponatremia within 72 hours with a p value 0.000. This also correlates well with other studies like Sijoy Kurian et al. (2017)¹¹ Our findings of hyponatremic cases were more often associated with higher Killip class, which is comparable to Goldberg et al.^{7,9}, Lazzari et al.¹², Vikas et al. (2018)¹⁰.

In our study it was found that survivors' group have mean age of 51.0±12.44, 18 patients (21%) were females and 66 patients (79%) were males, 18 patients (22%) with hyponatremia, 37 patients (44%) were smokers, 19 patients (23%) were diabetics, 14 patients (17%) were hypertensives, 66 patients (79%) were in Killip class I, 16 patients (19%) were in Killip class II, 1 patient (1%) in Killip class III and 1 patient (1%) in Killip class IV and mean ejection fraction was 43.23±3.35. In non-survivors' group have mean age 66.28±6.79, 3 patients (30%) were females and 7 patients (70%) were males, 8 patients (80%) with hyponatremia, 6 patients (60%) were smokers, 7 patients (70%) were diabetics, 5 patients (50%) were hypertensives, 3 patients (30%) were in Killip class I, 3 patients (30%) were in Killip class II, 3 patients (30%) were in Killip class III and 1 patient (10%) were in Killip class IV and mean ejection fraction was 41.54±2.72.

Odds ratio for 30day mortality is higher in groups with hyponatremia i.e., Group2 (6.88) and Group3 (4.00) when compared to Group1 i.e., (0.06) suggesting increased risk of mortality with hyponatremia. Maximum mortality in our study is observed in patients with sodium levels <130mEq i.e., 6(67%) of 9 patients and mortality

with sodium level 131-134mEq was 2(12%) of 17 patients suggesting high risk of mortality with increase in severity of hyponatremia.

In their study, Vikas et al. (2018)¹⁰ noted that survivors' group had 45 (25.7 %) patients with hyponatremia, 113 (64.5 %) patients with smokers, 43 (24.5 %) patients with diabetics, and 11 (6.2 %) patients with hypertension. Non survivors' group had 23 (92.5 %) patients with hyponatremia, 16 (64.0 %) patients with smokers, 7 (28 %) patients with diabetics and 8 (32 %) patients with hypertension. Maximum mortality 65.38% (17 of 26 patients) occurred in patients with serum sodium levels <130mEq. 16.6% (7 of 42 patients) of total deaths occurred in those with serum sodium levels between 131-134mEq.

Comparison of various risk factors and other variables among survivor and non-survivor groups revealed, apart from age, hypertension, diabetes, Killip class, and laboratory markers like Troponin and CKMB levels, hyponatremia was significant risk factor in determining mortality. Multivariate regression analysis was done among all the variables in survivors and non survivors that were significantly associated with mortality. Hyponatremia remained a significant independent predictor of mortality. This was in concordance with various other similar studies like Goldberg et al⁹., Vikas et al. (2018)¹⁰ and Sijoy Kurian et al. (2017)¹¹.

CONCLUSION:

Non osmotic release of AVP could be associated with early development hyponatremia after acute-STEMI. Plasma sodium levels may serve as a simple marker to identify patients at high risk. Hyponatremia on admission or early development of hyponatremia in acute-STEMI patients can be used as an independent predictor of 30day mortality.

REFERENCES:

1. Wilson PW. Established risk factors and coronary artery disease: the Framingham Study. *Am J Hypertens*. 1994 Jul;7(7 Pt 2):7S-12S
2. Canto JG, Kiefe CI, Rogers WJ, Peterson ED, Frederick PD, French WJ, Gibson CM, Pollack CV, Ornato JP, Zalenski RJ, Penney J, Tiefenbrunn AJ, Greenland P., NRM Investigators. Number of coronary heart disease risk factors and mortality in patients with first myocardial infarction. *JAMA*. 2011 Nov 16;306(19):2120-7
3. Hartikainen TS, Sörensen NA, Haller PM, Göföling A, Lehmacher J, Zeller T, Blankenberg S, Westermann D, Neumann JT. Clinical application of the 4th Universal Definition of Myocardial Infarction. *Eur Heart J*. 2020 Jun 14;41(23):2209-2216
4. Laslett LJ, Alagona P Jr., Clark BA 3rd, et al.: The worldwide environment of cardiovascular disease: prevalence, diagnosis, therapy, and policy issues. *J Am Coll Cardiol*. 2012, 60:S1-S49.
5. Rapsomaniki E, Timmis A, George J, et al.: Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet*. 2014, 383:1899-911
6. Roth GA, Huffman MD, Moran AE, Feigin V, Mensah GA, Naghavi M, Murray CJ: Global and regional patterns in cardiovascular mortality from 1990 to 2013. *Circulation*. 2015, 132:1667-78
7. Goldberg A, Hammerman H, Petcherski S, Zdorovyak A, Yalonetsky S, Kapeliovich M, et al. Prognostic importance of hyponatremia in acute ST-elevation myocardial infarction. *Am J Med* 2004; 117: 242- 8.
8. Klopotoski M, Kruk M, Przyłuski J, Kalinczuk L, Pregowski J, Bekta P, et al. Sodium level on admission and in-hospital outcomes of STEMI patients treated with primary angioplasty: The ANIN Myocardial Infarction registry. *Med Sci Monit* 2009; 15: CR477-83.
9. Goldberg A, Hammerman H, Petcherski S, Nassar M, Zdorovyak A, Yalonetsky S, et al. Hyponatremia and long-term mortality in survivors of acute ST-elevation myocardial infarction. *Arch Intern Med* 2006; 166: 781-86.
10. Dr Vikas, Dr Gurdeep Kaur. Prognostic Importance of Hyponatremia in Acute ST Elevation Myocardial Infarction (STEMI). *JMSCR Volume 06 Issue 08 August 2018*
11. Sijoy Kurian, Namita Mohanty, Suprabhat Giri, Rini George. Study of Hyponatremia in Acute ST-Elevation Myocardial Infarction and Its Prognostic Importance. *J Med Res Prac April 2017; Volume 06, Issue 02: 56-61*
12. Lazzeri C, Valente S, Chiostrì M, Attana P, Picariello C, and Gensini GF. Usefulness of Hyponatremia in the Acute Phase of ST-Elevation Myocardial Infarction as a Marker of Severity. *Am J Cardiol* 2012; 110: 1419-1424.