

Incidence of New-Onset Cardiac Complications among Requiring Invasive Mechanical Ventilation: Findings from a Retrospective Observational Study

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Abstract

Background: COVID-19 patients are prone to develop many systemic complications including cardiac complications.

Objective: This study aimed to determine the overall incidence of new-onset cardiac complications among patients admitted to COVID ICU and the possible role of cardiac complications in deciding the length of hospital or ICU stay and ICU mortality.

Methods: A retrospective observational study was conducted among critically ill COVID-19 patients admitted to the ICU of Aga Khan University Hospital in Karachi, Pakistan from June 2020 to May 2021. Medical Records of 159 adult COVID-ICU patients with no prior history of cardiac illness admitted between June 2020 till May 2021, were analyzed.

Results: The median age of COVID-ICU patients was 58 years (IQR =17 years). 48.4% (n=77) of all COVID-ICU patients developed one or more new cardiac events, with an incidence density rate of 92.9/1000 patient-days of COVID-ICU stays. Non-ST elevation myocardial infarction, ECG changes, and cardiac arrhythmias were identified as the most common cardiac complications. The study found a significantly higher frequency of cardiac events among patients having diabetes mellitus and septic shock. The study also found significant differences in ICU and hospital mortality among COVID-ICU patients with and without cardiac complications.

Conclusion: The incidence of cardiac complications is considerably high among COVID-ICU patients and is relatively higher among patients having diabetes mellitus and septic shock. Patients with cardiac complications showed considerably higher ICU and hospital mortality. Early identification of patients at higher risk of cardiac complications is crucial for better management of critically ill COVID-19 patients.

Keywords: Critically ill COVID-19, cardiac complications, invasive mechanical ventilation, Septic shock, Diabetes mellitus.

INTRODUCTION

Critically ill COVID-19 patients are at risk of developing many systemic complications [1]. Many such systemic complications among COVID-19 patients are also characterized as predictors of disease severity and COVID-19-associated mortality [1, 2]. Development of cardiovascular complications including myocardial injury and myocarditis, Acute Myocardial infarction, heart failure, and dysrhythmias have been reported among critically ill COVID-19 patients [3]. It is believed that cardiac event occurs in approximately 8–12% of all COVID-19 patients majorly due to viral involvement of cardiomyocytes causing inflammation and damage to cardiac tissue [4].

The severity of the disease makes a person more prone to develop cardiac events in the course of COVID-19 illness. Moreover, there is variation in the literature regarding the burden and types of COVID-19-associated cardiac complications reported from different populations due to various factors [5]. However, to design and implement effective and tailored prevention and treatment strategies is important to understand the

actual burden or incidence of cardiac events or complications among critically ill COVID-19 patients. Hence, this study aimed to determine the incidence of cardiac events or complications among the patients admitted to COVID-ICU. The findings from this study will also help in understanding the situation in the local context regarding common cardiac complications among severely ill COVID-19 patients to improve the current patient management practices.

METHODOLOGY

This retrospective observational study was conducted in the intensive care unit, of Aga Khan University Hospital, Karachi, Pakistan. Patients admitted between June 2020 till May 2021 to COVID ICU were included. The official approval for the conduct of this study was obtained from the Departmental Research Committee (DRC) of the Department of Medicine, Aga Khan University, Karachi. This study did not involve any active data collection, hence exemption for ethical approval was obtained from the Ethics Review Committee of Aga Khan University Hospital (ERC Registration #:2021-6602-18705).

All the adult patients of age 18 years or above who were admitted to COVID ICU in the period between June 2020 till May 2021 were included in the study. However, the patients who had a history of ischemic heart disease (IHD),

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arrhythmias, or history of cardiopulmonary resuscitation (CPR) before the COVID ICU admission were excluded from the study.

For the sake of this study, new onset cardiac arrhythmias were defined as arrhythmia lasting more than 30 seconds in patients with previously normal sinus rhythm or a sustained heart rate of 160 or above for more than 60 seconds or occurrence of symptomatic bradycardia presenting as elicited signs and symptoms such as chest pain, confusion, *etc.* at a heart rate less than 40 beats per minute. While the myocardial injury was defined as new ST elevations as per electrocardiogram (EKG) of more than 1mm in more than one contiguous lead or normal EKG with a troponin leak of 0.5ng/ml or above or echocardiography finding suggestive of cardiomyopathy.

Initially, a case log was developed for patients admitted to COVID ICU between June 2020 till May 2021, and then file records were retrieved and reviewed from the hospital Health Information Management System (HIMS) where all the patient data information is recorded carefully using the latest version of International Classification of Disease (ICD) which also facilitated the search for ICU admissions over one year for the study period. A structured data collection form was designed, and information was collected about patients' admission information, basic demographics, diagnosis, co-morbid, frequency, and type of cardiac events. The information was also collected regarding C – Reactive Protein (CRP), Lactate dehydrogenase (LDH) enzyme, Serum Ferritin, and D-Dimer levels at the time of ICU admission.

Data were analyzed using SPSS version 21. Descriptive statistics were calculated for socio-demographic and health-related characteristics such as age, sex, and co-morbid. The incidence density of various cardiac events or complications among COVID ICU patients was also estimated concerning patient days of COVID ICU stay [6]. The chi-square test or Fisher exact test will be applied to compare COVID-ICU patients with and without cardiac complications. Stratified sub-group analysis was applied for specific cardiac complications where indicated. A P-value of ≤ 0.05 will be considered statistically significant.

RESULTS

After reviewing the medical records in total 192 adult patients were identified as eligible participants for the study who were admitted in COVID ICU between June 2020 to May 2021. After excluding participants with prior history of cardiac diseases a final sample of 159 was included in the analysis.

The median age of study participants was 58 years (IQR= 51-68 years). 56.6% of all the patients included in this study were between 41 to 64 years of age. Most of the participants had a history of two or more medical co-morbid. The median length of overall hospital stays and ICU was 15 days (IQR = 9-23 days) and 9 days (IQR=8-15 days) respectively. Median serum levels for biochemical parameters at the time of ICU admission for CRP, D-Dimer, Serum Ferritin, and LDH were 116 units/L (IQR =36-173), 03 units/L (IQR=1-6), 1032 units/L (IQR=492-1504) and 666 units/L (IQR=462-775) respectively. **Table 1** shows the demographic and clinical features of study participants.

Table 1: Demographic and Clinical characteristics among COVID-19 patients admitted to COVID-ICU.

Patients' characteristics	Frequency	Percentage
Age		
40 years and less	19	11.9
41 years -64 years	90	56.6
66 years and above	50	31.4
Sex		
Male	117	73.6
Female	42	26.4
Burden of Co-morbid		
No co-morbid	14	8.8
Any one co-morbid	29	18.2
Two or more co-morbids	116	73.0
Types of Co-morbid		
Diabetes Mellitus	73	45.9
Hypertension	90	56.6
Chronic Kidney Disease	19	11.9
Chronic Liver Disease	5	3.1
COPD	10	6.3
Electrolytes imbalance	48	30.2
Septic Shock	91	57.2
DIC	1	0.6
Hospital Mortality		
ICU mortality	71	44.7
Non-ICU Mortality	14	8.8
No Mortality	74	46.5
Duration of Hospital Stay		
1-7 days	27	16.9
8-15 days	59	36.9
16 days or more	73	45.6
Duration of ICU Stay		
1-6 days	46	28.9
7-12 days	64	40.3
13 days or more	49	30.8

Among all 159 patients admitted to COVID-ICU, 77 (48.4%) developed one or more cardiac events or complications. The estimated incidence rate for cardiac events was 92.9 cardiac events per 1000 patient-days of COVID ICU stay. The incidence proportion for various cardiac events or complications was varied while most of the patients suffered only one kind of cardiac complication. The highest incidence proportion was observed for Non-ST elevation myocardial infarction (NSTEMI), EKG

changes, and cardiac arrhythmias with a proportion of 31.4% (n=50), 27.7% (n=44), echocardiography changes 26% (n=42) and 13.8% (n=22) respectively.

Fig. (1) depicts the incidence proportion of different cardiac events among patients.

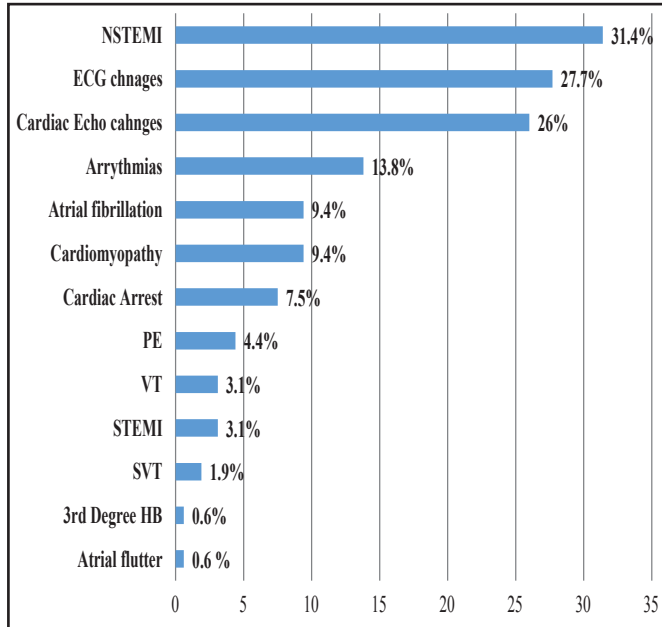


Fig. (1): Incidence Proportion for different types of cardiac events among COVID-ICU patients during ICU admission (n=159). SVT = Supra-Ventricular Tachycardia, VT = Ventricular Tachycardia, PE = Pulmonary Embolism, NSTEMI = Non-ST Elevation Myocardial Infraction.

Out of 85 (53.5%) mortalities, 71 (44.7%) were ICU mortalities. Table 2 presents the comparison of patients' features among those who developed and did not develop cardiac events. No significant differences were found among the patients admitted to COVID ICU who developed cardiac complications as compared to those who didn't develop any cardiac complication or cardiac event based on patients' age category, sex, number of comorbid, and type of comorbid. Statistically significant differences were observed among the two groups based on the frequency of septic shock with significantly higher septic shock frequency among those who developed cardiac complications (p=0.001). None of the biochemical parameters including CRP, LDH, serum ferritin, and D-dimer were significantly different among the two study groups. The study found statistically significant differences in the ICU and hospital mortality among patients who had a cardiac complication as compared to those who didn't develop any cardiac event in COVID ICU. However, no statistically significant differences were observed among the two groups based on overall hospital stay and ICU stay.

Table 2: Comparison of demographic and Clinical characteristics and in-hospital mortality among patients with and without cardiac complications (n =159).

Variables	Cardiac Complication		p-value
	Yes n (%)	No n (%)	
Age			
40 years and less	06(31.6)	13(68.4)	0.077
41 years -64 years	41(45.6)	49(54.4)	
66 years and above	30(60.0)	20(40.0)	
Sex			
Male	60 (51.3)	57(48.7)	0.229
Female	17(40.7)	25(59.5)	
Burden of Co-morbid			
No co-morbid	4(28.6)	10(71.4)	0.020
Anyone co-morbid	9(31.0)	20(69.0)	
Two or more co-morbid	64(55.2)	52(44.8)	
Diabetes Mellitus			
Yes	43(58.9)	30(41.1)	0.015
No	34(39.5)	52(60.5)	
Septic Shock			
Yes	54(59.3)	37(40.7)	0.001
No	23(33.8)	45(66.2)	
Hospital Mortality			
ICU mortality	44(62.0)	27(38.0)	0.005
Non-ICU Mortality	7(50.0)	7(50.0)	
No Mortality	26(35.1)	48(64.9)	
Duration of Hospital Stay*			
Median (IQR)	13 days (8-25)	15 days (9-23)	0.962
Duration of ICU Stay *			
Median (IQR)	9 (5-15)	8 (4.75-15)	0.701
CRP	116.0(39.5-175)	113.0(34-170)	0.562
LDH	666.0 (464-797)	594.5(509-1564)	0.246
Serum Ferritin	1100.0 (509-1564)	953.0(453-1470)	0.562
D-Dimer	3.0(1-6)	2.4(1-6)	0.527

*Mann-Whitney U test was applied for continuous variables.

DISCUSSION

This study is one of its kind as it provides evidence regarding the incidence of COVID-19-associated complications among COVID-ICU patients with no prior history of myocardial injury. The study found that the incidence of COVID-19-related cardiac complications is much higher in our study population as compared to the incidence reported in previous studies [7-9]. This difference in estimates among previous studies as well as in the current study can be explained by the differences in the study population and operational definitions among similar studies. Moreover, our study specifically represented COVID-ICU patients (unlike many previously conducted studies) who are critically ill patients and naturally more at risk for developing all kinds of systematic complications.

Our study found an obvious higher proportion of complications among COVID-ICU patients of age 66 years and above

but this finding was not statistically significant. However, old age has been identified as a risk factor for cardiac complications as well as disease severity by previously conducted international as well as local studies [2,10,11]. Nevertheless, contrary to previously available evidence our study couldn't find any significant differences in biochemical parameters (*i.e.* CRP, LDH, Serum Fe, and PF ratio) between COVID ICU Patients with and without cardiac events [10]. This can be explained by the fact that CRP is an indicator of severe disease, and all the ICU patients were critically ill which might have resulted in elevated CRP in most of the patients irrespective of cardiac complications [12, 13].

Furthermore, in our study population, the burden of cardiac complications was significantly higher among COVID-ICU patients with diabetes mellitus and septic shock. This finding suggests that high-risk stratification for cardiovascular complications must consider diabetes mellitus and septic shock as potential predictors for cardiac events among patients admitted to COVID-ICU. However, previous studies have also identified diabetes mellitus and septic shock as predictors of severe disease among COVID-19 patients [2, 14, 15]. Hence, special caution and strict monitoring are required while managing COVID-19 patients having diabetes mellitus or septic shock as comorbid.

This current study found a relatively longer length of hospital stay among COVID-ICU patients who didn't develop cardiac complications as compared to those who develop any cardiac event. This can be explained by high ICU mortality among COVID-ICU patients who develop complications. However, COVID-ICU patients with cardiac events had slightly longer stay in ICU as compared to those without cardiac complications which is in line with previous evidence [7]. The longer stay in ICU can be attributed to the severity of disease among patients who had cardiac events hence, requiring prolonged critical care as compared to those without cardiac events. However, both of these findings were not statistically significant probably due to limitations related to sample size.

The study found a significantly higher proportion of ICU mortality among COVID-ICU patients who had cardiac events as compared to those who didn't suffer any cardiac event during their ICU stay. This finding also indicates the possible contribution of cardiovascular complications in COVID-associated mortality [16]. This finding also supports that cardiac events among COVID-ICU patients can also be used as a potential disease prognosis indicator which is in line with previous studies [17-20]. A retro-

spective cohort study was conducted in Wuhan Jinyintan Hospital, China [18]. Another retrospective cohort study analyzed the data of 113 deceased COVID-19 patients at Tongji Hospital in Wuhan, China, and identified cardiac injury as one of the common complications among patients who died due to COVID-19 infection exacerbation [19]. A meta-analysis of 9 studies concluded that COVID-19 patients with cardiac complications have significantly higher mortality rates as also compared to COVID-19 patients without myocardial injury (OR = 13.68, 95% CI: 9.81–19.08, $P < 0.001$) [20].

This study provides valuable local evidence regarding the incidence of complications among critically ill COVID-19 patients admitted in one of the most well-equipped and well-managed ICUs in Karachi, Pakistan. This provides validity to study findings while decreasing the potential role of healthcare system-related issues or influences affecting COVID-19 management and diagnosis of clinical manifestations due to cardiac complications.

The considerably higher incidence of new-onset cardiac manifestation among COVID-ICU patients suggests extraordinary vigilance and proactive attitude towards the management of COVID-ICU patients for possible cardiac manifestations and related mortality. This study has a few characteristic limitations. First, the study was only confined to patients admitted to COVID-19 ICU. Hence this study had no comparison group to compare the incidence of cardiac events or complications with those of other viral illnesses or infectious diseases. The findings of this study are comparable to previous studies conducted among severely ill COVID-19 patients irrespective of their status regarding ICU admission. However, the study couldn't rule out the possibility of subclinical cardiac complications with no apparent clinical manifestations during ICU admission and which might have manifested after discharge from the hospital. This might have resulted in a slight underestimation of the incidence of cardiac events.

CONCLUSION

The incidence of new-onset cardiac events is considerably high among critically ill COVID-19 patients admitted to ICU especially those having diabetes mellitus and septic shock as comorbid. Hence, the management of COVID-ICU patients requires continuous monitoring of myocardial injury markers and cardiac function during hospitalization. A comprehensive management approach is needed to avoid the high risk of mortality among COVID-ICU patients with cardiac events or manifestations.

ETHICAL APPROVAL

The official approval for the conduct of this study was obtained from the Departmental Research Committee (DRC) of the Department of Medicine, Aga Khan University, Karachi. This study did not involve any active data collection, hence exemption for ethical approval was obtained from the Ethics Review Committee of Aga Khan University Hospital (ERC Registration #: 2021-6602-18705). All procedures performed in studies involving human participants were per the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

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Declared none.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTION

Dr. Sadaf Hanif:

Original idea, protocol, and perform development and Manuscript writing.

Dr. Muhammad Sohaib:

Protocol development and Manuscript writing.

Dr. Asma Rayani and Dr. Talha Sibtain:

Data Collection and Analysis.

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