

Hypertension and COVID-19

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Abstract: COVID -19 Pandemic is spreading very fast in whole world associated with severe acute respiratory syndrome and may cause death. Mortality further increases if COVID-19 disease is associated with comorbidities i.e., hypertension, diabetes etc. But it is not clear that uncontrolled blood pressure is risk factor for acquiring COVID-19. It is seen that renin angiotensin aldosterone system (RAAS) plays an important role in development of high blood pressure. Hypertension is often treated by angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). Both will cause increase activity and expression of ACE2, which is a protein found on many cells. It is abundant in lungs pneumocytes in alveoli. SARS-CoV-2 virus by using spike protein on its surface binds ACE2 and enter the human cells and can cause acute respiratory disease syndrome and myocarditis etc. On the other hand, ACE2 forms angiotensin (1-7) from angiotensin II. These angiotensin (1-7) potentiate anti-inflammatory effects and reduces inflammatory effects of angiotensin II. Thus ACE2 / angiotensin (1-7) seems to have protective effects on heart and lungs and ACE / angiotensin II may cause adverse effects on heart and lungs. The subjects with hypertension, even with treatment, are at higher risk with COVID-19 disease and should take extra precautions.

Key words: COVID -19, acute respiratory distress syndrome, angiotensin.

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There is outbreak of the COVID -19 pandemic in world caused by severe acute respiratory syndrome corona virus (SARS-CoV-2).The disease is associated not only with lung injury, but involves other systems also. It is seen that subjects with co-morbidities like hypertension (30%), diabetes (19%), coronary artery disease (8%) are prone to get infection, and may suffer from severe lung injuries and increased mortality.¹

World Hypertension day is celebrated on 17 May. Hypertension is said to be called silent killer. Every year death due to it and its related diseases is about one crore in whole world. It is increasing nowadays, may be because of stress due to coronavirus disease and also because of more use of wireless screen.As world is increasing towards digitalization (use of internet, online classes, use of social media, work from home, and also due to lock down and in

corona virus era subjects are spending more time on screen), subjects are exposed to electromagnetic waves emitted from mobile phone (MP)and wireless screen.

Normal blood pressure is 120/80 mmHg.² Hypertension is defined by American college of Cardiology (ACC) and American Heart association (AHA) as a systolic BP>130 or diastolic >80 mmHg. As age advances and over the age of 60 years, persons may likely to suffer from increased blood pressure. There is link between older age and increased incidence of COVID -19 disease.³

It is reported that disorders of rennin angiotensin aldosterone system (RAAS), a key regulator of blood pressure, is largely related to pathophysiology of hypertension, renal disease, and congestive cardiac failure.⁴ There occurs release of rennin from kidney, which acts on angiotensinogen, a product of liver, converting it in angiotensin I, which is converted in

angiotensin II, a very potent vasoconstrictor, by angiotensin converting enzyme (ACE) in lungs. ACE and ACE2, are key enzymes in formation and degradation of angiotensin II respectively.⁵ Angiotensin II acts via angiotensin receptor I (AT1), causes contraction of muscles surrounding the blood vessels, thus may result in hypertension. It is seen that hypertension and other forms of cardiovascular disease are frequently treated by angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs).³

There is controversy regarding role of ACE inhibitors and ARBs, which increases ACE2. This ACE2 could increase binding of SARS CoV-2 to the lung and may lead more lung injury. It is found that low ACE2 levels are associated with relatively low infection rates. In patients of hypertension more amount ACE2 is reported.⁶ In contrast it is shown that ACE2 forms angiotensin (1-7) from angiotensin II, and this angiotensin (1-7) reduces inflammatory action of angiotensin II, and potentiate anti-inflammatory effects.³ So, ACE inhibitors by reducing the formation of angiotensin and ARBs by blocking the action of angiotensin, may decrease the inflammation, which could otherwise cause acute respiratory disease syndrome, myocarditis and acute kidney disease.^{7,8}

It is demonstrated that in model of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) that lower ACE2 and angiotensin (1-7) are associated with poor prognosis. ACE, ACE2, angiotensin-II, AT1 receptor levels are high in lungs, which looks to be the primary site of complications from corona type virus. There is evidence that there is increase in ACE2 activity in patients of hypertension. Further, ACE inhibition and ARB increase the activity and expression of ACE2.⁶ ACE2 is a protein found on surface of many cells types and tissues including lungs, heart, blood vessels, kidney, liver and GIT. It is present on epithelial cells and providing protective barrier. In lungs it is highly abundant on type II pneumocytes present in alveoli.

SARS-CoV-2 virus by using spike protein on its surface binds ACE-2 like a key inserted in a lock, and enter in human cells.⁴ It is seen that ACE2/Angiotensin (1-7) seem to be protective to heart and lungs and ACE/ Ang-II may cause cardio-pulmonary dysfunction.

Thus, ACE inhibitors and ARBs contribute to reduction of acute respiratory distress syndrome, myocarditis and kidney injury. In fact, ARB is suggested as treatment of COVID-19 and its complications. Thus, recombinant ACE2 could be advised to COVID-19 patients, which will reduce the viral load. But not demonstrated in patients yet.³

It is interesting to note that angiotensin II, besides acting on AT1, also acts on angiotensin Type II receptor (AT2), which has low degree of expression compared to AT1. Role of AT2 in hypertension receiving AT1 antagonist is not clear. It is postulated that AT2 receptor opposes the functions mediated by AT1 receptor. As AT1 receptor increases cell proliferation, while AT2 inhibits cell proliferation, but stimulate cell differentiation. Similarly, AT1 stimulate protein phosphorylation and AT2 favours protein dephosphorylation. It is demonstrated that in contrast to AT1, which causes angiotensin II induced vasoconstriction and antinatriuretic effects, AT2 causes vasodilatation and natriuresis by autocrine fashion through bradykinin, nitric oxide, cyclic GMP and PGE2 and PGI2. It is thought that AT2 play a counterregulator protective role in regulation of blood pressure and sodium excretion. It is seen that long term use of AT1 blockers results in many folds increase in angiotensin II, and may be overstimulation of AT2, which is important both physiological and pathological situation.⁴

So, there is no evidence that hypertension is presented as outcome of COVID-19, and use of ACE inhibitors or ARBs use is harmful in COVID-19 disease. So, for prevention of hypertension, one should take following precautions:

1. 1 Select heart healthy diet –Approach for DASH—Dietary approaches to stop Hypertension, the diet should include fruits, vegetables, whole grains, poultry, fish, low fat dietary foods. Increase the food containing more amount of potassium. Avoid processed food, fast food.
 2. Decrease salt in diet –reduces to 2300 mg / day or less. Ideally it should be 1500 mg /day or less. Avoid adding salt on salad.
 3. Lose weight-even slight decrease in weight reduces BP. Overweight or obesity increases BP.
 4. Do Regular exercise – which releases stress, decreases weight, releases endorphin and make one happy, and thus reduces BP.
 5. Stress can be reduced by regular meditation, deep breathing, yoga. Avoid stress triggering agents.
 6. Avoid alcohol.
 7. Reduce intake of caffeine.
 8. Stop smoking as it may cause formation of atherosclerotic plaque in arteries.
 9. One should be regular to medication.
 10. Maintain the record of BP and check it on daily basis.
 11. Do activities by which one can enjoy i.e., music listening, dancing, reading and writing.
 12. Avoid overuse of mobile phone.
5. Gargaglioni LH, Marques DA. Let's talk about sex in control of COVID-19. *J Applied of Physiology* 1985; 128(6): 1533-38.
 6. Furuhashi M, Moniwa N, Mita T, Fuseya T, Ishimura S, Tanaka M, Watanabe Y, Akasaka H et al. Urinary angiotensin -converting enzyme 2 in hypertensive patients may be increased by Olmesartan, an angiotensin II receptor blocker. *Am J Hypertension* 2015; 28: 15-21.
 7. Phadke M, Saunik S. Rapid response: use of angiotensin receptor blockers such as Telmisartan, Losarsan in CoV Wuhan Corona virus infections-novel mode of treatment. Response to the emerging novel corona virus outbreak. *Br Med J* 2020; 368: m406.
 8. Gurwitz D. Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics. *Drug Dev Res* 2020, published online 4 March; doi:10.1002/ddr.21656.

Conflict of Interest :None

REFERENCES:

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J et al. Clinical course and risk factors for mortality of adult in patients with COVID -19 in Wuhan, China: A retrospective cohort study. *Lancet* 2020; 395: 1054-62.
2. Jain A K. Chapter 42, The arterial blood pressure. In text book of Physiology. APC, Volume I, 8th edition. 345.
3. Schiffrin EL, Flack JM, Ito S, Muntner P, Webb RC. Hypertension and COVID-19. *Am J Hypertension* 2020; 33 (5):373-74.
4. Henrion D, Kubis N, Levy BI. Physiological and pathophysiological functions of the AT2 subtype receptor of angiotensin II. *Hypertension* 2001; 38: 1150-1157.