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Study of hyponatremia as prognostic factor in acute ST elevation myocardial infarction (STEMI): a study in national institute of cardiovascular diseases and hospital, Dhaka, Bangladesh

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Abstract
Hyponatremia has been shown to be a predictor of cardiovascular mortality among patients with heart failure and the same mechanism of neurohormonal activation is also acting in cases of STEMI. Hence we aimed to investigate importance of hyponatremia in acute STEMI regarding prognosis and short term survival. 100 consecutive patients presenting with acute STEMI admitted to National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh from October 2017 to September 2018 were studied. Qualifying patients underwent detailed history and clinical examination. Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours thereafter along with other relevant investigations. Males made up 81% of patients who presented with hyponatremia on admission and 77% of patients who developed hyponatremia within 72 hours. Patients who presented with or developed hyponatremia more often were smokers(81%) and had diabetes(44%), anterior infarction(72%) and higher killip class, lower ejection fraction(40.36 ±6.14) compared to patients with normal sodium levels. The odd's ratio for 30-day mortality was found to be high in the hyponatremic groups compared to normal group. We also found a significant linear relationship between severity of hyponatremia and mortality. Multivariate analysis was performed which identified hyponatremia on admission or early development of hyponatremia as a significant independent predictor of 30 day mortality.

Keywords: acute myocardial infarction, STEMI, hyponatremia, prognosis

1. Introduction
Coronary heart disease is a major cause of death and is a global health problem reaching epidemic in both developed as well as in developing countries. It is the highest killer in developed countries and is rapidly assuming a similar role in developing ones. Globally, of those dying from cardiovascular diseases, 80 percent are in developing countries and not in the Western world. Myocardial infarction is a well-known clinical entity. It is one of the most fatal diseases which are worldwide in distribution, affecting all races and nationalities. Because myocardial infarction may strike any individual during the most productive years, it can have profound deleterious, psychological and economic ramifications [1]. Despite impressive studies in the diagnosis and management over past 4 decades, acute MI continues to be major public health problem in the industrialized world and is becoming an increasing important problem in developing countries [2]. With a decline in infectious disease related death accompanied by accelerated economic development and life style change promoting atherosclerosis, developing countries especially Bangladesh are expected to experience a sharp increase in ischemic heart disease and AMI. Given the wide disparity of available resources to treat AMI in developing countries, major efforts are needed to strengthen primary prevention programs at community level. Hyponatremia is a common electrolyte disorder amongst hospitalized patients, especially in postoperative period and in patients with heart failure, nephrotic syndrome or cirrhosis [4]. Hyponatremia has been shown to be a predictor of cardiovascular mortality among patients with heart failure. In fact, the neuro-hormonal activation that accompanies acute myocardial infarction is similar to that which accompanies heart failure [5]. Hyponatremia is common after MI, and clinical improvement is accompanied by a rise in plasma sodium concentration [6]. However, while the prognostic value of hyponatremia in chronic heart failure is well established, data on the prognostic importance of hyponatremia in the setting of acute myocardial infarction are lacking [7]. This study was done to determine the prognostic importance of hyponatremia in the setting of acute ST elevation MI and to determine its usefulness in predicting short term survival.

2. Material and Methods
100 consecutive patients presenting with acute ST-elevation myocardial infarction admitted to National Institute of Cardiovascular Diseases and Hospital, Dhaka, Bangladesh from October 2017 to September 2018 were studied. Qualifying patients underwent detailed history and clinical examination.

Plasma sodium concentrations were obtained on admission and at 24, 48 and 72 hours thereafter. The primary end point was all cause mortality within 30 days following myocardial infarction. 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 30 day mortality.

Inclusion Criteria

All myocardial infarction patients having: 1. Chest pain lasting more than 20 minutes. 2. Diagnostic ECG changes with characteristic ECG alterations consisting of new pathological Q waves or ST segment & T wave changes. 3. Elevated Creatine Kinase MB levels or Elevated Cardiac Troponin T levels.

Exclusion Criteria

Acute Coronary Syndrome without ST elevation. 2. Duration of Chest pain for more than 3 days (72 hrs.). 3. Renal failure patient 4.Chronic liver disease patient. 5. Hypokalaemia at the time of admission.

3. Results

The youngest age was 30 years. The eldest age was 85 years. The maximum numbers of patients were in the age group 51-60 which is 35% of the cases and next highest numbers of patients were found in the age group 61-70 (27%). Among 100 patients studied, 80% were males and 20 % were females. (M: F=4:1) (Table 1). Patients presented with hyponatremia on admission were older than patients with normal sodium levels. Males made up 81% of patients who presented with hyponatremia on admission and 77% of patients who developed hyponatremia within 72 hours. Patients who presented with or developed hyponatremia more often were smokers(81%) and had diabetes (44%), anterior infarction (72 and 83%), higher killip class, lower ejection fraction (40.36 ±6.14) compared to patients with normal sodium levels. (Table 1) 71 % patient presented with normal sodium level, 11% with preexisting Hyponatremia and 18% developed hyponatremia within 72 hours of hospitalization. Only 2 patients died in normal sodium group. But among those who had Hyponatremia, 6 patients lost their life in the period of next 30 days. Odds ratio for 30 day mortality was found to be high in hyponatremic groups. (Table 2) It was seen that serum sodium levels was statistically significant in determining mortality. Mean serum sodium level was 136.96 ±1.92 in the survivors and 134.09±3.53 in non survivors. Other factors such as Killip class, hypertension, diabetes, age and sex were found to be statistically significant in determining mortality. (Table 3) Multivariate analysis showed that along with other risk factors, hyponatremia was the significant independent predictor of 30 day mortality.

Table 1: Base line characteristics of patients (N=100).

Characteristics	Normal Sodium	Hyponatremia on	Hyponatremia	P value
	level (n=71)	Admission (n=11)	Within 72 hrs.(n=18)	
	MEAN±SD, NUMBER (%) OR MEDIAN			
Age(yrs)	57.8±11.7	64.9±13.1	56.61±11.54	F=1.97, p=0.145
Male sex	57(71)	9(81)	14(77)	χ^2=0.082, p=0.962
Diabetes	9(12.6)	3(27.5)	8(44.45)	χ^2=9.466, P=0.009
Smoking	50(70)	9(81)	11(61)	χ^2=4.938, p=0.0085
Hypertension	14(5.6)	2(18.18)	4(22.22)	χ^2=0.082, p=0.960
Anterior infarction	45(63)	8(72)	15(83)	χ^2=2.754, P=0.252
Killip class	1.06±0.23	1.18±0.40	1.06±0.24	F=1.18, p=0.312
Ejection fraction (%)	44.63±11.19	40.36±6.14	50.11±13.26	F=2.86, p=0.06

Table 2: Odds ratio for 30 day mortality (N=100).

	Survivors	Non survivors	Odds ratio	P value
Patients with normal sodium levels	69	2	-	-
Hyponatremia on admission	8	3	5.03	0.01
Hyponatremia within 72 hours.	15	3	6.9	0.02

Table 3: Survivors and non survivors were also compared for various factors (N=100).

	Survivors	Non survivors	T or χ^2	P value
N	92	8	-	-
Age(yrs.) (Mean±SD)	57.7±12.1	65.5±7.58	2.63	0.025
Sex				
Male	76(82%)	4(50%)	4.89	0.027
Female	16(18%)	4(50%)		
Hyponatremia(Mean±SD)	136.96±1.92	134.09±3.53	2.27	0.057
Smoking	66(72%)	4(50%)	1.65	0.198
Diabetes	16(17%)	4(50%)	4.891	0.027
Hypertension	16(17%)	4(50%)	4.891	0.027
Infarct site				
Anterior	63(68%)	5(63%)	0.002	>0.05
Inferior	29(32%)	3(37%)		

Killip class I	88(95%)	5(63%)	12.426	0.001
II	4(5%)	3(37%)		
EF (%) (Mean±SD)	47.7±12.7	38.6±10.9	2.24	0.05

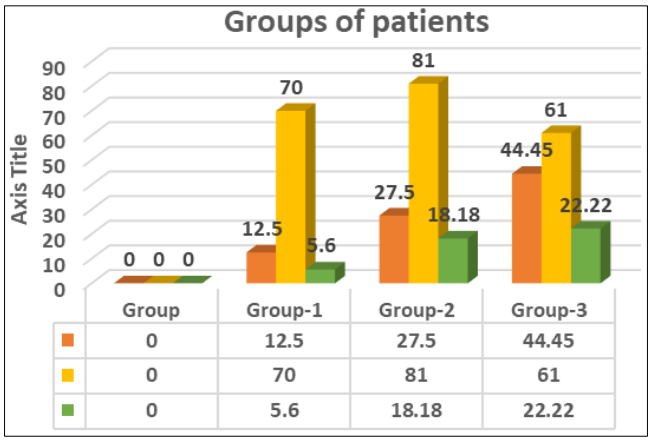

Fig 1: Bar diagram showing incidence of hyponatremia among diabetic, smokers and hypertensive patients

Group 1 = Patients with normal sodium level. Group 2 = Hyponatremia on admission. Group 3 = Hyponatremia within 72 hours.

4. Discussion

This study suggests that patients presenting with acute myocardial infarction who had hyponatremia on admission or developed hyponatremia after admission represent high risk population. In my study substantial proportion of patients who presented with acute ST-elevation myocardial infarction were hyponatremic on admission or developed hyponatremia shortly after admission. In this study hyponatremia was present on admission in 11 patients (11%). Hyponatremia developed in 18 patients (18%) during the first 72 hours of hospitalisation. Patients who presented or developed hyponatremia more often had diabetes, anterior infarction and higher Killip class and lower ejection fraction. In this study a total of 8 deaths (8%) occurred within 30 days of admission. 2.8% (2/71) of patients without hyponatremia, 27.5%(3/11) of patients with hyponatremia on admission, 16.67%(3/18) of patients who developed hyponatremia after admission. In study done by Goldberg *et al*, a total of 105 deaths (10%) occurred within 30 days of admission. 6.2% (44/708) of patients without hyponatremia, 19.8% (26/131) of patients with hyponatremia on admission and 16.8% (35/208) of patients who developed hyponatremia after admission [8]. In comparison with the above study, my study has higher mortality in patients with hyponatremia on admission whereas mortality was almost equal inpatients that developed hyponatremia after admission [10]. In this study, odd's ratio for 30 day mortality in patients with hyponatremia on admission and patients who developed hyponatremia after admission was high (5.03 and 6.9). This is in concordance with study done by Goldberg *et al*. [8]. A trend of increasing mortality with the severity of hyponatremia is observed in this study. The patients were divided in to two groups depending on the mean sodium level. The group with sodium level <130 mmol/L had 100% mortality and those with serum sodium in the range of 131-134 mmol/L suffered 12% deaths. This is in concordance with the study conducted by Goldberg *et al*., who showed increasing mortality with severity of hyponatremia [11]. A study in 1979 showed in their study that relation of mortality and plasma sodium level. 7% died with normalplasma sodium level, 17% with sodium level 135- 130 mmol/L and 22% died with plasma sodium level less than130 mmol/L [23]. In acute STEMI patients without hyponatraemia had a mortality rate 6.2% [22]. Patients with hyponatraemia on admission mortality rate were 19.8% and 16.8% in patients who developed hyponatraemia after admission. After logistic regression analysis and adjustment for other important co-variants they concluded that both hyponatraemia on admission and hyponatraemia developing after admission remained strong independent predictor of 30 –day mortality. When various risk factors and outcomes among the survivors and the non survivors are compared apart from age, sex, diabetes, hypertension, Killip class on admission, ejection fraction, and hyponatremia was found as a significant risk factor in determining mortality. All the variables among the survivors and non survivors that were significantly associated with mortality are included in the multivariate logistic regression analysis. Hyponatremia remained a significant independent predictor of mortality. This is in concordance to similar study conducted by Goldberg *et al* they found that hyponatremia was independently associated with 30 day mortality [5]. In a similar study on 235 patients admitted to a coronary care unit, Flear *et al*. found higher in hospital mortality rates among patients with low plasma sodium levels ≤130 mmol/L [2]. 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 neurohormonal activation [8]. Hence this study concludes that hyponatremia on admission or early development of hyponatremia in patients with acute ST elevation MI is an independent predictor of 30 day mortality.

5. Conclusion

In our study we concluded that hyponatremia on admission or early development of hyponatremia in patients with acute ST elevation myocardial infarction is an independent predictor of 30-day mortality. Plasma sodium levels may serve as a simple marker to identify patients at risk.

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