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Research Article

The Effect of Hyponatremia on Short Term Prognosis in Patients with acute ST-Elevation Myocardial Infarction

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ABSTRACT
The activation of the baroreceptor in acute STEMI, leads to activation of the sympathetic nervous system. this leads to release of hormones like vasopressin (AVP) and also activation of rennin-angiotensin system. This neurohormonal change is related to the severity of the myocardial damage. hyponatremia reflects these hormonal changes. So; serum sodium 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 elevation myocardial infarction with hyponatremia. This prospective observational study was included 116 patients presenting with acute ST-elevation myocardial infarction admitted to coronary care unit (CCU) , in AL-Sader Medical City , Najaf , Iraq , during the period from (April 2016 and February 2017) .Plasma sodium concentrations were taken on admission and at 24, 48 and 72 hours thereafter. The study subjects divided into three groups, group I,include 33 patients with hyponatraemia on admission, group II include 31 patients with hyponatraemia within 72 hours from admission, and control group include 52 patients with normal plasma sodium level (135-145 mmol/L).Study group is collectively of group I and group II (hyponatraemicpatients on admission and hyponatraemic patients within 72 hours), then compared with group III (control group " normonatremicpatient).In this study of 116 patients who presented with acute ST-elevation myocardial infarction (STEMI), hyponatremia was diagnosed in 33 patients (28.4%) at the time of admission , 31 patients (26.7%) within 72hours of admission (early developed hyponatremia) and 52 patients (44.9%) with normal serum sodium levelthe heart failure rate was statistically significant in the patients with hyponatremia (study groups) than in patient with normonatremia (control group) p -value < 0.001 , and statistically significant in sever hyponatremia p -value < 0.001 . The mortality rate was significantly higher in the patients with hyponatremia (study groups) than in patient with normonatremia (control group) p -value<0.001, and significantly higher in sever hyponatremia p –value <0.001. Hyponatremia in patients with acute ST-elevation myocardial infarction, is strongly associated with sever LV dysfunction and more mortality rate.

Keywords: *STEMI , Hyponatremia, heart failure, MI.*

INTRODUCTION

Hyponatremia

Hyponatremia, defined as a serum sodium concentration of <135 mmol/L, is the most common electrolyte abnormality in hospitalized patients and it is associated with increased mortality, morbidity and longer hospital stays [1]. This disorder is almost always due to increase in circulating arginin-vassopressen (AVP) and/or increased renal sensitivity to AVP, combined with an intake of free water; a notable exception is hyponatremia due to low solute intake. the underlying pathophysiology for the exaggerated AVP response differs in patients with hyponatremia as a function of their ECFV. Hyponatremia classified according to volume status into:(Hypovolemic hyponatremia, Euvolemic hyponatremia, Hypervolemic hyponatremia). Joint European guidelines classify hyponatremia according serum sodium concentration into:(Mild: 130-134 mmol/L, Moderat:125-129 mmol/L, sever:<125 mmol/L)Most common causes of hyponatraemia are (vomiting, diarrhea, burns, glucocorticoid deficiency, hypothyroidism, stress, SIADH, acute and chronic renal failure, nephrotic syndrome, liver cirrhosis, heart failure) [2].

Acute ST-Elevation Myocardial Infarction

Acute ST-elevation myocardial infarction (STEMI) is one of the most common diagnoses in hospitalized patients in industrialized countries. In the United States, approximately 525,000 patients experience a new STEMI, and 190,000 experience a recurrent STEMI each year. More than half of STEMI related deaths occur before the stricken individual reaches the hospital. in-hospital mortality rate after admission for STEMI has declined from 10% to about 6% over the past decade. The 1-year mortality rate after STEMI is about 15%. mortality is approximately fourfold higher in elderly patients (over age 75) as compared with younger patients (2).ST-elevation myocardial infarction is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic

(ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis [3].

Killip Class

The Killip class is a system used in individuals with acute myocardial infarction, doing physical examination and the development of heart failure in order to predict and stratify their risk of mortality. individuals with a high Killip class are more likely to die within the first 30 days after their myocardial infarction than individuals with a low Killip class. Patients were ranked by Killip class in the following way [4].

Killip class I: individuals with no clinical signs of heart failure, (Mortality rate was found to be 6%).

Killip class II: individuals with rales or crackles in the lungs, S3, and elevated jugular venous pressure, (Mortality rate was found to be 17%).

Killip class III: individuals with frank acute pulmonary edema, (Mortality rate was found to be 38%).

Killip class IV: individuals in cardiogenic shock or hypotension (systolic blood pressure lower than 90 mmHg), and evidence of peripheral vasoconstriction (oliguria, cyanosis or sweating),(Mortality rate was found to be 81%).

Mechanism of hyponatremia in acute ST elevation myocardial infarction

Hyponatremia is found more frequently in the early period of ST elevation myocardial infarction (STEMI), influences short term outcomes [5]. in STEMI, like congestive heart failure, arterial under filling (low effective circulating volume) causes stimulation of baroreceptors present in the left ventricle, arch of aorta and carotid sinus, leads to stimulation of cardio regulatory Centre in the brain, leads to stimulation of efferent pathway of the sympathetic nervous system. Activation of this sympathetic nervous system stimulates the non-osmotic release of arginine - vasopressin (AVP), rennin as well as angiotensin II, leading to activation of renin-an giotensin-aldosterone system. Hormones thus released bybaroreceptor stimulation reflects the severity of heart failure [6](AVP plays role in regulation of vascular tone and cardiac haemodynamics and myocardial remodeling) [7].In the early period of STEMI, release of AVP, also retards water excretion, leading to increase blood volume and thus leading to dilutionalhyponatremia. so hyponatraemia actually reflect the baroreceptor-mediated hormonal activation in an exaggerated manner and thus serves as a marker of underlying worsening haemodynamics. The release of AVP was not only triggered by a low effective circulating volume, but also could occur due to the acute development of left ventricular dysfunction, a response to any combination of pain, nausea or stress [8].Recently, some studies have shown that hyponatremia is linked to poor outcomes in patients with ST-elevation myocardial infarction (STEMI) and the risk of mortality increased with the severity of hyponatremia [9]. However, the effect of hyponatremia on the prevalence and prognosis in Iraqi patients with STEMI has been un clarified. Therefore, it is necessary to investigate the relationship of hyponatremia and in-hospital outcomes in Iraqi patients with STEMI. The aim of this study is to evaluate in hospital prognosis of acute ST segment elevation myocardial infarction with hyponatremia.

Material And Methods

Source of Data

This prospective observational study was included in patients presenting with acute ST-elevation myocardial infarction (STEMI), admitted to coronary care unit (CCU),in AL-Sader Medical City, Najaf,Iraq. During the period from (April 2016 and February 2017). Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours thereafter.

Inclusion Criteria

1-All acute myocardial infarction –ST elevation (STEMI) patients presenting to CCU of AL-Sader Medical City Hospital, having Chest pain lasting more than 20 minutes

2- Diagnostic ECG changes with characteristic ECG alterations consisting of:

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

ST elevation ≥ 2mm in ≥ two contagious precordial leads

3- Positive cardiac marker (s.TroponinI, CK-MB)

4- New left bundle branch block (LBBB).

Exclusion Criteria

1- Patients with previous ST elevation MI.

2- Non-Q wave myocardial infarction.

3- congestive Heart failure.

4- liver cirrhosis.

5-nephrotic syndrome, renal failure.

6- Patients with chest infection.

7- Patients on diuretics.

The study subjects divided into three groups

Group I wasincluding 33 patients with hyponatraemia on admission, Group II wasincluding 31 patients with hyponatraemia within 72 hours from admission,and Group III (control group) were include 52 patients withnormal plasma sodium level (135-145 mmol/L).Study groups are collectively of group I and group II(hyponatraemicpatients on admission and hyponatraemic patients within 72 hours),then compared with group III (control group – normonatremic patients).The study groups(group I and group II) were categorized into 3 sub-groups, according the severity of hyponatraemia into : Sever hyponatremia (plasma Na+ <125 mmol/L) , Moderate hyponatremia(plasma Na+ 125-129mmol/L) , Mild hyponatremia (plasma Na+ 130-134 mmol/L), in diabetic patients we added 1.6 mmol/L to the sodium level foreach 100 mg/dL increase in plasma glucose , (plasma sodium concentration falls by 1.6 mmol/L for each 100

mg/dL increase in plasma glucose concentration above the normal level) [10].Details clinical history was taken including history of present illness, drug history and past medical history, family history of coronary artery disease, physical examination were done and recorded. All the patients were treated with thrombolytics and usual treatment protocol of other medical therapy. For each patient on admission, 10ml blood was drawn with aseptic precaution and 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, serum Troponine I, CK-MB, serum lipid profile, blood urea, serum create nine, liver function test, serum electrolytes, were also measured on admission. Laboratory investigations were collected from medical report. Diagnosis of myocardial infarction (STEMI) was done according to the criteria of American College of Cardiology and the Joint European Society of Cardiology. Both groups (study groups and control group) were followed up till the end point of study in hospital, parameters of outcome were death and heart failure. occurrence of heart failure was followed up clinically by Killip class and by Echo cardio graphy. Echocardiography was performed in all patients with STEMI in hospital for assessment of left ventricular ejection fraction.

Statistical Analysis and Result

SPSS Software version 23.0 was used for performing statistical analysis. Continuous data are presented as mean ± standard deviation and qualitative data are presented as number and percentage. Comparisons of study groups characteristics were performed using chi-square test of significance. P value of < 0.05 was considered statistically significant.

Study patient

In this study of 116 patients, 73 was male and 43 was female who presented with acute ST-elevation myocardial infarction (STEMI), hyponatremia was observed in 33 patients (28.4%), at the time of admission, 31 patients (26.7%) within 72hours of admission (early developed hyponatremia) and 52 patients (44.9%) with normal serum sodium level. In group1 (hyponatremic on admission) shows they have older age group (62.24± 8.79) and have lower ejection fraction (43.30±7.27) compared with the other groups, and the majority of patients with STEMI were male (62.93%). the highest risk factor in our study was smoking (64.65%) with p value 0.882, followed by hypertension (50.86%) p value 0.589, diabetes (49.1%) p value 0.361, dyslipidemia (47.41%) p value 0.615 and family history of coronary artery disease (47.41%) p value 0.536, as shown in Table 1.

Table 1. Baseline characteristics of 116 patients

Characteristic		Group I hyponatremia on admission (n=33)	Group II hyponatremia within 72 hours after admission (n=31)	Group III Control group(n=52)	P-value
Age		62.24 ± 8.79	58.65 ± 7.55	57.87± 9.61	0.117
sex	Male	23 (69.70%)	19 (61.29%)	31 (59.62%)	0.505
	Female	10 (30.30)	12 (38.71%)	21 (40.38%)	
Hypertension		18 (54.55%)	16 (51.61%)	25 (48.08)%	0.589
Diabetes		17 (51.52%)	12 (38.71%)	28 (53.85)%	0.361
Smoking		21 (63.64%)	20 (64.52%)	34 (65.38%)	0.882
Dyslipidemia		17 (51.52%)	12 (38.71%)	26 (50.0%)	0.615
Family history of coronary artery disease		19 (57.58%)	13 (41.94%)	23 (44.23%)	0.536
Killip class	I&II	13 (61.9%)	12 (75%)	15 (83.33%)	0.218
	III&IV	8 (38.09%)	4 (25%)	3 (16.67%)	
Ejection fraction		43.30 ± 7.27	47.77 ± 31.0	50.25 ± 7.00	0.001

According to killipclass, there was 6 patient of study groups in class 4 , 2 patients of them (33.33%) had moderate hyponatremia and other 4 patients (66.66%) hade sever hyponatremia, while 1 patient in control group classified in class 4. as shown in Table2.

Table 2. Killip class in study groups and control group according to serum sodium level.

Killip class	Control group (n=52)	Study groups(n=64)		
	normonatremia	Mild hyponatremia (130-134mmol/L)	Moderate hyponatremia (125-129mmol/L)	Severe hyponatremia (< 125mmol/L)
I	7(38.89%)	3(18.75%)	0(0%)	0(0%)
II	8(44.44%)	12(75%)	10(66.67%)	0(0%)
III	2(11.11%)	1(6.25%)	3(20%)	2(33.33%)
IV	1(5.56%)	0(0%)	2(13.33%)	4(66.67%)
Total	18 (100%)	16(100%)	15(100%)	6(100%)
p-value	< 0.001			

X2 (6, N = 55) = 32.46, p< 0.001

Hospital Heart Failure

In hospital heart failure was 34 patients , 20 patients (60.61%) in group I , 14 patients (45.16%) in group II and 11 patients (21.15%) in group III (control group). According to age in study groups (group I and group II), the heart failure more frequent in older age group (4 of 5 patients "80%" with age > 70 years old) p value = 0.0634 as shown in Table 3 .

Table 3. Distribution of heart failure in hyponatremic patients according to age

Age	Study groups (hyponatremia)	Heart failure	P-value
40-51	11	3 (27.27%)	0.0634
51-60	21	9 (42.85%)	
61-70	27	18 (66.66%)	
> 70	5	4 (80%)	
Total	64	34 (53.12%)	

X2 (3, N=64) = 7.28, p = 0.0634

The majority of hyponatremia in study groups was male (65.63%) , 24 of 42 male patients (57.14%) had heart failure as shown in Table 4.

Table 4. Distribution of heart failure in hyponatremic patients according to sex

Sex	Study groups (hyponatremia)	Heart failure	P-value
Male	42	24 (57.14%)	0.373
Female	22	10 (45.45%)	
Total	64	34 (53.12%)	

X2 (1, N = 64) = 0.79, p = 0.373

All 6 patients with severe hyponatremia < 125 mmol/L had heart failure (100%), and 13 of 14 (92.85%) in moderate hyponatremia, while 15 of 44 (34.09%) in mild hyponatremia, p < 0.001 as shown in Table 5.

Table5.Distribution of heart failure in study groups according to level of serum sodium

Serum Na level	No. of cases	Heart failure	P -value
Severe hyponatremia (< 125mmol/L)	**6**	**6 (100%)**	**0.001**
Moderate hyponatremia (125-129mmol/L)	14	13 (92.85%)	
Mild hyponatremia (130-134mmol/L)	44	15 (34.09%)	
Total	64	34 (53.12%)	

X2 (2, N=64) = 20.57, p< 0.001

Hospital Mortality

The duration of hospitalization was (4 – 10 days) in all patient, all mortality was due to cardiogenic shock , and about15 of 116 patients (12.93%) , (10.34%) in study groups (hyponatremic group) and (2.59%) in control group (normonatremic group),According to age in study groups , the total mortality rate was 12 of 64 hyponatremic patients (18.75%) , and more frequent in older age group(4 of 5 patients" 80%" with age >70 years old) p value 0.207 as shown in Table 6.

Table 6. Distribution of mortality in hyponatremic patients according to age

Age	Study groups (hyponatremia)	Mortality	P -value
40-51	11	2 (18.18%)	0.373
51-60	21	3 (14.28%)	
61-70	27	3 (11.11%)	
> 70	5	4 (80%)	
Total	64	12 (18.75%)	

X2 (1, N = 64) = 0.79, p = 0.373

The majority of hyponatremia in study groups was male (65.63%) ,8 of 42 male patients (19.04%) were died while in females were 10 of 22 patients (45.45%) p value 0.933 as shown in Table 7.

Table7. Distribution of mortality in hyponatremic patients according to sex

Sex	Study groups (hyponatremia)	Mortality	P -value
Male	42	8 (19%)	0.933
Female	22	4 (18.18%)	
Total	64	12 (18.75%)	

X2 (1, N = 64) = 0,01, p = 0.933

5 cases of 6 patients (83.33%) with sever hyponatremia < 125 mmol/L was recorded as mortality rate , and 5 of 14 (35.71%) in moderate hyponatremia , while 2 of 44 (4.54%) in mild

hyponatremia p value < 0.001 as shown in Table 8. Figure 1 shows adverse in-hospital outcome of the study subjects.

Table 8. Distribution of mortality in study groups according to level of serum sodium

Serum Na level	No. of cases	Death	P -value
Severehyponatremia(< 125mmol/L)	6	5 (83.33%)	0.001
Moderate hyponatremia(125-129mmol/L)	14	5 (35.71%)	
Mild hyponatremia(130-134mmol/L)	44	2 (4.54%)	
Total	64	12 (18.75%)	

X2 (2, N=64) = 24.90, p< 0.001

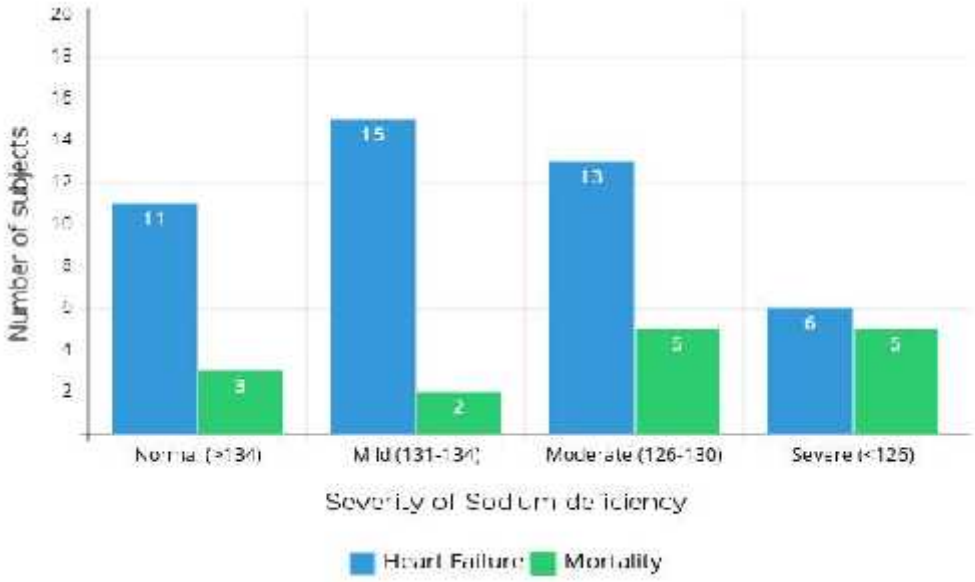

Figure 1. Bar graph.

Discussion

In this study, hyponatremia was present in (55.17%) of patients with acute STEMI admitted in coronary care unit. Hyponatremia remained a strong and independent predictor of in hospital mortality and morbidity, and the risk of mortality and morbidity increased with the severity of hyponatremia. In our study we found there was no significant difference of age and sex in the study groups (group I and group II) and control group (group III) according to heart failure and mortality rate, this agreed with by Qing Tang , Qi Hua et al [11] who reported that age and sex were not significantly associated with in- hospital heart failure and mortality. And among the risk factors in this study subjects, the highest percentage of patient had history of smoking, followed by hypertension, diabetes, dyslipidemia and family history of coronary artery disease. Also, we found hyponatremia was associated with heart failure and the incidence of heart failure in study groups (group I and group II) was (53.12%) and (21.15%) in control group (group III), also we found that patients with hyponatremia on admission had lower ejection fractions (LVEF%) was (43.30 ± 7.27%) than those with hyponatremia after 72 hours from admission (group II) and those with normal serum sodium level (control group). Similarly, Alexander G. et al [12] found reduced left ventricular ejection fraction (42 ± 13%) among patients with hyponatremia on admission than patient who developed hyponatremia after admission. In current study, heart failure developed in highest percentage in patients with serum sodium (s. Na+) level <125 mmol/L (6 of 6 patients 100%).So heart failure significantly associated with the severity of hyponatremia p value < 0.001. Similarly, Suresh Harsoor, Akshaya Kinagiel at [13], they reported, the Heart failure developed in highest percentage in patients with sodium level <130 mmol/L, also (6 of 6 patient 100%), and there is a relation between heart failure and severity of hyponatremia P-value 0.05, left ventricular ejection fraction was 37.82 ± 8.93% among patients with hyponatremia, and there was no significant difference of age and sex in two previous studies.Also, in our study the incidence of mortality in group I and group II (study groups) were (18.75%) and in group III (control group) was (5.77%) . also Alexander, G. et al ,found that acute

STEMI patients, the mortality rate was 19.8% in patients with hyponatraemia on admission and 16.8% in patients with hyponatremia developed after admission, and without hyponatremia had a mortality rate was 6.2% .also Flear et al [14] reported that in hospital mortality , the hyponatremia, hypochloremia and uremia in patients with confirmed myocardial infarction were common , in hyponatremic patients , other study by Goldberg et al [15], [16] showed, hyponatremia on admission or developing during the first 72 hours of hospitalization in STEMI was independently associated with increased short-term and 30-day mortality risk as well a higher incidence of post-discharge readmission for heart failure and death in long-term follow-up.In current study, we found the mortality rate was increased with hyponatremic patients compared with patients having normal sodium level .and mortality rate also increase with increasing severity of hyponatremia (s. Na+) level <125 mmol/L. The several studies support the present study results, like Suresh Harsoor, Akshaya Kinagi et al. they report 15 patients (15%) died, 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 normal Na+ level ≥135. Then Singla et al [17] found that hyponatremia was associated with adverse short-term and 30-day outcomes in patients admitted with acute coronary syndrome and degree of hyponatremia correlated with an increasing number of adverse events. Hence in our study, the data strongly suggest that the presence of hyponatremia, in acute STEMI, should be considered a marker of more ill patients.

Conclusion

Hyponatremia in patients with acute ST-elevation myocardial infarction, is strongly associated with sever LV dysfunction and more mortality rate. We recommended, from our study; hyponatremia is a simple parameter which reflect the presence of heart failure in patients with acute STEMI, and should be send for serum sodium examination for each patient admitted to CCU with acute STEMI to reduce the proportion of heart failure and therefore the proportion of mortality rate.

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