Original Contribution/Clinical Investigation

Prognostic value of hyponatremia in elderly Patients with Acute Coronary Syndrome

Amira H. Mahmoud
Hend M. Taha
Doha Rasheedy

Geriatrics and Gerontology department; Faculty of Medicine,
Ain shams University, Cairo, Egypt

Correspondence:
Amira Hanafey Mahmoud, M.D, Geriatrics and Gerontology department,
Faculty of Medicine, Ain shams University, Abbasia, Cairo, Egypt.
Tel: 02-01227285450
Email: *amira_mahmoud93@ yahoo.com*

Alternate correspondence:
Hend mahmoud taha, M.D , Geriatrics and Gerontology department, Faculty of Medicine, Ain shams University, Abbasia, Cairo, Egypt
Tel: 02-01222527754
Email: *hendtaha_80@ yahoo.com*

ABSTRACT

Objectives: to analyse in-hospital outcomes and prognostic implications of reduced sodium serum level (S-Na) in patients with acute coronary syndrome including ST elevation myocardial infarction (STEMI) and non ST elevation myocardial infarction (non-STEMI).

Design: A cross sectional study was conducted on elderly patients.

Participants: One hundred patients aged ≥ 60 years, both males and females.

Setting: Participants were recruited from cardiology intensive care unit in Ain Shams University hospitals.

Measurements: All patients had a sodium level determined at time of admission and after 48 hours, serial ECG and cardiac enzymes (creatine phosphokinase (CPK) and CPK-MB fraction) levels.

Results: Of 100 patients, 52 patients were admitted with STEMI and 48 with NSTEMI; 73 were hyponatremic (S-Na <135 mEq/L) and 27 were normonatremic (S>or=135 mEq/L). Patients who had hyponatremia were more likely to die or have recurrent myocardial infarction in the next 30 days (p <0.05). Hyponatremia, hypotension on admission, left ventricular ejection fraction (EF), mean level of cardiac enzymes were significantly associated with adverse outcome. On multivariate analysis, hyponatremia was a strong predictor of adverse outcome (odds ratio 2.4, 95% confidence interval).

In conclusion, hyponatremia is associated with 30-days adverse outcome in patients presenting with acute coronary syndrome.

Key words: hyponatremia; acute coronary syndrome; elderly;

Introduction

Hyponatremia, defined as a serum sodium concentration of <135 mmol/L, is the most common electrolyte abnormality in hospitalized patients (1,2). Hyponatremia often signifies poor prognosis(3). It is a predictor of mortality in patients with heart failure (4,5) and in patients with ST-elevation myocardial infarction (STEMI) (6,7). There is complex neuro-hormonal activation in acute myocardial infarction related to activation of the renin-angiotensin system, release of atrial natriuretic peptide and catecholamines (8,9). These mechanisms are similar to those in heart failure and lead to peripheral vasoconstriction and myocardial hypertrophy, with potential to worsen survival in acute myocardial infarction. The fall in sodium concentrations in patients with acute myocardial infarction is related to the previous mechanisms (6,10). 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, also few studies have focused on outcome in the elderly age group. This study is being undertaken to determine the prognostic significance of hyponatremia in the setting of acute coronary syndrome and to determine its usefulness in predicting short term (30-days) adverse outcomes.

Subjects and Methods

A cross sectional study was conducted on one hundred elderly males and females. Participants were recruited from cardiology intensive care unit in Ain Shams University hospitals. Elderly with the diagnosis of acute STEMI and non-STEMI were included. During the hospital stay, all participants underwent comprehensive geriatric assessment, medication review, cognitive assessment by which delirious patients were excluded, also subjects with history of heart failure, renal failure and hepatic patients were excluded; patients with history of diuretic use were also excluded.

Patients had clinical examination done and investigations in the form of serial ECG and cardiac enzymes, Echocardiography, laboratorial investigations for assessment of other Co- morbidities as complete blood picture, lipid profile, renal functions and blood glucose levels, also all participants had serum sodium levels obtained on admission and at 48 hours.

Laboratorial investigations were collected from medical reports. Diagnosis of myocardial infarction was done according to the criteria of the Joint European Society of Cardiology and American College of Cardiology in which diagnosis requires a finding of the typical rise and fall of biochemical markers of myocardial necrosis in addition to at least 1 of the following (11):

- Ischemic symptoms
- Development of pathologic Q waves
- Ischemic ST-segment changes on electrocardiogram (ECG) or in the setting of a coronary intervention

Renal insufficiency and anemia were defined as admission values for creatinine >1.4 mg/dl and <12 mg/dl for hemoglobin, respectively. The follow-up for myocardial infarction recurrence and mortality was done through post discharge phone calls and the follow up duration was 30 days.

Statistical methods:

The collected data were coded, tabulated, revised and statistically analyzed using SPSS program (version 20). Descriptive statistics were done using mean and standard deviation for numerical parametric data and by number and percentage for categorical data. Statistical analysis was done for quantitative variables by using independent t-test in case of two independent groups, and paired t-test in related samples with parametric data. Chi-square test was used for non parametric data and Logistic regression analysis for predictors of mortality. The level of significance was taken at P value < 0.05.

Results

Baseline sociodemographic and clinical Characteristics of Patients are shown in Table 1 - next page.

There is no statistically significant difference between Na level on admission and after 48 hours as shown in Table 2 - page 15.

Comparison between hyponatremic and normonatremic groups shows no statistically significant difference between the two groups as regards sociodemographic variables, Co morbidities (diabetes, hypertension, anemia, renal impairment or hypercholesterolemia or old stroke), presence of hypotension on admission, pulmonary edema on admission or type of myocardial infarction, while ejection fraction was significantly lower in the hyponatremic group (Table 3).

Relation between baseline patients' characteristics and outcome is demonstrated in Table 4, which shows that both hypotension on admission and hyponatremia are significantly associated with poor outcome (mortality, MI recurrence).

Significant relation between poor outcome, EF, cardiac enzymes and sodium level on admission is shown in Table 5.

Significant clinical variables were entered into a multivariate regression model which showed that hypotension on admission and hyponatremia are each significantly associated with 30-days adverse outcomes (Table 6).

Discussion

The results of this cross sectional study demonstrated that hyponatremia is common in elderly patients presenting with acute coronary syndrome and that hypotension on admission and hyponatremia were each significantly associated with recurrent myocardial infarction or death within 30 days of hospitalization.

Reviewing literature, data from several studies support the present study results. Flear et al (12) reported that hyponatremia, hypochloremia, and uremia were common in patients with confirmed myocardial infarction, with higher in-hospital mortality in hyponatremic patients, also Hochman et al (13) reported that hyponatremia in these patients was correlated with higher mortality and reflected severity of underlying disease; another study by Goldberg et al (7) showed an association between hyponatremia and increased 30-days mortality in patients with STEMI.

Bogdan et al (14) reported a high prevalence of hyponatremia within the first 72 hours of transmural myocardial infarction and Klopotowski et al (15) reported that patients with acute myocardial infarction developed hyponatremia on admission or within the first 48 after admission.

In this study age, sex, smoking, diabetes, hypertension, anemia, renal impairment, hypercholesterolemia, and pulmonary edema on admission were not associated with death/myocardial infarction. On the other hand hypotension on admission, hyponatremia on admission, ejection fraction and CPK & CPK -MB levels were significantly associated with recurrent myocardial infarction and death within 30 days and that is agreed with by Qing Tang & Qi Hua (16) who reported that gender, diabetes, hypertension, renal insufficiency, and hyperglycemia were not significantly associated with inhospital mortality and also with Singla et al (10) who reported that hypotension on admission and hyponatremia on admission were each significantly associated with the primary end point (combined incidence of death or new myocardial infarction within 30 days of index hospitalization), while diabetes mellitus and hypertension were not associated with death/myocardial infarction.

Qing Tang & Qi Hua (16) observed that patients with hyponatremia had lower ejection fractions than those without and stated that large infarct size resulted in ventricular dysfunction and might be responsible for these adverse outcomes therefore hyponatremia may be a simple parameter which reflects the presence of heart failure and that was in agreement with our study results as well.

Finally, it can be concluded that hyponatremia is considered a strong predictor for poor short term outcome in elderly with acute coronary syndrome.

Study limitations :
Our study has some limitations. Importantly, this was a small single site observational study also patients with hyperglycemia were not excluded which may be a contributing factor for hyponatremia.

Conclusion
Hyponatremia is associated with 30days adverse outcome in patients presenting with acute coronary syndrome.

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References
1. Upadhyay A, Jaber BL, Madias NE, 2006. Incidence and prevalence of hyponatremia. Am J Med .119: S30-S35
2. Funk GC, Lindner G, Druml W, et al, 2010. Incidence and prognosis of dysnatremias present on ICU admission. Intensive Care Med. 36: 304-311

Age Range	60-79	
Mean±SD	63.42±5.02	
Sex	N	%
Female	68	68.0
Male	32	32.0
Smoking		
Current	49	49.0
Ex-smoker	25	25.0
Non smoker	26	26.0
Diabetes	46	46.0
Hypertension	64	64.0
Other comorbidities		
Anemia	6	6.0
Renal impairment	17	17.0
Hyper cholesterolemia	6	6.0
Stroke	7	7.0
MI		
ST	52	52.0
NST	48	48.0
Hypotension on admission	10	10.0
Pulmonary edema on admission	1	1.0
Hyponatremic patients	73	73.0
Normonatremic patients	27	27.0
Outcome		
Mortality	16	16.0
MI recurrence	14	14.0
Good prognosis	70	70.0
EF		
Range	15-77	
Mean±SD	46.440±12.802	
Peak CPK		
Range	200-2850	
Mean±SD	813.0±690.1	
MB		
Range	41-1820	
Mean±SD	176.85±307.27	

Table 1 : Baseline Characteristics of Patients

				Paired	Paired Samples Test	
	Range			Mean(± SD)	Mean (SD)	t	P-value
Na on admission	111.000	-	152.000	131.060 (± 7.393)	0.430 (5.360)	0.802	0.424
Na after	111.000	-	153.000	130.630 (± 6.932)			

Table 2: Sodium levels at different time points

		Groups						Chi-Square	
		Hyponatremia		Normonatremic		Total			
		N	%	N	%	N	%	X^2	P-value
SEX	Female	50	68.49	18	66.67	68	68.0	0.030	0.862
	Male	23	31.51	9	33.33	32	32.0		
SMOKING	Current	38	52.05	11	40.74	49	49.0	1.293	0.524
	Ex-smoker	18	24.66	7	25.93	25	25.0		
	Non smoker	17	23.29	9	33.33	26	26.0		
	Diabetes	32	43.84	14	51.85	46	46.0	0.510	0.475
	Hypertension	45	61.64	19	70.37	64	64.0	0.651	0.420
Other comorbidities	Anemia	3	4.11	3	11.11	6	6.0	2.267	0.686
	Renal impairment	13	17.81	4	14.81	17	17.0		
	Hyper cholesterolemia.	4	5.48	2	7.41	6	6.0		
	Old Stroke	6	8.22	3	11.11	9	9.0		
MI	ST	39	53.42	13	48.15	52	52.0	0.220	0.639
	NST	34	46.58	14	51.85	48	48.0		
	Hypotension on admission	8	10.96	2	7.41	10	10.0	0.292	0.589
	Pulmonary edema on admission	1	1.37			1	1.0	0.633	0.426
								t	P-value
AGE	Mean±SD	63.356±5.012		63.593±5.116				-0.208	0.835
EF	Mean±SD	44.822±12.480		50.815±12.863				-2.114	0.037*
CPK	Mean±SD	795.562±685.520		860.222±713.587				-0.414	0.680
MB	Mean±SD	145.685±219.976		261.111±464.119				-1.683	0.096

Table 3: Comparison between hyponatremic and normonatremic groups as regard sociodemograhic and clinical variables

		Outcome						Chi-Square	
		Poor		Good		Total			
		N	%	N	%	N	%	X^2	P-value
SEX	Female	22	73.33	46	65.71	68	68.0	0.560	0.454
	Male	8	26.67	24	34.29	32	32.0		
SMOKING	Current	16	53.33	33	47.14	49	49.0	2.029	0.363
	Ex-smoker	9	30.00	16	22.86	25	25.0		
	Non smoker	5	16.67	21	30.00	26	26.0		
Hyponatremic patients		28	93.33	45	64.29	73	73.0	7.577	0.005*
Normonatremic patients		2	6.67	25	35.71	27	27.0		
Diabetic		13	43.33	33	47.14	46	46.0	0.123	0.726
Hypertensive		19	63.33	45	64.29	64	64.0	0.008	0.928
Other comorbidities	Anemia	1	3.33	5	7.14	6	6.0	8.520	0.074
	Renal impairment	10	33.33	7	10.00	17	17.0		
	Hyper cholesterolemia	2	6.67	4	5.71	6	6.0		
	Old Stroke	2	6.67	7	10.00	9	9.0		
MI	ST	19	63.33	33	47.14	52	52.0	2.205	0.138
	NST	11	36.67	37	52.86	48	48.0		
Hypotension on admission		7	23.33	3	4.29	10	10.0	7.651	0.006*
Pulmonary edema on admission		1	3.33			1	1.0	2.357	0.125
Age	Mean±SD	63.5±4.7		63.3±5.1				T=0.147	0.883

Table 4: Relation between patient characteristics and outcome

3. Clayton JA, Le Jeune IR, Hall IP, 2006. Severe hyponatremia in medical in-patients: aetiology, assessment and outcome. Q J Med.99:505-511

4. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV, 2003. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA. 290:2581-2587

5. Kearney MT, Fox KA, Lee AJ, Prescott RJ, Shah AM, Batin PD, et al ,2002 .Predicting death due to progressive heart failure in patients with mild-to-moderate chronic heart failure. J Am Coll Cardiol. 40:1801-1808

6. Goldberg A, Hammerman H, Petcherski S, Nassar M, Zdorovyak A, Yalonetsky S, et al, 2006. Hyponatremia and long-term mortality in survivors of acute ST-elevation myocardial infarction. Arch Intern Med. 166:781-786

7. Goldberg A, Hammerman H, Petcherski S, Zdorovyak A,

	Outcome						T-Test
	Poor			Good			
	Mean	±	SD	Mean	±	SD	t	P-value
Na on admission	128.733	±	6.544	132.057	±	7.554	-2.095	0.039*
Na after 48hrs	128.900	±	6.707	131.371	±	6.941	-1.648	0.103
EF	39.700	±	12.595	49.329	±	11.843	-3.656	<0.01*
CPK	1030.1	±	805.29	919.98	±	617.74	2.02	0.03*
MB	305.46	±	524.63	121.72	±	97.52	2.83	0.006*

Table 5 : Relation between hyponatremia at different time points, cardiac enzymes and cardiac function and outcome

Logistic regression	B	S.E.	Wald	P-value	Odd ratio	95.0% C.I. for odd	
						Lower	Upper
CPK	-0.001	0.000	2.455	0.117	0.999	0.999	1.000
MB	-0.002	0.001	3.305	0.069	0.998	0.995	1.000
EF	-0.041	0.020	4.332	0.037	0.959	0.923	0.998
Na	0.876	0.587	7.227	0.0136*	2.402	4.760	7.591
Hypotension on admission	1.692	0.762	4.937	0.026*	5.433	1.221	24.177
Constant	-2.979	1.674	3.166	0.075	0.051		

Table 6: Logistic regression analysis for significant clinical variables

Yalonetsky S, Kapeliovich M, et al, 2004. Prognostic importance of hyponatremia in acute ST-elevation myocardial infarction. Am J Med. 117:242-248

8. Dei Cas L, Metra M, Visioli O ,1993. Neurohormonal assessment in heart failure: from the sophisticated laboratory to practical indications. G Ital Cardiol. 23:193-204

9. Sigurdsson A, Held P, Swedberg K ,1993. Short- and long-term neurohormonal activation following acute myocardial infarction. Am Heart J. 126:1068-1076

10. Singla I, Zahid M, Good CB, Macioceb A, Sonel AF, 2007. Effect of hyponatremia (<135 mEq/L) on outcome in patients with non- ST elevation acute coronary syndrome. Am J Cardiol. 100: 406-408,

11. Alpert JS, Thygesen K, Antman E, Bassand JP, 2000. Myocardial infarction redefined-a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol. 36(3):959-69.

12. Flear CT, Hilton P, 1979. Hyponatremia and severity and outcome of myocardial infarction. Br Med J. 1:1242-1246

13. Hochman I, Cabili S, Peer G, 1989. Hyponatremia in internal medicine ward patients: causes, treatment and prognosis. Isr J Med Sci. 25:73-76

14. Bogdan M, Nartowicz E,1993. Magnesium, potassium and sodium in serum and erythrocytes in acute myocardial infarction. Kardiol Pol. 38:263-266

15. Klopotowski M, Kruk M, Przyluski J, et al, 2009. Sodium level on admission and in-hospital outcomes of STEMI patients treated with primary angioplasty: the ANIN Myocardial Infarction Registry. Med Sci Monit. 15: CR477-CR483,

16. Qing Tang& Qi Hua, 2011. Relationship between Hyponatremia and In-hospital Outcomes in Chinese Patients with ST-Elevation Myocardial Infarction. Intern Med 50: 969-974.