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Impact of comorbid heart failure among hospitalized patients with sarcoidosis: A United States population-based cohort study

Bruce Adrian Casipit [a,c,*], Kevin Bryan Lo [a,c], Carlo Gabriel Casipit [d], Abdiodun Idowu [a,c], Aman Amanullah [b,c]

[a] Department of Medicine, Einstein Medical Center Philadelphia, Philadelphia, PA, United States
[b] Department of Cardiovascular Disease, Einstein Medical Center Philadelphia, Philadelphia, PA, United States
[c] Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, United States
[d] University of Santo Tomas Faculty of Medicine and Surgery, Manila, Philippines

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ABSTRACT

Background: There is paucity of data regarding the impact of concomitant heart failure (HF) on the in-hospital outcomes among hospitalized sarcoidosis patients. We aim to investigate the factors associated with concomitant HF and its impact on in-hospital outcomes among hospitalized sarcoidosis patients.

Methods: We utilized the 2018–2020 National Inpatient Sample (NIS) Database in conducting this study. Multivariable logistic and linear regression models were used to examine the factors associated with HF and hospital-associated outcomes among patients with sarcoidosis.

Results: A total of 36,864 hospitalized patients with sarcoidosis were identified, of which 24.78 % (n = 9135/36,864) had concomitant HF. Factors associated with concomitant HF were age (aOR 1.03; 95 % CI: 1.02–1.03, p value $\leq$ 0.001), black race (aOR 1.74; 95 % CI: 1.47–2.05, p value $\leq$ 0.001), not being female (aOR 0.79; 95 % CI: 0.69–0.91, p value $\leq$ 0.001), and arrhythmias (aOR 2.50; 95 % CI: 2.10–2.98, p value $\leq$ 0.001) specifically atrial fibrillation and ventricular tachycardia. Comorbidities associated with concomitant HF in this population were hyperlipidemia, obesity, coronary artery disease, cardiac device implantation history, and chronic kidney disease stage 1–4. Concomitant HF was not an independent predictor of in-hospital mortality or length of stay (LOS). However, age (aOR 1.04; 95 % CI, 1.03–1.06; p $\leq$ 0.001) and arrhythmia burden (aOR 2.08; 95 % CI, 1.47–2.95; p $\leq$ 0.001), specifically ventricular tachycardia and fibrillation, were independently associated with in-hospital mortality among sarcoidosis patients.

Conclusion: Traditional cardiovascular risk factors were associated with concomitant HF among hospitalized sarcoidosis patients. Moreover, concomitant HF among sarcoidosis patients was not significantly associated with in-hospital mortality or LOS.

1. Introduction

Sarcoidosis is a systemic granulomatous disease of unknown etiology affecting various organ systems [1] including the heart [2,3]. In the majority of cases, patients remain asymptomatic or present with nonspecific constitutional symptoms [4]. However, among those who present with cardiovascular manifestations, only 5 % is attributable to cardiac sarcoidosis [5]. Cardiac sarcoidosis is uncommon, although it can occur in up to 25 % of patients with sarcoidosis in other organ systems [6] and is associated with fatal outcomes including death [7]. Sarcoidosis patients with concurrent cardiovascular manifestations including atrioventricular block, ventricular arrhythmias, and HF were found to have more complications with a greater risk for sudden cardiac death [8,9]. The sarcoid inflammatory granulomas infiltrate the myocardium causing infiltrative cardiomyopathy which can present as HF and alters the myocardial conduction system leading to atrioventricular blocks and tachyarrhythmias due to increase automaticity from myocardial granuloma scarring [10]. The degree of left ventricular dysfunction is one of the most important predictors of prognosis in patients with symptomatic sarcoidosis with cardiac manifestations [11]. Due to the paucity of data regarding the burden of HF among hospitalized patients with sarcoidosis and its impact on in-hospital outcomes,

* Corresponding author at: Einstein Medical Center Philadelphia, 5501 Old York Road, Philadelphia, PA 19141, United States.
E-mail address: Bruce.Casipit@jefferson.edu (B.A. Casipit).

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we conducted a study utilizing the National Inpatient Sample (NIS) database from 2018 to 2020 to investigate the prevalence of HF, factors associated with HF, and hospital-related outcomes of HF among patients with sarcoidosis. These findings will add to the literature on HF burden and its associated factors among hospitalized sarcoidosis patients, thus increasing physician awareness of the health outcomes in this population.

2. Methods

Data analyses were conducted utilizing the Health Care Utilization Project National Inpatient Sample (HCUP-NIS) database of the years 2018–2020. Briefly, the HCUP-NIS is sponsored by the Agency for Healthcare Research and Quality (AHRQ) and is the largest publicly available all-payer inpatient database in the United States that utilizes a survey design database of discharge data for inpatient hospital care from non-federal, non-rehabilitation, acute care, and short-term hospitals. In addition, it approximates about 20 % of hospital admissions and discharges which includes about 97 % of the total population. Moreover, the NIS is an annual sample of hospital discharges providing national estimates of the characteristics of the patients, diagnoses, and hospital-based procedures performed in US acute-care hospitals. All hospital discharges from the sample are recorded and weighed to ensure that they are nationally representative.

In our study population of interest, all patients aged 18 and older who were hospitalized with a diagnosis of sarcoidosis and HF during the index hospitalization between January 2018 and December 2020 were included in the analysis. We then utilized the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) to identify eligible discharge records that had sarcoidosis and HF. Stratification based on the presence or absence of HF was subsequently made (see supplementary Fig. S1). Further, comorbidities and other relevant past medical history was obtained based on the hospital discharge records containing the validated ICD-10 CM codes for the patient's diagnoses during the index hospitalization. (See Supplementary Table 1 for ICD-10-CM codes used in this study.)

The main clinical outcome of interest in this study was to investigate the factors associated with HF among hospitalized sarcoidosis patients. Secondarily, we are looking into hospital outcomes including in-hospital mortality and hospital LOS among admitted sarcoidosis patients with HF.

All date analyses performed in this study were conducted utilizing StataBE 17.0 (StataCorp, College Station, Texas). The NIS is based on a complex sampling design which employs stratification, clustering, and weighing of variables in order to provide an analysis that produces nationally representative results, variance estimates, and p values. Continuous variables were presented as median and interquartile range (IQR). Categorical variables were presented as numbers and/or percentages. Proportions were compared using the chi-square test, and continuous variables were compared using the student *t* test. Moreover, we utilized Survey univariable and multivariable logistic and linear regression analysis to calculate both adjusted and unadjusted odds ratios (ORs) for the primary and secondary outcomes. Subsequently, outcomes were adjusted for potential patient and hospital level confounders, including age, gender, race, Charlson Comorbidity Index, median income, hospital bed size, hospital location, and teaching status, insurance type, and comorbidities. The variables entered into the multivariable model were chosen based on the possible association with the outcome of interest on univariate regression analysis with P value < 0.25 and based on variable exploration using the backward elimination method of variable selection. Variables were tested for collinearity, odds ratios and beta coefficients with 95 % confidence intervals were provided as appropriate. A p value of <0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

There was a total of 36,864 hospitalized patients with sarcoidosis, of which 24.78 % (n = 9135/36,864) had concomitant HF including 3955 HFrEF and 5180 HFpEF patients during the index hospitalization. Table 1 summarizes the baseline characteristics of the study population. Among hospitalized sarcoidosis patients, the median age for those with and without concomitant HF were 67 years old (IQR, 57–75 years) and 61 years old (IQR, 52–71 years), respectively. Compared to admitted patients without HF, hospitalized sarcoidosis patients with concomitant HF were less likely to be female (59.39 % versus 63.63 %, p value $\leq$ 0.001) but were more likely to be black (49.53 % versus 43.56 %, p value $\leq$ 0.001), have more comorbidities (79.53 % versus 38.89 %, p value $\leq$ 0.001), on Medicaid (69.62 % versus 55.73 %, p value $\leq$ 0.001), admitted on the Midwestern region of the US (29.06 % versus 24.02 %, p value $\leq$ 0.001), was admitted in an urban teaching hospital (81.01 % versus 77.66 %, p value = 0.011) and have a higher prevalence of hyperlipidemia, obesity, chronic obstructive pulmonary disease (COPD), CAD, history of cardiac device implantation (Implantable Cardioverter-Defibrillator [ICD], Cardiac Resynchronization Therapy Defibrillator [CRT-D], Cardiac Resynchronization Therapy Pacemaker [CRT-P], pacemaker), CKD stages 1–4, and end-stage renal disease (ESRD). Further, hospitalized sarcoidosis patients with HF were more likely to have a higher overall arrythmia burden (22.22 % versus 7.68 %, p value $\leq$ 0.001), specifically atrial fibrillation (15.65 % versus 4.90 %, p value $\leq$ 0.001), supraventricular tachycardia (2.90 % versus 1.60 %, p value $\leq$ 0.001), ventricular tachycardia (4.60 % versus 1.26 %, p value $\leq$ 0.001), ventricular fibrillation (0.82 % versus 0.27 %, p value $\leq$ 0.001), and premature atrial complex/premature ventricular complex (0.49 % versus 0.18 %, p value = 0.032). However, regardless of the presence of HF, the study population was comparable in terms of median annual income and hospital bed-size (see Table 1).

3.2. Factors associated with heart failure among hospitalized patients with sarcoidosis

On multivariate analyses that adjusted for patient and hospital level confounders, age was found to be significantly associated with HF (aOR 1.03; 95 % CI: 1.02–1.03, p value $\leq$ 0.001). Additionally, compared to males, females were less likely to have a HF diagnosis (aOR 0.79; 95 % CI: 0.69–0.91, p value $\leq$ 0.001). Further, black patients were 74 % more likely (aOR 1.74; 95 % CI: 1.47–2.05, p value $\leq$ 0.001) to have HF when compared to their white counterparts. Furthermore, those with overall arrhythmias have higher odds (aOR 2.50; 95 % CI: 2.10–2.98, p value $\leq$ 0.001) of having HF compared to those without HF, specifically those who have atrial fibrillation (aOR 2.43; 95 % CI: 2.00–2.94, p value $\leq$ 0.001) and ventricular tachycardia (aOR 2.07; 95 % CI: 1.35–3.18, p value $\leq$ 0.001). Moreover, certain comorbidities were associated with HF among admitted sarcoidosis patients including those with hyperlipidemia, obesity, CAD, history of cardiac device implantation (ICD, pacemaker, CRT-D, CRT-P), and CKD stage 1–4 (see Table 2).

3.3. In-hospital mortality based on heart failure status

The overall in-hospital mortality rate among patients hospitalized for sarcoidosis from 2018 to 2020 was 2.89 % (n = 1065/36,864). Among those with concomitant HF, the in-hospital mortality rate was significantly higher at 4.16 % (n = 380/9135, p $\leq$ 0.001). Supplemental Table 2 shows the annual in-hospital mortality rates from 2018 to 2020 in this population. On HF subtype analysis, there was a significantly higher rate of in-hospital mortality among those with HFrEF (4.16 % versus 2.74 %, p value = 0.021) and HFpEF (4.15 % versus 2.68 %, p = 0.011) compared to those without HF. On univariate and multivariate analyses that adjusted for patient and hospital level confounders,

Table 1
Baseline characteristics of hospitalized sarcoidosis patients with comorbid heart failure.

Patient characteristics	With Heart Failure	Without Heart Failure	P-value
Number of patients	9135	27,729	–
Age at index admission, years (IQR)	67 (57–75)	61(52–71)	<0.001
Women, no. (%)	5425 (59.39)	17,644 (63.63)	<0.001
Race/ethnicity, no. (%)			
Caucasian	4085 (44.72)	13,584 (48.99)	<0.001
Black	4525 (49.53)	11,996 (43.26)	<0.001
Hispanic	275 (3.01)	1226 (4.42)	0.021
Others	250 (2.74)	926 (3.34)	0.262
Arrythmias (%)	2030 (22.22)	2130 (7.68)	<0.001
Atrial Fibrillation	1430 (15.65)	1359 (4.90)	<0.001
Supraventricular Tachycardia	265 (2.90)	444 (1.60)	<0.001
Ventricular Tachycardia	420 (4.60)	349 (1.26)	<0.001
Ventricular Fibrillation	75 (0.82)	75 (0.27)	<0.001
Premature atrial contraction/ Premature ventricular contraction	45 (0.49)	50 (0.18)	0.032
Comorbidities (%)			
Hypertension	160 (1.75)	12,614 (45.49)	<0.001
Hyperlipidemia	4915 (53.8)	11,410 (41.15)	<0.001
Diabetes Mellitus	1120 (12.26)	3824 (13.79)	0.114
Obesity	2960 (32.4)	6946 (25.05)	<0.001
Chronic Obstructive Pulmonary Disease	2020 (22.11)	3591 (12.95)	<0.001
Coronary Artery Disease	3570 (39.08)	4356 (15.71)	<0.001
Chronic Kidney Disease, stage 1–4	3390 (37.11)	5199 (18.75)	<0.001
End-stage renal disease	730 (7.99)	1276 (4.6)	<0.001
History of cardiac device implantation (ICD, pacemaker, CRT-D, CRT-P)	445 (4.87)	516 (1.86)	<0.001
Charlson Comorbidity Index score, no. (%)			
1	445 (4.87)	6685 (24.11)	<0.001
2	1425 (15.6)	5479 (19.76)	<0.001
3	7265 (79.53)	10,784 (38.89)	<0.001
Median annual income in patient's zip code, US$, no. (%)			
$1–$49,999	3455 (37.82)	9813 (35.39)	0.102
$50,000–$64,999	2235 (24.47)	6880 (24.81)	0.791
$65,000–85,999	1935 (21.18)	5854 (21.11)	0.963
≥$86,000	1510 (16.53)	5180 (18.68)	0.062
Insurance type, no. (%)			
Medicaid	6360 (69.62)	15,453 (55.73)	<0.001
Medicare	1110 (12.15)	4126 (14.88)	0.013
Private	1480 (16.2)	7420 (26.76)	<0.001
Uninsured	185 (2.03)	729 (2.63)	0.172
Hospital characteristics			
Hospital region, no. (%)			
Northeast	1975 (21.62)	6336 (22.85)	0.341
Midwest	2655 (29.06)	6661 (24.02)	<0.001
South	3590 (39.3)	11,929 (43.02)	0.013
West	915 (10.02)	2806 (10.12)	0.914
Hospital bed size, no. (%)			
Small	1945 (21.29)	6156 (22.2)	0.452
Medium	2600 (28.46)	8064 (29.08)	0.654
Large	4590 (50.25)	13,510 (48.72)	0.312
Location and teaching status of the hospital (%)			
Rural	565 (6.19)	1960 (7.07)	0.241
Urban non-teaching	1170 (12.81)	4234 (15.27)	0.023
Urban teaching	7400 (81.01)	21,534 (77.66)	0.011

ICD: Implantable Cardioverter-Defibrillator, CRT-D: Cardiac Resynchronization Therapy Defibrillator, CRT-P: Cardiac Resynchronization Therapy Pacemaker.

Table 2
Multivariable logistic regression table of factors associated with comorbid heart failure among hospitalized sarcoidosis patients.

Variable	Adjusted Odds Ratio	95 % confidence interval [CI]	P value
Age	1.03	1.03–1.04	<0.001
Sex			
Male	Reference		
Female	0.79	0.69–0.91	<0.001
Race/ethnicity			
Caucasian	Reference		
Black	1.74	1.47–2.05	<0.001
Hispanic	0.95	0.64–1.39	0.781
Others	1.02	0.57–1.85	0.931
Median annual income in patient's zip code, US$			
$1–$49,999	Reference		
$50,000–$64,999	0.89	0.74–1.09	0.272
$65,000–85,999	1.05	0.84–1.30	0.683
≥$86,000	0.92	0.74–1.14	0.441
Charlson Comorbidity Index score			
1	Reference		
2	3.21	2.41–4.32	<0.001
>3	6.19	4.51–7.97	<0.001
Location and teaching status of the hospital			
Rural	Reference		
Urban non-teaching	0.85	0.58–1.24	0.393
Urban teaching	1.03	0.73–1.46	0.861
Insurance type			
Medicaid	Reference		
Medicare	1.21	0.91–1.60	0.191
Private	0.83	0.66–1.05	0.122
Uninsured	1.35	0.74–2.47	0.334
Arrhythmias, overall	2.50	2.10–2.98	<0.001
Atrial Fibrillation	2.43	2.00–2.94	<0.001
Supraventricular Tachycardia	1.48	0.98–2.24	0.072
Ventricular Tachycardia	2.07	1.35–3.18	<0.001
Ventricular Fibrillation	1.96	0.98–2.24	0.291
Premature atrial contraction/ Premature ventricular contraction	1.86	0.67–5.15	0.231
Comorbidities			
Hypertension	0.02	0.01–0.03	<0.001
Hyperlipidemia	1.35	0.01–0.03	<0.001
Diabetes Mellitus	0.98	0.81–1.31	0.971
Obesity	1.73	1.48–2.02	<0.001
Chronic Obstructive Pulmonary Disease	1.15	0.96–1.38	0.141
Coronary Artery Disease	2.09	1.78–2.46	<0.001
History of cardiac device implantation (ICD, pacemaker, CRT-D, CRT-P)	2.17	1.43–3.29	<0.001
Chronic Kidney Disease (CKD), stage 1–4	1.51	1.16–1.81	<0.001
End-stage renal disease	1.32	0.89–1.91	0.311

ICD: Implantable Cardioverter-Defibrillator, CRT-D: Cardiac Resynchronization Therapy Defibrillator, CRT-P: Cardiac Resynchronization Therapy Pacemaker.

concomitant HF was not an independent predictor of in-hospital mortality (aOR 1.08; 95 % CI, 0.75–1.57; p = 0.662), even after HF subtype stratification (see Table 3). However, age (aOR 1.04; 95 % CI, 1.03–1.06; p ≤ 0.001) and overall arrhythmia burden (aOR 2.08; 95 % CI, 1.47–2.95; p ≤ 0.001) specifically ventricular tachycardia (aOR 2.43; 95 % CI, 1.12–5.29; p = 0.031) and ventricular fibrillation (aOR 13.27; 95 % CI, 4.73–37.25; p ≤ 0.001) were associated with higher risk for in-hospital mortality among hospitalized sarcoidosis patients (see Table 4).

3.4. Total hospital length of stay based on heart failure status

The median LOS for hospitalized sarcoidosis patients was similar between those with (4 days; IQR, 3–7 days) and without (4 days; IQR, 3–7 days) comorbid HF. On univariate and multivariate analyses that adjusted for patient and hospital level confounders, our analysis showed that among hospitalized sarcoidosis patients with comorbid HF, HF did not significantly increase the hospital LOS (aOR 1.89; 95 % CI: 0.95–3.75, p value = 0.072) (see supplementary Table 3), even after stratifying for HF subtypes (see Table 3).

4. Discussion

To the best of our knowledge, this study is the first retrospective population cohort analysis from a nationally representative database that investigated the characteristics and clinical outcomes of hospitalized sarcoidosis patients with concomitant HF. In this study, we investigated the factors associated with concomitant HF among hospitalized sarcoidosis patients as well as its impact on in-hospital mortality and hospital LOS. Our study suggests that among hospitalized sarcoidosis patients, concomitant HF was associated with increasing age, black race, and certain comorbidities including arrhythmias, history of cardiac device implantation (ICD, pacemaker, CRT-D, CRT-P), hyperlipidemia, diabetes mellitus, obesity, CKD stage 1–4, and CAD. Further, concomitant HF among admitted sarcoidosis patients was not significantly associated with in-hospital mortality or hospital LOS, even after stratifying for HF subtype. However, age and overall arrhythmia burden, specifically ventricular tachycardia and ventricular fibrillation, were associated with a higher risk for in-hospital mortality.

A study by Patel et al. (2018) [12] looking at the prevalence of cardiac manifestations and outcomes of hospitalized patients with sarcoidosis in the United States from 2005 to 2014 showed that the prevalence of concomitant HF among sarcoidosis patients was 15.5 %, compared to 24.78 % in our study. This increase in the prevalence of sarcoidosis with concomitant HF is multifactorial likely because of the recent publication of formalized guidelines [13–15] in the past decade, leading to a more organized and algorithmic way of approaching the diagnosis of sarcoidosis, especially if with cardiac manifestations such as HF. This is further complemented by the advancement of different myocardial imaging modalities including cardiac magnetic resonance imaging (CMR) and 18F-fluoro-2-deoxyglucose positron-emission tomography/computerized tomography (FDG PET/CT) scan [16–18], thus enhancing the early detection of sarcoidosis with cardiac involvement and effectively increasing the incidence of this disease entity [13,16,18].

Table 3
Impact of comorbid heart failure among hospitalized sarcoidosis patients in terms of in-hospital mortality and hospital length of stay.

	In-hospital mortality		Length of stay	
	OR (95 % CI)	P value	OR (95 % CI)	P value
Overall	1.08 (0.75–1.57)	0.662	1.89 (0.95–3.75)	0.072
HF subtype				
HFrEF	1.25 (0.84–1.86)	0.281	2.27 (0.89–5.84)	0.091
HFpEF	1.11 (0.76–1.62)	0.602	1.31 (0.63–2.69)	0.461

Table 4
Multivariable logistic regression table of factors associated with in-hospital mortality among hospitalized sarcoidosis patients.

Variable	Adjusted Odds Ratio	95 % confidence interval [CI]	P value
Heart Failure, overall	1.08	0.75–1.57	0.662
Age	1.04	1.03–1.06	<0.001
Sex			
Male	Reference		
Female	0.71	0.52–0.96	0.031
Race/ethnicity			
Caucasian	Reference		
Black	1.15	0.79–1.65	0.472
Hispanic	0.41	0.13–1.34	0.141
Others	1.89	0.76–4.70	0.172
Charlson Comorbidity Index score			
1	Reference		
2	0.89	0.51–1.68	0.681
>3	1.51	0.91–2.61	0.211
Hospital Bed size			
Small	Reference		
Medium	1.38	0.89–2.16	0.152
Large	1.60	1.06–2.41	0.033
Location and teaching status of the hospital			
Rural	Reference		
Urban non-teaching	0.51	0.26–1.03	0.061
Urban teaching	1.01	0.58–1.74	0.982
Insurance type			
Medicaid	Reference		
Medicare	1.33	0.80–2.22	0.271
Private	1.05	0.69–1.61	0.812
Uninsured	1.17	0.39–3.48	0.781
Arrhythmias, overall	2.08	1.47–2.95	<0.001
Atrial Fibrillation	1.48	0.98–2.19	0.062
Supraventricular Tachycardia	1.72	0.79–3.76	0.171
Ventricular Tachycardia	2.43	1.12–5.29	0.031
Ventricular Fibrillation	13.27	4.73–37.25	<0.001
Premature atrial contraction/ Premature ventricular contraction	1	–	–
Comorbidities			
Hypertension	0.71	0.47–1.06	0.092
Hyperlipidemia	0.46	0.33–0.63	<0.001
Coronary artery disease	0.83	0.58–1.19	0.311
History of cardiac device implantation (ICD, pacemaker, CRT-D, CRT-P)	0.22	0.04–1.09	0.061
Diabetes mellitus	0.90	0.56–1.45	0.682
Obesity	0.77	0.53–1.11	0.161
Chronic Kidney Disease (CKD), stage 1–4	0.59	0.38–1.09	0.061
End-stage renal disease	0.97	0.53–1.75	0.912
Chronic Obstructive Pulmonary Disease	0.86	0.58–1.27	0.442

4.1. Factors associated with heart failure among sarcoidosis patients

Our findings were concurrent with the results of previous studies which elucidated that sarcoidosis and concomitant HF are more common among hospitalized black individuals [19,20]. In terms of sarcoidosis, African Americans tend to be more symptomatic [21] and exhibit more extrapulmonary involvement [22–24], thus leading to more extensive multiorgan involvement and higher rates of hospitalization [25,26]. On the other hand, traditional risk factors for incident HF such as hypertension, diabetes, obesity, and CKD are more prevalent among black individuals compared to other race/ethnic groups [19,27]. In contrast to previous studies [28,29], our analysis has shown that female patients with sarcoidosis and concomitant HF were less likely to be hospitalized compared to their male counterparts. This is likely related to some evidence suggesting that male sarcoidosis patients tend to have more cardiac manifestations [30,31]. Also, female patients with concomitant HF receive a less aggressive treatment [32] approach leading to lesser hospitalization rates, even though their cardiac

manifestations appear to be more severe [33]. Taken together, sarcoidosis with cardiac involvement among female black individuals represents a substantial risk for hospitalization and increased risk for morbidity and mortality [27–29,33,34], indicating a need for more robust research regarding racial and sex health disparities in this population.

Further, the results of our analyses were concurrent with a recent study by Rossides et al. (2022) [35] exploring the risks and predictors of HF among sarcoidosis patients which showed that increasing age and higher number of comorbidities tend to be associated with the development of HF among sarcoidosis patients. This is likely because age is a well-recognized risk factor for the development of certain comorbidities including hyperlipidemia, diabetes mellitus, obesity, and CAD [36–38] which impacts overall cardiovascular health. Thus, it follows with sarcoidosis. This is further supported by a study of Zhou et al. (2017) [39] indicating that among cardiac sarcoidosis patients, increasing age was a significant predictor of mortality. The underlying reason is likely due to the chronic low-grade inflammation that is seen among aging individuals even in the absence of overt inciting factor, thus, leading to the development of age-related conditions such as hyperlipidemia, CAD and diabetes mellitus [40] as well as the aggravation of certain conditions including sarcoidosis which is in itself induces a proinflammatory state [41]. Interestingly, our study showed that the rate of hypertension was significantly lower among those with HF compared to their non-HF counterparts, which is clinically unsound since hypertension is a known risk factor for the development of HF. This is likely attributable to coding errors in the reporting of previous chronic comorbidities, especially among patients who are hospitalized with a complicated hospital course [42]. Thus, caution should be exercised in interpreting these findings as these are speculative and hypothesis generating.

Moreover, cardiac arrhythmias are a common manifestation among sarcoidosis patients with cardiac involvement [43,44]. In particular, a study by Rossides et al. (2022) indicated that cardiac arrhythmias among sarcoidosis patients is a strong predictor of HF development. This is consistent with the findings of our study which showed that cardiac arrhythmias were significantly associated with HF among hospitalized sarcoidosis patients. Moreover, this strong association between cardiac arrhythmias and heart failure development is further supported by the higher rate of prior cardiac device implantation in this patient population. Additionally, similar to our findings, other studies [35,45] showed that atrial fibrillation was the most common arrhythmia associated with concomitant HF among sarcoidosis patients. The underlying mechanism underpinning the development of cardiac arrhythmias among sarcoid patients is the scarring associated with the inflammation incited by the sarcoid granuloma leading to conduction abnormalities, and due to its patching involvement, may lead to the development of either atrial or ventricular arrhythmias [44,46,47]. Taken together, further evaluation for possible sarcoidosis should be pursued among patients with new-onset cardiac arrhythmias in the background of new-onset or worsening HF, without any plausible obvious cause.

4.2. In-hospital mortality among hospitalized sarcoidosis patients with heart failure

Previous studies [12,48] have suggested that sarcoidosis with cardiac manifestations including HF is associated with higher overall mortality, likely due to the underlying mechanisms underpinning the development of HF in this population including atherosclerotic CAD or treatment related to sarcoidosis including steroid-induced hypertension or diabetes, which in turn increases the disease burden in this population. This was in contrast with our study which did not show that concomitant HF among hospitalized sarcoidosis patients increased the risk for in-hospital mortality, although this could be explained by the fact that previous studies were longitudinal in nature and the scope of our study was limited by in-hospital events only, thereby potentially missing out on outcomes that occur after hospitalization. Further, if the said risk-enhancing mechanisms related to HF among sarcoidosis patients are stable during the said hospitalization, it might skew the outcomes to show that HF to not likely impact overall in-hospital mortality even though in reality it might impact overall clinical outcomes in the long term just like what previous studies suggested [12,48].

However, our study suggested that overall arrhythmia burden significantly increased the risk for in-hospital mortality in this population, particularly ventricular tachycardia and ventricular fibrillation. This is consistent with the findings of previous studies [45,48] indicating that the development of arrhythmias significantly increased the risk of in-hospital mortality in this population. Taken together, concomitant HF and sarcoid-related arrhythmias lead to higher disease burden and thus, effectively increasing mortality [45,48]. Although the patients in our study did not have confirmed cardiac sarcoidosis, it is imperative to have a timely diagnosis and treatment of concomitant HF among hospitalized sarcoidosis patients due to the inherent risks of increased morbidity and mortality among HF [32,49] patients and the risks associated with the development of sarcoid-related arrhythmias [35,45,48] in this population.

4.3. Hospital length of stay among hospitalized sarcoidosis patients with heart failure

Our study suggested that concomitant HF among hospitalized sarcoidosis patients is not an independent predictor of a longer LOS. This is concurrent with a previous study by Ungprasert et al. (2018) [50] which explored the hospitalization outcomes among sarcoidosis patients, indicating that the LOS was comparable among those with and without sarcoidosis, although their study did not specify whether the hospitalization is related to any sarcoid-related cardiac involvement or not. Similarly, our study did not specifically indicate concomitant HF as the reason for hospitalization among sarcoidosis patients, hence, regardless of the presence or absence of sarcoidosis, hospitalized patients with concomitant HF would have been treated similarly based on true medical need, thus leading to similar outcomes in terms of hospital LOS.

5. Limitations

Our study has several notable limitations owing to the use of an administrative dataset and the cross-sectional nature of our study design. This results in an inability to capture patient level data including the availability of radiographic, echocardiographic, laboratory results as well as treatment strategies pursued such as the use of certain pharmacological therapies which may have value in terms of stratifying the severity of the patients' condition. Further, given the lack of histologic evidence for cardiac sarcoidosis, we cannot validate that the cardiac manifestations including arrhythmias and HF are secondary to cardiac sarcoidosis or not. Moreover, the use of a large administrative database like NIS are prone to coding errors in terms of reporting previous chronic comorbidities, especially among hospitalized patients with life-threatening conditions, hence, caution should be exercised in interpreting findings such as what was seen in our study which showed that hypertension was associated with reduced HF development, as these are merely speculative and hypothesis generating. Additionally, the ICD-10 code for COVID-19 was released on April 1, 2020 which potentially missed a significant amount of the total number of true COVID-19 cases. Finally, the study captured in-hospital events only, hence, certain outcomes that may have occurred after hospitalization could have been missed specifically out-of-hospital sudden cardiac deaths, which constitutes a significant event in this subset of population.

6. Conclusion

Our study showed that among hospitalized patients with sarcoidosis, HF was significantly associated with increasing age, black race, and

certain comorbidities including arrhythmias, hyperlipidemia, obesity, CAD, history of cardiac device implantation, and CKD stage 1–4. Further, female gender is less likely to have a HF diagnosis compared to their male counterparts. Lastly, age and overall arrhythmia burden, specifically ventricular tachycardia and ventricular fibrillation were associated with higher risk for in-hospital mortality. Hence, patients need to be educated regarding their medical diagnoses and the need for treatment adherence, while physicians need to ensure adequate continuity of care between the hospital and the primary care setting to optimize the patients' health and therefore outcomes. With these, prospective studies with a larger sample size utilizing patient level data and control of other possible confounders are warranted in order to better delineate these associations.

7. Clinical study registration number

None.

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CRediT authorship contribution statement

Bruce Adrian Casipit: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Project administration. **Kevin Bryan Lo:** Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization, Supervision. **Carlo Gabriel Casipit:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – review & editing, Visualization, Supervision. **Abdiodun Idowu:** . **Aman Amanullah:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – review & editing, Visualization, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2023.101275.

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