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THE OCCURRENCE OF HYPONATREMIA AND ITS EFFECT ON IN-HOSPITAL OUTCOME IN PATIENT OF ACUTE ST ELEVATED MYOCARDIAL INFARCTION

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ABSTRACT:

INTRODUCTION: *Hyponatremia is regarded as the most commonly occurring disorder of electrolyte observed in patients in diverse hospital settings. Hyponatremia if becomes severe, may become life-threatening leading to drastic neurological complications. Being a marker for identification of underlying medical conditions, it is often associated with inadequate prognostication, even when level of sodium in serum is reduced mildly. Development of hyponatremia begins during ST-elevation myocardial infarction's acute phase due to neurohormonal activation. The aim of this study is to ascertain hyponatremia's prognostic value amidst acute phase of myocardial infarction.*

AIMS & OBJECTIVE: *To ascertain hyponatremia's frequency and the impact on the outcome of in-hospital patients suffering with acute ST elevated myocardial infarction.*

MATERIAL & METHODS: *This was a descriptive study which was carried out at Aga Khan University Hospital, Karachi (AKUH) over a period of six months. After obtaining consent of the patients, their data was collected prospectively. Inclusion of the patients was dependent upon diagnostic criteria and 225 individuals were selected. For quantitative data we used mean±standard deviation while the categorial variables were expressed as percentages and frequency. Scarification was used to control effect modifiers to observe their effect on output variable. A chi-square test was carried out post stratification and a p-value of ≤0.05 was determined as significant.*

RESULTS: *Overall, 225 patients admitted in department of Cardiology, Aga Khan University Hospital, Karachi were made part of this study. The mean age was 56.80±7.56 years in the present study. There were 135 (60%) male and 90 (40%) female patients. Out of 225 patients, 43 (19.1%) had hyponatremia. In-hospital mortality was 22 (100%) who had hyponatremia.*

CONCLUSION: *Hyponatremia in patients with acute STEMI is observed as a major predictor related to cardiovascular mortality. Level of sodium in the plasma might serve to be a relatively simple marker for the identification of patients who are at risk.*

KEY WORDS: *Hyponatremia, acute ST elevated myocardial infarction and in-hospital.*

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INTRODUCTION

Acute myocardial infarction (AMI) is among the most frequently diagnosed conditions for the people living in developed countries.[1]It is beginning to be a leading cause of death on a global scale.13 million deaths per annum globally are credited to sudden cardiac arrest.[2] Pakistan and India contribute >75% to worldwide cardiovascular mortalities.[3] The imbalance of electrolytes after an episode of AMI are common. Modifiability of the levels of electrolytes in patients of MI serves a significant role in changing its prognosis. Changes in several electrolytes have been observed following AMI.[1] Concentration of sodium in serum <135mmol/l is termed as hyponatremia and is fairly commonly in the in-hospital patients of AMI.[4]

According to some recent studies, patients with non-ST elevation acute coronary syndrome and ST-elevation myocardial infarction (STEMI) patients both bear poor outcomes related to hyponatremia and that severity of hyponatremia is directly proportional to the increase in the risk of mortality.[5,6] As per some studies, presence of hyponatremia in AMI and percutaneous coronary intervention (PCI) patients is independently associated to an elevated risk for the development of cardiogenic shock,[7] mortality during hospital stay,[8] and a general decrease in 1 year long-term survivalbility.[7] Hyponatremic patients are reportedly at 60 times greater risk of mortality as in comparison to normonatremic controls.[5] Hyponatremia was noticed in 3.6% of the patients at time of their admission, 20.7% at 72 hours of admission and 9.3% at the time of discharge in the acute STEMI, and was linked to congestive heart failure as outcome in both short and long term inpopulation of Japan.4A study from January 2002 to May 2008 consisting of 1620 patients with AMI, conducted in Xuan wu Hospital, Beijing by Qi Hua and Qing tang revealed the presence of hyponatremia in 13.1% of the patients with general mortality of in-hospital patients suffering with hyponatremia to be at 13.7% as compared to 8.1%:7.3% in normonatremic patients. Rate of adverse outcomes was higher significantly in in-hospital patients from China suffering with hyponatremia in comparison with the people who had normal level of sodium in their serum.[9]

MI and heart failure both demonstrates a similar neurohormonal activation,[10] But there is insufficient available data to link plasma sodium and risk of mortality in long-term in patients of myocardial infarction.[10] Prognostic importance of hyponatremia with regard to myocardial infarction with left ventricular dysfunction (LVSD) is of major significance as the patients suffering from this condition vary from the patients of chronic heart failure holding in view the risk of mortality, furthermore prognostic importance might indicate that latest treatments that might be able to rectify hyponatremia and this can prove to be helpful as it is presumed in the case of heart failure. Hyponatremia is the most common electrolyte abnormality encountered in clinical practice.[11]

It is to be kept in mind that if there is consistency in the prognostic importance, it might be an indication that hyponatremia is an indicator of heart failure and myocardial damage and not just serves as a marker of acute disturbances related to sodium and water. Severe hyponatremia is common in hospitalized patients.[12] Acute STEMI and other cardiovascular diseases are quite prevalent in Pakistan and are exerting a continuously increasing burden with each passing day, contributing to the mortality and morbidity. While hyponatremia being a curable condition, it is the major cause of mortality and morbidity in individuals with cardiovascular conditions. How hyponatremia influences prognosis and prevalence in the patients suffering with acute ST elevation myocardial infarctions is not yet clear. Thus, there is a dire need to investigate hyponatremia's relationship to the in-hospital patient's outcomes who are dealing with acute STEMI.

MATERIAL AND METHODS:

This was a descriptive case series which was conducted at Aga Khan University Hospital, Karachi (AKUH) over a period of six months. The requirement of the sample size to obtain an estimated frequency relating to hyponatremia in patients with STEMI present in Aga khan university hospital is constructed around the prior estimates of 13% as reported by Qi Hua and Qing Tang. Hence, for proportion of hyponatremia's estimate

to be between 10%-15%, employing 95% confidence level alongside 5% of error margin, sample size was calculated to be at 225 patients diagnosed with STEMI. Sample size was adjusted to inflation by 15% to consider for non-response. The size of the sample also serves adequately in testing out the increased 15% rate of mortality in hyponatremic STEMI patients as compared to 7% rate of mortality in patients with sodium levels in the normal range, with the confidence level of 95% and 80% statistical power. Non-Probability consecutive sampling technique was used. Patient having a definite diagnosis of ST elevation myocardial infarction, age 20-75 years regardless gender were included. Patients with chronic kidney disease, congestive heart failure, chronic liver disease, sepsis, metastatic cancer, syndrome of inappropriate diuretic hormone, hypothyroidism were excluded from the study.

PROCEDURE FOR DATA COLLECTION:

This study was carried out after permission from the institutional review board. Patients were explained about the study and informed consent obtained. All patients with acute STEMI meeting the inclusion criteria as assessed by the investigator were enrolled in study through outpatient or emergency departments. All subjects were admitted in Cardiology Unit of the hospital for further assessment. The history of the patients was taken in detail after a thorough examination at admission. Blood sample (5 ml) was drawn for measuringthe serum level of sodium at the instance of admission and after that the sample was transferred to AKUH standardized laboratory properly labeled along with the investigation that was requested. In-hospital outcomes with respect to the survival of patients under 72 hours of them being admitted was evaluated and recorded by investigator using the study proforma.

DATA ANALYSIS PROCEDURE:

SPSS 16.0 was used for the analysis of the data. Data related to the demographics such as continuous variables like age was represented as simple descriptive statistics as mean + SD. Percentages along with frequencies were calculated with respect to the categorical variables such as diabetes mellitus, gender, being coronary artery disease positive due to family history, smoking, hypertension and hyponatremia. To control the effect modifiers, age, positive family history for CAD, smoking, hypertension, presence of diabetes, hyponatremia and gender were all stratified so their effect becomes apparent on the outcome variable. In order to test for the relationship between hyponatremia and In-hospital outcome in terms of survival within 72 hours, the chi-square wasapplied, with a level of significance set at ≤ 0.05.

RESULTS:

In total, 225 patients that were admitted in Department of Cardiology, AKUH, Karachi were made part of this study.

From those 225 patients under study, the minimum age of the patients was found to be 29 while upper age limit of the patients was found to be 71 years. In our study the mean age was found to be56.80 years with standard deviation being ± 7.56. As shown in Table 1.

From the 225 patients under study, 43 (19.1%) had hyponatremia and 182 (80.9%) did not have hyponatremia.

From the 225 patients under study, 135 (60%) were male and 90 (40%) were female.

Frequency distribution pertaining to age exhibited that from 225 patients under study, 07 (3.1%) were found to be in age group 20-30 years, 37 (16.4%) in age group 31-40 years, 69 (30.7%) in age group 41-50 years, 64 (28.4%) in age group 51-60 years, and 48 (21.3%) patients were found to be in age group 61-75 years.

Frequency distribution of type 2 diabetes mellitus showed that out of 225 patients, 101 (44.9%) and 124 (55.1%) had and did not have diabetes mellitus respectively.

Frequency distribution done for hypertension revealed that from 225 patients included in the study, 119 (52.9%) and 106 (47.1%) had and did not have hypertension respectively.

Frequency distribution done for smoking status exhibited that from 225 patients included in the study, 68 (30.2%) and 157 (69.8%) smoked and did not smoke respectively.

Frequency distribution done for family history of coronary artery disease demonstrated that from225 patients included in the study, 41 (18.2%) were with previous CAD family history and 184 (81.8%)were with no family history of coronary artery disease.

Frequency distribution done for in-hospital mortality exhibited that that from225 patients included in the study, 203 (90.2%) and 22 (9.8%) survived and expired respectively.

Stratification done for age regarding hyponatremia exhibited that 01 (2.3%), 14 (32.6%), 05 (11.6%), 12 (27.9%) and 11 (25.6%) that belonged to age group of 20-30 years, 31-40 years, 41-50 years, 51-60 years and 61-75had hyponatremia, respectively. Whereas 06 (3.3%), 23 (12.6%), 64 (35.2%), 52 (28.6%) and 37 (20.3%) were in age group 20-30 years, 31-40

years, 41-50 years, 51-60 years and 61-75 years demonstrated the presence of hyponatremia respectively. P-value was set to 0.01.

Stratification done for gender with regard to hyponatremia demonstrated that 27 (62.8%) and 108 (59.3%) had and did not have hyponatremia in the male gender respectively. Whereas 16 (37.2%) and 74 (40.7%) had and did not have hyponatremia in the female gender respectively. P-value was 0.40.

Stratification done for type 2 diabetes mellitus with regards to hyponatremia demonstrated that 23 (53.5%) and 78 (42.9%) had and did not have hyponatremia in patients who had type 2 diabetes mellitus respectively. Whereas 20 (46.5%) and 104 (57.1%) had and did not have hyponatremia in patients who did not have type 2 diabetes respectively. P-value was observed at 0.13.

Stratification done for hypertension with regard to hyponatremia demonstrated that 27 (62.8%) and 92 (50.5%) had and did not have hyponatremia in patients who had hypertension respectively. Whereas 16 (37.2%) and 90 (49.5%) had and did not have hyponatremia in patients who did not have hypertension respectively. P-value was observed at 0.10.

Stratification done for smoking status with regards to hyponatremia demonstrated that 12 (27.9%) and 56 (30.8%) had and did not have hyponatremia in patients who smoked respectively. Whereas 31 (72.1%) and 126 (69.2%) had and did not have hyponatremia in patients who did not smoke respectively. P-value was observed at 0.43.

Stratification done for family history of CAD with regard to hyponatremia demonstrated that 06 (14%) and 35 (19.2%) had and did not have hyponatremia in patients who had family history

Table-1: Descriptive Statistics (n=225)

Variable	Mean	Standard Deviation	Min-Max
AGE (YEARS)	56.80	±7.56	29-71

Table-2: Hyponatremia with respect to age (n=225)

Age	Hyponatremia		Total
	Yes	No	
20-30	01 (2.3%)	06 (3.3%)	07 (3.1%)
31-40	14 (32.6%)	23 (12.6%)	37 (16.4%)
41-50	05 (11.6%)	64 (35.2%)	69 (30.7%)
51-60	12 (27.9%)	52 (28.6%)	64 (28.4%)
61-75	11 (25.6%)	37 (20.3%)	48 (21.3%)
TOTAL	43 (100%)	182 (100%)	225 (100%)
P-value	**0.01**		

Table-3: Hyponatremia with respect to gender (n=225)

Gender	Hyponatremia		Total
	Yes	No	
Male	27 (62.8%)	108 (59.3%)	135 (60%)
Female	16 (37.2%)	74 (40.7%)	90 (40%)
Total	43 (100%)	182 (100%)	225 (100%)
P-value	**0.40**		

Table-4: Hyponatremia with respect to type 2 diabetes mellitus (n=225)			
Type 2 Diabetes Mellitus	Hyponatremia		Total
	Yes	No	
Yes	23 (53.5%)	78 (42.9%)	101 (44.9%)
No	20 (46.5%)	104 (57.1%)	124 (55.1%)
Total	43 (100%)	182 (100%)	225 (100%)
P-value	0.13		

Table-5: Hyponatremia with respect to hypertension (n=225)			
Hypertension	Hyponatremia		Total
	Yes	No	
Yes	27 (62.8%)	92 (50.5%)	119 (52.9%)
No	16 (37.2%)	90 (49.5%)	106 (47.1%)
Total	43 (100%)	182 (100%)	225 (100%)
P-value	0.10		

Table-6: Hyponatremia with respect to smoking status (n=225)			
Smoking Status	Hyponatremia		Total
	Yes	No	
Yes	12 (27.9%)	56 (30.8%)	68 (30.2%)
No	31 (72.1%)	126 (69.2%)	157 (69.8%)
Total	43 (100%)	182 (100%)	225 (100%)
P-value	0.43		

Table-7: Hyponatremia with respect to family history of coronory artery disease (n=225)			
Family history of cad	Hyponatremia		Total
	Yes	No	
Yes	06 (14%)	35 (19.2%)	41 (18.2%)
No	37 (86%)	147 (80.8%)	184 (81.8%)
Total	43 (100%)	182 (100%)	225 (100%)
P-value	0.28		

of CAD respectively. Whereas 37 (86%) and 147 (80.8%) had and did not have hyponatremia in patients who did not have family history of CAD respectively. P-value was observed 0.28. As shown in Table 7.

Stratification done for hyponatremia with regards to In-hospital mortality showed that 22 (100%) and 21 (10.3%) had and did not

Table-8: In-hospital mortality with respect to hyponatremia (n=225)			
Hyponatremia	In-hospital mortality		Total
	Yes	No	
Yes	22 (100%)	21 (10.3%)	43 (19.1%)
No	00 (00%)	182 (89.7%)	182 (80.9%)
Total	22 (100%)	203 (100%)	225 (100%)
P-value	0.00		

have In-hospital mortality in patients who had hyponatremia respectively. Whereas 00 (00%) showed and 182 (89.7%) did not show in-hospital mortality in patients who did not have hyponatremia respectively. P-value was observed at 0.00. As shown in Table 8.

DISCUSSION

Hyponatremia is described as the relative excessive concentration of total water content of the body to sodium levels. It is the most frequently occurring abnormality of electrolytes in hospitalized patients and is observed during a number of health conditions, such as, liver disease, inappropriate antidiuretic hormone syndrome, congestive heart failure (CHF) and as an effect of certain medicines. Hyponatremia is correlated with mortality in the cases of heart failure, severe dysfunction of multiple organs, STEMI, right heart failure, elevated hypertension of the pulmonary artery and pneumonia. This trend is also observed in older patients.

A research study conducted regarding hyponatremia was based on 218 patients (144 males with a mean age of 64 ± 13 years) enrolled consecutively in the study admitted in the hospital with acute STEMI with no prior history of heart failure. Among the total 218 patients, 193 (88.5 %) underwent PCI and the mean period of follow-up was 39 ± 21 months. Value of S-Na < 135 mmol/L was defined as hyponatremia. Overall, 72 (33 %) developed hyponatremia: 51 (23.4 %) patients at the time of admission and 21 (9.6 %) of them latterly during the hospitalized period. The patients with hyponatremia were mostly presented with reduced left ventricular systolic function and Killip class III or IV. As compared to normanotremic patients, patients with hyponatremia possessed greater risk of cardiogenic shockdevelopment. Patients with hyponatremia developed latterly during hospitalized period were observed with significantly greater incidence rate of acute renal failure (5 patients/25.5% vs. 12 patients/6.1%, p < 0.05) as compared to other patients. A significant difference was observed between normanotremia and hyponatremia regarding the long-term patient survival (p = 0.01, log-rank test). The multiple variance analysis revealed the independent association of decreased levels of S-Na at the time of admission with overall mortality (p = 0.05).[7]

The preliminary study was conducted at the Department of Cardiology, Aga Khan University Hospital, Karachi which included 225 patients [mean age: 56.80±7.56 years, 135 (60 %) males and 90 (40 %) females]. Among the total 225 patients, hyponatremia was present in 43 (19.1 %) patients and 182 (80.9 %) did not present hyponatremia.

In a study conducted by Tada et al., the short-term prognosis (CHF and in-hospital mortality) long-term prognosis (re-admission due to CHF and cardiac death) and the association of serum level of sodium with the plasma AVP were investigated. In the patients with hyponatremia, significantly higher incidence rates of in-hospital hear failure were observed (p = 00018), higher rates prolonged cardiac death is also demonstrated (17.2% vs. 6.3%, P=0.19) and more frequent re-admission because of CHF is observed as well (20.7% vs. 4.5%, P=0.0024). The patients of hyponatremia group presented greater level of plasma AVP (4.5 vs. 2.7 pg/ml, P=0.003), which was inversely correlated with serum level of sodium (r=-0.28, P=0.02).[4]

Goldberg et al. demonstrated the presence of hyponatremia (mean serum sodium level < 136 mEq/L) at admission in 108 (11.0 %) patients. In a multivariable Cox proportional hazards model adjusted for left ventricular ejection fraction and other clinical potential predictors of mortality, the independent predictor of death after the discharge showed up to be hyponatremia at the time of admission (hazard ratio [HR], 2.0; 95% CI, 1.3-

3.2; P = .002). Re-admission for heart failure was also reported to be correlated independently with hyponatremia (HR, 1.6; 95% Confidence interval, 1.1-2.6; P = .04). The HR adjusted for heart failure or death was 1.12 for every 1-mEq/L decrease when serum sodium concentration was taken as a continuous variable (95% CI, 1.07-1.18; P<.001).[5]

In a study conducted by Singla et al. 1,478 patients were included, hyponatremia (sodium <135 mEq/L) was observed in 341 (23.1%) patients on presentation. Individuals who were hyponatremic on admission were at significantly increased risk of death or recurrent MI during the following 30 days (odds ratio 1.98, 95% confidence interval 1.35 to 2.89, p <0.001). The persistence of this trend was observed after the adjustment of factors that included age, diuretics use before admission, left ventricular ejection fraction, hypotension on presentation, chronic renal insufficiency, anemia, elevated levels of troponin and pulmonary edema (odds ratio 1.7, 95% CI 1.1 to 2.5, p = 0.01).[6]

Another study conducted by Havránek et al. comprised of 218 acute STEMI patients enrolled consecutively (mean age: 64 ± 13 years, 144 males) with no previous heart failure history. From the total number of patients, 193 (88.5%) underwent primary PCI. The mean period for follow-up was 39 ± 21 months. S-Na < 135 mmol/l was documented as hyponatremia. Overall, 72 (33 %) developed hyponatremia: 51 (23.4 %) patients at the time of admission and 21 (9.6 %) of them latterly during the hospitalized period. The patients with hyponatremia were mostly presented with reduced left ventricular systolic function and Killip class III or IV. As compared to normanotremic patients, patients with hyponatremia possessed greater risk of development of cardiogenic shock. Patients with hyponatremia developed latterly during hospitalized period were observed with significantly greater incidence of acute renal failure (5 patients/25.5% vs. 12 patients/6.1%, p < 0.05) as compared to other patients. A significant difference was demonstrated between normanotremia and hyponatremia regarding the survival of the patients in the long-term (p = 0.01, log-rank test). The multiple variance analysis revealed the independent association of decreased levels of S-Na at admission with overall mortality (p = 0.05).[7]

CONCLUSION:

Hyponatremia was most commonly observed

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