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General Medicine

PROGNOSTIC IMPORTANCE OF HYPONATREMIA IN ACUTE STEMI

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ABSTRACT **Background:** Hyponatremia is the most common electrolyte disorder in clinical settings and in hospitalized patients and is found to be the most important predisposing factor of cardiovascular mortality among patients with heart failure. So, our aim was to investigate the prognostic importance of hyponatremia in acute STEMI and to establish its usefulness in predicting mortality. **Method:** A total of 175 consecutives patients admitted with acute STEMI in ICU of tertiary care hospital, during the period from DEC 2020 to NOV 2022 were enrolled and divided into 3 groups. Group 1= 75 patients with normal sodium level and thereafter; Group 2a= 50 patients with hyponatremia on admission and thereafter. Group 2b= 50 patients who developed hyponatremia within 72 hours of admission. **Result:** Patients of acute STEMI having hyponatremia had higher occurrence of Major Adverse Cardiovascular Events (MACE) and higher mortality compared to normonatremic patients. Patients who developed hyponatremia at admission had higher occurrence of MACE and higher mortality rate than the patients who developed hyponatremia at 72 hrs and normonatremic patients. Patients of acute STEMI having serum sodium level 127.57meq/l or less on admission or develops thereafter within 72 hr of admission were at more risk of development of MACE and mortality. Hyponatremia cases had low Ejection Fraction and higher killip class (>1) were at more risk of occurrence of MACE. **Conclusion:** Hyponatremia is a significant independent predictor of in-hospital mortality and morbidity in patients with acute STEMI. However, plasma sodium levels may help identify patient at risk.

KEYWORDS : Hyponatremia, Acute STEMI, Normonatremia, Major Adverse Cardiovascular Events (MACE); Killip class

INTRODUCTION

Acute myocardial infarction (AMI) is a common diagnosis in hospitalized patients in industrialized countries. In Indian population ST segment elevation myocardial infarction (STEMI) is the most common type of acute coronary event and contributes to 60.6% of overall incidence of acute coronary syndrome. The overall mortality in STEMI is approximately 4 to 7% or even less in the published clinical trials. However, this is not the case in the real-world situation [1,2]. This is because the patients enrolled in the randomized trials are selected ones and represented low-risk subgroup. Therefore, the results of these trials are not applicable to 50% of patients in clinical practice [3].

Hyponatremia, a commonly occurring electrolyte deficiency found in hospitalized patients, more especially in cardiac care units, in surgical postoperative wards and in patients with cardiac failure [2-5], It has been shown as important prognostic indicator of cardiovascular morality in patients of cardiac failure [5-7]. In congestive cardiac failure (CCF), decreased sodium levels are linked with over activity of renin-angiotensin-aldosterone system. Catecholamine's arginine vasopressin (AVP) and baroreceptor-mediated hormones,

However, hyponatremia develops in early phases of acute myocardial infarction, recently, several studies show the importance of hyponatremia as important early prognostic tool. Many studies from all over India shown that significant increase in plasma AVP level was in patients who had associated with complication as heart failure and fatal outcome after AMI, and clinical improvement was noted following the rise in serum plasma level of sodium. So, we therefore hypothesized, presence of hyponatremia in the initial settings of AMI suggest, at least in parts, cause increased neuro hormonal activity and affects left ventricular remodelling in acute phase of STEMI [8]. Thus, patients present with decreased plasma sodium levels may be attributable at much long-term risk in development cardiac failure arrhythmias and mortality. Since lack of such studies in central India we studied the prognostic importance of hyponatremia in acute ST elevation myocardial infarction and also to determine its usefulness in finding its short-term survival.

MATERIALS AND METHODS

After obtaining Institutional Ethical Committee approval and written informed consent from all the patients, this hospital based cross-sectional observational study was conducted during the period from DEC 2020 to NOV 2022. A total 175 adult patients of chest pain diagnosed as STEMI according to AHA (American Heart Association) / ACC (American College of Cardiology) criteria were included in the study. Patients with previous history of STEMI, duration of chest pain more than 3 days (72hr.), renal failure patient, chronic liver disease patient, hypokalaemia at the time of admission and patients on diuretics and malignancy were excluded from the study.

Diagnosis of STEMI: According to ACC/AHA/ ESC criteria Various laboratory investigations such as complete blood count, random blood sugar, electrocardiography and other investigation included serum electrolytes (Sr. Sodium, Sr. Potassium) were done, On basis of Ion Selective Electrode Method (ISE) and Spectrophotometry and Poteintiometry principal. Hyponatremia was defined as sodium level less than 135mmol/L ((<135 mEq/L). However, a biochemical study was carried out in each patient. Liver function test was done which included total protein, enzyme levels of SGOT (Serum Glutamic-oxaloacetic transaminase), SGPT (Serum Glutamic-pyruvic transaminase) and ALP (Alkaline Phosphatase), Bilirubin level (Direct and Indirect). Renal function was done which included Sr. creatinine and urea level. Lipid Profile was done which included Triglycerides (TG), Total Cholesterol (TC), LDL Cholesterol (Low density lipid cholesterol), HDL Cholesterol (High density lipid cholesterol). Beckman coulter au5800 automated biochemistry performing above tests with principles of spectrophotometry and potentiometry.

Patients were divided into- Group1= patients with normal sodium level and thereafter; Group 2a= Patients with hyponatremia on admission and thereafter. Group 2b= patients who developed hyponatremia within 72 hours of admission.

Demographic data and past medical history, including cardiovascular risk factors and comorbidities, were collected. Plasma sodium concentrations were obtained on admission and at 24hr ,48hr and 72hr. All patients were followed up till hospitalization with blood investigation reports. The composite end point of study was correlation of hyponatremia with outcomes and MACE during hospital stay. Also, hospital other complication was noted.

Statistical Analysis

Data were coded and analysed in statistical software STATA version 10.1, 2011. Descriptive statics were calculated to summarise quantitative variables by mean and standard deviation and qualitative

variables by frequency and percentages. Inferential statistics was including confidence interval and test of significance (p- value). Prevalence of Hyponatremia in acute STEMI patients overall and in 3 groups were expressed as percentage along with 95% confidence interval. Z test for difference in proportion was used to compare prevalence in 3 groups. P- value <0.05 was considered statistically significant.

OBSERVATION AND RESULTS

The study comprised of 75 cases with normal sodium levels (Group 1), 50 cases with hyponatremia on admission (Group 2a), and 50 cases who developed hyponatremia after admission within 72 hrs (Group 2b). Table 1 show that group 2a and group 2b patients were older than group 1 and male preponderance was seen in all studied groups. The association of risk factors with hyponatremia and normonatremia was statistically insignificant (p>0.05). Lipid profile was more deranged in hyponatremic group than normonatremic group. However, association of dyslipidemia was statistically insignificant with hyponatremia.

Table 1: Baseline Characteristics Of Patients

Demographics		Group 1	Group 2a	Group 2b	P value
Age	Mean	56.06	58.24	57.64	0.847
Sex	Male	57 (76%)	32 (64%)	36 (72%)	0.345
	Female	18 (24%)	18 (36%)	14 (28%)	
Risk Factors	Sedentary lifestyle	55(73.3%)	37 (74%)	38 (76%)	0.944
	Dyslipidemia	36 (48%)	32 (64%)	30 (60%)	0.168
	Hypertension	43 (57.33%)	22 (44%)	27 (54%)	0.298
	Smoking	22 (29.33%)	17 (34%)	14 (28%)	0.803
	Diabetes	25 (33.33%)	12 (24%)	13 (26%)	0.438
	History of Stroke	13 (17.33%)	5 (10%)	7 (14%)	0.516
	Multiple Risk Factors	33 (44%)	27 (54%)	23 (46%)	0.373
	Class-I	41 (54.67%)	54 (54%)		0.375
	Class>1	34 (45.33%)	46 (46%)		
Ejection fraction (%)		46.46 ± 9.71	44.5± 11.21		0.4067

Figure 1 showing Anterior wall myocardial infarction (AWMI) was more common in all studied group followed by Inferior wall myocardial infarction (IWMI). But hyponatremia was not significantly associated with types of STEMI.

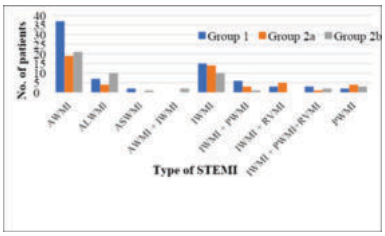

Figure 1: Distribution Of Type Of STEMI In Three Groups

Patients who develop HFpEF more in normonatremic group compared hyponatremic group. Although hyponatremia was not statistically significant correlation with reduced Ejection fraction. Figure 2 shows that hyponatremic group were more prone to develop reduced ejection fraction in acute STEMI.

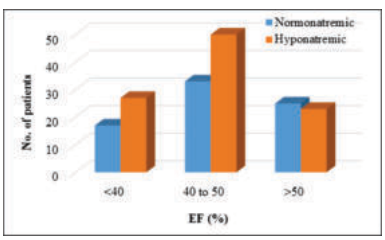

Figure 2: Ejection Fractions Among Groups

Major adverse cardiovascular events like arrhythmia, congestive cardiac failure, Cardiogenic shock, and A-V blocks were higher in hyponatremics, especially in patients who developed hyponatremia on admission and thereafter compared to who develops hyponatremia within 72 hours of hospitalization compared to normonatremic and all were significantly associated with hyponatremia, (p<0.05), (Table 2).

It was seen that serum sodium levels were statistically significant in determining MACE. The mean serum sodium level was 130.93±2.19 in the NO MACE and 129.40±3.36 in MACE. Other factors such Age, Dyslipidemia, Hypertension, Diabetes, History of Stroke, Ejection fraction and higher killips class were found to be statistically significant in determining MACE.

Table 2: In Hospital Complications

Groups	MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE)			
	Arrhythmia	CCF	C shock	AV BLOCK
Normonatrmic	10 (13.33%)	22 (29.33%)	15 (20%)	02 (2.67%)
Hyponatremic	29 (29%)	45 (45%)	38 (38%)	12 (12%)
P value	0.014, S	0.035, S	0.010, S	0.026, S
Group 2a	21 (42%)	30 (60%)	25 (50%)	10 (20%)
Group 2b	08 (16%)	15 (30%)	13 (26%)	02 (4%)
P value	0.008, HS	0.003, HS	0.013, HS	0.028, HS

In the present study mortality was more hyponatremic groups (23%) than normonatremics group (10.67%) and the difference was statistically significant with p value 0.034, (Table 3).

Table 3: Showing Mortality Rates Among Groups.

Group	Frequency	Mortality (%)	P value
NORMONATREMIC [Group-1(N=75)]	75	08 (10.67%)	0.034, S
HYPONATREMIC Group-2a + 2b (N=100)	100	23 (23%)	

However, mortality was more in patients who had hyponatremia on admission (group 2a) as compared to that who developed hyponatremia within 72hr of hospitalization (group 2b) and their difference was statistically significant with p-value 0.009, (table 4).

Table 4: Showing Mortality Rates Among Hyponatremics

Group	Frequency	Mortality (%)	P value
HYPONATREMIC on admission (2a)	50	17 (34%)	0.009, S
HYPONATREMIC in 72 of admission (2b)	50	06 (12%)	

Table 5 shows that serum sodium level <125meq /l had highest incidence of MACE (80%) and Mortality (40%), compared to serum sodium ranges 125-129meq/l and 130-134 meq/l.

Table 5: Severity Of Hyponatremia And Outcomes

Sodium level(meq/l)	MACE	DEATH
130 – 134(N=69)	35 (50.72%)	9 (13.03%)
125 – 129 (N=27)	20 (74.04%)	12 (44.44%)
<125(N=5)	4 (80%)	2(40%)
P value	0.010, s	0.001, HS

Figure 4 shows that significant serum sodium level for MACE and DEATH Is 126.95 and 127.57 respectively. And serum sodium level below 126.95meq/l had significant risk of developing MACE and below 127.57 meq/l had significant risk for mortality, this was statistically significant. (p<0.0001), (Figure 3).

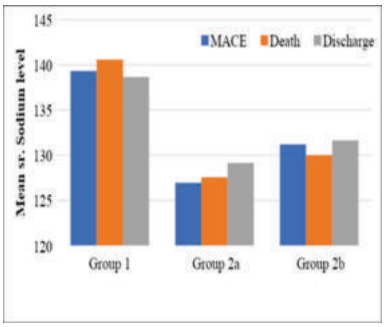

Figure 3: Highest Value Of Serum Sodium Level In Outcomes.

Multivariate analysis of variables showed that although other risk factors were significant in univariate analysis, but hyponatremia (P=0.019), higher Killips class (>1) and lower ejection fraction were having significant independent prediction for in hospital MACE. Whereas arrhythmia (p value <0.001) were having significant independent prediction for mortality, (Table 6).

Table 6: Multiple Logistic Regression Analysis Of Variables Of Independent Risk Factors For MACE And Mortality

Risk factors		Odds Ratio	95% confidence Interval	P-value
MACE	Smoking	2.38	0.55-10.28	0.244, NS
	Stroke	2.54	0.18-34.98	0.484, NS
	Hyponatremia	1.07	1.01-1.13	0.019, S
	Ejection fraction (%)	0.89	0.79-0.99	0.045, S
	Killips(>1)	0.001	0.001-0.16	<0.0001, HS
Mortality	Arrhythmia	38.64	7.86-189.93	<0.001, S
	CCF	16.35	1.99-133.89	0.009, S
	Killips(>1)	0.12	0.016-0.09	0.040, S

DISCUSSION

In the present study, patients who presented with hyponatremia on admission or develops hyponatremia in 72hr of admission belonged to a higher age when compared to patients with normal sodium levels who belonged to younger age. these results were comparable with study conducted by Goldberg A et al [9], Kurian S et al [10] and Singh S et al [11]. The incidence of anterior wall MI among patients with normal sodium levels, hyponatremia on admission or within 72 hours of admission was 61.33% and 68% respectively. This is similar to the results of Goldberg A et al [9] and Aziz M et al [12]. Mean ejection fraction was 46±12.96 in normal sodium group, 45±11.90 in hyponatremia on admission group and 44±5.26 in hyponatremia within72-h group. Patients with hyponatremia belonged to killip class 1 and >1 are 54%and 46% , among patients with normonatremia ,54.67% belonged to killip class1 , 45.33% belonged to class >1. These are almost similar to the studies done by Goldberg A et al [9] and Tada Y et al [13].

Among the patients presented with normal sodium levels (Group1) MACE during hospitalization was 46.6%, when compared to 53% in hyponatremic group and 88 in total. Out of 88 patients who developed MACE, 58 were males and 29 were females. In terms of percentage of MACE in each group during hospitalization hyponatremia was highly significant (P=0.0087). These results are consistent with other studies [9]. Patients who developed MACE also correlated well with severity of hyponatremia. A total of 27 patients had sodium levels less than 125-129mmol/l and 16 developed MACES, when compared to 33 MACE among 71 patients with sodium levels between130–134 mmol/l. 4 of 5 patients had sodium levels <125 mmol/l develops MACE. In current study severity of hyponatremia was statistically significant (p=0.010) with MACE, these results are comparable with study done by Kurian S et al [10] and Flear et al [14]. MACE and no MACE groups were analysed in terms of variables. The mean age in MACE group was 59.22 ±11.51 years compared to 55.06 ±12.21 years in no MACE group. Mean serum sodium value was 129.40±3.36 in MACE group and 130.93±2.19 in no MACE group. Mean ejection fraction was 39.08 ± 9.63 in MACE group and 51.42 ± 5.91 in no MACE group and 89.77% in MACE group had killip class >1. Sedentary lifestyle, dyslipidemia, hypertension, diabetes, smoking and history of stroke were also prevalent in MACE group constituting 79.54%,66.67%, 63.63%, 36.78%,36.78% and 21.84% respectively. Statistical analysis turned out be significant for age (p=0.0216), hypertension (p=0.006), diabetes (p=0.019), hyponatremia (p=0.0087), ejection fraction (p< 0.05), were included in the multivariate logistic regression analysis. Hyponatremia remained a significant independent predictor hospitalization MACE with p value of 0.019 in multiple logistic regression. This is concordance to a similar study conducted by Kurian S et al [10] and Tada Y et al [13].

The overall mortality rate in current study was 17.72%. The mortality was more hyponatremic groups (23%) than normonatremics group (10.67%) and the difference was statistically significant with p value 0.034. However, mortality was more in patients who had hyponatremia on admission (group 2a) as compared to that who developed hyponatremia within 72hr of hospitalization (group 2b) and their difference was statistically significant with p-value 0.009. These findings are in accordance with the previous studies [9, 15].

Mean serum sodium level was 130.57 ±2.76 in the survivors and 128.0 ± 2.97 in non survivors. Other factors such as lower ejection fraction, higher Killips, smoking, history of stroke and MACE (arrhythmia, CCF, Cardiogenic shock, AV block) were found to influence mortality in our study. Multivariate analysis and analysis of variance was performed which showed that along with other risk factors, hyponatremia on admission or during 72hr of hospitalization (p<0.0001) is an independent risk factor in predicting in hospital MACE and mortality in studied acute STEMI Cases. These findings are correlated with the other studies [9, 16].

Thus, the development of hyponatremia is a marker that most likely incorporates different prognostic entities, including the severity of left ventricular dysfunction, hemodynamic alterations, and the extent of neuro- hormonal activation. In AMI, there occurs non osmotic release of vasopressin due to the acute left ventricular dysfunction either 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, in this setting, vasopressin levels increase concomitantly with the activation of other neuro-hormones, such as renin and norepinephrine. However, vasopressin level does not correlate with serum osmolality in MI, suggesting that nonosmotic mechanisms are involved unlike in congestive cardiac failure where hypo osmolality is the predominant mechanism. In patients with AMI, hyponatremia may be aggravated further by the concomitant activation of the renin-angiotensin system and increased catecholamine production.

CONCLUSION

From the results of present study, it can be concluded that in patients with Acute ST elevation myocardial infarction who presented with hyponatremia at the time of admission and within 72 hours of admission had high mortality and so hyponatremia is an independent predictor of mortality. Patient at risk can be identified by a simple marker plasma sodium level.

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