REVIEW ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: www.ijrps.com

Clinical Linkage of COVID-19 with Hypertension, Diabetes and Cardiovascular Disease

Bimal Chhajer[1], Vikram Singh[*2], Girija Kumari[3]

[1]Department of Preventive Cardiology, SAAOL Heart Center, Farm No. 5, DLF Westend, Mandi Road, Chhattarpur, New Delhi-110030, Delhi, India
[2]Department of Medical Laboratory Technology, Amity Medical School, Amity University Haryana, Amity Education Valley Gurugram, Panchgaon, Manesar-122412, Haryana, India
[3]Department of Clinical Research, Amity Medical School, Amity University Haryana, Amity Education Valley Gurugram, Panchgaon, Manesar-122412, Haryana, India

Article History:

Received on: 20 Jun 2020
Revised on: 27 Jul 2020
Accepted on: 28 Jul 2020

Keywords:

Hypertension,
Diabetes,
Cardiovascular Disease,
COVID-19,
Prevention,
Treatment

ABSTRACT

The coronavirus outbreak caused by the pandemic Coronavirus Disease (COVID-19) is heart-rending millions live around the globe, and it is the foremost major human tragedy in history. World Health Organization (WHO) declared the coronavirus disease (COVID-19) a pandemic and global outbreak with a severe public health concern. This outbreak caused by a novel infectious coronavirus of Severe Acute Respiratory Syndrome Coronavirus- 2 (SARS-CoV-2) sequences leading to an emergent crisis with significant loss of health and global economy. COVID-19 is more prone to exacerbate health concerns in hypertensive, diabetes, and cardiovascular disease patients, however, COVID-19 incidence outcomes are inconsistent. Prevention and control of the outbreak are very challenging due to the complex nature of the virus and its pathogenesis. WHO, CDC, and every national health authority are taking necessary actions to combat the contagious novel infection. The purpose of the review is to discuss potential mechanisms and clinical linkages between high blood pressure, diabetes, cardiovascular diseases, and SARS-CoV-2. We hope that we can identify information deficiencies that need more review and clinical evidence of the COVID-19 for hypertension and cardiovascular problems in patients with diabetes. This article will provide a comprehensive integrative strategy to control and manage of current outbreak and related mortality around the world.

*Corresponding Author

Name: Vikram Singh
Phone: +918802552461
Email: vsmicroaiims@gmail.com

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v11iSPL1.3441

Production and Hosted by

IJRPS | www.ijrps.com

INTRODUCTION

SARS-CoV2 is a virus enveloped by a single-stranded, positive RNA virus-like other members of the Coronaviridae family. Any SARS-related coronavirus was shown to be the original zoonotic host for SARS-CoV2 in bats, and the working hypothesis is that it is having a genome of 96.2 per cent similar to a coronavirus related to bat. Studies showed that angiotensin-converting enzyme 2 (ACE2) protein could be used for cell input by SARS-CoV2 and other coronaviruses. ACE2 is a membrane protein integral type I that performs many essential physiological functions. The virus' leading site of entry

into human hosts is strongly expressed in lung alveolar cell. SARS-CoV2 reaches cells after ligand binding via the receptor-mediated endocytosis close to the HIV. ACE2 also plays a role in lung protection, which leads to a deregulation of the viral binding to this receiver and a contribution to viral disease (Andersen *et al.*, 2020; Bai *et al.*, 2020; CDC, 2020).

COVID-19 is more than influenza contagious. In particular, the rate of death for COVID-19 is also significantly higher associated to the latest WHO estimation of the death rate for seasonal influenza of below 0.1 per cent, and may rise to significantly higher rates in elderly, comorbid patients and lack of efficient intensive care support. Whilst the corresponding levels of 9.6 per cent and 34.4 per cent, respectively of other zoonotic coronaviruses, like the 2002-2003 Extreme ARSE and the Middle East Respiratory Syndrome (MERS-CoV) were low, COVID-19 resulted in far low deaths than the previous outbreaks combined, which was attributed, partially, to more significant infection. Uncertain and unreliable discernment triggered variable recorded cases for many causes, including 1) the illness then, in an overall proportion, be asymptomatic or mildly symptomatic 2) insufficient testing capacities in most geographical regions contributing to often underdiagnosed disorders (Cui *et al.*, 2019), especially in those with a lesser disorder, and 3) the complication (Chang *et al.*, 2020; Chen *et al.*, 2020, 2003).

Notable is that the assessment of SARS-CoV-2, which can significantly contribute to immunocompromised infection, can also complicate further spread of the infection in large part of the individual (at 20 per cent). COVID-19 is very flexible in its clinical appearance. A major analysis by the Chinese Center for CDC has found that the clinical severity is moderate in 81.4 per cent and extreme in 13.9 per cent, and vital in 4.7 per cent. The clinical aspects of moderate COVID-19 tend to involve signs similar to respiratory infections (e.g. nausea, cough, dyspnea, myalgia, weakness, and diarrhoea), and lab anomalies such as lymphopenia. At the same time, there is a regular improvement of information regarding the clinical characteristic of the disorder. The acute respiratory distress syndrome (ARDS), which is most common to ageing patients with known medical co-morbidities and is familiar to or without both distributive and cardiovascular shock, can manifest as pneumonia in severe cases (COVID-19). Although concomitant concentrations of certain viruses (Danser *et al.*, 2020; Zhu *et al.*, 2019) and bacterial superinfections in the preliminary results seem small, co-infection is likely to occur in patients with the most severe clinical appearance and worse (Deng and Peng, 2019; Guan *et al.*, 2020; Peng *et al.*, 2020).

Children are a subset of positive cases of COVID-19 in China. They are less susceptible to severe diseases, likely as a consequence of improved innate immunity, fewer co-morbidities, variations in viral receptacle maturation and/or previous exposure to certain types of coronavirus. In infants, however, the moderate-to-grave disease was also identified. Therefore, the amount of children examined is not explicit. Since the prevalence of COVID-19 is extraordinarily high and that, it is vital to classify prognostic factors linked to morbidity and mortality. Currently, COVID-19 does not have an authorised preventive vaccine or treatment, although others are closely researched (Fang *et al.*, 2020; Huang *et al.*, 2020; Liu *et al.*, 2020).

Hypertension

Hypertension, commonly known as moderate or high blood pressure, has persistently elevated the strain of the blood arteries. The blood pressure is caused by the force of the blood, which is pumped by the heart and pushed against the walls of blood vessels (arteries). The higher the pressure, the more difficult it is to pump the heart. Hypertension is a severe health issue that may improve the pulse, head, renal and other conditions. It is a leading global cause of early death, with more than 1 out of 4 men and 1 out of 5 women – more than one billion people – suffering. In low to intermediate-income countries with two-thirds of incidents, most of which arise due to the rise in risk factors in these populations in recent decades, the incidence in hypertension is especially important (Wang *et al.*, 2020; Tianxin *et al.*, 2020).

Linkage of Hypertension and COVID-19

The correlation of hypertension and diabetes in the patients of COVID-19 because of the growing incidence of these chronic conditions worldwide is not surprising. Hypertension as major co-observance with COVID-19 Ironically, in the pooling of evidence from the ten studies in China (n 1/4 2209) recording co-morbidity characteristics in COVID-19, hypertension combinations and diabetes correlations and cardiovascular (CVD) disorders of establishment range from 15 to 30 per cent (average of 21%), 5-20% (average of 11%) and 2-40% (average of 7%); In an Italian sample of 355 COVID-19 patients, proven CVD was also present in almost 43%. Although the strong correlation of hypertension in all these trials in patients with COV ID-19 is remarkable, the issue is the rise in mortality that must be seriously considered. The Chinese

Disease Control and Prevention Center recorded a 2.3 per cent (1023 deaths from 44,672 verified cases) case-fatality rate in the COVID-19 overview study (CFR). CFR for hypertension was improved to 6%, diabetes was elevated to 7.3%, and CVD was graded to 10.5% (Juan *et al.*, 2020; Jing *et al.*, 2020; Zhang *et al.*, 2019). No surprise, based on the observations above, scientists recently proposed that COVID-19 depends on the presence of a group of co-morbidities. There is a great concern that hypertension and CVD could be confused with the COVID treatment with certain antihypertensive medications such as RASB (Donoghue *et al.*, 2000).

Diabetes

Diabetes is a persistent metabolic disease, which contributes over time to severe heart, blood flow, eye and nerves injury. Diabetes, though, is a disorder of an elevated blood glucose level. Diabetes is more prevalent in adolescents where the body is insulin-responsive or does not contain sufficiently insulin. The most extreme is type 2 diabetes. Diabetes type 2 prevalence in all income countries has grown dramatically over the past three decades. Type 1 diabetes is a recurrent pancreatic disease itself develops little to zero insulin, formerly known as juvenile diabetes to insulin-dependent diabetes. The target of stopped diabetes and obesity by 2025 is settled to internationally. About 422 million people worldwide have diabetes and are directly linked annually to diabetes, particularly in low and middle revenue countries (Jiang *et al.*, 2014; Imai *et al.*, 2005). Over the last few decades, both the number of cases and the incidence of diabetes have risen gradually.

Diabetes and COVID-19

Potential linkages between diabetes and COVID-19 infections. In the region of 20 per cent of patients, diabetes is a significant risk factor for severe pneumonia to occur and for virus infection to establish a septic condition. Diabetes has been identified as a major contributory to the harshness and the life span of the Middle East Respiratory Syndrome (MERS-CoV). Several hypotheses explain the higher incidence of infection with COVID-19 among people with diabetes. The risk for infection is increased for people with all types of diabetes due to defects of immunity. Besides, the cardiovascular disease associates older diabetes and could itself help explain how the fatal COVID-19 results are associated (Patel *et al.*, 2016).

The COVID-19 infection could be characterised by two different mechanisms at least. First, to get into its target cell, the SARS-CoV-2 virus is catching a systematic route which is crucial to the control, metabolism and inflammation of blood pressure. The coronavirus-spike-protein receptor is having the angiotensin-converting-enzyme 2 (ACE2). ACE2, mainly with inflammation, has protective effects. The ACE2 expression of COVID-19 infection reduces cell injury, hyper inflammation and respiratory failure. It was shown that acute hyperglycaemia upregulates ACE2 expression on cells that could facilitate the entry of viral cells. Chronic hyperglycemia, however, is known to reduce the ACE2 expression. Besides, pancreatic ß cell activation of ACE2 can affect the activity of β-cells. Although this is not tested in humans, it indicates that diabetes may not only be a risky cause in severe COVID-19 diseases but that infections may also contribute to new incipient diabetes. The finding of those Italian authors who documented specific cases of extreme diabetic ketoacidosis (DKA) while admitted to the hospital is confirmed by the possible β-cell failure attributable to the disease of insulin (Wrapp *et al.*, 2020; Piao *et al.*, 2012).

The tremendous requirement of insulin in patients with a severe course of infection was another critical observation reported for COVID-19. In this high insulin resistance, COVID-19 has no specific role to play directly. The level of insulin resistance in diabetes patients tends to be comparable to severe disease induced by certain factors according to the clinical observations by the co-authors of professional opinions. Dipeptidyl-peptidase-4 (DPP-4) enzyme is a second possible mechanism which elucidates the relationship of Diabetes and COVID-19 and is usually pharmacologically targeted in patients with type 2 diabetes. DPP-4 was found to have an efficient receptor in cell studies to support the MERS virus, the Human Coronavirus-Erasmus Medical Center (HCoV-EMC). Antibodies inhibited HCoV-EMC infection with prime cells against DPP-4. DPP 4 enzyme is a transmembrane glycoprotein of type II omnipresently expressed. Glucose metabolism and insulin are essential, but inflammation in diabetes type 2 increases. It is not currently known whether these mechanisms also cover COVID 19 and whether in clinical practice the treatment of Diabetes with DPP-4 inhibitors impacts the infection process (Mortensen *et al.*, 2008; Haffner *et al.*, 1998).

Implications on diabetes management

The above-listed processes may not yet have strong clinical significance, but health-care practitioners need to learn their effect on patients with diabetes. For the metabolic testing of patients having Diabetes and COVID and related risk of metabolism, a simple flood chart has been compiled. This provides

recommendations both for primary diabetes control, as well as preventing serious diabetes sequelae triggered by unexplained or poorly controlled Diabetes (Donath *et al.*, 2019).

Cardiovascular Disease

Cardiovascular disease (CVDs), estimated to be around 17.9 million deaths a year, is the world's first leading cause of death. CVD's comprise lung failure, stroke and heart rheumatic failure, among other complications that are a category of cardiac-vessel diseases. CVD fatalities result in individuals under 70 years of age because of the heart attack and stroke; one-third of these accidents result prematurely.

CVD risk individuals may show increased blood pressure, glucose, lipids and overweight and obesity. All of them can be measured easily in primary care facilities. Identifying and ensuring adequate treatment for those with the highest risk of CVDs can prevent premature deaths (Drummond *et al.*, 2019). To ensure that those in need seek diagnosis and therapy, exposure to critical non-communicable disease medications and appropriate safety services in all primary health care facilities is vital.

Cardiovascular Disease and COVID-19

SARS-CoV-2 originated in the latest RNA beta coronavirus. Seven identified human-infected populations of beta-coronavirus with four mostly mild flu-like and three life-long diseases (SARS, MERS and the new COVID-19).

These diseases are considered to kill humans. Although SARS-CoV-2's primary objective is the air tract, it is possible, in many different ways, to involve the CV system. This is accompanied by the raising CV complications process in COVID-19.

Myocardial injury

SARSA-CoV-2, a strongly expressed membrane aminopeptidase in the heart and lungs, plays a significant function, both in regular health and in various disease situations, in the neurohumoral control of CV systems through interacting with angiotensin-converting enzyme 2 (ACE2) ACE2. The SARS-CoV-2 binding to ACE2 may lead to a major myocardial and pulmonary damage. It may lead to an altered ACE2 signalling pathway.

Inflammation

More severe causes of COVID-19 include intense systemic inflammation and a cytokine outbreak contributing to damage and multiple organ failures.

Studies have shown high blood levels of pro-inflammatory cytokines in patients with severe/critical COVID-19.

Changes in myocardial demand-supply

Increased need for cardio metabolism combined with systemic infection and hypoxia due to acute respiratory disorders will contribute to oxygen deficiency and an immediate injury to the myocardium.

Coronary thrombosis

Systemic inflammation and decreased shear stress due to enhanced coronary blood flow may contribute to acute myocardial infarction. The systemic inflammation created a prothrombotic environment increases the risk further.

Adverse effects

Several antiviral medicines, corticosteroids, and other COVID-19 therapies can also adversely impact the CV system.

Electrolyte disturbance

In acute systemic diseases and arrhythmia, the patients with underlying heart failure, electrolyte imbalances can occur. Concerning Hyperkalemia COVID-19 in particular, SARS-CoV-2 is correlated with the renin-angiotensin-aldosterone pathway. Hypokalemia raises the possibility of tachyarrhythmias Xu *et al.* (2020).

Role of Underling CV Comorbidities

Patients with pre-existing CVDs seem to be particularly vulnerable to COVID-19 and seem to be more severe with lower clinical outcomes. Specific risk factors influence the health of these people, but there seems to be little change in the potential for the occurrence of an infection. In six latest Chinese trials in China, which involved 1,527 patients with COVID-19, 9.7%, 16.4%, and 17.1% were recorded on principal diagnoses of diabetes, cardiovascular disease, and hypertension. The prevalence of diabetes and high blood pressure is significantly higher, although this sample was equivalent to the general population in China.

Most importantly, the risk of severe diseases, including the application of ICU, was two times, 3times and a 2-fold higher, which showed that the co-morbidity had a projecting effect, with diabetes, cardio-cerebrovascular diseases and hypertension. In a far broader report by the Chinese Centre for Disease Control and Prevention, the clinical findings of 44,672 VOCID-19 reports have been reported. The CFR overall risk for mortality was 2.3%, although significantly higher among people suffering from hypertension, diabetes and CVD.

Though there are few data, the prevalence and impact of different CV co-morbidities on clinical results in different geographical locations appear to vary significantly. Outside Hubei Province and many

other countries the CFRs are lower in China, but in some European countries much higher. There has been an especially grime scenario with a limited group of 21 patients from Washington, USA. Comorbidities in this cohort were common with 33.3% diabetes and 42.9% congestive heart failure. In 33.3% inpatients and 52.4% of patients dead, there was severe heart failure (Xu *et al.*, 2020; Liu *et al.*, 2016; Drummond *et al.*, 2019).

Cardiovascular Expressions of COVID-19

Acute myocardial injury

The furthermost common CV impediment in COVID-19 is acute myocardial injury. A variety of publications using various descriptions of acute myocardial damage like the rise in cardiac enzymes or electric disturbances (related biomarkers and cut-offs). The central concept is, however, the increase in heart troponin I (cTnI) high sensitivity above the 99th percentile maximum.

The estimated acute heart injury incidence was small, but about 8-12 per cent of stable patients reported significantly higher cTnI. Another research was carried out on Chinese trials with 17 per cent occurrence of cTnI-elevation, testing only patients with conclusive findings (death or hospital release). The frequency of 8% acute cardiac failure is reported in these meta-analyses. Acute heart injury was consistently shown in patients with COVID-19 as a distinctly negative measure, independent of the specific case.

The risk of raising troponin multiples is higher in patients admitted to or suffering from ICU / fatal illness. In comparison, in patients with the moderate disease who do not need ICU admission, there was a minimal occurrence of high troponin (only 1-2%). Acute cardiac injury and elevated heart troponins will occur in all pathways mentioned above in COVID-19 patients. There hasn't been a summary of the relative role of these different pathways, although the most prominent of them tend to be direct myocardial (noncoronary) injury or systemic inflammation. Such results have been supported by a recent analysis of SARS deaths since the Toronto SARS outbreak. In this analysis, 35% of the autopsy samples of the human heart were found with ribonucleic acid viral, which indicates the virus' immediate myocardial damage.

No research identified the occurrence of myocardial infarction in the ST-segment in COVID-19, but it does seem to be small. Also, no reports of systemic left ventricular instability, severe left ventricular collapse and cardiovascular pain have yet been reported. Only a study in China reported the prevalence of heart failure in COVID-19 patients. Heart disease has occurred in 52% of patients who died, and in 12% of patients who were released from the hospital.

Arrhythmias

Tachyrhythmia and bradyarrhythmia are well established in COVID-19. In 138 COVID-19 Chinese patients, study results reported a rhythmic incidence of 16.7 per cent. For people who seek ICU admission, the average was significantly greater (44.4%) than those who do not require ICU admission (8.9%). There was no description of the type of arrhythmia.

Potential long-term consequences

It is very challenging to forecast long-lasting outcomes of patients recovering from this condition. However, it might be necessary to derive any significant SARS-CoV-2-like messages of previous SARS experience triggered by the SARS CoV. 68% of the patients recovering from SARS continued to experience lipid metabolism anomalies for 12 years; 40% of CV-anomalies and 60% of glucose-related abnormalities were reported (Peng *et al.*, 2020). It is vital to closely track all that is recovering from the present COVID-19 to recognise the long-term impact of this disease and deter possible CVD (Donoghue *et al.*, 2000).

Management Implications

The general principles of management for COVID-19 patients who develop CV or with pre-existing CVD are the same in conjunction with all other patients without COVID-19. However, it is necessary to take account of some important points. We, as physicians have the enormous responsibility of ensuring that individual patients are not affected. Therefore, the necessary procedures have must extend to all workers interested in treating patients with COVID-19. We are therefore eligible to carry, use and display the personal security equipment, according to existing standards of operation.

A significant number of COVID 19 cases, all of whom need ICU and/or emergency cardiac surgery, will be ready for care by health-care systems. To treat, triage, isolate and handle COVID-19 CV-complicated patients, correct procedures should be established and proclaimed well. Speedy triages, and diagnosis of these patients is critical not only to allow successful use of health resources but also to minimise risk for care professionals. Delays in the provision of urgent heart treatment have also been reported as a consequence of increased measures to COVID-19.

Such gaps should be decreased. The avoidance of unjustified medical procedures of such cases

(e.g. heart troponins, echocardiography) will obtain considerable focus. This is important to reduce the mysterious concurrent diagnosis/treatments, which reinforce the current expanded health care services and thus raise the likelihood of infection exposure for caregivers. The American College of Cardiology has published a spontaneous analysis of cardiac biomarkers such as troponins and standard peptides.

It calls upon all clinicians to retain this assessment in circumstances where the management of COVID-19 patients contributes considerably. The American Society for Echocardiography also offered specific recommendations for the usage of echocardiography in such cases. The risk/benefit proportion of primary percutaneous operation against fibrinolysis will also need to be reconsidered for patients with COVID-19 with ST-segment elevation Myocardial infarction.

Questions were surrounding the health of ACEI and Angiotensin Receptor Blockers (ARBs) in the wake of the current COVID-19 pandemic. These agents enhance ACE2 expression in different tissues, including cardiomyocytes. Since the SARS-CoV-2 binds with ACE2, there is also the possibility of COVID-19 having 19 or more severe diseases in patients with ACEi / ARB history therapy (Huang *et al.*, 2020).

To date, however, these issues have been backed with no scientific or clinical evidence. The consequences of avoiding such procedures are often well established in the same period. Several leading professional societies have, therefore, strongly advocated that the patient should develop COVID-19 not suspend clinically indicated ACEi / ARB therapy.

Clinicians who care for these patients must also fully understand the potential CV side-effects of different viral infection treatment treatments. Additionally, many anti-retroviral have significant heart effects, and dosage changes need to be addressed.

More recently, based on preliminary evidence, a possible therapeutic option was proposed, chloroquine/hydroxychloroquine and azathioprine. Both are considered to stretch QT, and proper consideration needs to be given when administering such agents. In specific, in patients with liver or renal failure and such instances chloroquine/hydroxychloroquine, they will be paired with a daily electrocardiogram to track QT intervals (Xu *et al.*, 2020).

Prevention

Prevention strategies rely on clinical safety and vigilant infection control, including appropriate preventive and emergency care for patients affected. E.g., touch and airborne measures should be taken in the case of specimen collection droplets, and sputum induction prevented.

The WHO and other organisations have issued the following general recommendations

1. Maintain social distancing to avoid unwanted infections
2. Wash your hands often, particularly after you have contact with or around infected persons.
3. Avoid unprotected farm contact or wildlife contact.
4. People whose signs of acute inflammation of airways should stay far away, cover coughs or sneezes and wash their hands.
5. Strengthening of strict hygiene measures for preventing and controlling infections.
6. All public should avoid public meetings.
7. The important strategy for the populous is to use mobile hand sanitisers and frequently launder their hands and avoid touching the face and body after interacting with a potentially polluted environment.
8. Health care staff caring for infectious patients will use touch and airborne measures like PEP, eye cover, gowns and gloves for the prevention of pathogen transmissions, such as n95 or FFP3 masks.

Scientific research is now increasing to develop a vaccine for a coronavirus. China confirmed in recent days its first animal trials, and researchers in Australia at the University of Queensland have also confirmed that they are switching to animal studies after finishing the three-week in vitro trial. Besides, a Phase 1 study for novel coronavirus immunisation in the USA was launched by the National Institute for Allergy and Infectious Disease (Liu *et al.*, 2016).

Treatment Options

1. Antiviral therapy- Fabiravir and ribavirin, Lopinavir/ritonavir, Remdesivir and Arbidol
2. Chloroquine and hydroxychloroquine
3. Antibacterial therapy
4. Adjunctive interventions
5. Corticosteroids

6. Thymosin alpha-1
7. Cyclosporine A
8. Interferons
9. Gammaglobulin
10. Tocilizumab
11. Chinese traditional medicine
12. Convalescent plasma
13. Respiratory supportive strategies
14. Oxygen therapy and mechanical ventilation
15. Prone positioning ventilation
16. Extracorporeal membrane oxygenation (ECMO)
17. Circulatory support and fluid management
18. Plant-based Nutrition therapy

All the above is the treatment option of COVID-19. Appropriate nutritional approach with immune-boosting natural herbs can be used to control the rate of infection (Guo, 2017).

CONCLUSION

COVID-19 is more likely to be life-threatening in patients with a history of diabetes, hypertension and cardiovascular disease. It is perilous that the clinical and biochemical parameters of diabetes, hypertension and cardiovascular disease using comprehensive datasets are established using a multi-omics approach which predicts the severity of COVID-19. There is an immediate need, by using telehealth, online patient care, and wearable devices, for modern methods of caring for our patients. As the global pandemic evolves and progresses exponentially around the world, there will be a change from social exclusion steps. Still, critical and scientific studies are desperately required to resolve the very essential yet unresolved questions to contain this SARS-CoV-2 epidemic.

ACKNOWLEDGEMENTS

Authors are very thankful for the kind support to professionals of SAAOL Heart Center, New Delhi and Amity University Haryana, India.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that there is no conflict of interest for this study.

REFERENCES

Andersen, K. G., Rambaut, A., Lipkin, W. I., Holmes, E. C., Garry, R. F. 2020. The proximal origin of SARS-CoV-2. *Nature Medicine*, 26(4):450–452.

Bai, Y., Yao, L., Wei, T., Tian, F., Jin, D.-Y., Chen, L., Wang, M. 2020. Presumed Asymptomatic Carrier Transmission of COVID-19. *JAMA*, 323(14):1406–1406.

CDC 2020. Centres for Disease Control and Prevention. National Diabetes Statistics Report, US Department of Health and Human Services.

Chang, D., Xu, H., Rebaza, A., Sharma, L., Cruz, C. S. D. 2020. Protecting health-care workers from subclinical coronavirus infection. *The Lancet Respiratory Medicine*, 8(3):e13–e13.

Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., Qiu, Y., Wang, J., Liu, Y., Wei, Y., Xia, J., Yu, T., Zhang, X., Zhang, L. 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*, 395(20):30211–30218.

Chen, X., Hu, W., Ling, J., Mo, P., Zhang, Y., Jiang, Q., Ma, Z., Cao, Q., Deng, L., Song, S., Zheng, R., Gao, S., Ke, H., Gui, X., Lundkvist, A., Li, J., Lindahl, J. F., Xiong, Y. 2003. Hypertension and diabetes delay viral clearance in COVID-19 patients. *Medrxiv*. Published on: 24 March 2020.

Cui, J., Li, F., Shi, Z.-L. 2019. Origin and evolution of pathogenic coronaviruses. *Nature Reviews Microbiology*, 17(3):181–192.

Danser, A., Epstein, M., Batlle, D. 2020. Renin-angiotensin system blockers and the COVID-19 pandemic: at present, there is no evidence to abandon renin-angiotensin system blockers. *Hypertension*, 120:12015082–12015082.

Deng, S. Q., Peng, H. J. 2019. Characteristics of and Public Health Responses to the Coronavirus Disease Outbreak in China. *Journal of clinical medicine*, pages 575–575.

Donath, M. Y., Dinarello, C. A., Mandrup-Poulsen, T. 2019. Targeting innate immune mediators in type 1 and type 2 diabetes. *Nature Reviews Immunology*, 19(12):734–746.

Donoghue, M., Hsieh, F., Baronas, E., Godbout, K., Gosselin, M., Stagliano, N., Donovan, M., Woolf, B., Robison, K., Jeyaseelan, R., Breitbart, R. E., Acton, S. 2000. A Novel Angiotensin-Converting Enzyme–Related Carboxypeptidase (ACE2) Con-

verts Angiotensin I to Angiotensin 1-9. *Circulation Research*, 87(5):1–9.

Drummond, G. R., Vinh, A., Guzik, T. J., Sobey, C. G. 2019. Immune mechanisms of hypertension. *Nature Reviews Immunology*, 19(8):517–532.

Fang, L., Karakiulakis, G., Roth, M. 2020. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *The Lancet Respiratory Medicine*, 8(4):e21–e21.

Guan, W. J., Ni, Z. Y., Hu, Y. 2020. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*, 382:1708–1720.

Guo, J. 2017. Research progress on the prevention and treatment of glucolipid metabolic disease with integrated traditional Chinese and Western medicine. *Chin J Integr Med*, 23:403–409.

Haffner, S. M., Lehto, S., Ronnemaa, T. 1998. Mortality from coronary heart disease in subjects with type 2 diabetes and nondiabetic subjects with and without prior myocardial infarction. *New Engl J Med*, 339:229–234.

Huang, C., Wang, Y., Li, X. 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan. *China. Lancet*, 395:497–506.

Imai, Y., Kuba, K., Rao, S. 2005. Angiotensin-converting enzyme 2 protects from severe acute lung failure. *Nature*, 436:112–116.

Jiang, F., Yang, J., Zhang, Y. 2014. Angiotensin-converting enzyme two and angiotensin 1-7: novel therapeutic targets. *Nature Reviews Cardiology*, 11:413–426.

Jing, Y., Yanyu, S., Yujie, Z. 2020. Analysis of clinical characteristics of 223 patients with novel coronavirus pneumonia in Chongqing. *Journal of Southwest University Natural Science Edition*, pages 1–15.

Juan, X., Wanli, Qian, Z., Xiaoqing, H., Chunying, L. 2020. Clinical characteristics, treatment, and prognosis in 89 cases of COVID-2019. *Medical Journal of Wuhan University*, 4(41):542–546.

Liu, Q., Zhou, Y. H., Yang, Z. Q. 2016. The cytokine storm of severe influenza and the development of immunomodulatory therapy. *Cellular & molecular immunology*, 13:3–10.

Liu, W., Tao, Z. W., Lei, W. 2020. Analysis of factors associated with disease outcomes in hospitalised patients with 2019 novel coronavirus disease. *Chinese medical journal*, 133(9):1032–1038.

Mortensen, E. M., Restrepo, M. I., Copeland, L. A., Pugh, J. A., Anzueto, A. 2008. Association of Hydrophilic Versus Lipophilic Angiotensin-Converting Enzyme Inhibitor Use on Pneumonia-Related Mortality. *The American Journal of the Medical Sciences*, 336:462–466.

Patel, V. B., Zhong, J.-C., Grant, M. B., Oudit, G. Y. 2016. Role of the ACE2/Angiotensin 1–7 Axis of the Renin–Angiotensin System in Heart Failure. *Circulation Research*, 118(8):1313–1326.

Peng, Y. D., Meng, K., Guan, H. Q. 2020. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. *Chinese Journal of Cardiology*, 48(6).

Piao, S. H., Guo, J., Hu, Z. P. 2012. Clinical research of Chinese medicine syndromes of hyperlipidemia inpatients. *Chin J Integr Tradit West Med (Chin)*, 3:1322–1325.

Tianxin, X., Jiaming, L., Fei, X. 2020. Analysis of clinical characteristics of 49 patients with Novel Coronavirus Pneumonia in Jiangxi province. *Chinese Journal of Respiratory and Critical Care Medicine*. Updated on: 30 May 2020.

Wang, D., Hu, B., Hu, C. 2020. Clinical Characteristics of 138 Hospitalised Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*, 323(11):1061–1069.

Wrapp, D., Wang, N., Corbett, K. S., Goldsmith, J. A., Hsieh, C.-L., Abiona, O., Graham, B. S., McLellan, J. S. 2020. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science*, 367(6483):1260–1263.

Xu, Z., Shi, L., Wang, Y. 2020. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *The Lancet Respiratory Medicine*, 8(4):420–422.

Zhang, J. J., Dong, X., Cao, Y. Y. 2019. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy*, 75(7):1730–1741.

Zhu, N., Zhang, D., Wang, W. 2019. A Novel Coronavirus from Patients with Pneumonia in China. *N Engl J Med*, 382:727–733.