CARDIAC INVOLVEMENT IN PATIENTS SUFFERING FROM COVID-19 AND ITS ASSOCIATION WITH DISEASES SEVERITY AND PROGNOSIS

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ABSTRACT

Objective: To determine frequency of cardiac involvement in patients of COVID-19. Secondary objective was to determine association of cardiac involvement with prognosis.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Pak-Emirates Military Hospital, Rawalpindi Pakistan, from Apr to Jul 2020.

Methodology: We prospectively assessed the laboratory data, Electrocardiogram and transthoracic echocardiography of all the COVID-19 patients admitted to our institute. Outcomes of interest included length of hospital stay, admission to Intensive Care Unit and mortality. Acute myocardial injury was defined by a value of high-sensitivity troponin I (hs-TnI) above the 99th percentile upper reference limit. Statistical Package for the Social Sciences (SPSS) version 23 was used for all the analysis.

Results: Our study included 1015 patients, mean age 50.34 (SD 13.71) years, 887 (87.3%) males and 128 (12.6%) females. Three hundred and thirty (n=330, 32.5%) patients had evidence of acute cardiac injury as shown by raised cardiac troponins, but 50, 4.92% had left ventricle dysfunction. Raised cardiac enzymes were associated with marginally prolonged hospital stay (10.03 versus 9.32 days, *p*-value 0.07) and higher mortality (OR 2.634, confidence interval 1.252-5.543, *p*-value 0.01).

Conclusion: Cardiac involvement is quite common among patients suffering from COVID-19 and predicts worse prognosis.

Keywords: Cardiac Injury, COVID-19.

INTRODUCTION

COVID-19 pandemic has affected almost every country in the world by now. Respiratory involvement is the dominant clinical manifestation but other complications including pneumonia, deranged renal and liver functions[1], myocardial injuries[2], immune deficiency[3] and coagulation activation. It has been documented that around 12% of patients with COVID-19 suffered acute cardiac injury. Pre-existing cardiovascular disease (CVD) as well as CV risk factors enhance vulnerability to COVID-19[4]. COVID-19 can worsen pre-existing CVD and even precipitate de novo cardiac complications[5].

METHODOLOGY

All COVID-19 patients who were <18 years and confirmed by RT-PCR were considered for this descriptive cross sectional study. A consective sampling technique was used. Keeping a confidence level of 95%, Margin of error 2% and population proportion 12%[3] sample size was 1015. Unwilling patients, those with previous history of heart failure and suffering from MODS (Multi Organ Dysfunction Syndrome) were excluded from the study. All the patients gave a written informed consent. A detailed history including risk factors was obtained. Demographic characteristics (name, age, gender, residence, and contact number) were recorded. Laboratory investigations included Total Leucocyte Count (TLC), CRP, Serumferritin, LDH, CKMB, high sensitivity Troponin I, NT-Pro BNP ECG and 2-D Echocardiography was performed on all patients. Cardiac injury wasdefined if the serum level of troponin I was above referencelimit. Keyoutcomes of interest included length of hospital stay, admission to Intensive Care Unit (ICU) and mortalityrate. Continuous variables were expressed as means and standard deviations and compared by student's t-test. Categorical variables have been expressed as frequencies and percentages and compared by chi-square test. Multifactor logistic regression analysis was used to investigate the impact of factors on length of hospital stay, ICU admission and mortality. All statistical analyses were performed used SPSS-23 and *p*-value <0.05 was considered significant.

RESULTS

This study included 1015 patients.mean age of the patients was 50.34 (SD 13.71) years, 887 (87.3%) were males and 128 (12.6%) females. Out of 330 (32.5%) patients had evidence of acute cardiac injury as shown by raised cardiac hs-Troponin I levels. Baseline charac-

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teristics of patients with and without cardiac involvement is shown in table-I.

Table-I: Baseline characteristics of patients with and without cardiac involvement.

Characteristic	Total	Hs-Trop I Normal	Hs-Trop I raised	*p*-value
Total	1015	685	330	
Age	50.34 (SD 13.71)	50.49 (SD 14.064)	50.01 (SD 12.959)	0.598
Male	887	589	298	0.05
Female	128	96	32	0.05
Raised NT-Pro BNP	108	79	29	0.184
ECG Changes	288	195	93	0.03
LV Dysfunction on Echo	50	35	15	0.697
Hospital Stay (In Days)	9.53 (SD 5.855)	9.32 (SD 5.527)	10.03 (SD 6.578)	0.07
ICU Admissions	309	204	105	0.50
Mortality	29	13	16	0.008

ECG changes were present in 28.37% of the total patients. Sinus tachycardia was the most common arrhythmia present in COVID-19 (13.8%) patients followed by nonspecific ST/T changes, sinusbradycardia, NSTEMIand finally STEMI. Raised cardiac enzymes were associated with marginally prolonged hospital stay (10.03 versus 9.32 days) and this association was statistically significant (*p*-value 0.07). Raised cardiac injury biomarkers (Troponin) was also associated with higher mortality rates among COVID-19 patients (OR 2.634,Confidence interval 1.252-5.543, *p*-value 0.01) but raised NT-Pro BNP and left ventricular dysfunction did not have statistically significant association with higher mortality (table-II). Overall mortality was higher among patients with acute cardiac injury compared to those with normal cardiac status (4.85 versus 2.20, *p*-value 0.008).

Table-II: Factors predicting mortality among COVID-19 patients.

Parameter	OR	Confidence Interval	*p*-value
Raised Troponins	2.634	1.252-5.543	0.01
Raised NT-Pro BNP	0.968	0.288-3.253	0.95
LV Dysfunction	0.683	0.091-5.124	0.71

DISCUSSION

COVID-19 can result in various cardiac complications including acute myocardial infarction[6] myocarditis[7] takotsubo cardiomyopathy and acute cardiac injury. Various studies have reported incidence of cardiac injury, as evidenced by raised cardiac troponins level, from 12%[9] in patients with mild severity to 42.6%[8,9] in severe and critically ill patients. Our study has shown 32.5% of the total patients had cardiac involvement shown by raised troponin level. Most of these patients had mild elevation in troponin level but those with severe injury had higher elevation. Mean age of the patients in our study group was 50 years so it can be postulated that a higher number of patients might be having either pre-existing cardiac illnesses or risk factors for cardiac disease. NT-proBNP elevation occurred in 10.65% of our study group. Troponin is a widely accepted biomarker of myocardial injury, and elevated serum levels have been a notable feature during recent epidemics of respiratory virus infections [10,11]. There are various mechanisms of acute cardiac injury during SARS CoV-2 infection including but not limited to cardio myocyte damage and apoptosis due to infiltration of inflammatory cells, cytokine storm, hypoxemia, acidosis, pulmonary hypertension, increased myocardial oxygen, microembolism causing cardiac injury, ACE2 mediated direct damage of cardiomyocyte, plaque instability in patients with previous coronary artery disease and fulminant myocarditis accompanied with pneumonia[16].

Cardiac arrhythmias are frequent in COVID-19 patients[12]. In our study group ,sinus tachycardia was the most frequent arrhythmia encountered and it has also been reported in various other studies[13]. Other arrhythmic complications include sinus bradycardia and transient atrioventricular blocks. Around 5% patients in our study group had severe left ventricular dysfunction. Dweck *et al.* observed cardiac disease (severe ventricular dysfunction or tamponade) in 15% of their patients[14]. In our study group, association between left ventricular dysfunction and higher mortality was not statistically significant. Acute left and right ventricular failure may be a direct consequence of cardiac pathology, with the latter being also caused by elevations in right ventricular afterload due to pulmonary embolism or pneumonia. Other echocardiograp-

hic presentations of COVID-19 cardiac involvement include pericardial effusion, signs of pulmonary hypertension and right ventricular dysfunction[8].

Mortality data from 44672 cases of COVID-19 released by the Chinese Centre for Disease Control and Prevention showed that patients with cardiovascular comorbidities have a much higher mortality (10.5% vs 0.9%) in COVID-19 patients[15]. A study from Shi *et al* showed that compared to those without cardiac injury, patients with cardiac injury required more noninvasive ventilation (46.3% vs 3.9%; p<001) and invasive mechanical ventilation (22% vs 4.2%; p<001), and also had a higher mortality (51.2% vs 4.5%; p<001)[17]. This study has shown that mortality was higher among patients with acute cardiac injury compared to those with normal cardiac status (4.85 vs 2.2, p-value 0.008). This study results are in line with various studies done during the current pandemic. In another study by Guo *et al*. Mortality was markedly higher in patients with elevated plasma TnT levels than in patients with normal TnT levels (59.6% vs 8.9%)[18]. But there are few studies with contrary to above results. Zhou *et al* showed that hs cTnI>28pg/mL was not associated with mortality in multivariate analysis in their study[18].

This study limitations include lack of stratification of data keeping in view the pre-existing cardiac illnesses and elevated cardiac troponins were not categorized as per severity.

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CONCLUSION

Increasing clinical and epidemiological evidence, as described by the literature view and our study results, suggests that acute myocardial injury, as indicated by troponin elevation, is common in patients with COVID-19. Patients with raised cardiac injury biomarkers have prolonged hospital stay as compared to patients without any cardiac involvement in COVID-19. Cardiac injury is also associated with worse prognosis.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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