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Prevalence of Alzheimer Disease in Hospitalized Patients with Congestive Heart Failure

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Abstract

Background: Alzheimer's disease (AD) may be the most critical medical condition of the 21st century in part because it affects more than 5 million Americans, including one out of eight Americans aged 65 or older, and nearly half of those being over the age of 85. It is also recognized that cardiovascular disease (CVD) risks can catalyze the development of AD. AD and congestive heart failure (CHF) often occur together and thus increase the cost of care and health resources. We investigated the prevalence of AD in patients hospitalized with CHF. In addition, factors that affect the outcomes of this special population were determined.

Methods: Data from the National Inpatient Samples (NIS) were extracted and analyzed using ICD 9 codes (CHF 428, PD 331) for the main diagnosis. For continuous variables, we calculated the mean and standard deviations and evaluated significant differences of these factors by Alzheimer disease status using the t-test. For categorical variables, we obtained the counts (proportions) and evaluated significant differences using the Chi-square and Fisher's exact test Propensity score was utilized to match age, gender and race using logistic model for hospital death and generalized linear model for length of stay (LOS) and hospital charges.

Results: The overall characteristics of matched participants with CHF and AD status showed that average age of inpatients was ~84 (SD=6.31). The prevalence of inpatients with both CHF and AD was significant ($p < .0001$) for females, 62.91% (n = 12,054) and for males, 37.09% (n = 7,107). White patients with CHF and AD were predominant with 76.20% (14,600) when compared with other races. While diabetes (26.05%), obstructive sleep apnea (5.67%), morbid-obesity (3.36%) were prevalent for inpatient without AD, renal insufficiency (3.60%) and stroke (2.10%) were prevalent in patient with AD. Patients with low income ($1 - $38,999) were admitted more with 6,290 (33.40%) than those with higher income ($39,000 - > $63,000). Finally, patient with CHF and AD stayed longer with higher mortality rates than those without AD, $p< 0.0001$. Age and race significantly affected all the outcomes, $p< 0.0001$ while gender showed significance for hospital death and charges ($p< 0.0001$). Hospital death was not affected by patient's household income but its interesting to note that LOS was affected by patients with household income between $39,000 - $62,999 and hospital charge by patients with higher household incomes from $48.000 and above. Stroke was the only comorbidity that significantly ($p<0.0001$) affected hospital death while diabetes significantly ($p< 0.0001$) affected LOS. However, diabetes, stroke and morbid obesity significantly ($p< 0.0068$) influenced the patient hospital charges. For hospital characteristics, it is important to note that LOS and hospital charge were significantly ($p =0.0001$) affected irrespective of the hospital teaching status.

Conclusion: The prevalence of CHF and AD may be higher in females than males, with white patients admitted more often than other races. Patient age, gender, comorbidities, economic status, LOS and mortality rates play a significant role in the prevalence of CHF and AD. In addition, this study has confirmed that Alzheimer's disease and CHF may occur together and increase the cost of care and health resource utilization. Impaired cognition in AD patients may lead to more frequent hospital readmissions with CHF patients and even more for patients with comorbidities such as diabetes, stroke and morbid obesity. Readmission leads to increase in length of stay and increased mortality rates for this population.

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Introduction

Health care expenditures have maintained a relatively stable share of the Gross Domestic Product since 2009, reaching 17.5 percent in 2014 [1]. Alzheimer's disease is increasingly an epidemic in the United States, in the 21st century in part because it affects more than 5 million Americans, including one out of eight aged 65 or older. Aging of the population with proportionate increased disease burden, will escalate medical care cost for AD far beyond the ~$200 billion/year to treat ~5 million cases of AD in the US [1]. It is also recognized that cardiovascular disease (CVD) can catalyze the development of AD.

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There are approximately 5.1 million patients with congestive heart failure (CHF) in the United States, who account for 1 million hospital admissions, 6.5 million hospital days, and $37.2 billion in healthcare expenditure. The cost derives mainly from inpatient services including length of stay (LOS) [2]. The average of each episode of hospitalization was estimated at $10,775 [3]. The impetus has been to decrease LOS while improving patient outcomes [2].

Highest-cost were associated with urban and teaching hospitals. Highest-cost of hospitalization was also associated to 5 times longer LOS, 9 times more expensive and higher in-hospital mortality (5.6% vs 3.5%) when compared with lowest- cost hospitalizations [3]. Among Medicare beneficiaries hospitalized for congestive heart failure, 30-day all-cause readmission was associated with a higher risk of subsequent all-cause mortality, higher number of cumulative all-cause readmission, longer cumulative length of stay, and higher cumulative cost [4]. Older patients, with median age of 72 years hospitalized with acute CHF, had a higher prevalence of comorbidities, including hypertension and atrial fibrillation [5]. It was reported that plasma urea nitrogen and hemoglobin levels were predictors of 90-days mortality in the younger patients, while respiratory rate and albumin levels were associated with 90- days mortality in the older patients [5]. Extremely high brain natriuretic peptide (BNP) upon hospital admission is an independent risk factor of elevated LOS and 6-month all-cause-mortality in CHF [6]. In patients with CHF and reduced ejection fraction (HFrEF) and anemia presents a higher risk of mortality and morbidity in older males, with renal dysfunction [7]. Dyspnea at rest is associated with higher 30-day mortality and CHF readmission, longer length of stay, and higher healthcare costscompared with dyspnea with moderate activity [8].

Cognitive deficits in executive function, processing speed, and memory are common among older adults patients hospitalized with acute decompensated heart failure (ADHF) [9]. However, healthcare providers do not routinely record cognitive changes [10]. Recognition and documentation of these deficits is paramount for the clinical management of these high-risk patients [9,10]. Women hospitalized with acute heart failure present differently than men, more often, with preserved left ventricle ejection fraction (LVEF) and higher rates of hypertension, diabetes, and depression. Also, diuretics were less intensively utilized in women than men. However, risk-adjusted 180-day post-hospital discharge outcomes were not different between men and women [11].

Data from Centers for Medicare & Medicaid Services beneficiaries hospitalized with CHF indicate that socio-economic status (SES) characteristics have a modest association with post-discharge outcomes. Median household income was inversely associated with a 30-day mortality risk. When SES is not included in the model, Hispanics and African Americans had higher 30-day re-admission rates than Whites [12,13]. Asians had similar rates with whites. However, when SES is included in the model, Hispanics and African Americans had modestly lower 30-day and 1-year mortality rates than Whites, but there were similar 30-day re-hospitalization rates among these ethnic groups [12,13]. A recent randomized trial of 2331 patients, with CHF and an ejection fraction (EF) ≤ 35 showed that compared to Whites, African-Americans patients (N=749) tended to be younger, had lower SES, higher rates of hypertension and diabetes with less ischemic etiology [8]. Additionally, African Americans had increased prevalence of modifiable risk factors, lower exercise performance and higher rate of CHF related re-hospitalization, than Whites [8].

with cardiovascular disease alarming growth rate and lack of a cure, Alzheimer diseases (AD) may become one of the most critical medical conditions of the twenty-first century. This devastating neurological condition progressively destroys one's memory and ability to think. Alzheimer's now affects more than 5 million Americans, including one out of eight Americans aged 65 or older and nearly half of those over the age of 85. Someone in the United States develops Alzheimer's every 72 seconds, and according to current projections, by 2050 a new case of Alzheimer's disease will emerge every 33 seconds. Alzheimer's disease and heart failure often occur together and thus increase the cost of care and health resource utilization. There is little or no study done on the prevalence of AD inpatient hospitalized with CHF in 2012. The major risk factor for the development of Alzheimer's disease (AD) is increasing age [14]. Other known risk factors include family history, hypertension and hypotension, high cholesterol levels, low levels of physical activity and of education, obesity, and the presence of epsilon 4 alle of the apolipoprotein E gene (APOE4) [15-17]. A recently proposed risk factor for AD is CHF [18]. There is little or no study done on the effects of patients and hospital characteristics on the outcomes of inpatient with CHF and AD. Alzheimer's disease and CHF often occur together and thus increases the cost of care and health resources. The purpose of this study is to determine the prevalence of CHF and AD, impacting factors including the costs of hospital stays in a National Inpatient Sample. The results from this study may provide guidance for reducing frequent readmission, length of stay, total charges and mortality rate in this special population.

Research Designs and Method

This study is a secondary analysis that utilizes data from the HCUP Nationwide Inpatient Sample (NIS). The HCUP manages the health care datasets and related software tools and products developed through a Federal-State-Industry partnership and sponsored by the Agency for Healthcare Research and Quality (AHRQ). HCUP aggregates the data collection efforts of State data organizations, hospital associations, private data organizations, and the Federal government to create a national information resource of patient-level health care data (HCUP Partners). HCUP includes acute care hospital data in the United States, with all-payer (source of payment for the hospital length of stay). This database has all-payer data on hospital inpatient stays from selected states, however only few studies have focused on CHF and AD, hospital characteristics and reported studies are mainly on cost effectiveness [12-14] with few in longitudinal and population based studies [15].

Study population: In this study, data of patients with CHF were selected from the 2012 hospital discharge information according to hospital and patients' characteristics such as age, gender, race, insurance, family median income, comorbidities, hospital location and teaching status and hospital charge. This range was selected due to data availability. Selection of samples was aided by the existing NIS database and ICD-9-CM [16].

Inclusion and Exclusion Criteria: The NIS data samples were selected and extracted on the basis of the following criteria: (a) inpatient diagnosed with CHF and related comorbidities (b) inpatient admitted to nonfederal hospitals, (c) age 55 years and above. The exclusions were (a) pediatric inpatients and age below 55 years (b) discharges from federal and government hospitals. Figure 1 showed the inclusion and exclusion criteria used for the extraction of inpatient CHF with or without AD by age, gender and rac (e) [17,18].

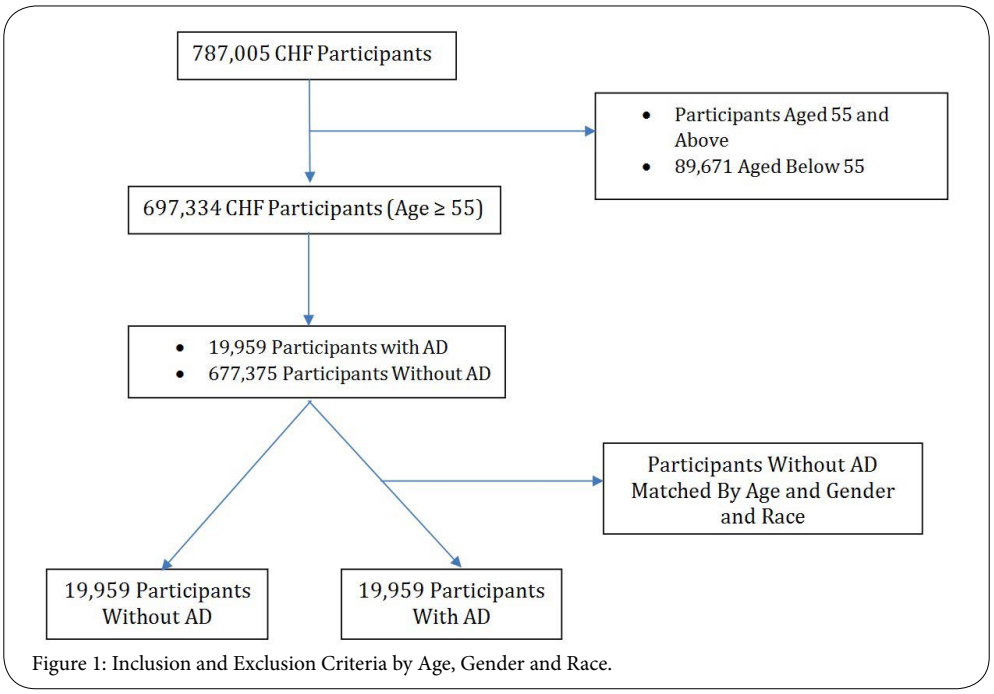

Figure 1: Inclusion and Exclusion Criteria by Age, Gender and Race.

Patient Measures: Measures were as follows: Age (55 years and above); gender (male, female); race (white, black, others); income ($1,000-38,999; $39,000-$47,999; $48,000-$62,999; $63,000 and above); insurance (Medicare, Medicaid, private including HMO, Others); primary diagnosis (CHF and AD); comorbidities (diabetes, stroke, obstructive sleep apnea, morbid obesity, renal insufficiently); hospital characteristics (rural, urban non-teaching, urban-teaching).

Statistical Analysis

In this study, descriptive statistics were computed to assess baseline clinical and demographic factors associated with AD among participants with CHF. For continuous variables we calculated the mean and standard deviations and evaluated significant differences of these factors by Alzheimer's disease status using the t-test. For categorical variables we obtained the counts (proportions) and evaluated significant differences using the Chi-square and Fisher's exact test (Table 1). We evaluated the relationship between the primary outcomes (Hospital Charges, Length of Stay, Mortality Rates) and Alzheimer disease status using multiple regression analysis. Propensity score was utilized to match participants with age, gender and race using logistic model for hospital death and generalized linear model for LOS and hospital charges. Univariate analysis was performed to assess potential confounders for the association between AD Status and the outcome measures. The factors that were significantly associated with the primary outcome measures and AD status (primary independent) were included in the multivariate stepwise regression analysis (Table 2). An interaction test and graphical plots were performed to assess the association between diabetes and AD status with the outcome measures. P-value less than 0.05 were considered statistically significant and confidence intervals (CI) were calculated at the 95% level (Table 3). Data analysis was conducted using the Statistical Analysis System (SAS) software 9.3 (SAS Institute, Cary, NC) and Statistical Analysis and Graphics (NCSS 9.0.7, Kaysville, UT) [19].

Results

Participants with CHF by AD status

The overall characteristics of matched participants with CHF and AD status showed that average age of inpatients was ~84 (SD=6.31). The prevalence of inpatients with both CHF and AD was significant ($p < .0001$) for females, 62.91% (n = 12,054) and for males, 37.09% (n = 7,107). White patients with CHF and AD were predominant with 76.20% (14,600) when compared with other races. While diabetes (26.05%), obstructive sleep apnea (5.67%), morbid-obesity (3.36%) were prevalent for inpatient without AD, renal insufficiency (3.60%) and stroke (2.10%) were prevalent inpatient with AD. Patients with low income ($1 - $38,999) were admitted more with 6,290 (33.40%) than those with higher income ($39,000 - > $63,000). Results of the hospital characteristics after matching showed that more patients with CHF and AD were discharged from urban non-teaching hospitals (42.97%), while patients without AD were discharged more from urban teaching hospitals (43.58%). Finally, our results showed that the LOS and hospital death were more among the patient with AD than those without, p = 0.0002 (table 1).

Mortality rate, length of stay and total charge: These results showed differences between patient with AD and those without in both adjusted and unadjusted analysis of the outcomes when matched with age, gender and race as shown in table 2. Logistic analysis for hospital death showed Odds (1.163, $p = 0.0002$) for unadjusted and Odds (1.151, $p = 0.0006$) for adjusted. For LOS unadjusted analysis showed Beta (0.496, $p = < 0.0001$) and adjusted Beta (0.533, $p = 0.0001$). While hospital charge showed Beta (-3144.98, $p = <.0001$) and adjusted Beta (-2415.43, $p = 0.0001$).

Patient and hospital characteristics by outcomes: Finally, patient with CHF and AD stayed longer with higher hospital deaths than those without AD, $p< 0.0001$. Age and race significantly affected all the outcomes while gender showed significance for hospital death and

Characteristics	No AD (N = 19,161)	AD (N = 19,161)	P value
Age – yrs.	83.75 (6.31)	83.75 (6.31)	1.000
Gender (%)			
Male	7,107 (37.09%)	7,107 (37.09%)	1.000
Female	12,054 (62.91%)	12,054 (62.91%)	
Race (%)			
White	14,600 (76.20%)	14,600 (76.20%)	1.000
Black	2,267 (11.83%)	2,267 (11.83%)	
Hispanics	1,440 (7.52%)	1,440 (7.52%)	
Asian or Pacific Islander	329 (1.72%)	329 (1.72%)	
Native Americans	90 (0.47%)	90 (0.47%)	
Others	435 (2.27%)	435 (2.27%)	
Hospital Death (%)			
Yes	1,219 (6.36%)	1,403 (7.32%)	0.0002
No	17,941 (93.64%)	17,757 (92.68%)	
Length of Stay (IQR)	4 (3, 7)	5 (3, 8)	<.0001
Total Charge (IQR)	26,684 (14,627, 50,726)	26,172 (14,866, 48,001)	0.014
Median Household Income (%)			
$1 – $38,999	5,659 (30.02%)	6,290 (33.40%)	<.0001
$39,000 – $47,999	4,684 (24.85%)	4,529 (24.05%)	
$48,000 – $62,999	4,429 (23.49%)	4,277 (22.71%)	
$63,000 or More	4,079 (21.64%)	3,738 (19.85%)	
Renal Insufficiency (%)	656 (3.42%)	690 (3.60%)	0.345
Diabetes (%)	4,992 (26.05%)	4,896 (25.55%)	0.262
Stroke (%)	345 (1.80%)	403 (2.10%)	0.032
Morbid Obesity (%)	644 (3.36%)	340 (1.77%)	<.0001
Obstructive Sleep Apnea (%)	1,087 (5.67%)	657 (3.43%)	<.0001
Hospital Characteristics			
Rural	2,773 (14.47%)	3,381 (17.65%)	<.0001
Urban Non-Teaching	8,038 (41.95%)	8,233 (42.97%)	
Urban Teaching	8,350 (43.58%)	7,547 (39.39%)	

Values are Mean (SD) for Continuous Variables and Count (%) for Categorical Variables.
For normally distributed variables p values were computed with t-tests; Wilcoxon Rank-sum Test for non-normally distributed.
Chi-square test for Categorical Variables.
AD = Alzheimer's Disease; Participants are matched by Age, Gender and Race.

Table 1: General Characteristics of the CHF Patients.

	Alzheimer' Disease Status (AD vs. No AD)							
	Unadjusted Analysis			Adjusted Analysis				
Logistic Model	Odds	95% C.I.	P	Odds	95% C.I.	P		
Hospital Death	1.163	1.074	1.259	0.0002	1.151	1.062	1.248	0.0006
GLM Model	Beta	SE	T	P	Beta	SE	T	P
Length of Stay	0.496	0.065	7.650	<.0001	0.533	0.065	8.150	<.0001
Total Charge	-3144.98	586.24	-5.360	<.0001	-2415.43	578.51	-4.180	<.0001

Unadjusted and Adjusted Association of Outcomes and Alzheimer's Disease Status
Hospital Death: Model = Logistic Regression Analysis; Odds, 95% Confidence Interval; P-values
Length of Stay and Total Charge: Model = Generalized Linear Model; Estimate, Standard Error, T-value, P-value
AD = Alzheimer's Disease; Participants are matched by Age, Gender and Race;

Table 2: Hospital Death, Length of Stay and Total Charge.

Characteristics	Hospital Death				Length of Stay			Total Charge		
	Odds	95% C.I.		P	Beta	SE	P	Beta	SE	P
Age – yrs.	1.033	1.026	1.041	<.0001	-0.044	0.005	<.0001	-743.78	47.65	<.0001
Gender (Female vs. Male)	0.823	0.757	0.894	<.0001	-0.111	0.068	0.104	-2619.37	603.89	<.0001
Race										
Whites vs. Blacks	0.954	0.836	1.088	0.002	-0.313	0.105	0.003	-3105.40	935.98	0.0009
Hispanics vs. Blacks	1.018	0.842	1.231	0.154	0.117	0.153	0.444	17120.05	1357.96	<.0001
Asians vs. Blacks	1.392	1.040	1.863	0.115	0.276	0.267	0.301	24677.45	2424.82	<.0001
Native Americans vs. Blacks	1.365	0.803	2.320	0.432	-0.548	0.485	0.259	-9285.34	4353.68	0.033
Others vs. Blacks	1.229	0.934	1.616	0.551	0.353	0.238	0.137	9053.55	2095.23	<.0001
Median Household Income										
$1 – $38,999)	ref	ref	ref	ref	ref	ref	ref	ref	ref	Ref
$39,000 – $47,999	0.950	0.851	1.061	0.754	-0.182	0.090	0.042	-787.44	792.02	0.3201
$48,000 – $62,999	0.907	0.806	1.020	0.125	-0.292	0.094	0.002	1670.43	832.64	0.0448
$63,000 or More	0.990	0.877	1.117	0.444	-0.164	0.099	0.098	6166.00	879.16	<.0001
Renal Insufficiency	0.945	0.759	1.177	0.614	-0.342	0.177	0.053	-3335.82	1558.90	0.0324
Diabetes	0.916	0.833	1.008	0.073	-0.341	0.075	<.0001	-2420.50	664.62	0.0003
Stroke	2.020	1.619	2.520	<.0001	0.410	0.236	0.083	7288.05	2090.98	0.0005
Morbid Obesity	0.842	0.611	1.161	0.293	0.395	0.215	0.066	5128.35	1893.28	0.0068
Obstructive Sleep Apnea	0.827	0.657	1.041	0.105	0.028	0.162	0.862	432.71	1440.94	0.764
Urban Non-Teaching vs. Rural	0.857	0.758	0.970	0.046	0.662	0.103	<.0001	20083.13	902.03	<.0001
Urban Teaching vs. Rural	0.879	0.777	0.995	0.250	0.878	0.103	<.0001	19501.57	906.59	<.0001

Hospital Death: Model = Logistic Regression Analysis; Odds, 95% Confidence Interval; P-values
Length of Stay and Total Charge: Model = Generalized Linear Regression Model; Estimate, Standard Error, T-value, P-value
AD = Alzheimer's Disease; Participants are matched by Age, Gender and Race; ref = reference group

Table 3: Hospital Death, Length of Stay and Total Charge

charges ($p< 0.0001$). Hospital death was not affected by patient's household income but its interesting to note that LOS was affected by patients with household income between $39,000 - $62,999 and hospital charge by patients with higher household incomes from $48.000 and above. Stroke was the only comorbidity that significantly ($p<0.0001$) affected hospital death while diabetes significantly ($p< 0.0001$) affected LOS. However, it is important to note that LOS and hospital charge were significantly ($p =0.0001$) affected irrespective of the hospital teaching status. Finally, diabetes, stroke and morbid obesity significantly ($p< 0.0068$) influenced the patient hospital charges (table 3).

Discussion

Gender wise, the prevalence of AD in CHF patients appears to increase at higher rates in females than males in this study, and white patients were admitted more often than other races. Patient age, gender, economic status, LOS and mortality rates were significantly associated with comorbidities such as diabetes, obstructive sleep apnea, morbid obesity and with hospital charges observed more in CHF patients discharged from urban teaching hospitals in 2012. In addition, inpatients with CHF and AD tend to stay longer in the hospital, and experienced more hospital deaths than their counterparts without AD. However, the hospital charges showed that patients with only CHF paid more in hospital charges than those with both disorders. This may be accounted for by the high profile treatment protocol that are involved with cardiac patients, coupled with higher comorbidities (diabetes, stroke and morbid obesity) often observed to have a strong relationship with CHF than hospital charges for patients admitted with CHF and AD. However, after adjusting for age, gender and race, the results showed that hospital death was not affected by patient's household income but it is important to note that patients with CHF and AD stayed longer and were charged more irrespective of the hospital teaching status. Hence, patients with lower household income were significantly affected by LOS and hospital charge, though higher household incomes population were affected as well. Stroke was the only comorbid condition that affected hospital deaths, while diabetes affected LOS. However, of interest was the finding that diabetes, stroke and morbid obesity affected hospital charges. Finally, all patients with CHF and AD were affected by LOS and hospital charges irrespective of the teaching status of the hospital they were admitted.

Conclusion

CHF is a progressive condition that may be defined as inadequate cardiac output to meet metabolic demands. Accordingly, the prevalence of CHF increases sharply with age in up to 10% of individuals over 65 years [20] and 20% in those over 75 years [21] within the age group for AD. CHF is the most common cause of hospitalization in patients over 65 years of age [22], another age group with increased AD. Thus, this study confirms that Alzheimer's disease

and CHF may occur together, and then increase the cost of care and health resource utilization when they do. This observation is in agreement with Pressler et al. [23] and highlights the need to investigate further, the relationship between these two conditions with patient and hospital characteristics. Impaired cognition in AD patients significantly leads to more frequent hospital readmissions when patients are also diagnosed with CHF as reported by Pressler et al., [23], and even more so for patients with comorbidities such as diabetes, stroke and obesity. Readmission leads to increase in length of stay and increased mortality rates for this population. Unfortunately, patients with low SES stay are readmitted more frequently, do experience longer LOS, high mortality rates and higher hospital charges. This in turn may affect outcomes in minority communities residing in rural areas. Hence, the authors conclude that the clinical implications of this study mandates healthcare providers to regularly evaluate CHF patients for cognitive impairments, along with obesity, and diabetes to prevent stroke shown to associate with high hospital deaths and charges in patients with CHF and AD.

Competing Interests

The authors declares that they have no competing interests.

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