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Vikas Sunder, MD
Thomas Jefferson University

Rene Alvarez, MD
Temple University

Evan Carabelli, MD
Temple University

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Vikas Sunder MD, Sidney Kimmel Medical College at Thomas Jefferson University

Rene Alvarez MD, Lewis Katz School of Medicine at Temple University

Evan Carabelli MD, Lewis Katz School of Medicine at Temple University

Corresponding Author: Vikas Sunder MD

833 Chestnut Street Suite 220

Philadelphia, PA 19107

Email: Vikas.Sunder@Jefferson.edu

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Abstract:

Background: Hyponatremia, defined by a serum sodium concentration less than 135 mEq/L, is seen in approximately 25% of patients admitted with congestive heart failure (CHF). Hyponatremia on admission has been shown to increase in-hospital mortality and to be an independent predictor of 6month mortality. Prior work has shown that CHF patients with hyponatremia on admission are more likely to be Caucasian. Given its prognostic significance, hyponatremia and its association with patient characteristics warrants further study

Methods: We queried for unique admissions to Temple University Hospital between 2011 and 2015 with a DRG code of "291-293" to represent a heart failure admission. We

identified admissions that had a first sodium lab value after admission available. Chi-square tests were performed to examine association between first Na<135 mEq/L and ethnicity, gender, or ethnic/gender sub-group. Statistical significance was defined as $p<0.05$.

Results: 884 admissions were identified by ethnicity as either "African-American", "Caucasian (Non-Hispanic)" or "Hispanic". There was no association between first Na<135 mEq/L and ethnicity (Chi-squared=2.31; p=0.31). 976 admissions were identified as either "male" or "female". There was no association between hyponatremia on admission and gender (Chi-squared=1.17; p=0.27). 768 patient admissions could be classified by both ethnicity and gender. The association between hyponatremia on admission and ethnic/gender sub-group did not achieve statistical significance (Chi-squared=9.49; p=0.09).

Conclusion(s): In conclusion, our study demonstrates no statistically significant association between hyponatremia and the patient characteristics ethnicity and gender in a small sample of heart failure admissions. There was a trend toward a lower proportion of "African-American/Female" admissions having hyponatremia.

Introduction: Heart failure is a complex clinical syndrome that affects more than 5.7 million Americans and more than 23 million people worldwide. [1] For several decades now, hyponatremia, defined by a serum sodium concentration less than 135 mEq/L, has been recognized as a not uncommon electrolyte abnormality in patients with congestive heart failure (CHF).[2] Patients with CHF and hyponatremia have been shown to exhibit neurohormonal upregulation. Increases in sympathetic stimulation and activation of the renin angiotensin aldosterone system cause constriction of renal vasculature and sodium and water retention.[3] Studies have shown that approximately 20-25 percent of patients

admitted with CHF have hyponatremia at baseline.[2] Hyponatremia can develop in an additional 15-25 percent of patients during decongestive treatment.[4] Baseline hyponatremia at time of admission has been shown to be an independent predictor of 6-month mortality in CHF patients.[2,5-6] Baseline hyponatremia has also been associated with an increase in in-hospital mortality and early post-discharge mortality.[5-6] What has to be clarified is whether there is an association between CHF patient characteristics and likelihood of having baseline hyponatremia. Analysis of the OPTIME-CHF registry showed that patients with baseline hyponatremia were more likely to be Caucasian, but without further investigation.[6] Heart failure does not affect patients of different ethnicities in the same manner. African Americans, although a heterogeneous patient group, are disproportionately affected by heart failure and have not derived the same treatment benefit as Caucasian patients.[7] Given the disparity in clinical impact, the purpose of this study is to examine the association between hyponatremia (Na<135 mEq/L) and the patient characteristics ethnicity and gender in a sample of acute heart failure admissions to further understanding of the heart failure syndrome.

Methods: This study was approved by the Institutional Review Board at Temple University Hospital.

Administrative data on all patients admitted to Temple University Hospital between August 2011 and July 2015 was drawn from the Mckesson system maintained by TUH. This data was merged with clinical data from the EPIC clarity system which contained laboratory results on all inpatients in this timeframe.

All patients included in analysis were greater than 18 years. We created a crosswalk of real identifiers with pseudo-identifiers so the analytical data set did not contain names or medical record numbers. The data was stored on a protected TUcloud server and uploaded

into directly Microsoft Access for analysis. We queried for all admissions with a DRG code of “291-293” for a heart failure related diagnosis. We identified unique admissions using non-duplicate dates of admission and discharge. We then queried the admissions that had a first sodium lab value after admission available. We used the identifiers “ethnicity” and “gender” to further categorize the data for statistical analysis. Chi-Square tests were performed to look for association between first Na<135 mEq/L and race, gender, or race/gender subgroup. All statistical analyses were performed with SAS 9.4 (SAS Institute, Cary, NC). Statistical significance was defined as $P < 0.05$. There was no adjustment for multiple comparisons.

Results:

1954 unique CHF admissions were identified. Of these, 976 admissions had a first sodium lab value after admission available through the merged data set.

Table 1 contains the percentage of patients of each ethnicity, gender, and ethnic/gender subgroup admitted with a first Na<135 mEq/L

884 patient admissions were identified by ethnicity as either "African-American", "Caucasian (NonHispanic)" or "Hispanic". 123 of these admissions had baseline hyponatremia (first Na<135 mEq/L). There was no statistically significant association between baseline hyponatremia and ethnicity (p=0.315).

976 admissions were identified as either "male" or "female". 154 of these admissions had baseline hyponatremia. There was no statistically significant association between baseline hyponatremia and gender (p=0.278).

768 patient admissions could be classified by both ethnicity and gender. 115 patients had baseline hyponatremia. The association between baseline hyponatremia and ethnic/gender sub-group did not reach statistical significance (p=0.091).

Discussion:

This study demonstrates no statistically significant association between admission hyponatremia and the patient characteristics ethnicity and gender in a small sample of acute heart failure admissions. There was a trend in our data toward a greater proportion of Caucasian patient admissions having hyponatremia at baseline. This trend is in line with prior study of baseline hyponatremia and heart failure.[6] There was also a trend toward a lower proportion of "African-American/Female" admissions having baseline hyponatremia as compared to other ethnic/gender sub-groups. Although there was no statistically significant association, further investigation of this trend using a larger sample size is needed.

There is a clear disparity in the clinical impact of the heart failure syndrome. African Americans have an increased risk of developing heart failure despite adjusting for the higher prevalence of CHF risk factors.[8] African Americans have more than twice the rate of hospitalization for heart failure compared to Caucasians.[9] Hispanic patients have similarly been shown to have a higher rate of hospitalization than Caucasians. Even among a commercially insured population with few barriers to care, African American patients have been shown to have a higher incidence of heart failure and a higher rate of hospitalization after diagnosis.[10] Further study is needed to elucidate the pathophysiology

of heart failure in different ethnic patient populations and the dynamic interplay between vasopressin and heart failure.

Hyponatremia may not simply be a prognostic indicator or marker of disease severity, but a contributor to the pathophysiology of the heart failure syndrome.[2] Admitted CHF patients with baseline hyponatremia could thus represent a population with a pathophysiology that differs from that of normo-natremic patients. Additional research may be needed to determine whether vasopressin antagonists, which are known to normalize serum sodium levels, are associated with improved clinical outcomes in specific patient populations. Future work should be directed at the level of vasopressin or copeptin, a fragment of vasopressin precursor, in different patient populations to identify which patients would theoretically benefit the most from vasopressin antagonist therapy. Measuring vasopressin levels allows us to examine the basis of the effect of vasopressin antagonists as previous studies have not done so.[11]

This study has several limitations. For one, it was conducted using admissions to a single academic medical center whose patient population is predominantly African American. Also, it must be stated that the African-American, Hispanic, and Caucasian populations each consist of a very heterogeneous patient group. Race, after all, has been said to be a sociopolitical construct having no scientific basis. However, there may be some differences in how patient populations are affected by heart failure and those differences should be explored in the best interest of patient care. Another limitation of the study is that only about half of the identified heart failure admissions did not have first sodium after admission available in our merged data set, thereby limiting our sample

size. Further studies examining the association between baseline hyponatremia and patient characteristics should be a conducted with a larger sample of CHF patients.

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Table 1: Proportion of Patients with Hyponatremia at time of Admission (

Patient Characteristic			
Ethnicity	Total Admissions	First Na<135 mEQ/L	Percentage with First Na<135mEQ/L
African American	637	79	12.4%
Hispanic	147	27	15.5%
Caucasian(Non-Hispanic)	100	17	17.0%
		P=0.315	
Gender			
Male	527	77	14.6%
Female	449	77	17.1%
		P=0.278	
Ethnic/Gender Sub-group			
African American/Male	330	41	12.4%
Hispanic/Male	99	15	15.2%
Caucasian(Non-Hispanic)/Male	53	7	13.2%
African American/Female	307	32	10.4%
Hispanic/Female	47	12	25.5%
Caucasian(Non-Hispanic)/ Female	47	8	17.1%
		P=0.091	