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A Review of Cardiovascular Complications in Patients with COVID-19 Infection

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Abstract

So far, it has been reported that the Covid-19 infection mainly involved respiratory system. During second wave, a rising number of cardiovascular complications have been described by many institutions. The literature is regularly updating the cardiovascular complications of Covid-19 infections in hospitalized patients or those who recovered. Also, it has been a matter of concern especially for those patients who have co-morbidities or pre-existing cardiovascular diseases because they are vulnerable in the setting of Covid-19. The mortality and morbidity increase in such patients due to cardiac injury caused by Covid-19 infection. We have reviewed the latest literature from 2019 onwards on this issue in order to summarize the pathophysiology, mechanism and effects of COVID-19 on cardiovascular system including their clinical consequences in patients with SARS-CoV-2 infections.

Keywords: COVID-19; Arrhythmia; SARS-CoV-2; Pandemic; Cardiac; Myocarditis

Abbreviations

SARS-CoV-2: Acute Respiratory Syndrome Coronavirus 2; ACE-2: Angiotensin-Converting Enzyme; ECG: Electrocardiogram; MRI: Magnetic Resonance Imaging

Introduction

According to the World Health Organization (WHO), the COVID-19 or severe acute respiratory syndrome coronavirus 2 (SARS- COV-2) pandemic has involved 172,637,097 cases and 3,718,944 deaths (cumulative) all over the world as on 6th June, 2021. The Alfa and Beta genera of Corona virus can infect human cells. The other two genera namely, Gama and Delta infect animals [1-2]. Sometimes coronaviruses that infect animals can evolve and make people sick and become a new human coronavirus. Three recent examples of this are 2019-nCoV, SARS-CoV-2, and MERS-CoV [1-2]. The Corona virus is single stranded enveloped RNA virus, have a crown-like morphology, consisting of four structural proteins known as Spike (S), Envelop (E), Membrane (M) and Nucleocapsid (N) proteins [2]. The 'WHO' has recently classified variants of SARS-CoV-2 and these include alpha, beta, gamma, delta, epsilon, zeta, eta, theta, iota and kappa [1].

The Covid-19 (SARS-CoV-2) infection mainly involves respiratory system. However, as the second-wave has infected more patients, a rising number of cardiovascular complications have been reported. The literature is regularly updating the cardiovascular complications of Covid-19 infections in hospitalized patients or those who recovered. It has been a matter of concern especially for those patients who have co-morbidities or pre-existing cardiovascular diseases because they are vulnerable in the setting of Covid-19. The mortality and morbidity is expected to increase due to cardiac injury caused by SARS-CoV-2 infection [3].

Approximately 10-30% of the hospitalized Covid-19 patients have evidence of cardiac involvement. It is acute or chronic in nature [4].

Material and Methods

The present study comprised of review of published English literature on impact of COVID-19 infection on cardiovascular system and morbidities in patients with cardiac conditions during or after the Corona virus infection. An attempt has been made to update the pathophysiology, mechanism and types of cardiovascular complications of SARS- COV-2 viral infections. The literature search included "PubMed, "google search" and other published reports in the English language journals, 2019 onwards.

Results and Discussion

The information archived has revealed various cardiovascular complications associated with corona virus infections during and after the initial episode. The objective measures used to identify cardiovascular complications included clinical findings, histopathological examinations, imaging studies and autopsy examinations.

Cardiovascular Manifestations of Covid-19

1. Myocardial injury and myocarditis
2. Arrhythmia
3. Acute coronary syndrome
4. Thromboembolism
5. Hyper inflammatory shock and Kawasaki-like disease (in children).

The Mechanism of Cardiac Injury

The lung and heart are both covered with protein molecules called Angiotensin-Converting Enzyme-2 (ACE-2). The ACE-2 protein is the doorway that the new coronavirus uses to enter cells

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and then multiply. The ACE2-virus complex starts an endosomal entry pathway where priming of the 'S' protein facilitates binding and translocation of the virus complex to endosomes and subsequent release into the cytoplasm. The ACE-2 receptors normally play a favorable role in protecting cells from inflammation. Unfortunately, the coronavirus somehow disables those molecules and subsequently makes the cells and tissues unprotected when the immune system reacts and liberates cytokines and inflammatory metabolites. The resultant systemic inflammation, cytokine storm and microthrombi formations due to deranged coagulation cascade further damages the myocytes and endothelial cells in the cardiovascular, respiratory and other organ-systems [3-4].

Myocardial injury with elevated troponin levels is described in patients hospitalized with COVID-19infection found to be associated with poor outcomes. The origin of myocardial injury could be associated with ischemia as a consequence of thrombotic coronary obstruction. However, heart failure, pulmonary embolism, myocarditis, tachycardia, and sepsis may play a crucial role in the pathogenesis [3-4].

The risk of cardiovascular complications is higher in men and in patients with predisposing conditions, such as older age, hypertension, obesity, diabetes and atherosclerosis. All these conditions are seemingly associated with endothelial dysfunction [3-5]. In general, cardiac involvement could be multifactorial due to direct myocardial damage related to the viral invasion, hypoxia, hypotension, inflammatory response, ACE-2 receptors down-regulation, catecholamine response, medications, coagulation derangement and psychological trauma [5].

The histopathological examination of involved hearts in autopsy specimens have revealed absence of infiltrates of inflammatory cells in the myocardium. However, an increase in the number of proinflammatory genes and virus presence in the cardiac cells has been demonstrated which presumably associated with viral load [6].

Myocarditis

As per Cochrane review in 2020, only three out of 205 studies, have reported possible cases of myocarditis complicating severe COVID-19 infection (incidence 2.6%). The myocarditis was suspected because of elevated serum troponin, Echocardiographic findings of pericardial effusion and electrocardiographic (ECG) abnormalities. However, majority of the patients had either a history of pre-existing heart failure, myocardial infarction in the recent past or hypertrophic cardiomyopathy in some cases. In addition, others had cardiovascular comorbidities, including hypertension and diabetes [3].

Cardiac Magnetic Resonance (MRI) findings in patients with recent Covid-19 infection have confirmed cardiac involvement in 15-78% patients and ongoing myocardial inflammation in 60%cases. However, these findings were independent of preexisting conditions, severity, overall course of the acute illness, and the time from the original diagnosis [7-8]. The cardiac MRI criteria of myocarditis included myocardial edema by elevated T2 signal and myocardial injury by presence of non-ischemic late gadolinium enhancement [8].

Arrhythmia

The prevalence of conduction abnormalities and arrhythmias in Covid-19 patients is variable [3,5,9]. From the available cohorts, palpitations were presenting symptoms in 7.3% patients. In addition, other studies have reported arrhythmias in 17 % in general cohort and 44% of patients admitted in the intensive care units. Moreover, 2.9 percent patients had ventricular tachyarrhythmia [3]. Atrial fibrillation is also a common presentation in approximately 8.5-17%patients. [3,9]. The heart block is very rare (0.1%). Potential risk factors for arrhythmias in Covid-19 patients include presence of other cardiovascular complications, hypoxia, shock, electrolyte imbalance, drugs that prolong the QT interval, and presence of fever [9]. A 12-lead ECG with continuous recording is essential to diagnose various arrhythmias. The management of all types of arrhythmias depends on the type, cause and hemodynamic stability and usually follows the standard management pathways.

Acute Coronary Syndrome

In a Cochrane review, out of 16 studies, the incidence of myocardial infarction or Acute Coronary Syndrome (ACS) in people hospitalized with COVID-19 was 1.7% (range 0% to 3.6%). Surprisingly, the rates of hospitalization for acute myocardial infarction in non-Covid-19 patients were found to be less during the Covid-19 period presumably due to patient- centered and logistic issues in 2020 [3].

The diagnosis of ACS can be made on the basis of chest pain, troponin rise and ECG changes. It has been proposed that plaque rupture, coronary spasm or microthrombi formation in the coronary arteries may be involved in the pathogenesis. The activation of macrophages that secretes collagenase enzyme is responsible for degradation of collagen of the fibrous cap of the atheromatous plaque. Similarly, systemic inflammatory response and 'cytokine storm' associated with intravascular thrombosis and microthrombi formations may lead to coronary events. The patients who recently were recovered from Covid-19 had been investigated using cardiac MRI and, in few studies, compared with healthy controls and risk factor–matched controls, patients who recovered from COVID-19 had lower left ventricular ejection fraction, higher left ventricle volumes, and raised native T1 and T2 signals in with gadolinium in the MRI study. Similarly, many studies have detected evidence of pericarditis, features of myocarditis and elevated cardiac enzymes in the recovery phase [3, 8].

The most prevalent abnormality seen in the cardiac MRI was myocardia inflammation (defined as abnormal native T1 and T2 measures). The cardiac injury is defined as a serum troponin concentration above a reference range or the '99th percentile upper reference limit', with or without new abnormalities at echocardiography or ECG. As per literature, the incidence of cardiac injury ranged from 4.8%, in a study that enrolled participants older than 60 years with a mild COVID-19 infection (overall mortality 2.9%) to 54% in critically-ill participants (mortality 41% to 72%) [3,4,7-8].

Thromboembolism

The arterial and venous thromboembolism have been reported in patients with Covid-19 and the incidence is higher in those with higher serum D-dimer or troponin levels. For people hospitalized with COVID-19, the incidence of venous thromboembolism in 16 studies was found to be 7.4% (range 0% to 46.2%). The incidence of deep vein thrombosis and pulmonary embolism was rather similar (6.1% and 4.3%, respectively) [3,9].

In the review of published 20 studies, the incidence for stroke was 1.2% (range 0% to 9.6%). In a cohort of 219 people hospitalized with COVID-19, 11 (6 men) developed ischemic (4.6%) or hemorrhagic (0.5%) stroke with overall mortality of 54% [3].

Hyper Inflammatory Shock and Kawasaki-Like Disease (In Children)

Kawasaki disease was first characterized in 1967 by Tomisaku Kawasaki. This included children suffering from "acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes. The current concept is that this syndrome results from an immunologic response to an exposure in the respiratory system or gastrointestinal tract or both in genetically susceptible children. The immunologic cascade presumably triggered by infection that leads to systemic inflammation in medium-sized arteries including multiple organs during acute phase [10-12].

1. The diagnostic criteria include presence of fever for at least 5 days, and presence of at least 4 of 5 principle clinical featuresExtremity changes with erythema and edema of palms and soles during the acute phase. Skin peeling can be seen in the convalescent phase.

2. Diffuse polymorphic rash including maculopapular, diffuse erythroderma or erythema multiforme-like findings.

3. Bilateral non-exudative bulbar conjunctivitis, typically sparing the limbus.

4. Oral mucosal changes with cracked lips, oral and pharyngeal erythema, "strawberry tongue" (erythema of tongue with prominent fungiform papillae).

5. Cervical lymphadenopathy, typically unilateral, at least 1.5 cm in diameter.

Recently, there are many reports published from the UK, Italy and USA, have described Kawasaki-like symptoms and shock like features in children infected with the Covid-19. The main features included laboratory findings of neutrophilia, lymphopenia, thrombocytopenia, and marked elevation of inflammatory markers. In addition, elevated levels of ferritin, triglycerides, and D-dimer were also found. Most of the patients had significantly elevated levels of pro-BNP (B-type natriuretic peptide) or Troponin-T or both suggesting compromised cardiac function or shock state or both [10-13].

Common clinical presentations include fever, rash, abdominal pain, diarrhea, and vomiting. Unlike the adult presentation of COVID-19, most pediatric patients have no significant respiratory involvement. Some children develop coronary artery aneurysms [10-11].

Conclusion

The COVID-19 pandemic has affected people of all age groups involving all the organ-systems. The cardiovascular system is affected in many ways during acute infection or recovery phase. The mortality and morbidities due to cardiovascular complications of Covid-19 are significant. Therefore, constant vigilance, anticipation, timely treatment and a regular close follow up should be integral part of COVID-19 management in all age-groups. Appropriate investigations and treatment of cardiac conditions is crucial. In addition, recommended protocols and safety measures have to continue. The full impact of SARS-CoV-2 virus on cardiovascular system is yet to be known in the long term and therefore regular updates and reviews are required.

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