



IN HOSPITAL MORTALITY AND HYPONATREMIA IN PATIENTS PRESENTING WITH HEART FAILURE.

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ABSTRACT

INTRODUCTION: Hyponatremia is a common electrolyte abnormality in patients with heart failure(HF). It is independently associated with increased short-term and long-term morbidity and mortality.

OBJECTIVE: The objective of the study was to find the association between in-hospital mortality and hyponatremia in patients presenting with heart failure.

MATERIAL AND METHODS:This cohort study was conducted at Department of Cardiology, Punjab Institute of Cardiology, Lahore from 18-12-2015 to 17-06-2016 (six months). Informed consent and demographic details were taken. Then baseline investigations were done and sodium level was noted. The factors like LV ejection fraction, anemia (Hb<11.5g/dl in females and <12.5g/dl in males) and serum potassium levels (3.5-4.5mcq/L) were also noted in both the groups. Then patients were followed-up in cardiology ward for 5 days. During hospital stay, if any patient expired then in-hospital mortality was labeled. All this information was collected on a pre-designed Proforma.360 patients in each group (patients with and without hyponatremia) were studied.

RESULTS: Mean age of cases and controls was 60.66 ± 11.59 and 60.09 ± 11.96 years respectively. Among cases there were 167(46.4%) male and 193(53.6%) female patients while in control group there were 159(44.2%) male and 201(55.8%) female patients. There were 75(20.8%) cases and 30(8.3%) controls who had in hospital mortality. RR=2.50 for in hospital mortality among cases, p-value<0.001.

CONCLUSION: Hyponatremia in hospitalized patients with a diagnosis of HF, either present on admission or developing during the hospital stay, is common and independently associated with poor outcomes like short term and long mortality and other relevant co morbidities.

KEY WORDS: In-hospital mortality, serum sodium level, Hyponatremia, Heart failure

INTRODUCTION:

Heart failure (HF) is a clinical syndrome, resulting from structural or functional cardiac disorders that impair the ability of the cardiac pump to support a physiological circulation.¹

Recent evidence suggests that an epidemic of HF is emerging both in the developed and the developing countries. There is an increasing trend seen in the presentation of HF to the cardiology units along with an increasing bed occupancy rate in a developing country like Pakistan. This implies an escalating trend in hospitalization costs of HF management, necessitating serious consideration for some drastic steps for controlling the ever-growing epidemic of HF.²

Patients with HF often develop hyponatremia

(*J Cardiovasc Dis* 2018;14(1):1 - 4)

owing to the activation of many neurohormonal systems leading to decreased of sodium levels.³ The complications of HF are lengthy hospital stay, higher readmission rate and increasing morbidity apart from the eventually high mortality.

Hyponatremia, is a relatively common but ignored parameter in these patients. Hyponatremia in HF patients poses a significant overall risk as compared to those who were normonatremic.⁴ A study conducted recently showed that 24% patients with CHF develop hyponatremia.⁵

One study has found that among HF patients who had hyponatremia, in hospital mortality was 6.0% which was significantly higher than HF patients without hyponatremia i.e. 3.2% ($P<0.0001$).⁶ In another study it was reported that there is no difference in in-hospital mortality whether patients have hyponatremia (8.2%) or no hyponatremia (3.8%). The difference was insignificant ($P=0.23$).⁷

The rationale of the study was to establish the association between in-hospital mortality and hyponatremia in patients presenting with heart failure. We conducted this study to confirm that whether hyponatremia may be a risk factor for in-hospital mortality among HF patients and to

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Date of Submission : 23-12-2017
Date of Revision: 30-12-2017
Date of Publication: 05-04-2018



improve our knowledge and practice to plan management protocols of HF patients with hyponatremia to control and minimize the cause of death among HF patients.

OBJECTIVE:

The objective of the study was to find the association between in-hospital mortality and hyponatremia in patients presenting with heart failure.

MATERIAL & METHODS:

OPERATIONAL DEFINITIONS

Heart Failure: Presence of shortness of breath and impaired myocardial performance (estimated by Echocardiography as LV ejection fraction <40%). Patients with onset of symptoms during last 24 hours were included.

Hyponatremia: It was measured as sodium (natrium) <135mmol/L at the time of admission of heart failure patients.

In-hospital mortality: It was labeled if patient die within hospital stay i.e. 5 days after heart failure.

The study was conducted at Department of Cardiology, Punjab Institute of Cardiology, Lahore from 18-12-2015 to 17-06-2016 (six months). Informed consent and demographic details were taken. Sample size of 720 patients; 360 patients in each group was calculated with 80% power of test, 5% level of significance and taking expected percentage of in-hospital mortality i.e. 8.2% in HF patients with hyponatremia and 3.8% in HF patients without hyponatremia.

Patients of age 40-80 years of either gender presenting with HF(as per operational definition) with onset of symptoms during last 24 hours were included and divided into two groups.

Group I: Patients of HF with hyponatremia (as per operational definition)

Group II: Patients of HF without hyponatremia (Normal sodium level >135mmol/L)

Patients with renal diseases (creatinine>1.2mg/dl) or on hemodialysis, liver disease(AST>40IU, ALT>40IU) and patients with hypothyroidism (TSH>5IU), nephrotic syndrome (on medical record) were excluded from the study.

Total 720 patients (360 cases / 360 controls), who fulfilled the inclusion criteria, were enrolled in the study from Emergency of Punjab Institute of Cardiology, Lahore. Then baseline investigations were done and sodium level was noted. The factors like LV ejection fraction, anemia (Hb<11.5g/dl in females and <12.5g/dl in males) and serum potassium levels (3.5-4.5meq/L) were measured in both the groups. Then patients were followed-

up in cardiology ward for 5 days. During hospital stay, if any patient died, then in-hospital mortality was labeled (as per operational definition). All this information was collected on a pre-designed.

Data was entered and analyzed in SPSS version 21.0. Mean and Standard deviation was calculated for quantitative variables like age and sodium level. Frequency and percentage were calculated for qualitative variables like gender and in-hospital mortality. Relative Risk was calculated to find association between hyponatremia and in-hospital mortality. RR>1 was taken as risk of association. P-value ≤0.05 was taken as significant.

RESULTS:

Mean age of cases and controls was 60.66±11.59 and 60.09±11.96 years (Table-1) respectively. Among cases there were 167(46.4%) male and 193(53.6%) female patients while in control group there were 159(44.2%) male and 201(55.8%) female patients (Table-1). Mean BMI of cases and controls was 26.75±4.40 and 27.687±4.07 Kg/m² (Table-1). Mean sodium level among cases and controls was 119.71±6.25 and 142.56±4.22 respectively (Table-1). There were 75(20.8%) cases and 30(8.3%) controls who had in hospital mortality. RR for in hospital mortality among cases control turned out to be 2.50 which means that cases had significantly 2.50 times more chances of in hospital mortality as that of controls.i.e. RR=2.50, p-value=<0.001 (Table-2). In hospital mortality was significantly higher in patients in the age group 51-60 years and >60 years. However patients who were in the

Table-1 Baseline Demographic Variables

Variables	Cases(n=360)	Control(n=360)	P-value
Gender	Male	167(46.4%)	0.603
	female	193(53.6%)	
Age	60.66±11.59	60.09±11.96	0.516
BMI	26.75±4.40	27.68±4.07	0.003
BMI Cat-egory	Normal Weight	90(25%)	0.0061
	Over Weight	128(35.6%)	
	Obese	142(39.4%)	
Sodium Level	119.71±6.25(110-130)	142.56±4.22(136-150)	0.001

age group 40-50 years among them in hospital mortality was higher as that of controls but it did not show any statistically significance (Table-2). Among male and female patients in hospital mortality was significantly higher among cases as that of controls (Table-2). In hospital mortality was significantly higher in all BMI categories (except obese patients) in cases. i.e. Normal Weight (In Hospital mortality): Cases: 33.3% vs. Controls: 0%, Overweight (In Hospital mortality): Cases: 35.2% vs. Controls:



Table-2 In Hospital Mortality

Variables with respect to mortality		Cases (n=360)	control(n=360)	p-value
MORTALITY		75(20.8%)	30(8.3%)	0.001
gender	Male	36(21.6%)	11 (6.9%)	0.001
	female	39(20.2%)	19(9.5%)	0.003
Age groups	40-50 years	15(18.5%)	10(10.3%)	0.116
	51-60 years	22(22%)	5(5.4%)	0.001
	>60 years	38(21.2%)	15(8.8%)	0.001
BMI category	Normal weight	30(33.3%)	0(0%)	0.001
	Over weight	45(35.2%)	22(18%)	0.002
	obese	0(0%)	8(4.5)	0.011

18% & Obese (In Hospital mortality): Cases: 0% vs. Controls: 4.5% (Table-2).

DISCUSSION:

Hyponatremia in patients with CHF signifies poor prognosis and is associated with significantly higher rates of in-hospital and follow-up mortality and longer hospital stays. An incremental increase in the risk of in-hospital death, follow up mortality and re-hospitalization was reported in one study for each 3mmol/L decrease in admission serum sodium below 140mmol/L.⁸

Klein et al reported 5.9% in-hospital mortality in a similar group of patients.⁹ Another study OPTIMIZE-HF registry by Gheorghiadé et al showed a total of 3.8% in-hospital mortality in patients hospitalized with heart failure. His study reported similarly high mortality in hyponatremic group 6.0% as compared to 3.2% in normonatremic group.¹⁰ In another study it was reported that there is no difference in in-hospital mortality whether patients have hyponatremia (8.2%) or no hyponatremia (3.8%). The difference was insignificant (P=0.23).⁷

In this study in hospital mortality among patients of HF with hyponatremia was 20.8% which was a bit higher as that of reported by Liviu Klein and Gheorghiadé. However like Gheorghiadé in this study in hospital mortality was higher in patients with hyponatremia as compared to those patients without hyponatremia. i.e. In hospital mortality (with hyponatremia) 20.8% vs. (without hyponatremia) 8.3%

One study reported that the risk of death appeared to increase linearly with serum sodium levels <140mmol/L. Hyponatremia in heart failure is also associated with increased short and long term mortality as compared to normonatremia.^{11, 12}

In this study relative risk for in hospital mortality among patients of HF with hyponatremia was 2.50. Recently Ali et al, from Ethiopia in their study reported that the in hospital mortality rate was also found to be higher in those with hyponatremia than those with normal serum sodium, 11.4% vs 1.0%.¹³ The same findings were obtained in this study for patients with and without hyponatremia.

In the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) and the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF), and sodium(per 3-mEq/L decrease from 140 mEq/L), there was an OR of 1.25, 1.18, and 1.10 for in-hospital mortality, 60-day mortality, and 60 to 90 day mortality, respectively.^{8, 9}

The above mentioned 2 trails calculated OR for long term mortality however in this study relative risk was calculated for short term mortality. Relative risk for short term mortality for patient with hyponatremia was 2.50.

The increased mortality due to hyponatremia, though the magnitude of this effect varied based on the population studied, is well-documented in multiple large-scale studies from around the globe.^{9, 10, 14-17}

Indeed, the critical question is whether mild to moderate hyponatremia in HF (as well as in other chronic disorders) is simply a prognostic marker of poor outcomes as a reflection of the severity of the underlying condition or actually imparts risk contributing directly to morbidity and mortality. The prevailing view favors the former option. So it can be said that serum sodium levels in patients with heart failure and hyponatremia may serve not only as a marker for adverse clinical outcomes but also as a potential therapeutic target.

There is neither routine electrolyte assessment at the hospital nor is there any guideline addressing this issue in high-risk patients. As a result, patients hospitalized with HF who also have hyponatremia remain untreated, which in turn may contribute to poor treatment outcome.

CONCLUSION:

In hospitalized patients with a diagnosis of HF, either present on admission or developing during the hospital stay, hyponatremia is common and independently associated with poor outcomes like short term mortality and other relevant co morbidities.



Author's Contribution

MAN: Consultant incharge of the study. AS: Helped in conducting the study and analysis of data. ME: Collected the data and conducted the study. AS: Data analysis and proof reading

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