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# FREQUENCY OF HYPONATREMIA, HYPOKALEMIA AND RENAL DYSFUNCTION IN PATIENTS WITH CHRONIC HEART FAILURE

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#### Contribution

MRH,MF conceived the idea, planned the study. MHD, AH, & I did the data collection and drafted the manuscript. All the author contributed significantly in manuscript submission.

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# ABSTRACT

**Objective:** To determine the frequency of hypokalemia, hyponatremia and renal dysfunction in patients with chronic heart failure.

**Methodology:** This was a cross sectional study including patients admitted with heart failure in Department of Cardiology, Lady Reading Hospital, Peshawar. The duration of the study was eight months from January to September 2014. Sample was non-probability consecutive sampling. Diagnosis of heart failure was made on clinical examination and echocardiography. Blood sample were collected from all admitted patients for serum electrolytes and serum creatinine and results were recorded on pre-specified study proforma. Data was stored and analyzed via SPSS version 16.

**Results:** A total of 264 patients of chronic heart failure were admitted to the hospital. There were 147 (55.68%) females. Male to female ratio was 1:0.80. Mean age of the patients was  $52.25 \pm 12.55$  years with range of 26-73 years. Heart failure was more prevelant in age range of 46-60 years. Hypokalemia in chronic heart failure was observed in 65(24.6%), hyponatremia in 75(28.4%) and renal dysfunction was observed in 71(26.9%) of heart failure patients. Hypokalemia was present in 30.8%, hyponatremia in 37.2% and renal dysfunction in 24.4% of patients with 60 years of age. Gender wise distribution of hypokalemia, hyponatremia and renal dysfunction showed no association.

**Conclusion:** Hypokalemia, hyponatremia and renal dysfunction were documented in a high number of patients with chronic heart failure associated with increased mortality.

**Key Words:** Hypokalemia, Hyponatremia, Renal dysfunction, Chronic heart failure.

## INTRODUCTION

Heart failure (HF) is a complex syndrome, resulting from structural or functional cardiac disorders that impair the ability of the cardiac pump to support a physiological circulation.<sup>1</sup> Congestive heart failure affects about 2% of the western population, with prevalence increasing sharply from 1% in 40 years old to 10% above age 75 and it is the most common cause of hospitalization in patients over 65 years of age.<sup>2</sup>

Electrolyte abnormalities and renal dysfunction are common among patients with chronic heart failure (CHF) and may be caused by the disease itself or its treatment.<sup>3</sup> All patients with evidence of volume overload or a history of fluid retention should be treated with diuretics.<sup>4</sup> The minimum required dose should be used because over-diuresis exacerbates the activation of the Renin Angiotensin System and may result in prerenal azotemia and electrolyte abnormalities.<sup>5,6</sup> Hypokalemia makes ventricular myocardium more susceptible to potentially lethal arrhythmias. It has been shown that 22% patients with congestive heart failure develop hypokalemia.<sup>7</sup>Hyponatremia and renal dysfunction in patients with CHF signifies poor prognosis.<sup>8,9</sup> Hyponatremia in CHF is associated with significantly higher rates of in-hospital and follow-up mortality and longer hospital stays.<sup>10</sup> It has been shown that 24% patients with CHF develop hyponatremia.<sup>11</sup> Even mild to moderate elevations in baseline blood urea nitrogen predicts increased post discharge mortality in patients hospitalized for heart failure.<sup>12</sup>In a meta-analysis 29%CHF patients were found to have moderate to severe renal impairment.9

Electrolyte disorders including (hypokalemia, hyponatremia) and renal dysfunction is a common finding in CHF that is a frequently overlooked. These easily diagnosed abnormalities require correction with appropriate drug adjustments. As there is no local data available on the frequency of these abnormalities in CHF patients, this study will provide us data regarding the magnitude of problem in local population that could be used for risk stratification and evaluation of therapeutic strategies for heart failure patients. This will help in identification and correction of these common, treatable factors in patients with CHF.

## **METHODOLOGY**

It was a cross sectional study, conducted in the Department of Cardiology of Lady Reading Hospital, Peshawar. Duration of the study was eight months from January to September 2014.Sample size was calculated using (22%)proportion of hypokalemia with 95% confidence level and 5% margin of error under WHO software for sample size determination.<sup>7</sup> Sampling technique was non-probability consecutive sampling.

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Both male and female patients aged 14 years and above with congestive heart failure of  $\geq 6$  months duration were included. As per medical record, patients with chronic kidney disease, chronic liver disease, diabetic nephropathy and those with history of vomiting and diarrhea during the last one week, were excluded from the study.

The study was approved by the hospital ethical committee. An informed written consent were obtained. Detail medical history were taken for orthopnea, exertional dyspnea and paroxysmal nocturnal dyspnea. Then complete physical examination of the patient were done for distended neck veins, bilateral ankle edema, and bilateral lungs crepitation on chest auscultation. Blood sample were collected for serum electrolytes and serum creatinine and results were recorded on study proforma. To control the confounding variables previous medical record including discharge reports, prescriptions and investigation reports were checked and all patients with chronic kidney disease, diabetic nephropathy and chronic liver disease were excluded from the study.

Congestive heart failure was defined as patients with two or more of the following clinical features: orthopnea, exertional dyspnea, paroxysmal nocturnal dyspnea, raised jugular venous pressure, ankle oedema and lung crepitation. Hypokalemia was defined as serum potassium level of  $\leq$ 3.5mg/dl, detected by laboratory test. Hyponatremia was defined as a serum sodium level of  $\leq$  135mg/dl, detected by laboratory test. Renal dysfunction was defined as a serum creatinine of more than 1.5mg/dl, detected by laboratory test.

All the data collected with the help of proforma were entered and analyzed with SPSS version 16. Mean  $\pm$  standard deviation were calculated for continuous variables like age. Frequency and percentages were calculated for categorical variables like gender, hypokalemia, hyponatremia, and renal dysfuntion. Hypokalemia, hyponatremia and renal dysfunction were stratified among age and gender to see the effect of modification. All the results were presented as tables and graphs wherever needed.

## RESULTS

A total of 264 patients of chronic heart failure were included in the study. There were 147 (55.68%) females and 117(44.32%) males. Male to female ratio was 1:0.80.Mean age of the patients was  $52.25 \pm 12.55$  years with range 26-73 years. Patient's age was divided in four categories, out of which most common age group for chronic heart failure was 46-60 years . There were 17(6.4%) patients with age less than or equal to 30 years, 54 (20.5%) patients were in the age range of 31-45 years, 115 (43.6%) were in age range of 46-60 years, 78(29.5%) presented at age more than 60 years of age (Table 1). Hypokalemia in chronic heart failure was observed in 65(24.6%) patients while hyponatremia was seen in 75(28.4%) patients . Renal dysfunction was observed in 71(26.9%) patients. (Table 2)

Age wise distribution of hypokalemia, hyponatremia and renal dysfunction in chronic heart failure showed that elderly were more affected as compared to young patients. Patients having age less than or equal to 40 years had hypokalemia in 11.8%, hyponatremia in 5.9% and renal dysfunction in 35.3%. In patients with age between 46-60 years, hypokalemia ,hyponatremia and renal dysfunction was foundin 13%, 14.8% and 27.8% of patients respectively while patients with 60 years of age had hypokalemia in 30.8%, hyponatremia in 37.2% and renal dysfunction in 24.4% patients as shown in table 3.

Gender wise distribution of hypokalemia, hyponatremia and renal dysfunction showed no association. About 24.8% of males had hypokalemia while it was found in 24.5% of female patients. Similarly hyponatremia was found in 38.5% males and 20.4% of female patients. The similar pattern was found in renal dysfunction as shown in table 4.

#### Table 1: Age Wise Distribution of the Patients in Study Population (n=264)

Age	Frequency (n)	Percentage %
<= 30.00	17	6.4
31.00 - 45.00	54	20.5
46.00 - 60.00	115	43.6
61.00+	78	29.5
Total	264	100.0

# Table 2: Frequency of Hypokalemia, Hyponatremia and Renal Dysfunction in Patients with Chronic Heart Failure (n=264)

Variables		Frequency(n)	Percentage %	
llunakalamia	Yes	65	24.6%	
Hypokalemia	No	199	75.4%	
Hyponatremia	Yes	75	28.4%	
	No	189	71.6%	
Renal dysfunction	Yes	71	26.9%	
nenal dystanction	No	193	73.1%	

#### Table 3: Age Wise Distribution of Hypokalemia, Hyponatremia and Renal Dysfunction in Patients with Chronic Heart Failure (n=264)

		Hypokalemia		Hyponatremia		Renal dysfunction	
		Yes	No	Yes	No	Yes	No
		%	%	%	%	%	%
Age (in years)	<= 30.00	11.8%	88.2%	5.9%	94.1%	35.3%	64.7%
	31.00 <u>-</u> 45.00	13.0%	87.0%	14.8%	85.2%	27.8%	72.2%
	46.00 60.00	27.8%	72.2%	32.2%	67.8%	27.0%	73.0%
	61.00+	30.8%	69.2%	37.2%	62.8%	24.4%	75.6%

Table 4: Gender Wise Distribution Hypokalemia, Hyponatremia and Renal Dysfunctionin Patients with Chronic Heart Failure (n=264)

		Hypokalemia		Hyponatremia		Renal dysfunction	
		Yes No		Yes No		Yes No	
		%	%	%	%	%	%
Gender	Male	24.8%	75.2%	38.5%	61.5%	30.8%	69.2%
	Female	24.5%	75.5%	20.4%	79.6%	23.8%	76.2%

#### DISCUSSION

Although HF manifests primarily with cardiopulmonary symptoms, hyponatremia is very common in this patient population. In fact, hyponatremia (variably defined as serum sodium <1342–136mmol/L) is present in over 20% of patients admitted to hospital with HF.<sup>13,14</sup>

Not only is it a common occurrence, but it has repeatedly been shown to be a marker of increased mortality in the HF population.<sup>14,15</sup> In the general population, diuretic-induced hyponatremia is very common, with thiazides accounting for the 63% of the cases of severe hyponatremia, loop diuretics for 6%, and spironolactone for 1%.<sup>16</sup>

The most powerful predictor of cardiovascular mortality was pretreatment serum Na, with hyponatremic patients having a substantially shorter median survival than patients with a normal serum Na (164 versus 373 days, p = .006). Similarly, in the Outcomes of a Prospective Trial of IntravenousMilrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) study, both in hospital and 60-day mortality rates were highest for patients with the lowest admission serum sodium.<sup>17</sup>

In the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE HF) registry, patients with hyponatremia had significantly higher in-hospital and follow-up mortality rates and longer hospital stays.<sup>10</sup> In this study, for each 3 mmol/L decrease in serum Na below 140mmol/L at admission, the risk of in-hospital mortality and follow-up mortality increased by 19.5% and 10%, respectively. More recently, the importance of persistent hyponatremia in HF patients was described in a cohort of patients enrolled in the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) .<sup>18</sup> Hypokalemia generally is most pronounced and problematic in patients with advanced CHF receiving aggressive diuretic therapy and with greatest activation of the reninangiotensin system.<sup>19-21</sup>

While the elevation of plasma renin increases the renal loss of potassium by stimulating via angiotensin II the synthesis and release of aldosterone, data from animal models indicate that elevated serum potassium can directly inhibit the reninangiotensin-aldosterone system by blunting renin release and modulating vascular responsiveness to angiotensin,<sup>22-24</sup>

Thus, one might speculate that hypokalemia potentiates continued activation of the renin-angiotensin-aldosterone in CHF. Potassium also modulates the activity of the sympathetic nervous system; when elevated, potassium enhances there uptake of norepinephrine by sympathetic nerve terminals.<sup>25,26</sup>

For these reasons, potassium in CHF likely has an important role in heamodynamic regulation and, perhaps, myocardial

protection. These data might also explain why intracellular levels of potassium can be normalized in CHF patients in whom cardiac compensation and lower levels of neurohormonesue achieved with proper therapy, while often remaining low in the CHF patients with refractory symptoms<sup>19-21,27-29</sup>

Chronic renal failure (CRF) and CHF in an individual patient poses many management problems. The most common causes of CRF are diabetes, hypertension, glomerulonephritis and polycystic kidney disease. Cardiovascular disease is the leading cause of morbidity and mortality in patients requiring renal replacement therapy, accounting for all most 50% of deaths.<sup>30,31</sup> Standard risk factors for cardiovascular disease such as hypertension, diabetes, smoking, dyslipidaemia and preexisting atherosclerotic vascular disease are also risk factors for progressive renal dysfunction. <sup>31,32</sup> In addition to these 'traditional' risk factors, renal failure itself may accelerate development of cardiovascular disease and worsen prognosis in heart failure. Myocardial dysfunction is common in individuals with progressive renal dysfunction, with up to 80% of patients having an abnormal echocardiogram prior to initiation of dialysis, and over 30% of patients have evidence of congestive heart failure at onset of dialvsis.32,33

#### CONCLUSION

Hypokalemia, hyponatremia and renal dysfunction are easily identifiable clinical entities and are frequent in patients with chronic heart failure. Further studies are necessary to quantify the impact of these in patients with heart failure.

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