

## Study of suspected myocarditis in covid positive ICU patients

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### Abstract

**Background:** A novel beta-Coronavirus related to Severe Adult Distress Syndrome, named SARS-CoV was the cause of pandemic with more than 24 million people contaminated. COVID-19, the disease provoked by the virus, resulted in more than 80,000 deaths in quite 200 countries worldwide. Several cardiovascular complications were reported in literature like arrhythmias, myocarditis, pericarditis, heart failure, myocardial ischemia, myocardial infarction, and Takotsubo syndrome. To our knowledge several cases of myocarditis associated with SARS-CoV-2 have been reported so far; nevertheless, to date, there is a knowledge gap regarding the real prevalence of this cardiac involvement, its pathologic pathway and specific characteristics of patients who experience this complication. Thus, we will analyze the data of covid 19 cases on the basis of appropriate sample size of the patients admitted in our hospital. **Objectives:** 1. Study of hospital related outcome of Covid 19 patients with suspected myocarditis, 2. Correlation of NT-PROBNP levels, TROPONIN T in suspected case of myocarditis with outcomes. **Methods: Study Design:** Hospital based retrospective study **Setting:** Patients admitted in ICU in SMS Medical College and attached hospitals **Result:** Patients with myocarditis had significantly more prolonged hospitalization 14.75±8.53 days as compare to without myocarditis 10.44±4.16 days (P value .009), they had the non-significant values of IL-6 level, NT-pro-BNP and T-troponin patients without myocarditis **Conclusion:** Myocarditis is a severe cardiac complication in SARS-CoV-2 infection. Present study showed that in COVID-19 patients myocarditis was associated with more severe infection and a higher need for oxygen therapy, a higher rate of cardiac disease, and a longer hospitalization.

**Keywords:** Myocarditis, Covid 19 Infection, NT PROBNP, TROPONIN T, Length of Stay

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### Introduction

A novel beta-Coronavirus related to Severe Adult Distress Syndrome, firstly isolated in December 2019 in Wuhan, Central China and named SARS-CoV-2, is currently pandemic, with more than 24 million people contaminated. COVID-19, the disease provoked by the virus, resulted in more than 80,000 deaths in quite 200 countries worldwide.[1] Most patients have respiratory symptoms as fever, cold, cough, shortness of breath. However different clinical manifestations can be observed, from asymptomatic cases to mild and no-specific symptoms or severe complications as acute respiratory distress and death. Several cardiovascular complications were reported in literature like arrhythmias, myocarditis,

pericarditis, heart failure, myocardial ischemia, myocardial infarction, and Takotsubo syndrome.

To our knowledge several cases of myocarditis associated with SARS-CoV-2 have been reported so far; nevertheless, to date, there is a knowledge gap regarding the real prevalence of this cardiac involvement, its pathologic pathway and specific characteristics of patients who experiment this complication. Thus, we analyzed the data of covid 19 cases on the basis of appropriate sample size who were admitted in our hospital.

**Aims and Objective:** Study of suspected myocarditis and its prevalence in covid positive ICU patients and its associated factors like comorbidities, cardiac disease, need of oxygen support, cardiac markers, length of stay in hospital and mortality.

### Methodology

**Sample size:** To calculate the sample size based on the prevalence with 99% confidence level, we can use the following formula:

$$n = z^2 * P * (100 - P) / d^2$$

where, z= 2.58 at 99% confidence interval, P= 12% (Prevalence of suspected myocarditis) d= absolute error= 10%, Sample size n = 72 cases

**Statistical analysis:** All analyses were performed with SPSS statistical software version 21.0. Continuous variables are expressed as mean  $\pm$  standard deviation (SD); categorical data are given as counts and percentages. The Student's t test was used for groups' comparisons of continuous variables. The chi-squared test was used to compare proportions.

### Results

Present study mean age of the cases was 57.84 $\pm$ 15.75 years, median age 58.00 year, minimum age 32 year and maximum age was 84 year. 44(61.1%) cases were male and 28(38.9%) cases were female.

**Table: 1 Distribution of cases according to gender and age groups**

AGE GROUPS	GENDER			
	MALE		FEMALE	
21-40	5	11.4%	6	21.4%
41-60	18	40.9%	10	35.7%
61-80	17	38.6%	11	39.3%
>80	4	9.1%	1	3.6%
Total	44	100.0%	28	100.0%

Majority of cases were belongs to 41-80 year age groups among both male and female groups

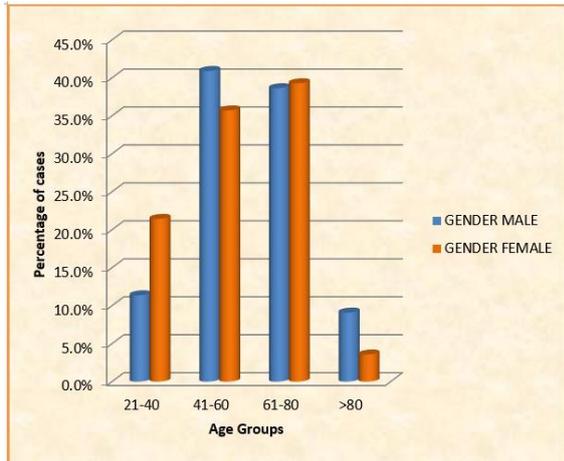


Figure 1: Distribution of cases according to gender and age groups

Table: 2 Characteristics in COVID-19 Patients

		N	%
Comorbidities	Yes	41	56.9%
	No	31	43.1%
Cardiac Disease	Yes	23	31.9%
	No	49	68.1%
Need of Oxygen Support	Yes	37	51.4%
	No	35	48.6%
Mortality	Yes	16	22.2%
	No	56	77.8%

Forty one (56.9%) patients had comorbidities like diabetes, COPD and CKD. Twenty three (31.9%) patients had a cardiac disease. Thirty seven (51.4%) need of oxygen-support and mortality rate of 16(22.2%).

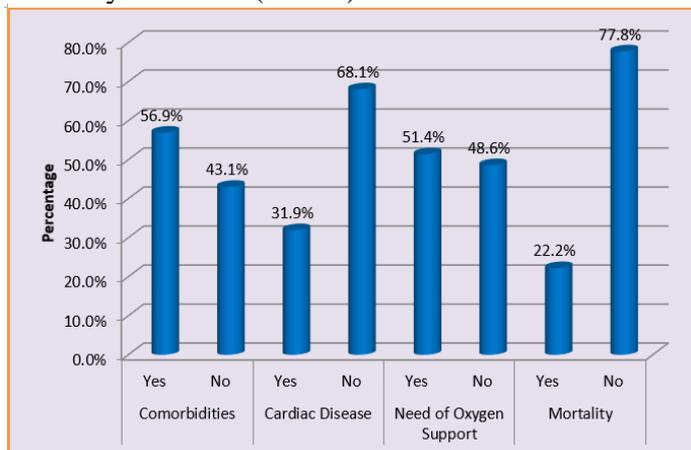


Figure 2: Characteristics in COVID-19 Patients

Table: 3 LOS and laboratory features of COVID-19 patients

	Mean	Standard Deviation
Length of stay	10.92	4.94
IL-6 level (pg/mL)	43.60	18.09
NT -proBNP (pg/mL)	904.31	702.19
T -troponine (pg/mL)	52.58	23.85

Length of stay of the cases was  $10.9 \pm 4.94$  days, IL-level  $43.60 \pm 18.09$ , NT -proBNP  $904.31 \pm 702.1$  and T -troponine was  $52.58 \pm 23.85$  among all cases

**Table: 4 Comparison between the group of myocarditis and the group without myocarditis**

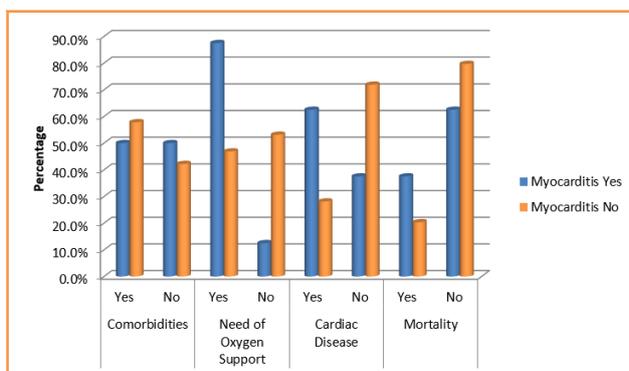
Myocarditis		N	Mean	SD	t	p
Length of stay	Yes	8	14.75	8.53	2.406	.019
	No	64	10.44	4.16		
IL-6 level (pg/mL)	Yes	8	33.13	14.00	1.762	.082
	No	64	44.91	18.21		
NT -proBNP (pg/mL)	Yes	8	595.50	566.45	1.326	.189
	No	64	942.91	711.63		
T -troponine (pg/mL)	Yes	8	61.13	20.46	1.076	.286
	No	64	51.52	24.16		

Patients with myocarditis had significantly more prolonged hospitalization  $14.75 \pm 8.53$  days as compare to without myocarditis  $10.44 \pm 4.16$  days (P value .009), they had the non-significant values of IL-6 level, NT-pro-BNP and T-troponin patients without myocarditis

**Table: 5 Comparison between the group of myocarditis and the group without myocarditis**

		Myocarditis				Chi-Square	p
		Yes		No			
Co morbidities	Yes	4	50.0%	37	57.8%	0.177	0.674
	No	4	50.0%	27	42.2%		
Need of Oxygen Support	Yes	7	87.5%	30	46.9%	4.698	0.03
	No	1	12.5%	34	53.1%		
Cardiac Disease	Yes	5	62.5%	18	28.1%	3.865	0.045
	No	3	37.5%	46	71.9%		
Mortality	Yes	3	37.5%	13	20.3%	1.215	0.27
	No	5	62.5%	51	79.7%		

Significant association was observed between myocarditis and need of oxygen, cardiac disease with  $p < 0.05$ . Need of oxygen support and cardiac disease was found higher in patient with myocarditis.



**Figure 3: Comparison between the group of myocarditis and the group without myocarditis****Discussion**

The available evidence regarding the association between COVID-19 and myocardial injury showed that cardiac involvement resulted in a substantial proportion of infected patients. The first Chinese report showed that 12% to 28% of patients had elevated cardiac troponin levels. Available data reported that acute cardiac injury is more frequently observed in patients with more severe COVID-19 infections, and patients with cardiac injury are often aged subjects with comorbidities including hypertension, CAD and diabetes; patients with a history of hypertension seem to be more exposed to cardiac damage. In the current literature, several mechanisms of cardiac involvement have been proposed: direct viral damage, adrenergic status, hypoxia, inflammatory response, drug toxicity. These mechanisms may result in different cardiovascular manifestations like arrhythmias, Takotsubo cardiomyopathy, heart failure, myocarditis, pericarditis, myocardial ischemia, myocardial infarction, microangiopathy with cardiac and peripheral involvement. Arrhythmia can be the result of underlying cardiac remodeling in pre-existent disease or the consequence of therapy with drugs such as azithromycin and hydroxychloroquine that can induce QT interval prolongation. Takotsubo cardiomyopathy in COVID-19 infection probably is triggered by both disease psychological stress and proinflammatory cytokine storm. Heart failure can result from the exacerbation of pre-existent cardiomyopathy.

In present study, the incidence of suspected myocarditis was 11.1%, myocarditis is currently underrated and misdiagnosed in COVID-19 infection clinical practice. Patients who experimented myocarditis had no difference in rate of death, and extracardiac comorbidities. On the contrary, we noted a significantly higher prevalence of previous cardiac diseases. Myocarditis in our COVID-19 patients was associated with significant prolonged hospitalization and a higher need for oxygen-support in patients.

IL-6 levels were lower in patients with myocarditis than in those without myocarditis, but this result did not reach a statistical significance. We can speculate that this can be due to different pathogenic mechanisms underlying myocarditis: prevalent overactivation of the immune system in patients without comorbidities, who showed a higher level of IL-6 and who responded earlier to corticosteroid therapy; prevalent direct viral damage and pathologic changes to the reninangiotensin- aldosterone system in patients with comorbidities, who were older, had a higher rate of cardiac diseases and needed longer support of inotropic therapy. We recognize that present has several limitations, first of all, the small sample of patients with suspected myocarditis. In clinical practice, myocarditis represents a growing challenge for physicians, because it presents in many different ways, ranging from mild symptoms of chest pain and palpitations associated with transient ECG changes to lifethreatening cardiogenic shock and ventricular arrhythmia. Viral myocarditis is mainly a diagnosis of exclusion, frequently supported by cardiac magnetic resonance imaging.

**Conclusion**

Myocarditis is a severe cardiac complication in SARS-CoV-2 infection. Present study showed that in COVID-19 patients myocarditis was associated with more severe infection and a higher need for oxygen therapy, a higher rate of cardiac disease, and a longer hospitalization. Since myocarditis patients had counterintuitive lower levels of IL-6, this finding deserves to be further investigated to better understand myocarditis prognostic and pathogenetic factors and to evaluate a specific target therapy.

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