Original Research Article

Study of hyponatremia as prognostic indicator in acute ST elevation myocardial infarction

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Abstract

Background: Myocardial infarction causes more deaths and disability and incurs greater economic costs than any other illness in the world. It is the most common, serious chronic, life threatening illness. **Aim and objective:** To study the prognostic importance of hyponatremia in acute ST elevation myocardialinfarction. **Methodology:** 100 consecutive patients presenting with acute ST- elevation myocardial infarction admitted to Bapuji Hospital and Chigateri General Hospital attached to JJM Medical college, Davanagere, from December 2014 to November 2016 were studied. Qualifying patients underwent detailed history and clinical examination. Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours thereafter. The primary end point was all cause mortality within 30 days following myocardialinfarction. **Results and discussion:** In our study substantial proportion of patients who presented with acute ST elevation myocardial infarction were hyponatremic on admission or developed hyponatremia shortly after admission. Univariate and Multivariate analysis showed hyponatremia on admission or early development of hyponatremia as a significant independent predictor of 30 day mortality.
Key Word: hyponatremia, prognostic indicator.

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INTRODUCTION

Myocardial infarction is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium, it typically occurs when there is an imbalance between myocardial Oxygen supply and demand. Because myocardial infarction may strike any individual during the most productive years, it can have profound deleterious, psychological and economic ramifications. The most common cause of myocardial ischaemia is atherosclerotic disease of an epicardial coronary artery (or arteries) sufficient to cause a regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery. With an decline in infectious disease related death accompanied by accelerated economic development and life style change promoting atherosclerosis, developing countries especially India are expected to experience a sharp increase in ischemic Heart disease and AMI. Given the wide disparity of available resources to treat AMI in developing countries, major efforts are needed to strengthen primary prevention programmes at community level1.Obesity, insulin resistance, and type2 diabetes mellitus are increasing and are powerful risk factors for IHD and AMI. Hyponatremia is a common electrolyte disorder amongst hospitalized patients[2], especially in postoperative period3and in patients with heart failure, nephroticsyndromeorcirrhosis[4,5] Hyponatremia has been shown to be a predictor of cardio vascular mortality among patients with heart failure[6,7] Hyponatremia is common after MI, and clinical improvement is accompanied rise in plasma sodiumconcentration.[8]

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However, while the prognostic value in hyponatremia in chronic heart failure is well established in data 9 prognostic importance of hyponatremia in the setting of acute myocardial infarction are lacking. Hyponatraemia is found more frequently in the early period of ST elevation myocardial linfarction, and influences short as well as long term outcomes10. In STEMI, like congestive heart failure, arterial under filling causes stimulation of high-pressure baroreceptors present in the left ventricle, arch of aorta and carotid sinus, causing stimulation of cardio regulatory centre in the brain, causing stimulation of efferent pathway of the sympathetic nervous system. Activation of this sympathetic nervous system stimulates the non-osmotic release of AVP, renin as well as angiotensin II, leading to activation of renin-angiotensin-aldosterone system. Hormones thus released by baroreceptor stimulation reflects the severity of heart failure[2,11] and also worsens cardiac remodelling (AVP plays role in regulation of vascular tone and cardiac contractility and negatively influences cardiac haemodynamics and myocardial remodelling).[1,12] In the early period of STEMI, release of AVP, also retards water excretion, leading to increased blood volume and thus leading to dilutional hyponatraemia. So hyponatraemia actually reflects the baroreceptor-mediated hormonal activation in an exaggerated manner and thus serves as a marker of underlying worsening haemodynamics. Hyponatraemia, though a marker, can also contribute to the worsening haemodynamics by impairing contraction and relaxation of myocardial cells, decreasing the diastolic membrane potential and abolishing electrical coupling between myocytes13,14. Hence, it is worth to evaluate the incidence of hyponatraemia in patients with acute ST elevation myocardial infarction in Intensive Coronary Care Unit and to find out whether hyponatraemia serves as a poor prognostic indicator in these patients.15,16,17 This study was done to determine the prognostic importance of hyponatremia in the setting of acute ST elevation MI and to determine its usefulness in predicting short term survival.

AIM AND OBJECTIVE

To study the prognostic importance of hyponatremia in acute ST elevation myocardial infarction.

METHODOLOGY

Present study is a prospective study carried out in a tertiary care centre.100 patients presenting with acute ST-elevation myocardial infarction admitted to, cardiac unit in a tertiary care centrewere studied. Goldberg A, Hammerman H, Petcherski S, Zdorovyak A, Yalonetsky S, Kapeliovich M *et al* in their study at Rambam Medical Center and Rappaport Medical School, Haifa, Israel have shown incidence rates of hyponatremia in acute ST-elevation myocardial infarction as 32% 83.With incidence rate 32% and allowable error 30%, sample size i.e. n = 94 (n = 4pq /L2) where, p = incidence rate q = 1-pL = Allowable error Study was approved by ethical committee. A written valid consent was taken from patients after explaining study to them.

Inclusion Criteria:

All acute myocardial infarction patients having

1. Chest pain lasting more than 20minutes
2. 2. Diagnostic ECG changes with characteristic ECG alterations consisting of new pathological Q waves or ST segment and T wave changes.
3. Elevated creatinine kinase MB levels or elevated cardiac tropinin Tlevels

Exclusion Criteria:

1. Acute coronary syndrome without STelevation.
2. Age less than 16 years of both sexes.
3. Pre-existing Renaldiseases.
4. Patients with Acute MI and cardiac failure and on Diuretictherapy.

Qualifying patients underwent detailed history and clinical examination. Patients of acute myocardial infarction received thrombolytic therapy (tissue type plasminogen activator or streptokinase). Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours thereafter. The primary end point was all cause mortality within 30 days following myocardial infarction. Mortality data after discharge but within 30 days of myocardial infarction were obtained by postcard returned by patients or their families. When no postcard was received, follow-up status was determined over telephone or visit to their house which ever possible. Plasma sodium concentrations were determined by using an ion selective electrode auto analyzer (Roche OMNI C) Hyponatremia was defined as sodium level less than 135mmol/L (<135 mEq/L).Data was analysed with appropriate statistical tests.

RESULTS

Mean age of the patients was 53.21± 3.2 years with range of 26-86 years. The maximum numbers of patients were in the age group 51-60 which is 31% of the cases and next highest numbers of patients were found in the age group 61-70 (24%). M: F ratio in our study was 4:1. Patients presented with hyponatremia on admission were older than patients with normal sodium levels. Males made up 75.9% of patients who presented with hyponatremia on admission and 100% of patients who developed hyponatremia within 72hours. Patients who presented with or developed hyponatremia more often were smokers (84.6%) and had diabetes (31%), anterior infarction (62.1% and 92.3%), higher killip class, lower

ejection fraction (47.86 ±7.145) compared to patients with normal sodium levels . (table 1) Table 2 showed distribution of patients according to hyponatemia and mortality. Mortality in patients with normal sodium levels was 2(3.44%) out of 58.Mortality in patients developing hyponatremia on admission was 7(24.1 %) out of 29. Mortality in patients developing hyponatremia within 72 hours was 1(7.69%) out of 13. A total of 10 deaths(10%) occurred out of 100. On calculating Odd's ratio we found that Odds ratio for 30 day mortality was found to be high in hyponatremic groups.(Group2=3.143, Group3=12.0)

Table 1: Table Showing Base Line Characteristics Of 100 Patients

Characteristics	Normal sodium level(n=58)	Hyponatremia on Admission (n=29)	Hyponatremia within 72 hrs (n=13)	P value
	MEAN ±SD, NUMBER (%) OR MEDIAN			
Age(yrs)	55.38 ± 12.333	58.59 ±12.836	48.46± 13.776	F=2.868 p=0.062
Male sex	43 (74.1)	22 (75.9)	13 (100)	χ 2= 4.284 p=0.12
Diabetes	22 (37.9)	9 (31)	1 (7.7)	χ 2= 4.48 p=0.106
Smoking	41 (70.7)	19 (65.5)	11 (84.6)	χ 2= 1.579 p=0.45
Hypertension	6 (10.3)	3 (10.3)	3 (23.1)	χ 2=1.736 p=0.42
Anterior infarction	38 (62.1)	18(62.1)	12(92.3)	χ 2=4.609 p=0.1
Killip class	1.05±0.22	1.12±0.41	1.08±0.28	F=1.18 p=0.312
Ejection fraction (%)	49.76±5.066	47.86±7.145	49.62±5.709	F=2.693 p=0.073

Table 2: Distribution of patients according to hyponatremia on admission and at 72 hours and outcome in terms of mortality

	Normal sodium levels	Hyponatremia on admission	Hyponatremia within 72 hours	Total
No. of patients	58	29	13	100
Mortality in each group at the end of 30days	2 (3.44%)	7 (24.1%)	1 (7.69%)	10 (10%)
Odd's ratio	-	**3.143**	**12.0**	
P value	-	**0.008**	**0.017**	

Table 3: Comparison of severity of Hyponatremia and outcome in terms of mortality

Range of Sodium levels in hyponatremia patients	No. of patients	Mortality
<130	7	4(57.14%)
131-134	25	4(16.11%)

Number of patients with sodium levels less than 130 is 7 and mortality was 4(57.14%). Number of patients with sodium levels between 131-134 is 25 and mortality was 4(16.11%).

Table 4: Comparison of Survivors and non survivors for various factors

	Survivors	Non survivors	T or χ 2	P value
N	90	10		
Age(yrs) (mean ±SD)	55.02 ±12.78	58.9 ± 14.15	-0.901	0.370
Sex M	69 (76.7%)	9 (90%)	1.00	0.452
Hyponatremia on admission(mean ±SD)	136.96 ±4.02	131.63±4.24	3.963	<0.0001
Hyponatremia on at 24 hours	136.92±3.422	134±1.19	2.505	0.014
Hyponatremia on at 72 hours	136.01±3.32	132±4.372	3.508	0.001
Smoking	66(72%)	4(50%)	1.65	0.198
Diabetes	27 (30%)	5(50%)	1.654	0.19
Hypertension	10 (11.1%)	2 (20%)	0.673	0.412
Infarct site Anterior Inferior	64(68.9%) 28(31.1%)	6(60%) 4(40%)	0.1323	0.6972
Killip class I	89(98.9%)	1(10%)	79.012	<0.0001
EF(%)	49.7±5.59	44.6±6.096	2.711	0.008

Table 5: Multivariate analysis of sodium levels in MI patient

	Mean Square	F	p value
Age	.007	.384	.537
Sex	.000	.026	.873
Smoking	.004	.210	.648
Diabetes	.015	.849	.359
Hypertension	.055	3.167	.079
Killip Class	4.948	**283.242**	**<0.0001**
Sodiumon Admission	.140	**8.021**	**.006**
Sodium at 72 hours	.009	.488	.487
Ejection Fraction	.002	.125	.725

It was seen that serum sodium levels was statistically significant in determining mortality. Mean serum sodium level was 136.96 ±4.02 in the survivors and 131.63±4.24 in nonsurvivors. Other factors such as Killip class, hypertension, diabetes, age and sex were found to be statistically significant in determining mortality. Multivariate analysis using logistic regression analysis was performed (table 5) including variables that had p value < 0.2 in the univariate analysis to identify the variables that were independently associated with 30 day mortality. Multivariate analysis showed that along with other risk factors, hyponatremia was the significant independent predictor of 30 day mortality.

DISCUSSION

Our study suggests that patients presenting with acute myocardial infarction who had hyponatremaia on admission or developed hyponatremia after admission represent high risk population. In our study substantial proportion of patients who presented with acute ST elevation myocardial infarction were hyponatremic on admission or developed hyponatremia shortly after admission. In our study, hyponatremia was present on admission in 29 patients (29%). Hyponatremia developed in 13 patients(13%) during the first 72 hours of hospitalisation. In a similar study conducted by Goldberg18 *et al*, hyponatremia was present in 131 patients (12.5%) and hyponatremia developed in 208(19.9%) during the first 72 hours of hospitalisation. Patients who presented or developed hyponatremia more often had diabetes, anterior infarction and higher Killip class and lower ejection fraction. This is in accordance to the study conducted by Goldberg18 *et al*. In study done by Goldberg18 *et al*, a total of 105 deaths (10%) occurred within30 days of admission. 6.2% (44/708) of patients without hyponatremia, 19. 8% (26/131) of patients with hyponatremia on admission and 16.8% (35/208) of patients who developed hyponatremia after admission. Klopotowski *et al*, in their study of 1858 ST-elevation MI patients concluded that hyponatremia independently correlated with in-hospital mortality. Hyponatremics had higher rates of in-hospital mortality (13.5% vs 3.8%,p<0.001) composite of death and heart failure(27.8% vs 18.4%p=0.022).19

Ahmad Sajadieh *et al* in their study of 671 men and women aged 55 to 75 years with no history of cardiovascular disease, stroke, or cancer, found an adverse outcome defined as death or Myocardial Infarction(MI) occurred in 43% of patients whose serum sodium level was less than 134mEq/L. They concluded that Hyponatremia is an independent predictor of death and myocardial infarction in middle-aged and elderlypatients.[20] Bae *et al* reported that in hospitalized survivors of acute myocardial infarction, the presence of hyponatremia at discharge was an independent predictor of 12-month mortality. The study involved 1290 patients[21] In comparision with the above study, our study had higher mortality in patients with hyponatremia on admission whereas mortality was almost equal in patients who developed hyponatremia after admission. In our study, odd‘s ratio for 30 day moratality in patients with hyponatremia on admission and patients who developed hyponatremia was high (3.143 and 12.0).This was in concordance with study done by Golderg18 *et al*. In our study, we found a trend of increasing mortality with the severity of hyponatremia. We stratified patients into two groups depending on the mean sodium level. The group with sodium level <130 mmol/L had 58% mortality and those with serum sodium in the range of 131-134mmol/L suffered 17% deaths. This was inconcordance with the study conducted by Goldberg18*et al*, who showed increasing mortality with severity of hyponatremia. When we compared the various risk factors and outcomes among the survivors and the non survivors, we found, apart from age, sex, diabetes, hypertension, Killip class on admission, ejection fraction, hyponatremia was significant risk factor in determining mortality. All the variables among the survivors and non survivors that were significantly associated with mortality were included in the multivariate logistic regression analysis. Hyponatremia remained a significant independent predictor of mortality. This is in concordance to similar study conducted by Goldberg18 *et al*. they found that hyponatremia was independently associated with 30 day mortality. In a similar study of 235 patients admitted to a coronary care unit, Flear *et al*., found higher in hospital mortality rates among patients with minimal plasma soidum levels ≤130mmol/L. Sigurdsson A, Held P, Swedberg K in their study of 55 patients with acute myocardial infarction concluded that sustained neurohormonal activation after myocardial infarction mainly occurs in patients with clinical heart failure and is related to the magnitude of myocardial damage, even in patients without heart failure.[22] Tang *et al* also

documented in their study that hyponatremia was independently associated with in hospital death and heart failure. Thus, Goldberg83 *et al*., concluded in their study that the development of hyponatremia is a marker that most likely incorporates different prognostic entities, including the severity of the left ventricular dysfunction, hemodynamic alterations and the extent of neurohumoralactivation.[23] It was observed that the development of hyponatremia is a biochemical marker for prognostic importance i.e. left ventricular dysfunction severity, hemodynamical changes and neurohumoral activation. Hence in our study, we concluded that hyponatremia on admission or early development of hyponatremia in patients with acute ST elevation MI is an independent predictor of 30 day mortality.

CONCLUSION

Hyponatremia on admission or early development of hyponatremia in patients with acute ST elevation myocardial infarction is an independent predictor of 30-day mortality. Plasma sodium levels may serve as a simple marker to identify patients atrisk.

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