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Cardiovascular Manifestations in Post Covid-19

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CARDIOVASCULAR MANIFESTATIONS, COVID-19, MYOCARDIAL INFARCTION, PULMONARY EMBOLISM, ARRHYTHMIA.

Abstract
BACKGROUND
COVID-19 is a pandemic which initially started in Wuhan, China and is still not under control worldwide. Because of evident spread in the many countries and increased death tolls WHO declared COVID-19 as a public health emergency on January 30 2020. Following recovery from COVID-19 many individuals have developed complications like clinical and sub clinical myocarditis, arrhythmias, pericarditis & pericardial effusion, heart failure and pulmonary embolism. So it is important to follow up with those patients who recovered from COVID-19 regularly for prompt diagnosis and treatment.
OBJECTIVE
To evaluate the cardiac status of the patient who recovered from post COVID-19 by electrocardiography.
PATIENTS AND METHODS
This cross-sectional study was comprising of 30 patients who were recovered from COVID-19 was selected as study subjects based on convenient sampling. History of symptoms, events following hospitalisation, use of anti-coagulants was elicited in the study participants followed by complete clinical evaluation and their cardiac status was assessed by electrocardiography, levels of CRP and D-dimer during the recovery phase was noted. Association of ECG with levels of CRP and D-dimer, presence/absence of symptoms are studied and compared.

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RESULTS:
Out of 30 patients we had no significant outcome but there is enough finding which has to be evaluated and followed with regular intervals to avoid the serious complications. So further highlights are need for a multifactorial analysis in more number with variable comparative factors to asses the prognosis in post-COVID-19.
CONCLUSION:
Cardiovascular morbidity and mortality in post COVID-19 does not depend on one individual factor. It is multifactorial, hence consideration of other factors, long term follow up, multi system approach with more number of samples are needed for further analysis and interpretation.

1. Introduction

Corona virus is a huge community of single positive stranded RNA enveloped viruses and it infectious in various species including Homo sapiens. Corona viruses which infects humans are classified by their pathogenicity. Variant coronavirus with very high pathogenicity include MERS-CoV,SARS-CoV and SARS-CoV2. The initial mode of transmission is through cross-species transmission by bat to human. It is believed that initial transmission was happened in Wuhan, China,2019. SARS-Co2 is more transmissible than SARS-CoV2. The outbreak of SARS-CoV2 in China was catastrophic and lead to changes in health care systems. Comparatively ability of encountering pandemic COVID-19 in India is lesser than China([1,2]).COVID-19 cases were started to drop from September 2020 after a surge of around 100000 confirmed positive cases per day. But it began to rise again in March 2021 with double strength than the previous wave. The nationwide vaccination campaign was kick started in January 2021 and more than 250 million people were vaccinated which doesn't count even the ten percent of Indian population([3]). sAfter Corona virus infection the quality of life is declined in individuals who were hospitalised for COVID-19 disease. Longer term sequelae in post COVID-19 patients is not well characterised. There is an increased incidence of heart failure as a one of the major sequela of COVID-19 is of concern[(4)].So we followed up the patients to look for cardiovascular complications in post COVID-19 patients.

2. Methods:

This cross-sectional study was comprising of 30 patients who were recovered from COVID-19 was selected as study subjects on post COVID follow up, based on convenient sampling. Informed consent was obtained from the patients and study is duly approved by ethical committee of Sree Balaji Medical College Hospital, Chromepet, Chennai.

INCLUSION CRITERIA

- Documented history of COVID-19
- Age >18 years
- Patients with comorbidities like Type2 Diabetes Mellitus, Systemic Hypertension and others

EXCLUSION CRITERIA

- Age <18 years
- History of Coronary Heart Disease, Heart Failure, Atrial Fibrillation
- History of Congenital Heart Defects

Post COVID-19, irrespective of COVID-19 pneumonia severity patients who were fulfilling the inclusion criteria of age >18 years, with or without co-morbidities who were recovered from COVID-19 . Patients <18years and previously known case of cardiovascular disorders were excluded from the study. History of symptoms, use of anticoagulants and events following hospitalisation or completion of treatment was elicited in the study participants and their cardiac status was assessed by electrocardiography, levels of CRP and D-dimer during the recovery phase are noted. Treatment was started according to the complication. Association of ECG with levels of CRP and D-dimer, presence/absence of symptoms are studied and compared. Data is then statistically analysed using analytical cross-sectional study

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CRP & D-dimer Statistical Comparison

	Value	df	p-value
Pearson Chi-Square	11.920[a]	10	.290
Likelihood Ratio	15.778	10	.106
N of Valid Cases	30		

a. 20 cells (90.9%) have expected count less than 5. The minimum expected count is .47.

Table 1.0

3. Results:

Figure 1. Interpretation of ECG manifestation among post COVID 19 infection.

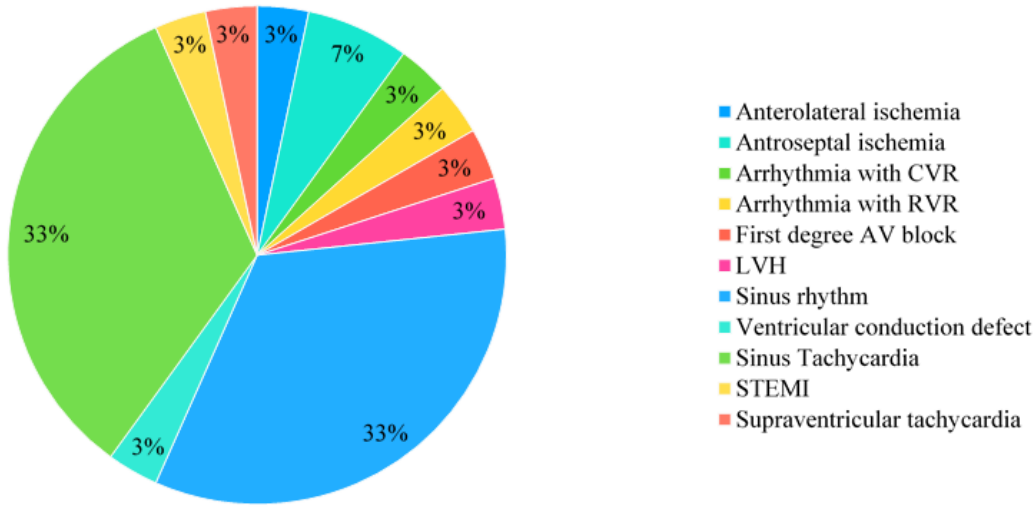

Figure 1.

Among the 30 patients who were recovered from COVID-19, the interpretation of ECG with symptoms, comorbidities and inflammatory markers were done. Though it is a cross-sectional study the sample size was 30 which is very lesser to get a significant outcome Under 30 study subjects ten subjects presented with symptoms, in that 33.3% showed significant ecg changes. C-reactive protein was elevated in 14 subjects among them 46.7% showed ecg abnormality which is similar in D-dimer levels. On people with comorbidities type2 diabetes mellitus had 40 % and systemic hypertension 30%

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significance in electrocardiography. And in subjects who were taking anticoagulants only 23.3% showed incidence.

12 variants of abnormal presentation of electrocardiography was noted, among them 33.3 % were normal presentation and another 33.3% showed sinus tachycardia. And some of them presented with myocardial infarction ,arrhythmias and heart blocks. By doing this study with various factors ,we couldn't point out a single factor as an independent predictor for this outcome which signifies elimination of any single factor as a marker on its own. Further, this highlights the need for a multifactorial analysis in long term basis in larger number to asses the post COVID-19.

4. Discussion:

PATHOPHYSIOLOGY OF COVID-19

S-spike protien of SARSCoV2 binds to ACE2 receptor at the access point. Type I and type II pneumocytes expresses ACE2 receptors. ACE2 receptors also expressed in endothelial cells and some others. ACE2 is an upright regulator of renin angiotensin aldosterone system. A likely primary target of SARSCoV2 is respiratory system[5,6,7]

Adaptive immune system will try to eliminate the virus in the incubation stage of the disease. Despite the failure of immune system in the first phase the virus disseminate and cause multi-organ damage which shows evident destruction of organs with peak expression of ACE2 receptors in lung endothelial cells, myocardial cells and glomerulus causing severe damage leading to second phase severe inflammation in involved organs(8). Immune system is down regulated by atherosclerosis, diabetes and obesity, which are also risk factors for cardiovascular disease. (9)

Acute respiratory distress syndrome and end organ damages occurs by severe inflammation where cytokines play a role in enhancing it[9,10]. Elevated pro-inflammatory cytokines like IL-2,IL-10,IL-6,IL-8 and TNF-alpha induces the inflammation cascade and causing multiple tissue injury including vascular endothelium and myocardial cells [11].

Cardio-metabolic demand in severe systemic infection and hypoxia by infected myocardium causing fatal pneumonia and ARDS. Thrombotic coronaries causing acute coronary syndrome is very evident in COVID 19 infection[12].

POST COVID-19 SEQUELAE

COVID-19 cardiovascular complications are more frequent comparatively and associated with increased morbidity and mortality with long term prognostic implication. It is very important to raise awareness for the post COVID-19 cardiovascular complications like clinical and sub clinical myocarditis, arrhythmias, pericarditis & pericardial effusion, heart failure and pulmonary embolism.It is to be believed that adaptive immune response to SARSCoV2 infection causes inflammation of the myocardium which influencing this cascade of events. So we followed the post COVID-19 patients who were hospitalised on out patient basis and elicited history with detailed clinical examination. Echocardiography and cardiac magnetic imaging is more specific comparatively but because of the economic burden cardiac evaluation was done by electrocardiography. Interpretation of ecg and clinical correlation is done here to raise the awareness about post cardiac manifestations and to avoid the mortality in post COVID-19 sequelae.

MYOCARDITIS

Myocarditis is inflammation of myocardium commonly associated with viral infection. Most common presentation of myocarditis is chest pain, breathlessness,palpitation and pounding heart. In severe cases it can lead to myocardial infarction, fulminant hear failure, stroke and sudden cardiogenic shock. The pathophysiology is mediated by cytokine storm syndrome where IL-6 enhances the pro-inflammatory response through immune cells like T-lymphocytes[12]. This stimulation of T-lymphocytes causes positive feedback of immune activation and myocardial damage. Most of the infected patients will have self limiting mild symptoms which are managed by local medical prcationers and they may not undergo any cardiac evaluation. These unnoticed patients will develop the risk of arrhythmias in future. So it is much important to screen the patients to exclude the devastating complication.

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ARRHYTHMIA

Conduction system of heart is involved in various viral infections like influenza virus, Epstein-Barr virus, Human Immuno Deficiency virus,etc. But arrhythmia in post COVID 19 infection is add on in that group. There's an evidence of cardiac arrhythmias in the family of corona virus like MERS and SARSCoV(13,14). Where sinus tachycardia is the secondary physiological response of the viral infection[15]. It can also be secondary due to adverse effects of medication[16]. QT prolonging drugs like azithromycin or hydroxychloroquine can also progress to arrhythmias. Without any history of arrhythmias atrial and ventricular arrhythmias have been witnessed in COVID-19 infection. Atrial fibrillation is most common arrhythmia comparitively[17]. Cardiac markers and complete evaluation of cardiac status required to avoid the unprecedented events.

PULMONARY EMBOLISM

Several countries like China, Italy and Ireland have done studies that confirms COVID-19 is linked with hypercoagulable state and an increased risk thromboembolism[18]. The International Society on Thrombosis and Haemostasis (ISTH) have shown that severe COVID pneumonia can cause sepsis leading to intravascular clotting state known as "sepsis induced coagulopathy"**[19]** . Hypercoagulation is mainly initiated by microvascular damage by SARS-COV-2 virus leading to cytokine release, in few cases can cause reactive thrombocytosis. The risk of thrombus formation increases with obesity, old-age and immobilisation. Most of the patients will have high D-dimer value, which is associated with increased risk of pulmonary embolism[20]. Association of thrombosis and COVID pneumonia during acute stage of infection has been proved by many studies, but not much information on occurrence of pulmonary embolism at the late stage of infection. In most of the cases of pulmonary embolism occurring in late stage of disease, the median time from diagnosis of COVID-19 to occurrence of symptoms is about 20 days. In such cases, inflammatory markers during the time of pulmonary embolism were normal. This leads to possibility of persistence of hypercoagulable state even after the stage of acute inflammation and cytokine storm, despite the anticoagulant prophylactic measures [21]. Among the 30 patients one of the young female patient developed fatal pulmonary thromboembolism with presentation of sinus tachycardia and D-dimer more than 10000. Incidence of thromboembolic events even in the healing phase shows the need for long-term anticoagulant therapy that should be started at the time of diagnosis and regular follow-up even after discharge from the hospital.

5. Conclusion:

This cross-sectional study was done by convenient sampling during the second wave of COVID-19. The limitation of this study is the sample size. Sample size of 30 was inadequate to generalise the genesis of cardiovascular manifestations in post-COVID-19 patients. This study proposes a hypothesis that cardiovascular manifestation in patients post-COVID-19 is multifactorial and it can also be due to some other external factors. People recovered from second wave of COVID-19 developed lot of cardiovascular symptoms , and it is necessary to have a long term follow up and also assess them by a multifactorial approach. Overall, despite the identification and evaluation of several factors which may contribute to cardiovascular manifestations in post COVID-19 patients, the exact mechanism behind each clinical occurrence are yet to be elucidated.

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ARTICLE INFORMATION

CONFLICT OF INTEREST: None

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AUTHOR CONTRIBUTIONS:

Dr.SARATH BHASKAR.S is the co-first author. They are responsible for the integrity of the data and had full access to all data in the study.

Study concept and Designing: Dr PADMA V

Acquisition, analysis and interpretation of data: Dr. SARATH BHASKAR.S

Critical revision of manuscript: Dr SHINY THOMSON

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