RESEARCH ARTICLE

The prognostic effect of hyponatraemia in determining mortality in patients with heart failure hospitalised in AL-Yarmouk Teaching Hospital

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Abstract

Objective: To assess the prognostic effect of hyponatraemia in determining mortality in patients with heart failure.

Method: The prospective observational study was conducted at the Internal Medicine Unit of Al-Yarmouk Teaching Hospital, Baghdad, Iraq, from September 1, 2019, to February 1, 2020, and comprised adult patients of either gender who were hospitalised due to heart failure and left ventricular ejection fraction <49% at admission. The endpoint was inpatient mortality from the index hospitalisation for decompensated heart failure according to the serum sodium levels.

Results: Of the 70 patients, 46(65.7%) were males and 24(34.3%) were females. A total of 30(42.9%) patients were aged 60-69 years. Serum sodium level was <135mmol/L in 40(57%) patients, and, among them, 29(67.4%) had normal body mass index and 21(70%) were ex-smokers. There was a significant association of serum sodium with body mass index and smoking status (p<0.05). Of the 25(35.7%) cases of inpatient mortality, 19(76%) had serum sodium level <135mmol/L (p= 0.004).

Conclusion: Hyponatraemia was found to be common in patients with heart failure. It is a significant modifiable risk factor in patients with heart failure.

Keywords: Hyponatremia, Heart failure, Sodium. (JPMA 71: S-101 [Suppl. 8]; 2021)

Introduction

Heart failure (HF) is a complex clinical syndrome and not a disease. It prevents the heart from fulfilling the circulatory demands of the body since it impairs the ability of the ventricle to fill or eject blood. It is characterised by symptoms such as breathlessness, ankle swelling and fatigue that may be accompanied by signs, like elevated jugular venous pressure, pulmonary crackles, and peripheral oedema caused by structural and/or functional cardiac or non-cardiac abnormalities.[1,2]

HF can be classified as predominantly left ventricular (LV), right ventricular (RV) or biventricular, based on the location of the defect. Depending on the time of onset, HF is classified as acute or chronic. Clinically, it is typically classified into two major types based on the functional status of the heart: HF with preserved ejection fraction (HFpEF), and heart failure with reduced ejection fraction (HFrEF).[3,4]

Cardiac imaging used for HF diagnosis include chest X-rays to evaluate heart size, pulmonary congestion and to detect alternative cardiopulmonary diseases that may cause or contribute to the patient's symptoms.[2] Electrocardiogram (ECG) suggests an acute tachyarrhythmia or bradyarrhythmia as the cause of HF, aids in the diagnosis of acute myocardial ischaemia or infarction (AMI) or the presence of coronary artery disease (CAD) as the cause of HF.[5] Transthoracic echocardiography assesses LV function, size, wall thickness, wall motion, valve function and ejection fraction (EF).[6]

Besides, specific laboratory tests include brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) which both have diagnostic power and are applicable to HFrEF and HFpEF.[7] Hyponatraemia is defined as a reduction in the serum sodium (Na) concentration to <135mmol/L. Hyponatraemia is one of the most common electrolyte abnormalities in hospitalised patients with HF, with a prevalence close to 35%.[8,9] It is associated with poor short- and long-term outcomes in HF patients.[10,11] Two opposite processes can result in hyponatraemia in this setting: volume overload with dilutional hypervolaemic hyponatraemia from congestion, and hypervolaemic hyponatraemia from excessive use of natriuretic.[4,12] These two conditions require different therapeutic approaches.

Several observational studies and clinical trials have been conducted to assess the prognostic impact of Na levels at admission and during hospitalisation of HF patients, showing a strong association between mortality among HF patients and hyponatraemia at admission.[13]

The current study was planned to assess the prognostic

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effect of hyponatraemia in determining mortality in HF patients.

Patients and Methods

The prospective observational study was conducted at the Internal Medicine Unit of Al-Yarmouk Teaching Hospital, Baghdad, Iraq, from September 1, 2019, to February 1, 2020. After approval from the institutional ethics review committee, A convenient random sample was raised from among adult HF inpatients of either gender with left ventricular ejection fraction (LVEF) <49% at admission. Those with LVEF >49%, age <18 years, and those having acute coronary syndrome (ACS), sepsis, hypertriglyceridaemia, chronic renal failure, hypothyroidism, hypertriglyceridaemia, hyperglycaemia and liver cirrhosis were excluded.

The HF diagnosis was based on clinical history, physical examination, electrocardiography (ECG), and echo study done by a cardiologist.

EF 40-49%was graded as mild HF, 30-39% as moderate HF and <30% as severe HF.[1]

Sociodemographic information, age, gender occupation, residence and smoking status, as well as body mass index (BMI), which was calculated using the standard formula.[14] Those with BMI $\leq$24.99kg/m^2 were categorised as normal, 25-29.99kg/m^2 as overweight, and $\geq$30kg/m^2 as obese.[14] All statistical analyses were completed with the use of Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 25. Summary data are presented as mean±SD.

Also noted were HF causes, history of previous hospitalisation, duration of hospitalisation, vital signs, like systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR), and LVEF by Echo study.

Laboratory investigations included complete blood count (CBC), fasting blood sugar (FBS), renal function, serum cholesterol, serum potassium, serum Na, serum triglyceride (TG), and thyroid function (DiaSys diagnostic system international).

Treatment strategy and hospitalisation outcome were also noted.

Hyponatraemia was defined as serum Na level <135mmol/L.[15]

The endpoint was inpatient mortality from the index hospitalisation for decompensated HF according to the serum Na level.

Results

Of the 70 patients, 46(65.7%) were males and 24(34.3%) were females. A total of 30(42.9%) patients were aged 60-69 years. Mean serum sodium 135± 5.1 mmol/L Serum Na level was <135mmol/L in 40(57%) patients, and, among them, 29(67.4%) had normal BMI and 21(70%) were ex-smokers. There was a significant association of serum Na

Table-1: Association between serum sodium level and general characteristics.

General Characteristics	Serum Sodium Level (mmol/L) n= 40	n= 30	Total (%) n= 70	P-Value
Age (Years)				
< 60	13 (54.2)	11 (45.8)	24 (34.2)	0.871
60 - 69	17 (56.7)	13 (43.3)	30 (42.9)	
≥ 70	10 (62.5)	6 (37.5)	16 (22.9)	
Gender				
Male	27 (58.7)	19 (41.3)	46 (65.7)	0.716
Female	13 (54.2)	11 (45.8)	24 (34.3)	
BMI Level				
Normal	29 (67.4)	14 (32.6)	43 (61.4)	0.043
Overweight	11 (44.0)	14 (56.0)	25 (35.7)	
Obese	0 (0)	2 (100.0)	2 (2.9)	
Occupation				
Housewife	16 (57.1)	12 (42.9)	28 (40.0)	0.866
Retired	14 (60.9)	9 (39.1)	23 (32.9)	
Private Work	10 (52.6)	9 (47.4)	19 (27.1)	
Residence				
Urban	33 (55.0)	27 (45.0)	60 (85.7)	0.375
Rural	7 (70.0)	3 (30.0)	10 (14.3)	
Smoking status				
Current smoker	6 (35.0)	12 (65.0)	20 (28.6)	0.047
Non-smoker	13 (60.0)	9 (40.0)	20 (28.6)	
ex-smoker	21 (70.0)	9 (30.0)	30 (42.8)	
Clinical Information	**< 135 n= 40**	**≥ 135 n= 30**	**Total (%) n= 70**	**P-Value**
Cause of Heart Failure				
Ischaemic heart disease	15 (51.7)	14 (48.3)	29 (41.4)	0.736
Atrial fibrillation	3 (100.0)	0 (0)	3 (4.3)	
Hypertension	4 (66.7)	2 (33.3)	6 (8.6)	
Valvular Heart Disease	5 (50.0)	5 (50.0)	10 (14.3)	
Dilated cardiomyopathy	2 (40.0)	3 (60.0)	5 (7.1)	
Diabetes mellitus	3 (75.0)	1 (25.0)	4 (5.7)	
COPD	4 (57.1)	3 (42.9)	7 (10.0)	
Unknown cause	4 (66.7)	2 (33.3)	6 (8.6)	
Previous Hospitalization				
Yes	34 (59.6)	23 (40.4)	57 (81.4)	0.375
No	6 (46.2)	7 (53.8)	13 (18.6)	
Inpatient Treatment				
Nitrate + Statin	32 (80.0)	26 (86.7)	58 (82.9)	0.463
Diuretics	38 (95.0)	22 (73.3)	60 (71.7)	0.01
ACEI or ARB	9 (30.0)	21 (70.0)	30 (42.8)	0.125
Dopamine	13 (32.5)	4 (13.3)	17 (24.3)	0.064

BMI: Body mass index.
COPD: Chronic obstructive airway disease.
ACEi: Angiotensin converting enzyme inhibitors.
ARB: Angiotensin receptor blockers.

Table-2: Association between inpatient death and serum sodium level.

Serum Sodium Level (mmol/L)	Inpatient Death		Total (%)	P-Value
	Yes n=25	No n=30	n=70	
< 135	19 (47.5)	21 (52.5)	40 (57.1)	0.004
≥ 135	6 (20.0)	24 (80.0)	30 (42.9)	

with BMI and smoking status (p<0.05). Age, gender, occupation and residence showed no significant associations with serum Na level (p>0.05) (Table-1)

Of the 25(35.7%) cases of inpatient mortality, 19(76%) had serum Na level <135mmol/L (p=0.004) (Table-2).

The duration of hospitalisation was longer in patients with serum Na level ≥135mmol/L compared to the rest (6.63± 1.06 versus 5.35±1.81 days, p=0.001). Other parameters showed no significant associations with serum Na level (p>0.05).

SBP and DBP in patients with serum Na level ≥135 mmol/L were significantly higher than the rest (129.63±26.04 versus 105.0±25.62mmHg, p=0.001; and 76.66±11.54 versus 63.75±16.12mmHg, p=0.001).

HR in patients with serum Na level <135mmol/L was significantly higher than the rest (86.82±14.12 versus 79.7±11.45 beats/min, p=0.027).

There was no significant difference (p=0.369) in mean LVEF values between patients with serum Na level <135mmol/L and the rest (35.6±7.34 versus 37.1±6.18, p=0.369).

Discussion

The current study found serum Na level <135 mmol/L in 57% of the sample. A study reported 51%, which is slightly lower than the current results.[16] Other studies have reported 16.8% 38%.[17] The difference might be ascribed to the difference in sample size in the studies.

The current study found significant association between BMI and serum Na level, which has also been reported earlier.[18]

The current study also found serum Na level to have a significant association with smoking status, and there was no significant association with age, gender, residence and occupation. One study noticed no relation of serum Na level with age, gender, occupation and residence.[18] Another study did not find a significant relation between smoking status and serum Na level.[18]

In the current study, 38(95%) patients with serum Na level <135mmol/L were treated with diuretics (p= 0.01) which was reported by an earlier as well,[18] while contrasting findings were reported by another study.[18]

Diuretics are one of the most common causes of drug-induced hyponatraemia.[19] The great majority of cases of diuretic-induced hyponatraemia are caused by thiazide diuretics, which act solely in the distal tubules and do not interfere with urinary concentration and the ability of arginine vasopressin (AVP) to promote water retention. Thiazide-induced hyponatraemia is usually mild, but acute severe hyponatraemia is occasionally developed as an idiosyncratic reaction.[20]

In the current study, no significant association was found between Na level and all other clinical information, as the HF cause. In contrast, a study reported that hyponatraemic patients had a higher frequency of chronic kidney disease (p<0.001), and had a lower frequency of myocardial infarction history (p=0.038).[18] Another study found no significant disparity in the HF aetiology except for valvular heart disease (VHD) (p=0.025).[18] Also, a study found that VHD) (14.1%) was the third leading cause of HF, preceded by hypertensive heart disease (39.2%) and cardiomyopathy (21.4%).[21] Another study showed valvular implication of VHD with findings of mitral regurgitation and mitral stenosis as the most common valvular involvement in Ethiopian HF cohort.[22] Differences observed can be attributed to different sample sizes in each study.

In HF patients, the low cardiac output and blood pressure lead to an increase in sympathetic tone. There is activation of the renin-angiotensin-aldosterone system, and, finally, there is non-osmotic release of vasopressin to preserve arterial blood volume and pressure.[23]

In the present study, mean SBP, DBP and HR in patients with serum Na level ≥135 mmol/L were significantly higher. Similar[17] and contrasting[18] results have been reported earlier. Different sample sizes, types of drugs used and other associated diseases would explain the differing results.

In the current study, there was no significant relation between mean LVEF and serum Na level which was in line with literature.[18]

The highest prevalence of inpatient death in the current study was seen in those with serum Na level <135mmol/L (p=0.004), which has also been reported earlier.[24] Lower results, however, have also been reported.[17]

In terms of limitations, the current study was conducted at a single centre, and the sample size was not calculated scientifically, which could influence the study's power.

Conclusion

Hyponatraemia was found to be common in patients with HF. It is a significant modifiable risk factor in HF patients.

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Conflict of Interest: None.

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Reference

1. Tripoliti EE, Papadopoulos TG, Karanasiou GS, Naka KK, Fotiadis DI. Heart Failure: Diagnosis, Severity Estimation and Prediction of Adverse Events Through Machine Learning Techniques. Comput Struct Biotechnol J 2016;15:26-47. doi: 10.1016/j.csbj.2016.11.001.
2. Inamdar AA, Inamdar AC. Heart Failure: Diagnosis, Management and Utilization. J Clin Med 2016;5:62. doi: 10.3390/jcm5070062.
3. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol 2016;13:368-78. doi: 10.1038/nrcardio.2016.25.
4. National Clinical Guideline Centre (UK). Chronic Heart Failure: National Clinical Guideline for Diagnosis and Management in Primary and Secondary Care: Partial Update. London, UK: Royal College of Physicians (UK); 2010. [Online] 2010 [Cited 2020 March 06]. Available from URL: https://pubmed.ncbi.nlm.nih.gov/22741186/
5. Dumitru I, Baker MM. Heart failure workup: Approach considerations, routine laboratory tests, natriuretic peptides. [Online] 2021 [Cited 2020 February 19]. Available from URL: https://emedicine.medscape.com/article/163062-workup#c17.
6. Paterson I, Mielniczuk LM, O'Meara E, So A, White JA. Imaging heart failure: current and future applications. Can J Cardiol 2013;29:317-28. doi: 10.1016/j.cjca.2013.01.006.
7. Maries L, Manitiu I. Diagnostic and prognostic values of B-type natriuretic peptides (BNP) and N-terminal fragment brain natriuretic peptides (NT-pro-BNP). Cardiovasc J Afr 2013;24:286-9. doi: 10.5830/CVJA-2013-055.
8. Kovesdy CP, Lott EH, Lu JL, Malakauskas SM, Ma JZ, Molnar MZ, et al. Hyponatremia, hypernatremia, and mortality in patients with chronic kidney disease with and without congestive heart failure. Circulation 2012;125:677-84. doi: 10.1161/CIRCULATIONAHA.111.065391.
9. Holland-Bill L, Christiansen CF, Heide-Jørgensen U, Ulrichsen SP, Ring T, Jørgensen JO, et al. Hyponatremia and mortality risk: a Danish cohort study of 279508 acutely hospitalized patients. Eur J Endocrinol 2015;173:71-81. doi: 10.1530/EJE-15-0111.
10. Sato N, Gheorghiade M, Kajimoto K, Munakata R, Minami Y, Mizuno M, et al. Hyponatremia and in-hospital mortality in patients admitted for heart failure (from the ATTEND registry). Am J Cardiol 2013;111:1019-25. doi: 10.1016/j.amjcard.2012.12.019.
11. Konishi M, Haraguchi G, Ohigashi H, Sasaoka T, Yoshikawa S, Inagaki H, et al. Progression of hyponatremia is associated with increased cardiac mortality in patients hospitalized for acute decompensated heart failure. J Card Fail 2012;18:620-5. doi: 10.1016/j.cardfail.2012.06.415.
12. Liamis G, Milionis H, Elisaf M. In Reply to 'Drug-Induced Hyponatremia Adding to the List'and 'Tramadol-Induced Hyponatremia'. Am J Kidney Dis 2008;52:1027. doi:10.1053/j.ajkd.2008.07.014
13. Bae MH, Chae SC. Hyponatremia in acute heart failure: a marker of poor condition or a mediator of poor outcome? Korean J Intern Med 2015;30:450-2. doi: 10.3904/kjim.2015.30.4.450.
14. World Health Organization. Obesity and overweight. [Online] 2021 [Cited 2020 March 04]. Available from URL: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
15. Shea AM, Hammill BG, Curtis LH, Szczech LA, Schulman KA. Medical costs of abnormal serum sodium levels. J Am Soc Nephrol 2008;19:764-70. doi: 10.1681/ASN.2007070752.
16. Abebe TB, Gebreyohannes EA, Tefera YG, Bhagavathula AS, Erku DA, Belachew SA, et al. The prognosis of heart failure patients: Does sodium level play a significant role? PLoS One 2018;13:e0207242. doi: 10.1371/journal.pone.0207242.
17. Yoo BS, Park JJ, Choi DJ, Kang SM, Hwang JJ, Lin SJ, et al. Prognostic value of hyponatremia in heart failure patients: an analysis of the Clinical Characteristics and Outcomes in the Relation with Serum Sodium Level in Asian Patients Hospitalized for Heart Failure (COAST) study. Korean J Intern Med 2015;30:460-70. doi: 10.3904/kjim.2015.30.4.460.
18. Vazquez R, Bayes-Genis A, Cygankiewicz I, Pascual-Figal D, Grigorian-Shamagian L, Pavon R, et al. The MUSIC Risk score: a simple method for predicting mortality in ambulatory patients with chronic heart failure. Eur Heart J 2009;30:1088-96. doi: 10.1093/eurheartj/ehp032.
19. Liamis G, Milionis H, Elisaf M. A review of drug-induced hyponatremia. Am J Kidney Dis 2008;52:144-53. doi: 10.1053/j.ajkd.2008.03.004.
20. Liamis G, Milionis H, Elisaf M. Blood pressure drug therapy and electrolyte disturbances. Int J Clin Pract 2008;62:1572-80. doi: 10.1111/j.1742-1241.2008.01860.x.
21. Agbor N, Essouma M, Ntusi N, Nyaga U, Bigna JJ, Noubiap JJ. A5953 Heart failure in sub-Saharan Africa: a contemporaneous systematic review and meta-analysis. J Hypertens 2018;36:e157. doi: 10.1097/01.hjh.0000548638.47932.4b
22. Tefera YG, Abegaz TM, Abebe TB, Mekuria AB. The changing trend of cardiovascular disease and its clinical characteristics in Ethiopia: hospital-based observational study. Vasc Health Risk Manag 2017;13:143-51. doi: 10.2147/VHRM.S131259
23. Schrier RW, Abraham WT. Hormones and hemodynamics in heart failure. N Engl J Med 1999;341:577-85. doi: 10.1056/NEJM199908193410806.
24. Bettari L, Fiuzat M, Shaw LK, Wojdyla DM, Metra M, Felker GM, et al. Hyponatremia and long-term outcomes in chronic heart failure--an observational study from the Duke Databank for Cardiovascular Diseases. J Card Fail 2012;18:74-81. doi: 10.1016/j.cardfail.2011.09.005 diac Failure. 2012;18:74-81.