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Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Research paper

Retrospective analyses of the outcomes among hospitalized liver cirrhosis patients with heart failure and COVID-19 infection: Insight from the National Inpatient Sample

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ABSTRACT

Background: There is paucity of data regarding the impact of Coronavirus Disease 2019 (COVID-19) infection on the outcomes of hospitalized liver cirrhosis (LC) patients with heart failure (HF).
Methods: Utilizing the 2020 National Inpatient Sample (NIS) Database, we conducted a retrospective cohort study to investigate the outcomes of hospitalized LC patients with HF and COVID-19 infection, looking at its impact on in-hospital mortality, risk for acute kidney injury (AKI) and length of stay (LOS).
Results: We identified a total of 10,810 hospitalized LC patients with HF, of which 1.39 % (n = 150/10,810) had COVID-19 infection. Using a stepwise survey multivariable logistic regression model that adjusted for patient and hospital level confounders, COVID-19 infection among hospitalized LC patients with HF was found to be an independent predictor of overall in-hospital mortality (aOR 3.73; 95 % CI, 1.58–8.79; p = 0.00) and risk for AKI (aOR 3.06; 95 % CI, 1.27–7.37; p = 0.01) compared to those without COVID-19 infection. However, there were comparable rates of LOS among LC patients with HF regardless of COVID-19 infection status. Moreover, AKI was found to be an independent predictor of longer LOS (coefficient 4.40, 95 % CI 3.26–5.38; p = 0.00). On subgroup analysis, diastolic HF was found to be associated with increased risk for in-hospital mortality (aOR 6.54; 95 % CI, 2.02–21.20; p = 0.00), development of AKI (aOR 3.33; 95 % CI, 1.12–9.91; p = 0.03) and longer LOS (coefficient 4.30, 95 % CI 0.79–9.45; p = 0.03).
Conclusion: Concomitant COVID-19 infection among hospitalized LC patients with HF was associated with higher risk for in-hospital mortality and AKI but did not significantly affect hospital LOS.

1. Introduction

Heart failure (HF) is associated with increased morbidity and mortality, especially in the presence of comorbidities such as liver cirrhosis (LC), resulting in prolonged hospitalization and higher medical costs [1,2]. Mechanistically, LC may impair cardiac contractile and diastolic function leading to the worsening or development of cardiac dysfunction among those with and without pre-existing HF, respectively [3,4]. Previous research has established a relationship between the two diseases, classifying them both as a disorder known as cirrhotic cardiomyopathy (CCM) [4]. The interaction of the pathophysiological mechanisms of the two diseases triggers a chain of hormonal and physiological events causing changes in cardiac output and arterial blood volume leading to further deterioration of cardiac function [5–7]. The emergence of Coronavirus Disease 2019 (COVID-19) has brought about global concern due to its associated increase in morbidity and mortality especially among those with concurrent pre-existing medical diseases such as chronic cardiovascular and liver diseases [8–10]. While early research didn't establish a link between LC and COVID-19 infection severity [11,12], later studies have shown that patients with LC who have comorbidities such as congestive HF were found to have increased hospitalization and mortality rates in the presence of COVID-19

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infection [13]. In addition, research had shown that severe COVID-19 infection increases the risk for exacerbation among those with pre-existing HF by inducing a severe inflammatory reaction causing increased metabolic demand, coagulation dysfunction, direct myocardial injury, and cardiac electrical abnormalities leading to worsening cardiac dysfunction [14–16]. Moreover, previous studies suggested that COVID-19 infection increases the risk for the development of acute renal failure leading to circulatory volume overload which subsequently worsens cardiac dysfunction among those patients with pre-existing HF [17,18]. Although previous studies have shown that there is increased risk for morbidity and mortality among hospitalized LC with concurrent HF [19,20], there is still paucity of data regarding the incremental risk of COVID-19 in this population. With this, we aim to investigate the in-hospital outcomes among hospitalized LC patients with comorbid HF and concurrent COVID-19 infection by utilizing a large nationwide database.

2. Methods

We conducted a retrospective cohort study utilizing the Health Care Utilization Project National Inpatient Sample (HUCP-NIS) of the year 2020. Briefly, the NIS is sponsored by the Agency for Healthcare Research and Quality (AHRQ) and is the largest, publicly available inpatient database that encompasses a survey design to collect discharge information from non-federal, non-rehabilitation, acute-care, and short-term hospitals. It approximately covers about 20 % of total hospital admission and discharges in the United States. Further, the database is updated annually and provides national estimates of patient and hospital level characteristics performed on US acute-care hospitals. Additionally, all discharges are weighted to ensure that they are nationally representative. Based on the code of federal regulations, since the data are de-identified and is publicly available, this does not constitute human subjects research and therefore, no institutional review board (IRB) review was required.

We included all patients aged 18 and older in our study who were admitted between January 2020 and December 2020 with a principal diagnosis of LC with a known HF comorbidity during the index hospitalization. We utilized the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) in identifying all discharge records that had LC and HF. Stratification based on the presence or absence of COVID-19 infection was subsequently employed. Patient comorbidities and relevant past medical history were retrieved on the discharge records containing the ICD-10 CM codes during the index hospitalization and were recorded accordingly. (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 impact of COVID-19 infection on in-hospital mortality among hospitalized LC patients with comorbid HF. Secondary outcomes included other factors associated with inpatient mortality, the influence of COVID-19 infection on the development of AKI, and hospital LOS among admitted patients with LC and comorbid HF.

The patient information and data were analyzed by using StataBE 17.0 (StataCorp, College Station, Texas). The NIS utilizes a complex sampling design that includes stratification, clustering, and weighing of patient and hospital level data in order to facilitate analyses and produce nationally representative results, variance estimates, and p values. Continuous variables were presented as median and interquartile range (IQR) as well as mean ± standard error (SE) where appropriate. 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. Survey univariable and multivariable logistic and linear regression analysis were used to calculate both adjusted and unadjusted odds ratios (ORs) for the primary and secondary outcomes. 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. Univariate regression analysis was done to identify variables with a P value <0.2, indicating possible association with the outcome of interest, and was subsequently entered into the multivariable model for analysis. Survey multivariate linear regression analysis was used for the secondary outcome of hospital length of stay to adjust for possible patient and hospital level confounders as above. 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

There were a total of 120,595 hospitalizations with a principal diagnosis of LC identified in the NIS database in the year 2020, of which 11,170 had a diagnosis of HF including 2940 systolic, 6930 diastolic, and 1330 combined systolic and diastolic HF during the index hospitalization. Of these, 10,810 met our inclusion criteria. Table 1 summarizes the baseline characteristics of the study population. Patients with concomitant COVID-19 infection accounted for 1.39 % (n = 150/10,810) of the total study population. Further, the median age for those with and without COVID-19 were 62 years old (IQR, 52–73 years) and 64 years old (IQR, 57–73 years), respectively. Compared to patients admitted without COVID-19 infection, admitted LC patients with comorbid HF and concomitant COVID-19 infection had a similar proportion of females, number of comorbidities, median annual income, insurance type, characteristics of admitting hospitals (hospital bed size and teaching status) and prevalence of hypertension, hyperlipidemia, diabetes mellitus, obesity, coronary artery disease, chronic kidney disease, as well as tobacco use. Further, they were less likely to be white (33.3 % vs 65.8 %) and were more likely to be Hispanic (36.7 % vs 13.4 %).

The overall mortality rate among patients admitted for LC with HF was 5.92 % (n = 640/10,810). Among those with concomitant COVID-19 infection, the mortality rate was significantly higher at 23.33 % (35/150, p = 0.00). Further, there was a significantly higher rate of in-hospital mortality among those with diastolic HF (30 % vs 5.15 %; p = 0.00) but not those with systolic (12.5 % vs 6.91 %; p = 0.54) and combined systolic and diastolic HF (0 % vs 5.56 %; p = 0.73). On univariate and multivariate analyses that adjusted for patient and hospital level confounders, concomitant COVID-19 infection was found to be an independent predictor of overall in-hospital mortality (adjusted OR 3.73; 95 % confidence interval [CI], 1.58–8.79; p = 0.00). Moreover, age and the development of AKI were significantly associated with increased inpatient mortality among hospitalized LC patients with HF (see Table 2.) In terms of HF subtypes, although this was a smaller group of patients, COVID-19 infection increased the risk for in-hospital mortality among admitted LC patients with concomitant diastolic HF (adjusted OR 6.54; 95 % confidence interval [CI], 2.02–21.20; p = 0.00) but not for those with systolic or combined systolic and diastolic HF. (See Table 3).

The overall AKI rate among patients admitted for LC with HF was 42.04 % (n = 4545/10,810). Among those with concomitant COVID-19 infection, the AKI rate was significantly higher at 66.67 % (100/150, p = 0.01). Moreover, among HF subtypes, those with diastolic HF had a significantly higher rate of AKI (70 % vs 42.32 %; p = 0.01) but not for those with systolic (62.5 % vs 39.36; p = 0.19) and combined systolic and diastolic HF (50 % vs 43.25 %; p = 0.01). On multivariate analyses that adjusted for patient and hospital level confounders, concomitant COVID-19 infection among LC patients with comorbid HF was found to be an independent predictor for the development of AKI (adjusted OR 3.06; 95 % confidence interval [CI], 1.27–7.37; p = 0.01). Further, in terms of HF subtypes, those with diastolic HF had a significantly higher risk for AKI (adjusted OR 3.33; 95 % confidence interval [CI], 1.12–9.91; p = 0.03) compared to those with systolic (adjusted OR 2.70; 95 % confidence interval [CI], 0.62–11.77; p = 0.19) and combined systolic and diastolic HF (adjusted OR 6.35; 95 % confidence interval [CI],

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

Patient characteristics	With COVID-19	Without COVID-19	P-value
Number of patients	150	10,660	
Age at index admission, years (IQR)	62 (52–73)	64 (57–73)	
Women, no. (%)	0.3	0.4	0.4
Race/ethnicity, no. (%)			0.0
White	33.3	65.8	0.0
Black	13.3	13.5	1.0
Hispanic	36.7	13.4	0.0
Asian or Pacific Islander	6.7	1.6	0.0
Native American	3.3	1.2	0.3
Others	6.7	2.8	0.2
Comorbidities (%)			
Hypertension	0.0	1.3	0.5
Hyperlipidemia	26.7	37.4	0.2
Diabetes Mellitus	20.0	11.5	0.12
Obesity	16.7	23.1	0.4
Chronic Obstructive Pulmonary Disease	3.3	21.3	0.0
Coronary Artery Disease	26.7	32.0	0.5
Chronic Kidney Disease (CKD), stage 1–4	43.3	37.3	0.5
End-stage renal disease	9.7	9.7	1.0
Tobacco use	0.0	0.9	0.6
In hospital Complication (%)			
AKI	66.7	41.7	0.0
Charlson Comorbidity Index score, no. (%)			
1	0.0	0.0	–
2	6.7	5.9	0.9
3	66.7	57.7	0.1
Median annual income in patient's zip code, US$, no. (%)			0.45
$1–$49,999	46.7	34.9	0.2
$50,000–$64,999	16.7	28.1	0.2
$65,000–85,999	20.0	19.6	1.0
≥$86,000	13.3	15.0	0.8
Insurance type, no. (%)			0.57
Medicaid	46.7	58.3	0.2
Medicare	26.7	21.3	0.5
Private	20.0	13.7	0.3
Uninsured	3.3	4.1	0.8
Hospital characteristics			
Hospital region, no. (%)			0.0
Northeast	36.7	16.1	0.0
Midwest	26.7	23.0	0.6
South	20.0	45.5	0.0
West	16.7	17.4	0.9
Hospital bed size, no. (%)			0.6
Small	16.7	19.5	0.7
Medium	36.7	27.8	0.3
Large	46.7	52.7	0.5
Location and teaching status of the hospital (%)			0.1
Rural	0	7.0	0.1
Urban non-teaching	6.7	1.7	0.1
Urban teaching	93.3	76.3	0.0

0.56–71.83; p = 0.14). (See Table 4).

The median length of stay for admitted patients with LC and HF with concomitant COVID-19 infection was 9 days (IQR, 4–18 days) in contrast to 5 days (IQR, 3–9 days) in those without COVID-19 infection. After adjusting for patient and hospital level confounders, our analysis showed that among hospitalized LC patients with HF, COVID-19 did not significantly increase the hospital LOS (coefficient 3.10, 95 % CI 0.44–8.16; p = 0.07). However, when stratified in terms of HF subtypes, diastolic HF was associated with a longer LOS (coefficient 4.30, 95 % CI 0.79–9.45; p = 0.03) whereas systolic and combined systolic and diastolic HF did not. Further, concomitant AKI (coefficient 4.40, 95 % CI 3.26–5.38; p = 0.00) was significantly associated with a longer LOS (See Table 5).

Table 2
Multivariable logistic regression table of factors associated with inpatient mortality among hospitalized patients with liver cirrhosis and comorbid heart failure.

Variable	Adjusted odds ratio	95 % confidence interval [CI]	P value
COVID-19	3.73	1.58–8.79	0.00
Age	1.03	1.01–1.04	0.00
Charlson Comorbidity Index	1.06	0.96–1.16	0.24
Comorbidities			
Hyperlipidemia	0.61	0.40–0.95	0.03
CAD	0.66	0.42–1.03	0.07
Diabetes	0.42	0.18–0.95	0.04
Obesity	0.58	0.34–0.96	0.04
CKD Stage 1–4	0.57	0.37–0.89	0.01
COPD	0.46	0.24–0.85	0.02
In-hospital complication			
AKI	6.68	4.17–10.69	0.00

Table 3
Adjusted Odds Ratio for in-hospital mortality among hospitalized liver cirrhosis patients with heart failure and concomitant COVID-19 infection stratified based on heart failure subtype[a].

	Adjusted OR	95 % confidence interval [CI]	P value
Overall	3.73	1.58–8.79	0.00
Heart failure subtype			
Systolic HF	1.10	0.03–34.69	0.96
Diastolic HF	6.54	2.02–21.20	0.00
Combined systolic and diastolic HF	1	No patients with COVID-19 had combined systolic and diastolic HF	No patients with COVID-19 had combined systolic and diastolic HF

[a] Adjusted for age, gender, race, Charlson comorbidity index, median annual income, insurance type, hospital location, hospital bed size, hospital teaching status, hyperlipidemia, hypertension, diabetes mellitus, obesity, COPD, CAD, CKD, ESRD, Tobacco use.

Table 4
Adjusted Odds Ratio for acute kidney injury among hospitalized liver cirrhosis patients with heart failure and concomitant COVID-19 infection stratified based on heart failure subtype[a].

	AKI		
	Adjusted odds ratio	95 % confidence interval [CI]	P value
Overall	3.06	1.27–7.37	0.01
Heart failure subtype			
Systolic HF	2.70	0.62–11.77	0.19
Diastolic HF	3.33	1.12–9.91	0.03
Combined systolic and diastolic HF	6.35	0.56–71.83	0.14

[a] Adjusted for age, gender, race, Charlson comorbidity index, median annual income, insurance type, hospital location, hospital bed size, hospital teaching status, hyperlipidemia, hypertension, diabetes mellitus, obesity, COPD, CAD, CKD, ESRD, Tobacco use.

4. Discussion

This study is, to the best of our knowledge, the first retrospective population cohort study from a nationally representative database that investigated the clinical outcomes among hospitalized LC patients with

Table 5
Multivariate linear regression table of length of stay among hospitalized liver cirrhosis patients with comorbid heart failure and the association of acute kidney injury with hospital length of stay based on heart failure subtype[a].

	LOS			AKI		
	Coefficient	95 % confidence interval [CI]	P value	Coefficient	95 % confidence interval [CI]	P value
Overall	3.10	−0.22–6.42	0.07	4.32	3.26–5.38	0.00
Heart failure subtype						
Systolic HF	0.47	−6.87–7.82	0.90	3.69	2.44–4.94	0.00
Diastolic HF	4.30	0.44–8.16	0.03	4.99	3.49–6.49	0.00
Combined systolic and diastolic HF	−0.01	−3.94–3.92	1.00	1.97	0.43–3.50	0.01

[a] Adjusted for age, gender, race, Charlson comorbidity index, median annual income, insurance type, hospital location, hospital bed size, hospital teaching status, hyperlipidemia, hypertension, diabetes mellitus, obesity, COPD, CAD, CKD, ESRD, Tobacco use.

comorbid HF and concomitant COVID-19 infection. The outcomes investigated include in-hospital mortality, risk for AKI, and hospital LOS. Our findings suggested that hospitalized LC patients with HF and COVID-19 infection had significantly increased risk for in-hospital mortality and the development of AKI but did not impact hospital LOS. Moreover, when stratified according to HF subtype, our findings suggested that only diastolic HF was associated with increased risk for in-hospital mortality, development of AKI and longer hospital LOS. Further, our analysis suggested that there was a significantly increased LOS among those hospitalized LC patients with HF and COVID-19 infection who develop AKI regardless of the HF subtype.

Recent studies by Yazdanyar et al. (2021) [19] and Khalid et al. (2020) [20] which investigated the outcomes of hospitalized patients with HF and LC showed a similar 3.4 % in-hospital mortality rate in this population. Further, according to Ge et al. (2021) [21], the cumulative incidence of death at 30 days is 12.5 % among those patients with LC and HF with concurrent COVID-19 infection. Our analysis concurred with previous studies which showed a 5.92 % over-all in-hospital mortality rate among hospitalized patients with LC and HF. However, the mortality rate significantly increased to 23.33 % among those with concomitant COVID-19 infection. This significant increase in the in-hospital mortality rate among patients with concomitant COVID-19 infection is likely due to the implicating mechanisms of the SARS-CoV-2 virus causing cardiac and hepatic injury involving massive cytokine release and severe systemic inflammation with subsequent downstream pathophysiological effects targeting organs such as the liver and heart [22–24]. Mechanistically, hepatic injury in the setting of COVID-19 infection is multifactorial and is thought to be due to virus-induced systemic inflammation, hypoxia, hepatic congestion, and drug-induced liver disease which subsequently manifests as acute decompensation of pre-existing liver disease such as LC [22]. Similarly, COVID-19 induces myocardial injury by means of enhanced pro-inflammatory cascade, direct cytopathic effects and increased blood viscosity leading to clinical conditions including acute coronary syndromes, myocarditis, and the development or worsening of pre-existing HF [23,24]. Taken together, COVID-19 infection worsens the clinical outcomes among hospitalized patients with LC and HF as was evident in our study. Interestingly, our analysis concurred with the study by Alvarez-Garcia et al. (2020) [25] which demonstrated that there was a significantly increased risk for mortality among hospitalized COVID-19 patients with diastolic HF compared to the other HF phenotypes, adding to the mounting body of evidence that is pointing away from the idea that diastolic HF has a more favorable outcome compared to their systolic HF counterparts [25–27]. Furthermore, our analysis suggested that age and the development of AKI increased the risk of in-hospital mortality among hospitalized LC patients with HF likely due the inherent risks associated with aging and the underlying mechanisms by which AKI developed in HF and cirrhotic patients including cardiorenal and hepatorenal syndromes, which oftentimes presents as a therapeutic challenge [28,29].

AKI remains to be one of the major complications among hospitalized patients with LC [30] and HF [31] and is associated with increased morbidity and mortality. Previous studies demonstrated that the rate of development of in-hospital AKI among those with LC [31] and HF [32] were 27.9 % and 20 %, respectively. On the other hand, among those hospitalized LC patients with comorbid HF, the rate of AKI was noted to be 26.49 % [20]. In our study, the rate of AKI development among hospitalized LC patients with HF was 42.04 %, almost double the rate as compared to the results of previous studies. Further, our study showed that among those with concurrent COVID-19 infection, the risk for AKI increased to 66.67 %. This was almost similar to a study conducted by Fisher et al. (2020) [33] which demonstrated an AKI rate of 57 % among hospitalized COVID-19 patients, however, this was not exclusive to patients with LC and HF. The mechanisms implicated in the development of AKI in HF include hemodynamic alterations in the cardiorenal axis such as decreased forward flow leading to venous congestion and increased renal venous pressure which subsequently results in renal dysfunction [34]. Further, systemic venous congestion leading to impairment of renal perfusion trigger a cascade of maladaptive neurohormonal mechanisms including the activation of the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system (SNS) and antidiuretic hormone (ADH) secretion leading to a vicious cycle of circulatory overload and systemic congestion [35]. On the other hand, the underlying pathophysiological mechanisms implicated in the development of renal dysfunction in LC include splanchnic vasodilation leading to pooling of blood in the splanchnic circulation, thus causing a reduction in the effective circulating volume and decreases renal perfusion which subsequently activates the RAAS which, through Angiotensin II, induces renal vasoconstriction and decreases glomerular filtration rate (GFR) [36]. Further, COVID-19 induces renal dysfunction by means of direct renal cellular injury, cytokine storm, and hypovolemia [33]. Taken together, the significant interplay between the various pathophysiological mechanisms of AKI among hospitalized LC patients with HF and concurrent COVID-19 infection lead to a greater risk for in-hospital morbidity. Lastly, our analysis showed that among HF phenotypes, those with diastolic HF had increased risk for AKI which was consistent with the results of the study conducted by Choi et al. (2018) [37], however, their study also showed that systolic HF had increased risk for AKI in contrast to our study which did not show that association.

A study by Khalid et al. (2020) [20] showed that among hospitalized HF patients with LC, there was a 1.2-fold increase in hospital LOS. Further, previous studies suggest that concomitant COVID-19 infection significantly increased the hospital LOS among patients with LC [38] and HF [39]. This was contrary to the results of our study which showed that COVID-19 infection did not significantly impact hospital LOS among hospitalized LC patients with HF. However, when stratified according to HF subtypes, diastolic HF was associated with a significantly longer LOS. A study by Standl et al. (2021) [40] showed that among those with COVID-19 infection, diastolic dysfunction was more commonly seen than systolic dysfunction. This supports the idea that diastolic HF may not be as benign as previously thought and has

comparable outcomes to those with systolic dysfunction [25–27] which could possibly explain the similar or longer LOS in this population. In addition, our analysis was consistent with the results of previous studies [19,20] which showed that AKI among hospitalized LC with HF increased the hospital LOS. This is likely related to the increased morbidity associated with the development of AKI in this population, which could also be a variant of cardiorenal or hepatorenal syndrome, which in itself presents as a diagnostic and therapeutic challenge.

The cross-sectional nature of our study design and the utilization of an administrative database limits the ability of our analysis to capture certain patient level data including the severity of LC and HF during admission which could be ascertained by the availability of relevant information such as radiographic, echocardiographic, and laboratory values as well as the therapeutic approaches undertaken during hospitalization, all of which could confound the outcomes of interest among the study population. Moreover, the presence of possible coding errors as well as underreporting of some of the data might be a source of bias in our analysis given the nature of the administrative database itself, specifically the inability to distinguish the different HF subtypes accurately, determine the chronicity of HF, and obtain accurate baseline histories and comorbidities. Further, caution should be exercised in interpreting the low prevalence of hypertension and tobacco use in our study which could be the result of underreporting of previous chronic comorbidities owing to the use of an administrative database, especially among hospitalized patients with life-threatening conditions, as these findings are clinically unsound and are merely speculative and hypothesis generating. Additionally, a significant number of true COVID-19 cases might have been missed since the ICD-10 code for COVID-19 was released on April 1, 2020, which was several months since the pandemic started. Furthermore, due to the overall small number of COVID-19 infected patients in our study population, caution should be exercised when interpreting the findings associated with HF subtype stratification. Lastly, we are limited by inpatients events only, hence, certain disease outcomes that may have occurred after hospitalization would not be captured and could be missed.

5. Conclusion

Our study showed that hospitalized LC patients with HF and concomitant COVID-19 infection had increased risk for in-hospital mortality and development of AKI but had similar hospital LOS compared to those without COVID-19 infection. Prospective studies with larger sample size are warranted to control for other possible confounders in order to better delineate these associations.

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. **Hussein Al-Sudani:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – review & editing, Visualization, Supervision. **Ahmer Khan:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – review & editing, Visualization, Supervision. **Emmanuel Akuna:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – review & editing, Visualization, Supervision. **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.

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Appendix A. Supplementary data

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