Pak Heart J

FREQUENCY OF HYPONATREMIA AND ITS SHORT TERM CLINICAL OUTCOMES AFTER ACUTE ST ELEVATION MYOCARDIAL INFARCTION

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Date Received: July 02, 2019

Date Revised: Aug 27, 2019

Date Accepted: Sep 09, 2019

Contribution

MJ and UA conceived the idea and designed the study. JS and IUD did data collection and analysis. HUJ, TA and MA did review. All authors contributed equally to the submitted manuscript.

All authors declare no conflict of interest.

This article may be cited as: Jamil M, Ali U, Siraj J, Din IU, Ahmad T, Abbas M, Jan HU. Frequency of hyponatremia and its short term clinical outcomes after acute ST elevation myocardial infarction. Pak Heart J 2019; 52 (04):307-12

ABSTRACT

Objective: To determine the frequency of hyponatremia and its short term clinical outcomes after acute ST-elevation myocardial infarction.

Methodology: This cross sectional study was conducted at Department of Cardiology, Lady Reading Hospital Peshawar from 1st November 2014 to 30th April 2015. Patients of either gender aged between 18 to 60 years admitted with acute ST elevation myocardial infarction were included in the study. Serum sodium was measured in all patients at admission, 24 hrs, 48 hrs and 72 hrs post admission to detect hyponatremia. All hyponatremic patients were followed during their hospital stay for in hospital mortality, acute heart failure and cardiogenic shock. P value of less than 0.05 was taken as significant.

Results: The total numbers of patients were 159. Mean age was 51.8 ± 7.2 (18–60) yrs. Males were 70.4 % (n=112). Mean serum sodium was 138 ±6.8 mmol/L. Of the total 47.2% (75) were hypertensive. Diabetes was found in 28.3% (45) of study population. 37.1% (59) were smoker. Dyslipidemia was found in 32.1% (51). 18.9% (30) patients were having obesity. Hyponatremia (serum sodium ≤135mmol/L) was present in 22% (n=35) patients. Hyponatremia was equally common in male and female patients (21.4% vs 23.4%). Sub group analyses revealed a higher but statistically insignificant hyponatremia in patients with anterior MI and of older age. Of 35 hyponatremic patients all were followed during their hospital stay for in-hospital outcomes. In hospital mortality noted in these patients was 48.6% (p=0.001). Acute heart failure was in 60% of hyponatremic patients (p=0.001). Cardiogenic shock was in 54.3% of patients (p= 0.001).

Conclusions: Hyponatremia in hospitalized patients with acute ST elevation myocardial infarction is relatively common and is associated with higher in-hospital and early post-discharge mortality.

Key Words: Hyponatremia, ST elevation myocardial infarction, In-hospital mortality, Acute heart failure, Cardiogenic shock.

INTRODUCTION

During the 20th century, cardiovascular disease became the most common cause of death worldwide. A century ago, cardiovascular disease (CVDs) accounted for less than 10 percent of all death. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Of these deaths, an estimated 7.3 million were due to coronary heart disease and 6.2 million were due to stroke. Low- and middle-income countries are dis-proportionally affected. Over 80% of CVD deaths take place in low- and middle-income countries and occur almost equally in men and women.[1] The available treatment options for coronary artery disease are pharmacological, percutaneous interventions (PCI) and coronary artery bypass graft.[2,3]

Myocardial infarction (MI) is the irreversible necrosis of heart muscle secondary to prolonged ischemia. It is considered more appropriately, a part of a spectrum referred to as acute coronary syndromes (ACSs), which includes ST-elevation MI (STEMI), non–ST-elevation MI (NSTEMI) and unstable angina. Most of those with ST-segment elevation will develop Q waves. Those without ST elevations will ultimately be diagnosed with unstable angina or NSTEMI based on the presence of cardiac enzymes.[4]

Acute myocardial infarction (MI) is a common medical emergency and is the leading cause of death worldwide. One hundred thousands individuals suffered from acute myocardial infarction (AMI) all over world in the year 2000.[5] The estimated annual incidence of MI in the United States (including both STEMI and NSTEMI) is 600 000 new and 320 000 recurrent attacks. In 2004, AMI resulted in 695 000 hospital stays and $31 billion in hospital charges.[6] The risk of further cardiovascular complications, including recurrent MI, sudden cardiac death, heart failure, stroke and angina pectoris, for those who survive AMI is substantial.[7]

The South Asian countries of India, Pakistan, Bangladesh, Sri Lanka and Nepal account for about a quarter of the world's population and contribute the highest proportion of the burden of cardiovascular diseases including MI compared with any other region globally.[8-10] In Pakistan it is estimated that one in five middle-aged adults may have underlying coronary artery disease (CAD).[11] Deaths related to cardiovascular disease also occur 5 to 10 years earlier in South Asian countries than they do in Western countries. This has raised the possibility that South Asians exhibit a special susceptibility for acute myocardial infarction (AMI) that is not explained by traditional risk factors.[3,12]

Hyponatremia is frequently (9.2-15.4%) found in the early phase of ST-elevation myocardial Infarction(STEMI) and is associated with heart failure(HF).[13] Hyponatremia often complicates acute STEMI with an incidence of 11% and is associated with a poor prognosis.[17] Also acute heart failure was more common (11.7%) in patients who had hyponatremia during the acute STEMI.[14] Thus in the acute phase of STEMI it has been identified as an independent predictor of short term mortality, long-term mortality, acute and chronic heart failure and re hospitalization.[15] Hyponatremia was independently associated with in-hospital death and heart failure in patients admitted with STEMI.[16] Patients with STEMI (in whom percutaneous coronary intervention(PCI) was performed in 88.5%), hyponatremia in the acute phase showed increased risk for worse in-hospital clinical Outcomes.[17] Therefore on admission or early development of hyponatremia was an independent predictor of short term mortality in patients with acute STEMI.[18]

Electrolyte disorders especially hyponatremia is frequently overlooked in STEMI patients. There is no data available on the latest frequency of hyponatremia in STEMI patients locally. This study will provide us data regarding the magnitude of problem in local population and also the current study will provide us with its clinical outcomes in terms of mortality and acute heart failure among those patients with hyponatremia.

The objective of this study was to determine the frequency of hyponatremia and its short term clinical outcomes after acute ST elevation myocardial infarction.

METHODOLOGY

This cross sectional descriptive study was performed at Cardiology Department, Postgraduate Medical Institute, Lady Reading Hospital, Peshawar from 1st November 2014 to 30th April 2015. Non probability consecutive sampling was done. Male and female patients from 18 to 60 years of age who present with acute ST Elevation myocardial infarction were included in the study. While Patients with renal failure , liver failure, diagnosed congestive cardiac failure were excluded.

Sample size was calculated using 11.7% proportion of heart failure among hyponatremic patients with acute STEMI with 95% confidence level and 5% margin of error under WHO software for sample size determination.

The study was conducted after approval from hospital ethical and research committee. The diagnosis of STEMI was made with patient presenting with characteristic chest pain described as band like central chest pain radiating to left shoulder or jaw lasting more than 30 minutes not relieving with rest and/or sublingual nitrates with ST-segment elevation of more than 1mm in at least two consecutive limb leads or 2mm or more in two consecutive chest leads. Hyponatremia was defined as a serum sodium concentration less than 135 mmol/L.

Short term clinical outcomes measured within 72 hours of admission included in-hospital mortality occurring within 3 days, acute heart failure and cardiogenic shock defined as systolic blood pressure (SBP) $<$ 90 mm Hg for greater than one hour, not responsive to fluid resuscitation

The purpose and benefits of the study were explained to all patients and a written informed consent was obtained. All patients were subjected to detailed history, followed by complete routine examination and baseline investigations including serum sodium concentration (Auto Analyzer) and ECG (Cardio-fax). Venous blood samples for sodium levels were obtained on admission and at 24,48, and 72 hours thereafter.

All the above mentioned information including demographic features was recorded in a pre-designed proforma. Statistical analysis was done with the Statistical Package for the Social Sciences software SPSS 20.0 for Windows. Mean $\pm$ SD and CI was calculated for numerical variables like age and serum sodium concentration. Frequencies and percentages were calculated for categorical variables like gender, hyponatremia and short term

clinical outcomes. Hyponatremia and short term clinical outcomes were stratified among age and gender to see the effect modifiers. Post stratification was done through chi square test. Keeping $p < 0.05$ was significant. All results were presented in the form of tables and graphs

RESULTS

A total of 159 patients were included in the study. Mean age was 51.8 ±7.2 (18–60) years. Males were 112 (70.4%) and females were 47 (29.6%) . Of the total 47.2% (75) were hypertensive. Diabetes was found in 28.3% (45) of study population and 37.1% (59) were smokers. Dyslipidemia was found in 32.1% (51). 18.9% (30) patients were having obesity. Coronary interventions were done in 21.4% (34) of patients. These are shown in table 1.

All patients were stratified according to gender, age and STEMI type to see for effect modifiers (Table 2 and Table 3 respectively). Also the biochemical and echo profiles of the patients were recorded (Table 4). Hyponatremia (serum sodium ≤135 mmol/L) was present in 22% (n=35) patients. Overall, the enrolled patients displayed a wide distribution of admission sodium values (112-156 mmol/L) (Figure 1).

Of 35 hyponatremic patients all were followed during their hospital stay for in-hospital outcomes (Table 5). In hospital mortality noted in these patients was 48.6%(17) (p=0.001), acute heart failure was in 60% (21) hyponatremic patients (p=0.001) and cardiogenic shock was in 54.3% (19) (p= 0.001) (Table 6).The remaining 124 patients were discharged home on standard STEMI treatment..

Table 1: Base line Characteristics of Study Population (n=159)

Variables	Frequency (n)	Percentage (%)
Age	51.8±7.2	
Male	112	70.4
Hypertension	75	47.2
Diabetes	45	28.3
Dyslipidemia	51	32.1
Obesity	30	18.9
Symptoms time	7.55±5.2	
Current Smoker	59	37.1
Coronary interventions	34	21.4
Complete heart block	11	6.9
Arrythmias	36	22.6

Table 2: Age Distribution of Study Population (n=519)

Age Category(Years)	Frequency (n)	Percentage (%)
20 - 30	2	1.3
31 - 40	13	8.2
41 - 50	44	27.7
51 - 60	100	62.9

Table 3: STEMI Distribution of Study Population (n=519)

Type of MI	Frequency (n)	Percentage (%)
Anterior MI	60	37.7
Inferior MI	35	22.0
Lateral MI	26	16.4
Inferoposterior MI	11	6.9
Inferior+RV MI	11	6.9
Inferolateral MI	16	10.1

Table 4: Biochemical and Echo Characteristics of Study Population (n=519)

Biochemical and Echo profile	Mean value
CKMB	27.90±14.30
LDH	896±498.20
CHOLESTEROL	202.87±62.43
RBS	187.76±69.05
LVEDD	5.25±0.63
EF	52.43±11.7

Table 5: Mean Serum Sodium Levels of Study Population (n=519)

Serum Sodium	Mean(mmol/l)
At Admission	138.44±6.82
After 24 hrs	138.70±7.61
After 48 hrs	138.98±7.26
After 72 hrs	138.89±7.95

Figure 1: Distribution of Admission Serum Sodium (mmol/L) in Patients Hospitalized with STEMI

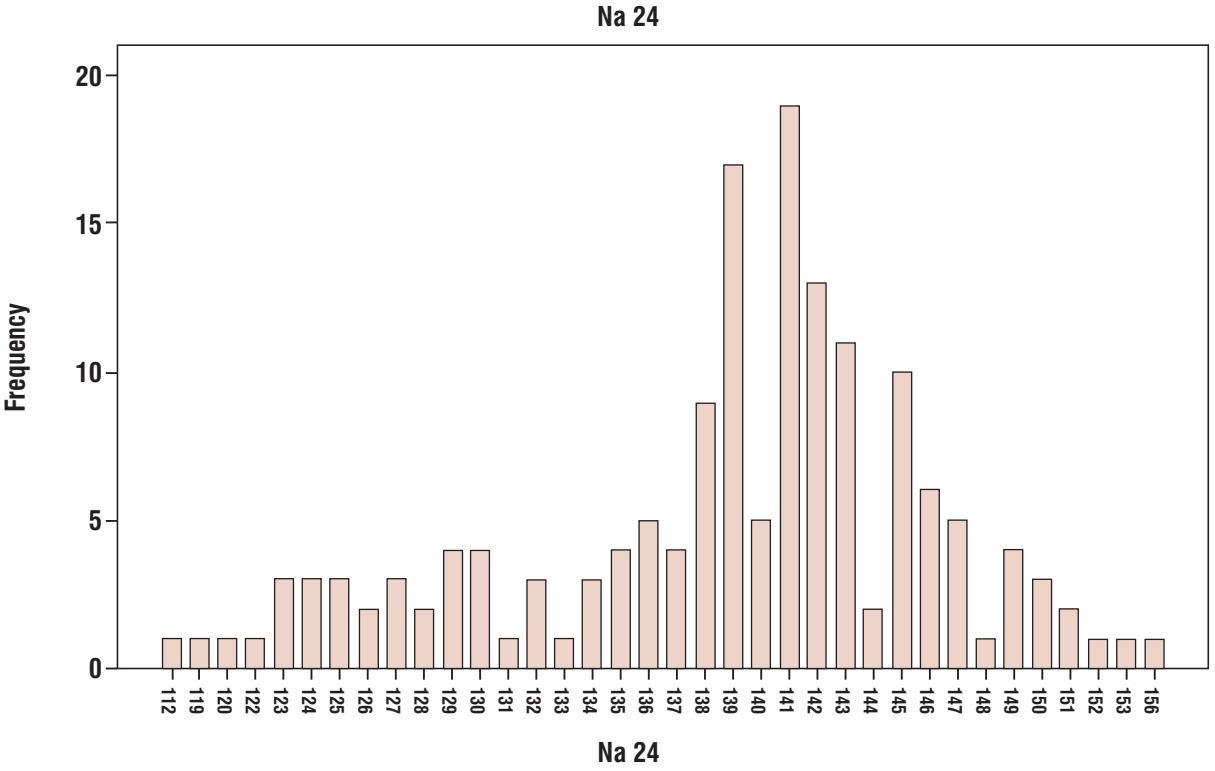

Table 6: Mean Serum Sodium Levels of Study Population (n=519)

Variables	Normonatremia	Hyponatremia	P value
Mortality	1(0.8)	17(48.6)	0.001
Acute heart failure	15(12.1)	21(60)	0.001
Cardiogenic shock	10(8.1)	19(54.3)	0.001

DISCUSSION

Acute myocardial infarction (MI) is a common medical emergency and is the leading cause of death worldwide. Hyponatremia is a common electrolyte abnormality among hospitalized patients, and is associated with poor outcomes in patients with acute and chronic cardiopulmonary diseases, such as left ventricular heart failure and acute myocardial infarction.

Hyponatremia has significant prognostic implications in patients with heart failure. However, little data is available regarding its significance in patients presenting with myocardial infarction.

The present study suggested that hyponatremia is not infrequently found in patients with an early phase of STEMI. The same has been shown by TADA Y et al who also studied acute STEMI patients who had successful revascularization. Early developed hyponatremia in patients with STEMI could be an independent predictor of deterioration of heart failure during hospitalization.[13]

Before the primary PCI era, several studies demonstrated that hyponatremia implicated poor prognostic outcomes in acute ST elevation myocardial infarction. Singla et al showed that a sodium concentration <135 mmol/L was associated with an increased 30-days mortality or recurrence of myocardial infarction in non-STEMI.[19] Klopotowski et al showed that hyponatremia at admission increased the risk of in-hospital death or heart failure in STEMI.[20] Goldberg et al reported that long-term mortality and re-admission for heart failure increased in hyponatremic patients. Hyponatremia developed in 12% of patients and the 3-month mortality was 24% in their study.[17]

In comparison with previous studies, the present study showed not only similar frequency of early-developed hyponatremia, but also its comparable importance as a predictor of heart failure, regardless of the difference of treatments.

High age was associated with hyponatremia in the present study. Aging is an established risk factor for hyponatremia in various diseases, including STEMI.[14,20] Acute MI also results in marked activation of the renin-angiotensin system and increased catecholamine production.[21] These factors promote renal vasoconstriction, leading to diminished GFR and subsequent delivery of tubular fluid to the diluting segment of the nephron, further contributing to the reduction of renal water excretion. Thus, neurohormonal activation in the acute phase of MI bears a striking resemblance to that seen in chronic HF. Consequently, patients with acute MI are predisposed to hyponatremia, especially if marked neurohormonal activation has occurred.

The present study demonstrates a strong association between hyponatremia in the early phase of MI and short-term mortality in survivors of acute MI. Hyponatremia remained a strong and independent predictor of mortality after adjustment for established clinical predictors of adverse outcome, including LVEF.

Whether hyponatremia (sodium <135 mEq/L) in the acute phase of ST-segment elevation myocardial infarction is just a marker of "more ill" patients or decreased sodium concentration is able to exert a direct adverse effect on the cardiovascular system is still unknown. Higher mortality rates were observed in patients with hyponatremia during intensive cardiac care unit stay and at follow-up. These data therefore strongly suggest that the presence of hyponatremia in the acute phase of ST-segment elevation myocardial infarction should be considered a marker of more ill patients.Patients who developed hyponatremia in the early phase of STEMI were at higher risk of worse in-hospital clinical outcome.

LIMITATIONS

There were certain study limitations. This was a single center study with a low number of patients, thus posing the possible risk of patient selection bias. There were differences in co-morbid conditions, such as gender and age, between the patients with and without hyponatremia. These differences might have influenced the results. These data were necessary to analyze long-term outcomes more exactly.

In addition, we collected no information on sodium levels after hospital discharge. Thus, the prognostic implications of transient vs persistent hyponatremia could not be analyzed.

Whether serum sodium concentration would be predictive of outcomes in patients hospitalized for STEMI deserves further investigation. Also Most of the patients were from low socioeconomic class therefore the study finding cannot be generalized to regional population.

CONCLUSION

Hyponatremia on admission or early development of hyponatremia in patients with acute ST-elevation myocardial infarction is an independent predictor of 30-days mortality, and prognosis worsens with the severity of hyponatremia. Further studies are required to determine if plasma sodium levels may serve as a simple marker to identify patients at high risk.

Patients who developed hyponatremia in the early phase of STEMI were at higher risk of worse in-hospital clinical outcome.

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