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# CARDIAC PROFILE OF COVID-19 PATIENTS IN INDIA AND ITS PROGNOSTIC IMPLICATIONS

Medicine

**Dr. Vipul Phogat*** Post Graduation Resident, Department Of General Medicine, Government Medical College, Kota, Rajasthan, India. *Corresponding Author

**Dr. Shyoji Ram Meena** Senior Professor, Department Of General Medicine, Government Medical College, Kota, Rajasthan, India.

**Dr. Mayank Sharma** Post Graduation Resident, Department Of General Medicine, Government Medical College, Kota, Rajasthan, India.

**Dr. Pramod Chaurasiya** Assistant professor, Department Of General Medicine, Government Medical College, Kota, Rajasthan, India.

## ABSTRACT

**OBJECTIVE:** The main aim of the study is to delineate the effects of COVID-19 infection on routinely available cardiac profile markers and to assess their use as a potential prognostic marker. **METHOD:** A retrospective cohort study was done using medical records of 500 laboratory confirmed COVID-19 patients admitted in Government Medical College, Kota, Rajasthan, India between April, 2020 to June,2020. Cases were divided into 3 groups depending on the disease severity. **RESULTS:** The sample population had 58.6% males. The highest number of cases were young adults (18-44 years) while severe disease was present mostly (80%) in people >45 years age. The mean values of CK-MB (63.7 U/L), LDH (829.2 U/L) and AST (63.8 U/L) in group 3 was significantly (p value < 0.05) more than other two groups. Positive C-reactive protein and electrocardiographic abnormalities were present in 57.5% and 62.5% cases respectively, while markedly less in other two groups. **CONCLUSION:** The levels of various cardiac markers included in the study were significantly raised in patients having severe disease and these levels were higher than in studies done in Chinese patients. Thus, cardiac involvement is evident in severe COVID-19 cases and cardiac profile monitoring is an important tool in assessing prognosis of the disease.

## KEYWORDS

Cardiac Profile, COVID-19, Prognosis

## INTRODUCTION

On 31st December,2019, WHO got a report of a cluster of pneumonitis cases in Wuhan city of Hubei province of china[1]. When the unusual increase in cases caught attention of health authorities, rapid search for the causative agent began. By January 7, 2020, the virus which was soon going to cause one of the biggest healthcare burdens in the history of mankind, was isolated and it was named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2). The disease was eventually named as Coronavirus Disease 2019 (COVID-19) in February, 2020, by WHO.

This is the third coronavirus disease that has gripped humans in last two decades, preceded by Severe Acute Respiratory Syndrome (SARS) in 2002 and Middle East Respiratory Syndrome Coronavirus (MERS) in 2012. Genetically it is a beta coronavirus of the same subgenus as SARS CoV-1(79% similarity) but of a different clade.[2]

The virus is mainly spread by droplets produced during coughing, sneezing or talking, although fomite spread is also possible but it does not seems to be a major way.[3]

The origin of the virus is presumed to be zoonotic as the epicentre is believed to be Huanan seafood market in Wuhan where a number of live animals and birds are also traded but still the topic is under heavy research & controversy.

The incubation period of the disease is presumed to be around 14 days. The clinical spectrum of disease appears to range from completely asymptomatic to very severe viral pneumonia requiring ventilatory support.[4]

Before its high communicability was sensed, it was already too late. The virus easily spread to other parts of the highly connected present world. WHO declared the disease as pandemic on 11th March,2020. As of 10th June,2020, there are already >72 lakh cases with > 4 lakh deaths worldwide. The highest toll of deaths has been registered in U.S.A, U.K, Brazil, Italy, Spain, France, Mexico. India being the 2nd most populous country and a developing economy with limited resources faces a big challenge. There are already >2.6 lakh cases and >7.4 thousand deaths till now, despite the national restrictions imposed from 25th,march,2020, during stage 1 of spread.[5] India has now entered stage 4 of transmission with rampant community spread.

The need of the hour is to promote more and more local studies to delineate the clinical characteristics of the indigenous patients so that efficient health planning suited to the local level can be made.

Since, cardiac involvement is being increasingly recognised in COID19, this study is aimed to delineate the cardiac profiles of COVID-19 cases in the Indian population, compare it with other populations and to determine its value in early identification of severe cases and to estimate prognosis.

## METHODS

### Study design and participants

This a retrospective cohort study of first 500 laboratory confirmed COVID-19 patients admitted in GMC, Kota, the only dedicated COVID-19 tertiary care facility in the region. The study spans from April,2020 to June, 2020. The study was conducted after prior permission from Institute's Ethics Committee (IEC).

### Case diagnosis

All suspected patients having symptoms suggestive of the disease with history of international travel or contact with a positive case in last 14 days were chosen for testing. Throat swabs were taken by appropriately trained laboratory staffs after taking all biosafety precautions. The samples were placed into a collection tube containing Viral Transport Medium (VTM). The samples were processed and RT-PCR was performed using U.S FDA approved or European CE certified testing kits as per recommendations of ICMR.[6]

### Data collection

After diagnosis all the positive cases were isolated and managed in dedicated wards. Routine biochemical and radiological investigations were performed on all the patients along with appropriate additional investigations.

The demographic, clinical and laboratory data of all the patients was collected in predefined proforma and tabulated.

### Statistical analysis

All continuous variables are presented as mean, standard deviation and categorical variables as proportion. The continuous variables were compared using ANNOVA t-test and categorical variables using chi-square test.

## RESULTS

To compare the results according to severity of disease, patients were divided into 3 groups of disease severity as per the clinical management protocol issued by Ministry Of Health and Family Welfare, version 2:

**Group 1:** no disease manifestations.
**Grade 2:** mild to moderate disease.
**Grade 3:** severe disease.

The number of patients falling in respective groups were 294(58.8%), 166(33.2%) and 40(8%).

**Table I: Demographic details of patients.**

| | All (n=500) | Group 1 (n=294) | Group 2 (n=166) | Group 3 (n=40) | P value |
|---|---|---|---|---|---|
| **Age** | | | | | |
| <18 | 41 (8.2%) | 20 (6.8%) | 21 (12.6%) | 0 (0%) | |
| 18-44 | 291 (58.2%) | 185 (62.9%) | 98(59%) | 8 (20%) | |
| 45-64 | 138 (27.6%) | 80 (27.2%) | 39 (23.4%) | 19 (47.5%) | |
| 65 | 30 (6%) | 9 (3%) | 8 (4.8%) | 13 (32.5%) | |
| Mean (years) | 38.14 | 36.5 | 36.8 | 56.6 | 0.033 |
| **Sex** | | | | | |
| Male | 293 (58.6%) | 148 (50.3%) | 120 (72.2%) | 25 (62.5%) | |
| Female | 207 (41.4%) | 146 (49.6%) | 46 (27.7%) | 15 (37.5%) | |
| **Comorbidities** | | | | | |
| Diabetes (DM) | 36 (7.2%) | 15 (5.1%) | 8 (4.8%) | 13 (32.5%) | 0.028 |
| Hypertension (HTN) | 48 (9.6%) | 16 (5.4%) | 14 (8.4%) | 18 (45%) | 0.005 |
| Pregnant & Post-partum | 15 (3%) | 12 (4%) | 3 (1.8%) | 0 (0%) | 0.299 |
| Chronic kidney disease (CKD) | 5 (1%) | 0 (0%) | 2 (1.2%) | 3 (7.5%) | 0.199 |
| Ischaemic heart disease (IHD) | 10 (2%) | 1 (0.3%) | 5 (3%) | 4 (10%) | 0.109 |
| others | 30 (6%) | 12 (4%) | 11 (6.6%) | 7 (1.75%) | 0.225 |

**Table II: Cardiac profile according to severity of disease. LDH(Lactate Dehydrogenase), CK-MB (Creatine Kinase-Myocardial Band), AST (Aspartate Aminotransferase), CRP (C-Reactive Protein), ECG (Electrocardiography).**

| Marker | Group 1 (n=294) | Group 2 (n=166) | Group 3 (n=40) | P value |
|---|---|---|---|---|
| LDH (U/L) | 498.7 | 562.2 | 829.2 | 0.024 |
| CK-MB (U/L) | 49.2 | 57.5 | 63.7 | 0.005 |
| AST (U/L) | 29.8 | 35.7 | 63.8 | 0.054 |
| Qualitative CRP | 14(4.7%) | 18(10.8%) | 23(57.5%) | 0.196 |
| ECG abnormalities | 64(21.7%) | 40(24%) | 25(62.5%) | 0.632 |

## DISCUSSION

SARS CoV-2 causes infection by binding of the viral coat spike glycoprotein to the Angiotensin Converting Enzyme 2 (ACE2). Moreover, SARS CoV 2 binds with ACE2 with higher affinity than SARS CoV.[7] . ACE2 is a membrane bound peptidase which degrades Angiotensin 2, the prime effector of Renin Angiotensin Aldosterone System (RAAS) which causes vasoconstriction, inflammation, oxidative stress and fibrosis. ACE2 is expressed most extensively in ileum and kidney but also in other organs like heart, brain, lungs and vessels as evidenced in mouse models, leading to its varied manifestations related to these organs.[8] The expression of ACE2 on heart makes it a potential viral target. Multiple mechanisms of injury have been proposed including:

1. Endothelial dysfunction leading to plaque rupture and thrombosis[9],
2. Direct or ACE2 dependant viral invasion of cardiomyocytes leading to arrythmia and loss of cardiac function[10] and
3. "Cytokine storm", an over-exuberant immune response[11].

In our study, only 8% of cases had severe disease who required transfer to Intensive Care Unit (ICU) which is significantly less than in study done by wang et al (26.1%).[12]

The sample population had 58.6% males which is due to the fact that males have higher occupation related exposures. Males were significantly higher than females in group 2 and 3. This may signify that males develop more severe disease as compared to females. This may be due to higher incidence of smoking and other abuses in males.

The age group of 18-44 years i.e. young adults had maximum number of patients which is consistent with the age distribution of the population of a developing nation. The mean age in group 3 was 56.6 years which was 1.5 times higher than in other two groups. Also, there were no cases in group 3 below 18 years age. Both these findings denote that severe disease was more common in older age group, which is consistent with the previous studies.

Hypertension was the most common (9.6%) comorbidity, present in 45% cases in group 3 while in less than 10% in the other two groups. Diabetes was 2nd most common comorbidity present in 32.5% cases in group 3 while in less than 5% in the other two groups. This denotes that underlying comorbidities pose a greater risk for developing severe disease.

Various studies have gauged the effect of SARS CoV 2 infection on cardiac profile of COVID-19 patients:

1. Huang et al did a study on 41 patients in china and found that in Intensive care unit (ICU) vs non-ICU patients, LDH (400 vs 281 U/L), AST (44 vs 34 U/L) and cTnI ( >28pg/ml in 31% vs 4%) were significantly raised.[13]
2. Wang et al did a study on 138 patients in china and found that in ICU vs non-ICU patients LDH (435 vs 212 U/L), AST (52 vs 29 U/L), CK-MB (18 vs 13 U/L), cTnI (11 vs 5.1 pg/ml) were raised significantly and new onset arrythmia was present in 44% having severe disease while in 8.9% in mild cases.[12]
3. Zhou et al did a study on 191 patients in china in which he found that Cardiac Troponin I (cTnI) was found to be significantly raised in around 50% of patients who died, while LDH was raised in 98% of non-survivors and heart failure was present in 53% who died vs 12% in survivors.[14]
4. Shi et al did a study on 416 patients in china in which he found that cardiac injury was a common complication (19.7%) and mortality rate was higher among patients with cardiac injury ( 51.2% vs 4.5%).[15]

In our study, the mean value of LDH in group 3 was 829 U/L, which is significantly higher than in other two groups. The mean value of CK-MB was 63.7 U/L which is also significantly higher than in other two groups. The value of AST is 63.8 U/L which is more than double than in other two groups. The value of all these biomarkers are higher than those found by Huang et al and wang et al in their studies based on Chinese population.

Wang L found in his study that CRP level positively correlates with COVID-19 disease severity and size of largest lung lesion.[16] Chen et al also found that plasma CRP levels correlated with severity of pneumonia.[17] In our study qualitative CRP was positive in 57.5% patients in groups 3 whereas only upto 10% in other two groups.

Angeli et al found ST abnormalities in 30% patients in his study including 50 patients.[18]

in our study, ECG abnormalities were present in 62.5% of patients in group 3 whereas less than in 25% in other two groups. The most common (15.7%) ECG findings was localised or generalised ST-T abnormality.

Other methods of identifying cardiac injury such as cTnI, NT-Pro BNP, echocardiography, angiography and cardiac magnetic resonance imaging were not used in the study because of limited availability of these methods in a resource poor setting which is further exacerbated by the restricted use in COVID-19 pandemic.

## CONCLUSION

Findings of the study signify that cardiac profile is evidently deranged in COVID-19 patients in India, especially in severe cases. But the proportion of patients having severe disease is less in India. The rise in level of cardiac markers is gradual, coinciding with increasing severity of disease. Thus, cardiac profile of patients COVID-19 patients should be regularly monitored for timely identification of high-risk cases and to estimate prognosis.

**Conflicts of interest:** none

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