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COVID-19 IN HYPERTENSIVE PATIENTS: A REVIEW OF COMORBIDITIES AND WORSE OUTCOMES

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ABSTRACT
The SARS-CoV-2 virus causes COVID-19, and the first case was reported in Wuhan in late 2019. The virus spreads via direct contact and respiratory droplets. It soon hit different countries, and the World Health Organization declared it a pandemic in early 2020. Most countries around the world started looking for possible pharmacological options against COVID-19. Vaccine trials were started, and countries adopted preventive measures to curb the disease spread. Patients with cardiovascular comorbidities such as hypertension were found to be at an increased risk of serious infections caused by SARS-CoV-2. The association between frequently prescribed hypertensive drugs such as ACE inhibitors/AR blockers, and severe COVID-19 cases have been studied. This review emphasizes the worse outcomes in COVID-19 patients suffering from hypertension and other cardiovascular diseases.

INTRODUCTION
The SARS-CoV-2 virus causes COVID-19, and the first case was reported in Wuhan in late 2019.[1] The virus spreads by direct contact and respiratory droplets and soon hit different countries, and World Health Organization declared it a pandemic in early 2020. Most countries worldwide started making vaccines and adopted preventive measures to curb the disease spread.[2] Travel restrictions were imposed, and it affected people at large, causing global chaos. Most of the elective procedures and primary care visits were canceled, jeopardizing patient care.

Clinically, the symptoms start manifesting after an incubation period of 2-14 days. The common symptoms reported are fever, fatigue, cough, and shortness of breath, while dyspnea, chest pain, and confusion represent alarm symptoms that should prompt people to seek medical attention immediately. One of the largest metanalysis reported that fever and cough are the presenting symptoms in 89% and 72% of patients, respectively.[3] Fatigue, body aches, and gastrointestinal symptoms were also frequently reported.[4] Diabetes and hypertension are frequently reported comorbidities in COVID patients. Acute respiratory distress syndrome, acute kidney injury, and cardiac injury were all reported in severe cases, with ARDS being the most common.[5] Leukopenia and, eosinopenia were reported to be the most typical laboratory findings, while bilateral ground-glass in the lungs were the common radiologic abnormalities. C reactive protein, D dimer, and procalcitonin levels were elevated, especially in severe disease cases.[6]

Hypertension is the leading cause of cardiovascular disease worldwide. Estimates suggest that 31.1% of adults (1.39 billion) worldwide had hypertension in 2010.[7] Hypertension is an independent risk factor for

predicting the adverse outcomes of patients with COVID-19.[8] This article reviews the impact of the SARS-CoV-2 infection on hypertensive patients and the factors that lead to the worse outcomes. As hypertension is one of the most frequent comorbidities of patients with severe SARS-CoV-2 infections, it is imperative to look more deeply into the relationship between the two conditions.

Review

The role of antihypertensive medications

The angiotensin-converting enzyme (ACE) enzyme is secreted from the lungs, and its dysregulation is linked with different clinical conditions, such as hypertension. Previously, studies were done to assess the potential role of ACE in Acute Respiratory Distress Syndrome. Multiple animal studies have shown a protective effect of ACE II inhibitors against ARDS development.[9] The SARS-CoV-2 virus uses the ACE II receptor to invade the alveolar epithelium in lungs and might be considered a potential target for future anti-COVID-19 therapies.[10] Cardiovascular pathologies and use of ACE inhibitors/angiotensin receptor (AR) blockers can lead to increased levels of ACE II, potentially increasing the risk of SARS-CoV-2 infections.[11] Hanff et al. also pointed some evidence that SARS-CoV-2 can lead to the downregulation of ACE II and toxic accumulation of angiotensin II.[12] SARS-CoV infections can be linked with gastrointestinal symptoms, cardiac damage, and Acute kidney injury as ACE is express[12] ed in other tissues such as the gut, heart and kidney and this speaks in favor of a strong correlation between ACE expression and COVID infection.[11] Hypertensive patients with a history of RAAS inhibitor treatment had lower levels of C-reactive protein and higher levels of $CD4^+$ cells.[14]

The ACE inhibitors and AR blockers are most commonly used in patients suffering from hypertension, congestive heart failure, and proteinuria. They reduce the activity of the renin angiotensin system (RAS). A study suggested that ACE inhibitors and AR blockers' administration lead to a high number of ACE II receptors in the pulmonary circulation.[15] Fang et al. recommend monitoring patients who are taking any of the controversial drugs and, when possible, choosing alternative treatments.[13]

Hypertension & COVID 19

Hypertension was among the most frequent comorbidities among COVID patients.[5] Li et al. reported a very high prevalence of hypertension and other cardiovascular comorbidities among COVID 19 patients treated in the ICU than those who did not require ICU treatment.[17] It was also reported that over 8% of those infected by SARS-CoV-2 developed cardiac injury. Chen et al. also reported a similar association between hypertension and COVID-19.[18] It is very difficult to see the impact of hypertension on the outcome of COVID patients. Previous studies point to a significant association between hypertension and adverse outcomes. Besides hypertension, other cardiovascular comorbidities such as coronary artery disease, congestive heart failure were also frequently correlated in patients with severe cases of COVID 19. Also, there is a notable association between heart and pulmonary diseases, such as pulmonary hypertension. Li et al. reported cardio-cerebrovascular disease was among the most prevalent comorbidities among patients with severe cases of COVID 19, secondary to hypertension 17.1% and 16.4%, respectively.[17] Zhou et al. also reported that coronary disease was the third most prevalent comorbidity after hypertension and diabetes.[17] Chen et al. also found that previous coronary disease history was an independent risk factor for adverse outcomes.[18] Cardiac muscle injury could then lead to endothelial dysfunction. Patients with already existing heart failure are more likely to have elevated ACE II expression due to underlying CHF's pathophysiology, which could then increase the risk of infection.[18] He et al. reported mortality among critically ill patients infected by SARS-CoV-2 virus who develop heart failure to be as high as 60%.[20] They also found a significant correlation between elevation in N-terminal pro-B-type natriuretic peptide levels (usually a biomarker for congestive heart failure) and myocardial damage caused by COVID 19 virus.

So all these studies highlight the association between cardiovascular comorbidities and worse outcomes in COVID patients. Most common finding which suggests the correlation is the observed myocardial damage in a subset of COVID 19 patients with pre-existing heart disease who are less likely to recover. Also, the increased expression of ACE II with congestive heart failure can also explain the increased susceptibility to the infection. Most important prognostic factor will be the physician's ability to manage the myocardial damage and associated complications in the ICU. Further large-scale studies are needed to establish guidelines to manage the cardiac complications in COVID patients.

Table 1: Study Characteristics.

Sr. No.	Study	Total no. of Pts (N)	Prevalence of hypertension (n)	Cardiac complication	In hospital death relative risk (RR)
1.	Li et al.	1527	261 (17.1 %)	Acute Cardiac injury 8%	2.03 (1.54 – 2.68)
2.	Zhou et al.	191	58 (30%)	Acute Cardiac Injury 2%	3.05 (1.57–5.92)
3.	Pan et al.	996	282 (28.31%)	Acute Cardiac Injury 20.9%	2.24, 1.36–3.70
4.	He at al.	54	24 (44.4%)	Myocardial injury 44.4%	NA

CONCLUSION

COVID 19, caused by SARS-CoV-19 virus, has been the most focused disease of the year. Patients who are at increased risk for adverse outcomes are elderly and those suffering from chronic conditions. Hypertension is the most frequently reported comorbidity among patients with severe infections, followed by diabetes and other cardiovascular diseases, possibly related to ACE II expression, which facilitates viral entry into cells. Some patients tend to stop using the antihypertensive drugs due to fear of disease. The relationship between ACEIs/ARBs use and the incidence of severe COVID-19 has not been studied in detail. Use of NSAIDs among the hypertensive patients has been questioned by most of the patients, so doctors recommend choosing alternative medicine due to lack of safety evidence of these drugs. The available evidence highlights the correlation between cardiovascular comorbidities and adverse outcomes among COVID patients as severe cases are associated with cardiac complications.

REFERENCES

1. Khan S, Siddique R, Shereen MA, Ali A, Liu J, Bai Q, et al. Emergence of a Novel Coronavirus, Severe Acute Respiratory Syndrome Coronavirus 2: Biology and Therapeutic Options. Kraft CS, editor. J Clin Microbiol, 2020; 58(5): 00187-20, /jcm/58/5/JCM.00187-20.atom.
2. Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents, 2020; 55(3): 105924.
3. Sun P, Qie S, Liu Z, Ren J, Li K, Xi J. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: A single arm meta-analysis. J Med Virol, 2020; 92(6): 612–7.
4. Zhang J, Dong X, Cao Y, Yuan Y, Yang Y, Yan Y, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy, 2020; 75(7): 1730–41.
5. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med, 2020; 8(5): 475–81.
6. Xu X-W, Wu X-X, Jiang X-G, Xu K-J, Ying L-J, Ma C-L, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ, 2020; 19: 606.
7. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol, 2020; 16(4): 223–37.
8. Liang X, Shi L, Wang Y, Xiao W, Duan G, Yang H, et al. The association of hypertension with the severity and mortality of COVID-19 patients: Evidence based on adjusted effect estimates. J Infect, 2020; 81(3): 44–7.
9. Cheng H, Wang Y, Wang G. Organ-protective effect of angiotensin-converting enzyme 2 and its effect on the prognosis of COVID-19. J Med Virol, 2020; 92(7): 726–30.
10. Kuba K, Imai Y, Penninger J. Angiotensin-converting enzyme 2 in lung diseases. Curr Opin Pharmacol, 2006; 6(3): 271–6.
11. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med, 2020; 46(4): 586–90.
12. Hanff TC, Harhay MO, Brown TS, Cohen JB, Mohareb AM. Is There an Association Between COVID-19 Mortality and the Renin-Angiotensin System? A Call for Epidemiologic Investigations. Clin Infect Dis, 2020; 71(15): 870–4.
13. Perico L, Benigni A, Remuzzi G. Should COVID-19 Concern Nephrologists? Why and to What Extent? The Emerging Impasse of Angiotensin Blockade. Nephron, 2020; 144(5): 213–21.
14. Pan W, Zhang J, Wang M, Ye J, Xu Y, Shen B, et al. Clinical Features of COVID-19 in Patients With Essential Hypertension and the Impacts of Renin-angiotensin-aldosterone System Inhibitors on the Prognosis of COVID-19 Patients. Hypertens Dallas Tex, 2020; 76(3): 732–41.
15. Diaz JH. Hypothesis: angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may increase the risk of severe COVID-19. J Travel Med, 2020; 27(3): 041.
16. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med, 2020; 8(4): 21.
17. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol, 2020; 109(5): 531–8.
18. Chen L, Li X, Chen M, Feng Y, Xiong C. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovasc Res, 2020; 116(6): 1097–100.
19. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet, 2020; 395(10229): 1054–62.
20. He XW, Lai JS, Cheng J, Wang MW, Liu YJ, Xiao ZC, et al. [Impact of complicated myocardial injury on the clinical outcome of severe or critically ill COVID-19 patients]. Zhonghua Xin Xue Guan Bing Za Zhi, 2020; 48(6): 456–60.