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ORIGINAL ARTICLE

A PROSPECTIVE STUDY OF IN HOSPITAL OUTCOME OF ACUTE PHASE OF STEMI WITH HYPONATREMIA

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ABSTRACT: BACKGROUND AND OBJECTIVE: In acute STEMI, due to activation of the Baro receptors, there is activation of the sympathetic nervous system. This leads to release of hormones like vasopressin and also activation of renin angiotensin system. Magnitude of this neurohormonal change is related to the severity of the myocardial damage. Hyponatremia is a reflection of these hormonal changes. So serum Na+ level may be an indicator of the severity of ST elevation MI (STEMI). The aim of this study is to evaluate in hospital prognosis of acute ST segment elevation myocardial infarction with Hyponatremia. **MATERIAL AND METHODS**: This prospective observational study was conducted in patients presenting with acute ST-elevation myocardial infarction admitted in ICCU, Basaveshwar Teaching and General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College during the period of Jan 2013 to July 2014.Qualifying patients underwent detailed history and clinical examination. Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours thereafter. Study population were grouped into two groups, 50 patients with hyponatraemia were included in Group-I and 50 patients with normal plasma sodium level were in Group-II. Hyponatremia defined as plasma sodium level less than 135 mmol/L. In hospital outcome of these two groups of patients were evaluated and compared. **RESULTS:** The hypo and normo natremic groups were comparable with respect to baseline characteristics and in-hospital management. There was no statistically significant difference between the two groups regarding the incidence of risk factors of IHD. Hyponatremics had higher rates of in-hospital mortality (24%vs 6%$p<0.01$) composite of death, heart failure (72% vs. 36%, $p=0.05$) and arrhythmias (30% vs 6% $p<0.01$) Anterior myocardial infarction was more frequent in patients with hyponatremia, who showed advanced Killip class. After adjustment for covariates, hyponatremia was independently correlated with in-hospital mortality. **CONCLUSION:** Hyponatremia on admission in patients with acute ST Elevation MI is a strong independent predictor of prognosis and sodium levels may serve as a simple marker to identify patient at high risk.

KEYWORDS: Acute myocardial infarction, Hyponatremia.

INTRODUCTION:

AIMS AND OBJECTIVES: To Study the usefulness of hyponatremia in predicting the in hospital outcome of acute phase of ST segment elevation MI.

MATERIAL AND METHODS:

Source of Data:

- This prospective observational study was conducted in patients presenting with acute ST-elevation myocardial infarction admitted in ICCU, Basaveshwar Teaching and General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College during the period of Jan 2013 to July 2014 were studied.

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- Qualifying patients underwent detailed history and clinical examination. Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours thereafter.
- Study population were grouped into two groups 50 patients with hyponatraemia were included in Group-I and 50 patients with normal plasma sodium level were in Group-II.
- Hyponatraemia defined as plasma sodium level less than 135 mmol/L. In hospital outcome of these two groups of patients were evaluated and compared.

Inclusion Criteria:

- All acute myocardial infarction patients presenting to ICCU, Basveshwar hospital, Gulbarga having Chest pain lasting more than 20 minutes
- Diagnostic ECG changes with characteristic ECG alterations consisting of:

  ST elevation ≥ 1 mm in ≥ two contigious limb leads.

  ST elevation ≥ 2mm in ≥ two contigious precordial leads

Exclusion Criteria:

- Patients with previous ST Elevation MI.
- Non Q wave MI, congestive cardiac failure.
- Cirrhosis of liver, nephrotic syndrome, renal failure.
- Patients with chest infection and bronchogenic carcinoma.
- Patients on diuretics were excluded.
- Study population were grouped into two groups 50 patients with hyponatraemia were included in Group-I and 50 patients with normal plasma sodium level 135-145mmol/L were in Group-II.
- Group I were categorized into 3 groups, Group Ia – Plasma Na+ ≤125, Ib – Plasma Na+ 126-130mmol/L, Ic – Plasma Na+ 131-134 mmol/L. Hyponatraemia defined as plasma sodium level less than 135 mmol/L. In hospital outcome of these two groups of patients were evaluated and compared.
- Details clinical history was taken including history of present illness, past illness, drug history and personal history. Relevant physical examination were done & recorded. All the patients were treated with thrombolytics and usual treatment protocol of the Institute.
- For each patient 10ml blood was drawn with aseptic precaution on admission. Blood was collected in a test tube and allowed to settle down for the formation of serum. Then serum was analyzed by auto analyzer using ion specific electrode. Blood glucose, CK-MB, Blood urea, Serum creatinine, Serum lipid profile were also measured on admission.
- Both the groups were followed up till death or discharge. Parameters of outcome were death, heart failure and arrhythmia. Occurrence of heart failure was followed up clinically by Killip class and by Echocardiography. Occurrence of arrhythmia was followed up clinically and by doing ECG.

Statistical Analysis: All collected data were checked and verified thoroughly to reduce inconsistency. Then data were edited, coded and entered into SPPS PC program. Baseline characteristics of two groups of patient were compared using analysis of variance by Chi-square test.

Univariate and multivariate logistic regression analysis were performed to determine the relation between hyponatraemia and in hospital mortality as well as other hospital outcomes

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(arrhythmia, heart failure). For the main analysis baseline characteristics (diabetes, hypertension, smoking, dyslipidaemia, and family history of CAD) were considered in multivariate procedure. Results were presented in the form of tables, graphs and chart.

OBSERVATIONS AND RESULTS:

Distribution of subjects by Age:

Age	Study group		Control group		Total	
	No	%	No	%	No	%
25-30	01	02.0	03	06.0	04	04.0
31-50	16	32.0	12	24.0	28	28.0
51-70	30	60.0	33	66.0	63	63.0
>70	03	06.0	02	04.0	05	05.0
Total	**50**	**100.0**	**50**	**100.0**	**100**	**100.0**
Mean±SD	56.50±11.48		54.78±11.02		55.64±11.21	

Table 1: Age Wise Distribution of Cases

Total 100 patients were studied. The mean age of patient was 55.64±11.21yrs. 5 patients (5%) were in >70 age group. 63 patients (63%) were in 51-70 age group, 28, (28%) in 31-50 age group and 4, (4%)) in 25-30 age

P-value & Significance t = 0.83, p>0.05, not significant

There is no significant difference of age among study and control group

Sex distribution of the study Group:

Groups	Male		Female		Total	
	No	%	No	%	No	%
Study group	35	74.0	15	26.0	50	50.00
Control group	38	70.0	12	30.0	50	50.0
Total	**73**	**73.0**	**27**	**27.0**	**100**	**100.0**

Table 2: Sex distribution

Among 100 patients studied, 73% were males, 27% females.

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Risk factors	Study group Group I		Control group Group II		P value
	No	%	No	%	
Hypertension	26	52.0	21	42.0	0.279 NS
Diabetes	19	38.0	13	26.0	0.147 NS
Smoking	32	64.0	30	60.0	0.582 NS
Dyslipidemia	15	30	14	28.0	0.415 NS
Family history of CAD	12	24.0	11	22.0	0.431 NS

Table 3: Distribution of cases according to risk factors

p>0.05, Not significant.

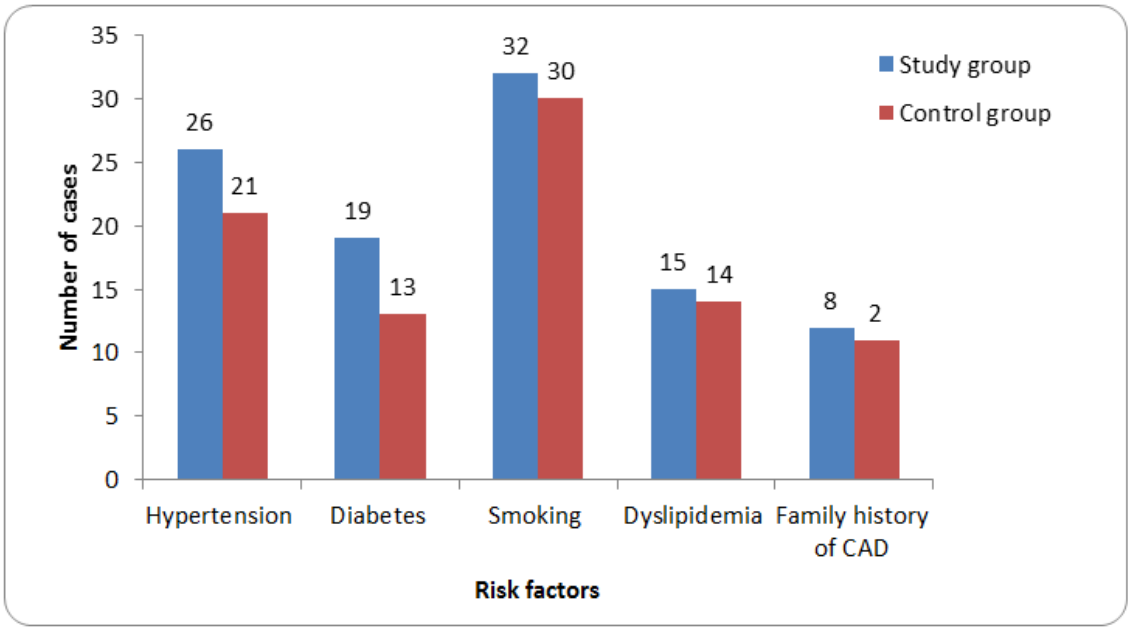
Group-I: Patients with hyponatremia.

Group-II: Patients with normal sodium levels.

P value obtained by chi-square level, NS-Non significant.

Risk factors are not statistically significant difference among study and control groups.

Bar graph showing Distribution of cases according to risk Factors:



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Characteristics	GROUP 1 NA <135	GROUP 2 NA ≥135	P VALUE
AGE(YRS)	56.50±11.48	54.78±11.02	0.49 NS
MALE SEX	35	38	0.53 NS
FAMILY HISTORY CAD	12	11	0.431 NS
DIABETES	19	13	0.147 NS
SMOKING	32	30	0.582 NS
DYSLIPIDEMIA	15	14	0.415 NS
HYPERTENSION	26	21	0.279 NS
ANTERIOR Wall MI	37	28	0.058 NS
INFERIOR WALL MI	13	20	0.085 NS
OTHERS	-	2	-
KILLIP CLASS 1 OR 2	27	46	0.00024 VHS
3 OR 4	23	4	0.00024 VHS
EJECTION FRACTION (%)	37.82±8.93	48.06±10.57	0.00078 VHS
ARRYTHMIAS	15	3	0.0023 HS
IN HOSPITAL DEATH	12	3	0.010 HS

Table 4: Base line characteristics of 100 patients

The hypo and normo natremic groups were comparable with respect to baseline characteristics and in-hospital management. There was no statistically significant difference between the two groups regarding the incidence of risk factors of IHD. Hyponatremics had higher rates of in-hospital mortality (24%vs 6% $p<0.01$) composite of death, heart failure (72% vs. 36%, $p=0.05$) and arrhythmias (30% vs 6% $p<0.01$) Anterior myocardial infarction was more frequent in patients with hyponatremia, who showed advanced Killip class.

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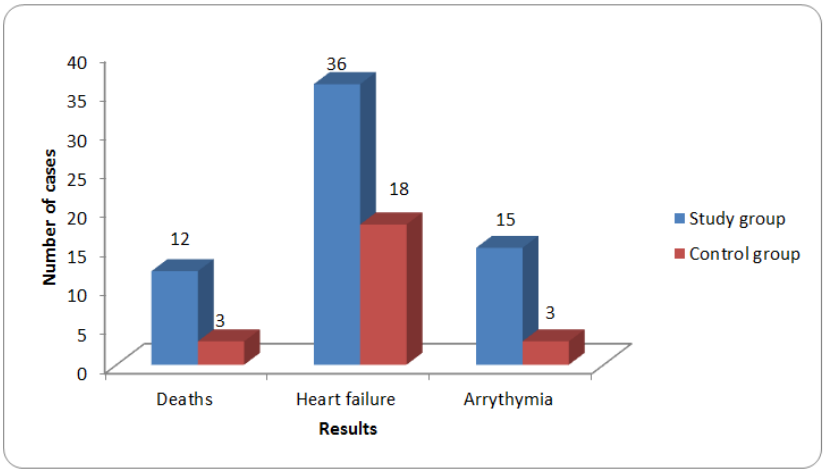
Results	Study group		Control group		P – value and significant
	No	%	No	%	
Deaths	12	24	03	6	$X^2 = 6.65$ p <0.01 HS
Heart failure	36	72	18	36	$X^2 = 3.87$ p <0.05 Sign
Arrhythmia	15	30	3	6	$X^2 = 8.83$ p <0.01 HS

Table 5: Adverse in-hospital outcome of the study subjects

Bar graph showing adverse in-hospital outcome of the study Subjects:



Study groups	Range	No. of Cases	No. of mortality cases	Percentage	Heart failure	Percentage
Group Ia	≤125	3	2	66.7	2	66.7
Group Ib	126-130	16	6	37.5	16	100.0
Group Ic	131-134	31	4	12.9	18	58.0
Control group	≥135	50	3	06.0	18	36.0
Total	**-**	**100**	**15**		**54**	

Table 6: Distribution of mortality and heart failure by serum sodium level

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Multivariate analysis using logistic regression analysis was performed including variables that had p value < 0.2 in the univariate analysis to identify the variables that were independently associated with in hospital mortality. So, multivariate analysis showed that along with other risk factors, hyponatremia was the significant independent predictor in hospital mortality.

Variable	p value
Age	0.492
Sex	0.534
Smoking	0.582
Dyslipidemia	0.415
Hypertension	0.265
Diabetes	0.147
Killip class	0.00024
Hyponatremia	0.0453
Ejection fraction	0.00078

TABLE 7

DISCUSSION: The main objective of this study was to ascertain the in hospital adverse outcomes of patient with hyponatraemia in setting of Acute ST elevation myocardial infarction. Among the important risk factors studied in patients the highest percentage of patients had history of smoking (62%) followed by hypertension (47%), diabetes (32%), Dyslipidaemia (29%) family history of coronary artery disease (10%).

In our study total of 15 patients (15%) died. Hyponatremic patients were categorized into four groups. 2 patients (66.7%) out of 3 patients died with plasma Na+ level <125 mmol/L. In patients with plasma sodium level 126-130 mmol/L deaths occurred in 6 (37.5%) patients out of 16 patients. 4(12.9%) patients died inNa+131-134mmol/L group out of 31 patients in this group. Death occurred in 3 (6%) patients having Na+ level ≥135.

Mortality increased with increasing severity of hyponatremia compared with patient having normal sodium level. This was is concordance with the study conducted by Goldberg et al, Hilton et al and Alexander et al, who showed increasing morality with severity of hyponatremia. Hilton, P. showed in their study that mortality of patients with MI is related to plasma sodium level [1.] Alexander, C. et al showed that acute STEMI patients without hyponatremia had a mortality rate 6.2% and the mortality rate was 19.8% in patients with hyponatraemia on admission and 16.8% in patients with hyponatremia developed after admission. After logistic regression analysis and adjustment for other important co-variants they concluded that both hyponatremia on admission and hyponatremia developing after admission remained strong independent predictors of 30-day mortality.[2]

In our study adverse hospital outcome other than mortality included heart failure, arrhythmia. Heart failure developed in highest percentage in patients with sodium level <130 mmol/L. So there was a relation between severity of hyponatremia and heart failure. Left ventricular ejection fraction was 37.82 ± 8.93% among patients with hyponatremia. Alexander, G. et al also found

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reduced left ventricular ejection fraction (42 ± 13%) among patients who developed hyponatremia after admission.[3]

Incidence of arrhythmia in this study was 18 %. Rahman et al. found that 9% of patients with MI had arrhythmia.[3,1] This contradiction is probably due to routine use of beta- blocker in that study and improvement in the monitoring of our study population. 3 patients (6%) developed arrhythmia in group II and 15 patients (30%) developed arrhythmia in group-I. Occurrence of ventricular fibrillation increased with degree of hyponatremia. Flear, C.T.et al. found that episodes of ventricular fibrillation occurred in relation to sodium level. They got significant ventricular fibrillation in patients with Na level 132 mmol/L and got no arrhythmia in patients with normal sodium level.[1]

Previously several studies have focused on the prognostic implications of hyponatremia in patients with chronic heart failure.[4,5] In the presence of heart failure, several mechanisms promote the development of hyponatremia. Vasopressin is essential to the development of hyponatremia because at least 15 liters of fluids can be excreted daily when vasopressin is appropriately inhibited.[5]

Activation of carotid baroreceptors has been implicated in the non-osmotic release of vasopressin due to arterial underfilling.[6,7] In addition, increased expression of messenger RNA for vasopressin in the hypothalamus has been described in animal models. Moreover, the renal effect of vasopressin is enhanced in heart failure, as the vasopressin-regulated water channel (AP2) in the collecting duct is upregulated[8]. The mechanisms leading to hyponatremia in heart failure may be responsible in part for the adverse prognosis associated with hyponatremia.

However, it is not clear whether the mechanisms that contribute to the development of chronic hyponatremia are involved in our study. For example, increased hypothalamic expression of vasopressin and up regulation of water channels in the collecting duct require several weeks of heart failure to develop.[4] In the setting of acute myocardial infarction, we observed hyponatremia on admission or a rapid reduction in plasma sodium level in a substantial number of patients. In addition, hyponatremia remained an independent predictor of mortality even after adjustment for the most important clinical and hemodynamic covariates that determine prognosis in ST elevation myocardial infarction.[9]

In acute myocardial infarction, nonosmotic release of vasopressin may occur due to the acute development of left ventricular dysfunction; in response to pain, nausea, and major stress, the most common mechanisms of hyponatremia in adults; or in response to the administration of analgesics and diuretics.[10,11] In this setting, vasopressin levels increase concomitantly with the activation of other neurohormones such as renin and norepinephrine.[12] However, vasopressin level does not correlate with serum osmolarity in myocardial infarction, suggesting that nonosmotic mechanisms are involved. In patients with myocardial infarction, hyponatremia may be aggravated further by the concomitant activation of the renin-angiotensin system and increased catecholamine production.[5]

These factors decrease the glomerular filtration rate and subsequent delivery of tubular fluid to the diluting segment of the nephron, further contributing to decreased renal water excretion.[5]

The mechanism of hyponatremia at cellular level occurs due to: 1) Increased cellular permeability initiated by anoxia or ischaemia and often enhanced by stress hormones. 2) Non-osmotic release of arginin-vasopressin leads to inappropriate amount of water retention. Administration of hypotonic fluid, non-steroidal analgesic and diuretic may add to the problem.[13]

Hyponatremia is a common hospital-acquired electrolyte disorder that is often associated with high mortality and morbidity due to progression of severe underlying disease. Chiara Lazzeri in

their study to assess the prognostic impact, in the short and long terms, of admission hyponatremia in 1, 231 consecutive patients with ST-segment elevation myocardial infarctions all submitted to primary percutaneous coronary concluded that the presence of hyponatremia in the acute phase of ST-segment elevation myocardial infarction should be considered a marker of more ill patients.[14]

Goldberg 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 neurohumoral activation.[15]

Hence in our study data therefore strongly suggest that the presence of hyponatremia, in the acute phase of STEMI, should be considered a marker of more ill patients.

CONCLUSION: Hyponatraemia on admission in patients with acute ST-Elevation MI is a strong independent predictor of prognosis. Prognosis worsens with increasing severity of hyponatraemia. Plasma sodium levels may serve as a simple marker to identify patient at high risk. These results will require further validation in other prospective studies.

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