ORIGINAL ARTICLE

Association of Mortality with Hyponatremia in patients of Heart Failure

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ABSTRACT

Aim: To assess the association of mortality with Hyponatremia in patients presenting with heart failure
Methods: Total310 cases fulfilling the selection criteria were selected from 1st January to 30th June 2016. Then patients were divided in two groups (155 in each group) i.e., Serum sodium <135meq/l (hyponatremia) and Serum sodium ≥135meq/l (normonatremia). Then patients were followed-up for 30 days. During follow-up patients were in contact for assessment of their status i.e. death or alive. If patient died within 30 days, then mortality was labeled.
Results: In this study risk of mortality was significantly higher in patients with hyponatremia (30.3%) who presented with heart failure when compared with patients who were normonatremia (12.3%). i.e., RR: 2.47, p-value=0.002. Patients in the age group 61-70 and 70-80 years had significant risk of mortality who had hyponatremia. While patients in the age group 40-50 years and 51-60 years did not show any significant risk towards morality with hyponatremia. Male patients had significantly 2.86 times more chances of mortality and female patients had 2.19 times more chances of morality who had hyponatremia. Risk of morality among patients who had hyponatremia was statistically significant. Patients who had normal BMI and overweight patients with hyponatremia had significant risk for morality as that of patients who were normonatremia. i.e., Normal BMI: RR: 2.08, p-value=0.047 & Over weight: RR:2.92, p-value=0.001
Conclusion: Results of this study showed that heart failure patients presenting with hyponatremia had higher risk of mortality.
Keywords: Heart failure, Mortality, Hyponatremia, sodium

INTRODUCTION

In United States, the estimated prevalence of heart failure is 5.8 million patients, with an annual incidence of 670,000 new cases per year. Heart failure results in 1.1 million hospital discharges and cause or contributes to 280,000 deaths per year. The major signs and symptoms of heart failure are attributed to compensative mechanisms aimed to restoring cardiac output to near normal levels.

Hyponatremia can develop in these patients[1]. Due to decrease in cardiac output and subsequent decreased renal perfusion leading to release of hypovolemic hormones resulting in retention of Na and water. Stimulation of carotid sinus and aortic arch receptors result in release of ADH (levels may be raised to 2-3 folds in patients with LVF) which stimulate the V2 receptors enhancing water uptake from collecting ducts. Nor-epinephrine and angiotensin 2 decrease the GFR and limit the water excretion, In addition there is potent thirst stimulation mediated by decreased cardiac output and angiotensin 2. In addition patients with LVF may be using diuretics which facilitate the Na loses through kidneys. Patients admitted with heart failure commonly have Hyponatremia. This relationship has prognostic significance[2].

One more cohort study, Rates of death were significantly higher in patients with hyponatremia, 15%, compared to 5.3%, in those with normonatremia ($p<0.05$)[5]. Another cohort showed that mortality was not significantly higher in patients with hyponatremia, 18.4%, compared to 17.5%, in those with normonatremia ($p=0.730$)[6].

The rationale of the study is to assess the association of mortality with Hyponatremia in patients presenting with heart failure. It has been noticed from literature that hyponatremia in HF patients is highly associated with high rates of mortality. But contradiction has also been reported which showed that whether the sodium level decrease or not, there may be equal chance of mortality. So to resolve the issue we want to conduct this study and confirm whether hyponatremia is associated with early mortality in such complicated cases. So that early screening and management can be done in HF patients with hyponatremia and patients can be prevented from hazardous outcome.

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MATERIAL &METHODS

Total310 cases fulfilling the selection criteria were selected form emergency of Department of Medicine, Mayo hospital Lahore from 1st January to 30th June 2016. Then patients were divided in two groups (155 in each group) i.e. Serum sodium <135meq/l (hyponatremia) and Serum sodium ≥135meq/l (normonatremia). Then patients were followed-up for 30 days. Frequency and percentages was calculated for qualitative variables (e.g., gender, and mortality). Relative risk was calculated to determine the strength of association between hyponatremia and mortality.

RESULTS

In hyponatremia group there were 84(54.2%) male and 71(45.8%) female patients while in normonatemia there were 77(49.75) male and 78(50.3%) female patients.Mean BMI of patients with and without hyponatremia was 24.59±2.86 and 25.76±2.93.Mean sodium level of patients with and without hyponatremia was 115.37±9.60 and 139.81±3.37.Patients with hyponatremia had significantly 2.47 times more chances of mortality as that of patients who were normonatremia i.e. (p-value=0.002) Patients in the age group 61-70 and 70-80 years had significant risk of mortality who had hyponatremia. While patients in the age group 40-50 years and 51-60 years did not show any significant risk towards morality with hyponatremia. Male patients had significantly 2.86 times more chances of mortality and female patients had 2.19 times more chances of morality who had hyponatremia. Risk of morality among patients who had hyponatremia was statistically significant. Patients who had normal BMI and overweight patients with hyponatremia had significant risk for morality as that of patients who were normonatremia. i.e. Normal BMI: RR: 2.08, p-value=0.047 & Over weight: RR:2.92, p-value=0.001

Table 1: Gender distribution of Patients

Gender	Hyponatremia	Normonatremia
Male	84(54.2%)	77(49.7%)
Female	71(45.8%)	78(50.3%)

Table 2: Descriptive statistics for BMI of patients

	Hyponatremia	Normonatremia
N	155	155
Mean	24.59	25.76
SD	2.86	2.93
Min	20.06	20.06
Max	30.00	30.00

Table 3: Descriptive statistics for Serum Sodium level

	Hyponatremia	Normonatremia
N	**155**	**155**
Mean	115.37	139.81
SD	9.60	3.37
Min	100	135
Max	132	145

Table 5: Mortality in study Groups

Mortality	Hyponatremia	Normonatremia	Total
Yes	47(30.3%)	19(12.3%)	66
No	108(69.7%)	136(87.7%)	244
Total	***155***	***155***	310

Relative Risk= 2.47 p-value= 0.0002

Table 6: Mortality in study Groups as per age stratification

Age Groups	Mortality	Hyponatremia	Normonatremia	RR	p-value
40-50	Yes	12(23.5%)	6(12%)	1.96	0.142
	No	39(76.5%)	44(88%)		
51-60	Yes	2(8.3%)	4(13.3%)	0.625	0.567
	No	22(91.7%)	26(86.7%)		
61-70	Yes	16(41%)	5(12.8%)	3.200	0.011
	No	23(59%)	34(87.2%)		
70-80	Yes	17(41.5%)	4(11.1%)	3.731	0.009
	No	24(58.5%)	32(88.9%)		

Table 7: Mortality in study Groups as per age stratification

Gender	*Mortality*	*Hyponatremia*	*Normonatremia*	*RR*	*p-value*
Male	*Yes*	25(29.8%)	8(10.4%)	*2.86*	*0.0049*
	No	59(70.2%)	69(89.6%)		
Female	*Yes*	22(31%)	11(14.1%)	*2.19*	*0.017*
	No	49(69%)	67(85.9%)		

Table 8: Mortality in study groups as per BMI stratification

BMI	Mortality	Hyponatremia	Normonatremia	RR	p-value
Normal	Yes	25(27.8%)	8(13.3%)	2.08	0.047
	No	65(72.2%)	52(86.7%)		
Over weight	Yes	22(34.9%)	11(12%)	2.92	0.001
	No	41(65.1%)	81(88%)		
Obese	Yes	0(0%)	0(0%)	1.33	0.876
	No	2(100%)	3(100%)		

DISCUSSION

Hyponatremia is a common disorder in patients with either acute or chronic heart failure, caused mainly by impaired water excretion instead of sodium depletion. The underlying pathophysiology may involve an increase of nonosmotic release of AVP attributed to baroreceptor activation and decreased distal renal tubularflow attributed to compromised glomerularfiltration.

Previous studies have demonstrated the prognostic impacts of on-admission serum sodium levels in patients hospitalized for AHF. A lower serum sodium level in AHF may indicate poor water excretion attributed to cardiorenal insufficiency, which was therefore related to a worse clinical outcome. In contrast, the prognostic value of the changes of sodium levels in AHF patients during hospitalization has been less clear. For example, treatment of hyponatremia in AHF patients with the vasopressin antagonist in the EVEREST study showed an improvement in serum sodium levels and heart failure signs and symptoms, but not clinical outcomes[8].

In addition, in observational studies, the changes of serum sodium levels during hospitalization for AHF were not a predictor of long-term survival, whereas on-admission hyponatremia indeed was related to their prognoses. These results may suggest that hyponatremia is a marker of more-severe disease, but not a treatment target in AHF.

In this study risk of mortality was significantly higher in patients with hyponatremia (30.3%) who presented with heart failure when compared with patients who were normonatremia (12.3%). i.e., RR: 2.47, p-value=0.002. Patients in the age group 61-70 and 70-80 years had significant risk of mortality who had hyponatremia. While patients in the age group 40-50 years and 51-60 years did not show any significant risk towards morality with hyponatremia.

Male patients had significantly 2.86 times more chances of mortality and female patients had 2.19 times more chances of morality who had hyponatremia. Risk of morality among patients who had hyponatremia was statistically significant. Patients who had normal BMI and overweight patients with hyponatremia had significant risk for morality as that of patients who were normonatremia. i.e., Normal BMI: RR: 2.08, p-value=0.047 & Over weight: RR:2.92, p-value=0.001

Sato N and his colleagues reported that the rates of death were significantly higher in patients with hyponatremia, 15.0%, compared to 5.3%, in those with normonatremia ($p<0.05$).[(5)]

BothGheorghiade M and Sato N findings are consistent with the results of this study showing that patients with hyponatremia had high risk for morality as that of patients without hyponatremia.

HoweverYoo BS study showed that mortality was not significantly higher in patients with hyponatremia, 18.4%, compared to 17.5%, in those with normonatremia ($p=0.730$)[6].

In another observational study of 322 AHF patients with hyponatremia at admission, Madan et al. showed that changes of sodium levels within 60 to 270 days were a strong predictor of long-term survival. [110] However, the treatment related change of sodium levels during hospitalization was not a predictor of mortality during a median follow-up duration of 20 months[12].

In contrast, Konishi et al. suggested that new onset hyponatremia during hospitalization for AHF in patients who were normonatremic at admission was related to an increase in 1-year death and cardiac events[14].

CONCLUSION

Results of this study showed that heart failure patients presenting with hyponatremia had higher risk of mortality.

REFERENCES

1. De Luca L, Klein L, Udelson JE, Orlandi C, Sardella G, Fedele F, et al. Hyponatremia in patients with heart failure. The American journal of cardiology 2005;96(12):19-23.
2. Leier CV, Dei Cas L, Metra M. Clinical relevance and management of the major electrolyte abnormalities in congestive heart failure: hyponatremia, hypokalemia, and hypomagnesemia. American heart journal 1994;128(3):564-74.
3. Gheorghiade M, Abraham WT, Albert NM, Stough WG, Greenberg BH, O'Connor CM, et al. Relationship between admission serum sodium concentration and

clinical outcomes in patients hospitalized for heart failure: an analysis from the Optimize-HF registry. European heart journal 2007;28(8):980-8.
4. Gheorghiade M, Rossi JS, Cotts W, Shin DD, Hellkamp AS, Pina IL, et al. Characterization and prognostic value of persistent hyponatremia in patients with severe heart failure in the Escape Trial. Archives of Internal Medicine 2007;167(18):1998-2005.
5. 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). The American journal of cardiology 2013;111(7):1019-25.
6. Yoo B-S, Park JJ, Choi D-J, Kang S-M, Hwang J-J, Lin S-J, 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. The Korean journal of internal medicine 2015;30(4):460-70.
7. Weintraub WS, Daniels SR, Burke LE, Franklin BA, Goff DC, Hayman LL, et al. Value of primordial and primary prevention for cardiovascular disease a policy statement from the American Heart Association. Circulation 2011;124(8):967-90.
8. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. Jama 2003;290(19):2581-
9. Rusinaru D, Tribouilloy C, Berry C, Richards AM, Whalley GA, Earle N, et al. Relationship of serum sodium concentration to mortality in a wide spectrum of heart failure patients with preserved and with reduced ejection fraction: an individual patient data meta-analysis†. European journal of heart failure 2012;14(10):1139-46.
10. Gheorghiade M, Konstam MA, Burnett JC, Jr., Grinfeld L, Maggioni AP, Swedberg K, et al. Short-term clinical effects of tolvaptan, an oral vasopressin antagonist, in patients hospitalized for heart failure: the Everest Clinical Status Trials. Jama [Multicenter Study. Randomized Controlled Trial. Research Support, Non-U S Gov't] 2007;297(12):1332-43.
11. Lee SE, Choi D-J, Yoon C-H, Oh I-Y, Jeon E-S, Kim J-J, et al. Improvement of hyponatraemia during hospitalisation for acute heart failure is not associated with improvement of prognosis: an analysis from the Korean Heart Failure (KorHF) registry. Heart 2012;98(24):1798-804.
12. Madan VD, Novak E, Rich MW. Impact of change in serum sodium concentration on mortality in patients hospitalized with heart failure and hyponatremia. Circulation: Heart Failure 2011;4(5):637-43.
13. Lu DY, Cheng HM, Cheng YL, Hsu PF, Huang WM, Guo CY, et al. Hyponatremia and Worsening Sodium Levels Are Associated With Long-Term Outcome in Patients Hospitalized for Acute Heart Failure. Journal of the American Heart Association 2016;5(3):e002668.
14. 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. Journal of cardiac failure 2012;18(8):620-5.
15. Schrier RW, Abraham WT. Hormones and hemodynamics in heart failure. New England Journal of Medicine 1999;341(8):577-85.