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Review Article

Covid-19 Infection and Cardiovascular System: A-Review

Warda Mustfa[1] and Hina Ayub[2]*

[1]PhD Scholar, Department: School of Space and Earth Sciences, University of Science and Technology of China, Hefei, Anhui, China

[2]BS Zoology, University of Narowal, Pakistan

***Corresponding Author:** Hina Ayub, BS Zoology, University of Narowal, Pakistan.

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Abstract

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) affects the cells by ACE, leading to infect the human respiratory system severely. Recently investigated that COVID-19 also damage the Cardiovascular System, leading to cause severe myocardial injury. The increased mortality and morbidity in COVID-19 patients are mainly because of hypertension. This paper interprets the relationship between COVID-19 with cardiovascular damage, hypertension (HTN), ACE, blood pressure, CK-MB, and Lipid Profile. Hypertension (HTN) continues to be a strong and widespread risk factor for IHD.

Keywords: COVID-19; Cardiovascular Disease; Angiotensin-converting Enzyme; CoV-2; Hypertension; Blood Pressure

Introduction

The respiratory viral infection is a leading cause of pandemic as the after-effects of abrupt transmission in the respiratory tract from human to human. In the last two centuries, influenza and coronavirus have succeeded in the world many times by producing economic loss, significant mortality, and global disaster. In 2002 the epidemic of SARS major cause of 916 deaths amongst over 8000 patients in 29 different countries worldwide, succeeded by the occurrence of MERS infection in 2012, which responsible for 800 deaths out of 2254 patients globally [1]. The outburst of pneumonia because of novel coronavirus appeared in Wuhan city, Hubei province. It dispersed instantaneously as an ongoing risk of the pandemic all over China. After the isolation and identification of pathogens for this type of pneumonia which was originally known as 2019 novel coronavirus (2019-nCoV) [2], but now WHO has been publicly named this virus as severe acute respiratory syndrome coronavirus2 (SARS-CoV-2). In 2002 and 2003, the SARS outbreak became an epidemic worldwide. Studies suggested that similarity exists between symptoms of SARS and COVID-19. However, there is a difference that exists between SARS-CoV and SARS-CoV-2 in their mechanism of infection, incubation time, and genomic structures. In this review, we emphasize on current demand for awareness of long term, acute and chronic effects of this viral epidemic on the cardiovascular system and the significance of knowledge that needed in future research.

Methods

We wrote this review article to summarize the effects of Covid-19 on human. We assessed the journal articles to compile the data. We searched articles based on cardiovascular disease, covid effect on human body, covid family effecting heart etc. Various authenticated databases like: 20 articles from PubMed, 10 articles from science direct, 50 articles from Elsevier direct were used to collect and compile data. Based on the inclusion and exclusion criteria, we narrow down our search to 100 articles and we selected 50 articles for this article as mentioned in references as well. Our inclusion and exclusion criteria mainly based on viruses' effect on cardiovascular system. Those were selected which explain their research on cardiovascular system and excluded who just mentioned cardiovascular system and didn't show diseases related to virus family.

This study found cardiovascular complications along with hypertension, diabetes, lipid profile, blood pressure, angiotensin-converting enzyme, and cardiac biomarker. Patients infected with SARS-CoV as well as previously diagnosed with CVD exhibited an adverse clinical prognosis.

Cardiovascular complications of respiratory virus

In 2003, severe acute respiratory syndrome (SARS) infection appeared globally [3]. Recent studies reported that the reasons for this epidemic were a strain of virus belongs to coronavirus family [4], 774 patients died among 8098 patients who were infected because of SARS [5], with a competency of this infection reoccurrence [6]. SARS is a virulent disease that influences many organs of the body, with many complications such as intravascular coagulopathy, pneumonia, neutropenia, myositis, lymphopenia, and derangement of the liver and renal functions [7,8]. Someone has not evaluated yet the complication of SARS in cardiovascular diseases. In some previous studies, we have shown that coronavirus infection affected the heart with subsequent acute and chronic heart failure observed in rabbits [9], from this we can assume that we might correlate it to human strains of coronavirus [10]. Another study concluded that coronavirus infection might affect the cardiovascular system by generating cardiomyopathy that affects cardiac chambers dilatation and damage systolic functions by simulating dilated cardiomyopathy in the animal model. Besides the above changes, electrocardiographic methods, also observed other abnormalities such as non-specific T wave reversal and ST depression [11]. Currently, the major cardiovascular complication has not been reported in humans after no strains of SARS-CoV. The coronavirus clinical activity causing SARS is much more virulent than other infections in humans. Hence, in this study we would analyze if SARS will cause cardiovascular complications and their normal course, including tachycardia, bradycardia, hypotension, cardiac arrhythmia, and cardiomegaly; and determine whether it linked those complications to an adverse outcome. SARS is a virulent infection produced by a coronavirus that becomes an epidemic and now pandemic within a short period [12].

The potential impact of ACE2 and COVID-19 on the Cardiovascular system

ACE2 (Angiotensin-converting enzyme 2) is a membrane-bounded amino-peptide that shows a significant role in defenses mechanism and cardiovascular systems [13]. ACE2 plays a vital role in the development of hypertension, diabetes, and heart functions. It also has been found that ACE2 is determined as a well-designed receptor for SARS-CoV and SARS-CoV-2. Infection of SARS-CoV-2 is triggered by binding the spike protein of the virus to the ACE2 receptor, which is profoundly expressed in the lungs, hearts and many other organs [13]. The action mechanism of acute and chronic myocardial injury progression caused by SARS-CoV-2 it may be associated with ACE2 that which can play an important role in cardiac injury. Another perspective mechanism for acute myocardial injury comprises a cytokines system activated by an imbalance in response of T helper cells (type 1 and type 2) [14,15]. The hypoxia and respiratory functional disruption caused by COVID-19 causes damage to myocardial cells. SARS-CoV can downregulate the ACE2 pathway by mediating myocardial inflammation, acute respiratory failure, and lung oedema [16]. The SARS-CoV spike proteins assist in viral entry into host cells. Spike proteins facilitate the entry and attachment of the viral cell to the target cells. Also, cofactor TMPRSS2 binding with the host cell membrane becomes very easy. Previous studies determined that ACE2 receptors support the entrance of SARS-CoV-2 inside the cell by binding S proteins with ACE2. Another current report proposes that the transmission mechanism of SARS-CoV-2 is capably determined by the ACE2 receptor. Therefore, a strong link was established between COVID-19 and RAS. According to a report, no evidence found that genes for ACE-2 present on X-chromosome and expression of loci also influence the perceptivity of COVID-19 infections [17].

The ACE2 acts as a SARS-CoV-2 target receptor. I consider ACE2 as a membrane-bound amino-peptidase chiefly present in many organs such as hearts, lungs, intestines and kidneys. I closely related the organ level distribution of ACE2 to COVID-19's clinical sequelae. SARS-CoV-2 has a 10-fold better affinity for binding with ACE2 than SARS-CoV, making it a more effective virus [18]. ACE2 is a component of the RAAS and is involved in diabetes development, hypertension and heart failure. Only at the tissue level, ACE2 expresses itself strongly in the lungs, kidneys, heart and blood vessels [19].

The link between blood pressure, cardiac biomarker and COVID-19

In the recent studies I have found that the blood pressure level was significantly higher in those patients which were analyzed in

the ICU as compared to those who were not kept in the ICU (mean systolic blood pressure 145 mmHg versus 122 mmHg; P < 0.001) [14]. A recent study showed that 138 patients of COVID-19 were evaluated in Wuhan city out of 36 patients who were found with severe symptoms and treated in the ICU. Someone highly expressed the cardiac biomarker levels of myocardial damage in ICU patients as compared to those patients which were not treated in ICU (median creatinine kinase (CK)- MB level 18 U/l versus 14 U/l, P < 0.001; hs- cTnI level 11.0 pg/ml versus 5.1 pg/ml, P = 0.004). These outcomes suggested complications like I saw acute myocardial damage in those patients who have worse symptoms of infection [20].

CK-MB is an appropriate diagnostic biomarker for myocardial infarction and ischemic heart disease (IHD). In a previous study, I found that the level of CK-MB was highly significant in the ischemic heart disease group than in the control group [21]. In previous studies, the level of CK-MB was higher in IHD patients, which shows myocardial damage to some extent including coronary artery blockage occurs in IHD subjects which caused the release of CK-MB from cardiomyocyte. Additional reports have supported the results of previous studies that there was an increased CK-MB level in IHD subjects.

Lipid profile with COVID-19 and adverse outcomes

The circulating low-density lipoproteins along with smaller triglyceride, very-low-density lipoproteins (VLDL) and remaining particles, freely pass through the endothelial membrane barrier, where they can combine with extracellular particles like proteoglycans to become reserved in the extracellular matrix [22]. Feedback response of an animal model of atherosclerosis, the accumulation of apo-B proteins comprises lipoprotein substances in the suboptimal arterial wall triggered complex, maladaptive inflammatory mechanisms that start the formation of atheroma [23]. Besides, the lipoproteins which remain in the artery walls with time the nascent atheroma gradually increases in size and causes the formation of larger mad more complicated atherosclerotic plaques.

Chronic cardiovascular damage may become unstable after viral infection because of dysregulation between diminishing cardiac reserve and infection induces an increase in metabolic demands. The patients with severe coronary artery diseases and heart failure might be at high risk because of plaque rupture in coronary arteries to virally induced systemic inflammation and strict use of stabilizing agents for plaque formation (angiotensin-converting enzyme inhibitors, stating, aspirin, and beta-blockers) considered as a possible therapeutic approach. Effects of pro-coagulation in systemic inflammation can be upregulated the probability of thrombosis and the estimated platelet role and strengthened antiplatelet therapy should have acknowledged in patients who already have a history of coronary intervention [24].

Hypertension as a risk factor for COVID-19

In several epidemiological studies, it has been found that hypertension is associated with the COVID-19 epidemic in China and one of the major causes of morbidity and mortality in COVID-19 patients. Current studies revealed that hypertension is found to be a great threat with a ratio of 1.82 in acute respiratory syndrome and 1.70 for death in 201 patients with COVID-19 [25]. I found hypertension to be a significant risk for hospital mortality in 191 patients of COVID-19, with a ratio of 3.05 [26]. In feedback to these studies, the council of Hypertension of the European Society of Cardiology stated that "The Council of Hypertension strongly confirmed that physicians, as well as patients, should continue with their normal anti-hypertensive therapy since there is no clinical evidence to suggest that treatment with angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) should be discontinued because of the COVID-19 infection" [27]. Above mentioned comments have been followed by several other similar statements from many other societies by recommending that patients should continue their current hypertensive medication. The American Heart Failure Society, The American College of Cardiology and the American Heart Association has given a combined statement protecting for patients to continue ARBs or ACEIs uses as prescribed by physician and changes in the medication about COVID-19 must be done after accurate evaluation [28].

Hypertension committed to increased myocardial oxygen demands because of the increase in the myocardium's workload, homologous with the other risk factors of IHD. Often it is well-defined as afterload or the aortic retardation to left ventricular ejection fraction. Reduction in coronary blood flow (because of the coronary artery stenosis-mediated decrease in myocardial oxygen supply) and added to enhance the workload by the heart (because of HTN) might be led to an oxygen supply demand ratio mismatch.

Therefore, this kind of approach produces symptoms like angina and myocardial infarction [29]. I project a pharmacy therapeutic approach in the presence of IHD to decrease myocardial oxygen consumption, which seems to be beneficial.

The relationship between mean arterial pressure (MAP) and cardiac output (CO) is proportional. Systemic vascular resistance (SVR), and CO further defined as the product of heart rate (HR and stroke volume (SV) [30], the action of various anti-hypertensive drug types can readily be showed. Reduction in BP (MAP) hence lowered the myocardial workload. Beta-blockers, verapamil, diltiazem and many other drugs of subclasses of calcium channel blockers (CCB) acts to lower cardiac contractility and heart rate. Reduction in stroke volume because of diuretic agents and Vasodilator compounds decreases systemic vascular resistance. Hence above mentions, I prefer beneficial hemodynamic responses in both situations, including chronic stable IHD and acute coronary syndromes. Oxygen-depriving results in sudden thrombotic arterial obstructions that might be enhanced by facilitating excessive myocardial oxygen demands. Hypertension also represents the occurrence of alternative cardiovascular risks such as organ damage and diabetes, all of which presented the prevalence with increasing age. RAS blockers are often used to treat the disease [31]. According to a recent report, In China, 23.2% adult population is expected to have hypertension. Indeed, in the current survey of 2020, 982 patients were detected with COVID-19, and the ratio of hypertensive patients was 12.6% [17].

Acute and long-term cardiovascular damage

In some previous studies, I have found that the MERS-CoV (Middle East Respiratory Syndrome Related Coronavirus) mainly affects the cardiovascular system and causes acute myocarditis and ultimately heart failure [32]. MERS-CoV and SARS-CoV-2 both showed similarity in pathogenicity, increase myocardial injury and the treatment of patients with COVID-19 hence be difficult and more complex. The myocardial injury correlated with SARS-CoV-2 appeared in 5 patients out of 41 firstly analyzed as COVID-19 in Wuhan city. These outcomes mainly illustrated as an increased level of high sensitivity cardiac troponin I (hs-can) levels (> 28 pg/ml) [33]. From this study, we can speculate that I admitted 5 patients with myocardial damage to the ICU (intensive care unit), which shows the severe nature of the myocardial injury with COVID-19.

In a previous study in which the 12 years follow up study was done in 25 patients who were in good health after SARS-CoV infection and it was found that 60% had glucose metabolism disorders, 44% had abnormalities in the cardiovascular system and 68% had hyperlipidemia. It was also identified from the metabolism that metabolism of lipid was disrupted in those patients who have the history of SARS-CoV infection and it was evaluated that the concentrations of lysophosphatidic ethanolamine, free fatty acids, phosphatidic glycerol, and lysophosphatidic choline were undoubtedly increased as compared with the patients without a history of SARS-CoV infection [34]. However, the mechanism of action with SARS-CoV infection disrupts the glucose and lipid metabolism are quite unknown. Given the structural similarity of SARS-CoV-2 with to SARS-CoV, this novel virus might also source of chronic damage to the cardiac system, and consideration should be give to cardiovascular protection while treating the COVID-19 [35].

Impact of COVID-19 on persistent cardiovascular disease

Systemic inflammation and pro-coagulation activity can persistent in survivors of hospitalized subjects for community-acquired pneumonia long after the perseverance of the index infection. I related the clinical effects of pneumonia to increased cardiovascular disease risk up to 10 years of follow-up [36], and subjects infected through respiratory virus epidemics will probably experience related adverse outcomes. The therapeutic consumption of corticosteroids further enhances the chances of adverse cardiovascular proceedings.

Wu., *et al*. conducted a study and explained that lipid metabolism dysregulation persists 12 years after clinical recovery. Mechanism of metabolism amongst 25 SARS surviving individuals studied [34] abnormalities in cardiac system observed in 8 patients during hospitalization with H7N9 influenza virus returned to normal at the time of 1-year follow-up [37]. The novel coronavirus' normal pattern of presentation is rather unspecific and is like other viral infections: most of the co-morbidities in the past viral outbreak included cardiovascular disorders (e.g. hypertension), smoking history, and diabetes: however, the number of chronic disorders is small and under-reported [38].

Drugs	Mechanism of Action	Effect on SARS-CoV-2	Adverse effect on the cardiac system	Ref
Hydroxy-chloroquine (HCQ)	Altered post-translational modifications.	Improved virus clearance	Frequent cardiotoxicity	[43]
Azithromycin	Macrolide antibiotic; used in combination with chloroquine or HCQ	Virus clearance in combination with (HCQ)	LQT	[19]
Chloroquine	Inhibit glycosylation and endosomal acidification	Block the viral entry into cell	Alteration in cardiac conductivity	[43]
SSAA09E1	Inhibit Cathepsin L	Inhibitors suppress SARS-CoV replication	Block ACE2 receptor interaction	[40]
Remdesivir	Inhibition of RNA-dependent RNA polymerase RdRP	Inhibit viral RNA replication, control viral infection	Not common	[45]
Angiotensin receptor 1 (AT1R)	Inhibit losartan	Reduce blood pressure and hypotension	Protect from SARS-CoV-2 infection	[44]
Arbidol	Block trimerization of SARS-CoV-2	Immature less infectious virus formed	Reduce viral yield in heart	[46,47]
Lopinavir and Ritonavir	Inhibit proteases	Virus replication inhibition	Metabolic derangement in heart	[48]

Table 1: Adverse effects of potential drugs on cardiovascular system to treat COVID-19.

Figure 1: Schematic overview of possible cardiovascular damage because of COVID-19.

Conclusion

The worldwide mobility rate has enhanced the percentage of microbial transmission worldwide. Global pandemics are threats due to increased human mobility. COVID-19 is a quickly developing pandemic with ambiguous clinical features. This study found cardiovascular complications along with hypertension, diabetes, lipid profile, blood pressure, angiotensin-converting enzyme, and cardiac biomarker. Patients infected with SARS-CoV, as well as previously diagnosed with CVD, exhibited an adverse clinical prognosis. Therefore, particularly we should pay attention to cardiovascular protection while treating COVID-19 patients with newly developing therapeutic approaches.

Disclosure Statement

The listed authors have no financial disclosures or conflicts of interest with the findings in this paper.

Author's Contribution

It involved only two authors in this article writing. Principal author did 60% article and 40% by co-author.

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