

# CARDIAC INVOLVEMENT IN CRITICALLY ILL COVID 19 PATIENTS: A SINGLE CENTER STUDY FROM PAKISTAN

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## ABSTRACT

**Background:** Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) causes a severe respiratory illness. Early studies suggest that COVID-19 can cause a wide range of cardiac complications. This prospective study was conducted to describe the cardiac abnormalities in patients with COVID-19 including cardiac enzymes, electrocardiogram, transthoracic echocardiographic findings and identifying the characteristics of different participant groups with positive and negative findings.

**Material and Methods:** All consecutive adult patients admitted to the ICU with confirmed COVID19 infection were included in the study. Data were recorded on demographics, comorbidities, ECG findings, cardiac enzymes, and echocardiography findings. Data were analyzed using SPSS ver.26 and a p-value of  $\leq 0.05$  was considered significant.

**Results:** A total of 129 patients were included with a median age of 53 years. High sensitivity troponin I was raised in 24.1% patients. Ischemic changes in electrocardiogram were found in 18.6% of the patients. Overall, 41.86% had some type of cardiac abnormality on echocardiography. This study found a significant association between the male gender and low ejection fraction (p-value of 0.019). This study also found a significant association between significantly raised troponin I and low ejection fraction (p-value 0.034). Overall, in-ICU mortality was 40.3% which does not differ significantly across normal and abnormal cardiac enzymes, ECG findings, and echocardiography groups.

**Conclusion:** The male gender, and significantly raised trop I are risk factors for having a low ejection fraction. Abnormal cardiac parameters have no effect on in-ICU mortality.

**Keywords:** Ultrasonography, Echocardiography, Troponin, COVID-19, Critical care

## BACKGROUND

In December 2019, a cluster of acute respiratory illnesses, now known as a novel coronavirus–infected pneumonia (NCIP), occurred in Wuhan, Hubei Province, China.<sup>1</sup> Given the rapid spread of this virus with consequences worldwide, the World Health Organization declared COVID-19 a pandemic on March 11, 2020. Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) causes a severe respiratory illness that is associated with high rates of intensive care unit (ICU) admissions and a high mortality rate.<sup>2</sup> Other common complications include hematological<sup>3</sup> neurological complications<sup>4</sup>, cardiovascular<sup>5</sup>, renal complications<sup>6</sup>, and long-term respiratory complications.<sup>7</sup>

Early studies suggest that COVID-19 can cause a wide

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range of cardiac conditions that include acute myocardial infarction<sup>8</sup>, myocarditis<sup>9</sup>, takotsubo cardiomyopathy<sup>10</sup>, pulmonary hypertension<sup>11</sup>, pericardial effusion, and tamponade physiology.<sup>12</sup> Echocardiography may provide useful information, especially in critical care patients, because it can be performed quickly at the bedside. Echocardiography has been shown to change management in at least a quarter of the patients with covid 19.<sup>13</sup> Earlier studies have recommended performing transthoracic echocardiography on admission as it can change the management and has proved to be of prognostic value.<sup>14</sup>

This study aimed to record the cardiac profile in covid 19 patients (cardiac enzymes, ECG changes, limited bedside echocardiography findings and identify the characteristics of different participant groups with positive and negative findings. There is a paucity of data assessing the patients at risk for developing cardiac abnormalities. This study aimed to describe the cardiac abnormalities in patients with COVID-19 and identify the characteristics of patients who would benefit most from echocardiography.

## MATERIAL AND METHODS

We conducted this prospective observational study in the intensive care unit of Sindh Institute of Urology and Transplantation from April 2021 to October 2021. All consecutive adult patients admitted with covid 19 pneumonia were evaluated with cardiac enzymes (Trop-I, CPK, CK-MB, LDH), electrocardiogram, and limited bedside transthoracic echocardiography. Only the patients with poor acoustic window were excluded. Echocardiography was performed by a cardiologist with more than 25 years of experience using the Toshiba Xairo 200 ultrasonography machine. Echocardiography was blinded with the patient's history, comorbidities, and cardiac enzyme status before final report documentation to cater to any personal bias. The recorded findings included left and right ventricular systolic and diastolic dysfunction, valvular abnormalities, chamber size assessment, wall motion abnormalities, pericardial effusion, and tamponade physiology. ASE guidelines were considered for reference ranges.<sup>15</sup> Written informed consent was obtained from all participants. The confidentiality of all participants was ensured. The data were analyzed in SPSS version 26.0. Normally distributed continuous variables were expressed as mean  $\pm$  SD. While non-normally distributed variables as median (IQR) Categorical variables were given as frequencies and percentages.

For comparison of categorical variables between groups was determined using the Chi-square test. A cut-off value  $<0.05$  was used to assess the statistical significance.

## RESULTS

In this study a total of 129 patients were included in the study. The median age of patients was 53 years with a male preponderance (64%). Coexisting conditions include hypertension – 76 (58.9%), diabetes – 53 (41.1%) and end-stage renal disease -29(22.5%). Overall, 54(41.86%) patients had some type of cardiac abnormality on echo-cardiography (Table-1). This study found a significant association between the male gender and low ejection fraction (p-value 0.019). This study found a significant association between significantly raised troponin I \and low ejection fraction (p-value 0.034) (Table-2). Overall, in-ICU mortality was 40.3% which does not differ significantly across normal and abnormal cardiac enzymes, ECG findings, and echocardiography groups. Increased in-ICU mortality was observed in diabetics (p-value 0.04) and renal transplant recipients (p-value 0.05).

**Table-1: Baseline patient's characteristics and echocardiography results.**

<b>Gender, n (%)</b>		
	Male	83(64.3)
	Female	46(35.7)
Age, y(IQR)		53(45-64.5)
<b>BMI, n (%)</b>		
	Underweight	18(14.0)
	Healthy	54(41.9)
	Overweight	34(26.4)
	Obese	23(17.8)
<b>Coexisting Disorders, n (%)</b>		
	Hypertension	76(58.9)
	Ischemic heart disease	7(94.6)
	Diabetes mellitus	53(58.9)
	Chronic kidney injury	29(22.5)
	Renal transplant recipient	12(9.3)
	Septic shock	37(28.7)
	Cardiogenic shock	5(3.9)
	History of Angioplasty	5(3.9)
<b>Cardiac Enzymes, unit (IQR)</b>		
	High sensitivity troponin I pg/ml (IQR)	62(15.1-295.9)
	Lactate dehydrogenase U/L(IQR)	593.00(472.5-877.50)
	Creatinine phosphokinase U/L(IQR)	127.00(50.00-262.00)
	Creatinine kinase-MB U/L(IQR)	30.0(22.0-47.00)

<b>ICU therapies, n (%)</b>		
	Invasive Mechanical ventilation	43(33.3)
	Vasopressors	37(28.7)
	Inotropes	5(3.9)
Ischemic changes in electrocardiography, n (%)	24(18.6)	
<b>Echocardiography Results, n (%)</b>		
	Low ejection fraction	18(14.0)
	Right heart dilatation	3(2.3)
	Right heart systolic dysfunction/ low TAPSE	10(7.6)
	Pericardial effusion	13(10.1)
	Mitral valve stenosis	1(0.8)
	Mitral valve regurgitation	3(2.3)
	Mitral valve calcification	20(15.5)
	Aortic valve stenosis	0(0)
	Aortic valve regurgitation	0(0)
	Aortic valve calcification	3(2.3)
	Tricuspid valve stenosis	0(0)
	Tricuspid valve regurgitation	4(3.1)
	Tricuspid valve calcification	0(0)
	Pulmonic valve stenosis	0(0)
	Pulmonic valve regurgitation	0(0)
	Pulmonic valve calcification	0(0)
<b>ICU mortality, n (%)</b>		<b>52(40.3)</b>

**Table-2: Differential characteristics of patients with and without low ejection fraction.**

Variables	Low ejection fraction (n=18)	Normal ejection fraction (n=111)	p-value
Male, N (%)	16(88.8)	67(60.3)	0.019
Hypertension, N (%)	11(61.1)	65(58.5)	0.838
Ischemic heart disease, N (%)	1(5.5)	6(5.4)	0.66
Diabetes Mellitus, N (%)	10(55.5)	43(38.7)	0.179
Chronic Kidney Injury, N (%)	4(22.2)	25(22.5)	0.623
Renal Transplant Recipient, N (%)	1(5.5)	11(9.9)	0.476
Septic Shock, N (%)	7(38.8)	25(22.5)	0.118
Cardiogenic Shock, N (%)	1(5.5)	4(3.6)	0.534
Invasive Mechanical Ventilation, N (%)	8(44.4)	35(31.5)	0.281
Raised High Sensitivity Troponin I, N (%)	8(44.4)	23(20.7)	0.034
Raised Lactate Dehydrogenase, N (%)	15(83.3)	107(96.3)	0.056
Raised Creatine Phosphokinase, N (%)	10(55.5)	45(40.5)	0.232
Raised Creatine Kinase-Mb, N (%)	7(38.8)	66(59.4)	0.102
Ischemic Changes In ECG	2(11.1)	22(19.8)	0.304
History Of Angioplasty, N (%)	1(5.5)	4(3.6)	0.534
ICU Mortality (%)	5(27.7)	47(42.3)	0.243

**Table-3: Differential characteristics of patients with and without In-ICU mortality.**

Variables, n (%)	Non-survivors (n=52)	Survivors (n=77)	p-value
Male	36(69.2)	47(61.0)	0.341
Hypertension	31()	45(58.4)	0.894
Diabetes Mellites	27(59.6)	26(33.7)	<b>0.04</b>
Ischemic Heart Disease	5(9.6)	2(2.5)	0.093
Chronic Kidney Disease	14(26.9)	15(17.4)	0.321
Renal transplant	8(15.3)	4(5.1)	<b>0.05</b>
Low ejection fraction	5(9.6)	13(16.8)	0.243
Right heart dilatation	1(1.9)	2(2.5)	0.645
Right heart systolic dysfunction/ low TAPSE	5(9.6)	5(6.4)	0.523
Pericardial effusion	8(15.3)	5(6.4)	0.886
Mitral valve stenosis	0	1 (1.2)	0.597
Mitral valve regurgitation	3 (5.7)	0 (0)	0.063
Mitral valve calcification	8 (15.3)	12 (15.5)	0.975

Aortic valve calcification	3 (5.7)	0 (0)	0.209
Tricuspid valve regurgitation	1 (1.9)	3 (3.8)	0.179
Raised High sensitivity troponin I	14 (26.9)	17 (22.0)	0.528
Raised Lactate dehydrogenase	48 (92.3)	74 (96.1)	0.291
Raised Creatine phosphokinase	21 (40.3)	34 (44.1)	0.671
Raised Creatine kinase-MB	34 (65.3)	39 (50.6)	0.098
Ischemic changes in ECG	11 (21.1)	13 (16.8)	0.541
History of Angioplasty	3 (5.7)	2 (2.5)	0.68

## DISCUSSION

Covid-19 infection is recognized as a systemic disease involving multiple organ systems, heart being one of the most important.<sup>16</sup> The evolving information about Covid-19 expanded exponentially but cardiac involvement remained an area of concern and needed further evaluation especially from Pakistan.<sup>17</sup>

The chief indication of admission to ICU remains respiratory involvement but the evidence is emerging about cardiac involvement in acute and chronic Covid-19 infection.<sup>18</sup> Both right and left ventricles were involved in previous studies with different frequencies, this study showed depressed left ventricular function in every 7<sup>th</sup> patient, which is comparable to previous studies.<sup>13</sup> The right ventricle was even less involved in this study group involving only 3 patients with the dilated right ventricle. No significant valvular involvement was present in acute Covid-19 infection, although a quarter of the patients had nonsignificant changes (24%). Although 13 patients (10.1%) had pericardial effusion; none of them had cardiac tamponade. While comparing normal ejection fraction patients (86%) with low ejection fraction patients (14%), there was no significant mortality difference. Other studies have shown that mortality directly correlates with the severity of reduced left ventricular ejection fraction.<sup>19</sup> A systemic review from 2019 to 2020 data mentioned acute cardiac injury and raised troponin to be risk factors for increased mortality.<sup>20</sup> In all the parameters measured, only the male gender and raised troponin I was significantly different in the low ejection fraction group. In a previous study, myocardial depression is completely reversible in patients in whom troponin I levels were not elevated in the acute phase of covid 19.<sup>21</sup> The mortality in this group of patients in the ICU was 40%. Notifying the fact that 29 patients were suffering from renal failure and 12 had a kidney transplant, this mortality is comparable to or less than the previous studies.<sup>22</sup>

Diabetes mellitus is a known risk factor for ischemic heart disease.<sup>23</sup> In this study, mortality was

significantly higher in diabetic patients as compared to non-diabetics (p-value of 0.04). This has been shown in multiple studies before where mortality was significantly higher in diabetic patients as compared to non-diabetic patients.<sup>24</sup> The other significant mortality risk factor was renal transplant (p-value of 0.05). This aspect is well studied in previous research conducted in different parts of the world.<sup>31</sup> High cardiac enzymes also known as Troponin was not significantly associated with low ejection fraction or mortality, contrary to Manocha KK *et al* and Zwaenepoel B *et al* studies<sup>25,26</sup> which showed increased troponin levels were associated with high 30 days in-hospital mortality.

The strength of this study is the significant proportion of patients with renal failure and post kidney transplants in which not many studies have been published on echocardiographic findings. Patients were compared according to the mortality and risk factors associated with mortality were identified. The limitation of this study is the unidentified type of covid-19 virus. As the mortality and morbidity of different viruses have been different in different covid 19 waves,<sup>27</sup> it is yet to determine which virus has more cardiac involvement and mortality due to cardiac involvement.

## CONCLUSION

Overall, 41.86% of patients have some type of cardiac involvement. The male gender, and significantly raised trop I are risk factors for having a low ejection fraction. Abnormal cardiac parameters have no effect on in-ICU mortality. Further studies are needed to know the effects of different covid-19 variants on the cardiac involvement of patients.

## AUTHOR CONTRIBUTION

**Heeralal:** Conception, the acquisition, analysis, interpretation of data and manuscript writing

**Fakhir Raza Haidri:** Conception, the acquisition, analysis, interpretation of data and manuscript writing

**Zakia Haq:** Conception, Analysis and interpretation of data, revision of manuscript after review by the journal

**Ramesh Kumar:** Data collection and analysis

**Syed Aftab Mehmood:** Data collection and analysis

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